Committee for Risk Assessment

RAC

Annex 1
Background document
to the Opinion proposing harmonised classification and labelling at EU level of

4-tert-butylphenol

EC Number: 202-679-0
CAS Number: 98-54-4

CLH-O-0000001412-86-112/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

3 June 2016

CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

Substance Name: 4-tert-butylphenol

EC Number: 202-679-0

CAS Number: 98-54-4

Index Number: 604-090-00-8

Contact details for dossier submitter:

Norwegian Environment Agency

PB 5672 Sluppen,

N-7485 Trondheim

Norway

Version number: 1.1 **Date: 9 October 2015**

CONTENTS

Part A.

Part B.

Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	4-tert-butylphenol
EC number:	202-679-0
CAS number:	98-54-4
Annex VI Index number:	604-090-00-8
Degree of purity:	>= 96% w/w
Impurities:	Formation of 2,4,6-tri-tert-butylphenol during the production of 4-tert-butylphenol theoretically is possible and cannot 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 (4-tert-butylphenol) is below 2 ppm. The situation for 2,4-di-tert-butylphenol is similar.

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation	**Directive 67/548/EEC (Dangerous Substances Directive; DSD)**
Current entry in Annex VI, CLP Regulation	Repr. 2; H361f Skin Irrit. 2; H315 Eye Dam. 1; H318	Repr. Cat. 3; R62 Xi; R38-41
Current proposal for consideration by RAC	Aquatic chronic 1; H410	N/A
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Repr. 2; H361f Skin Irrit. 2; H315 Eye Dam. 1; H318 Aquatic Chronic 1; H410	N/A

1.3 Proposed harmonised classification and labelling based on CLP Regulation

Table 3: Proposed classification according to the CLP Regulation

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives	none	N/A	none	not evaluated
2.2.	Flammable gases	none	N/A	none	not evaluated
2.3.	Flammable aerosols	none	N/A	none	not evaluated
2.4.	Oxidising gases	none	N/A	none	not evaluated
2.5.	Gases under pressure	none	N/A	none	not evaluated
2.6.	Flammable liquids	none	N/A	none	not evaluated
2.7.	Flammable solids	none	N/A	none	not evaluated
2.8.	Self-reactive substances and mixtures	none	N/A	none	not evaluated
2.9.	Pyrophoric liquids	none	N/A	none	not evaluated
2.10.	Pyrophoric solids	none	N/A	none	not evaluated
2.11.	Self-heating substances and mixtures	none	N/A	none	not evaluated
2.12.	Substances and mixtures which in contact with water emit flammable gases	none	N/A	none	not evaluated
2.13.	Oxidising liquids	none	N/A	none	not evaluated
2.14.	Oxidising solids	none	N/A	none	not evaluated
2.15.	Organic peroxides	none	N/A	none	not evaluated
2.16.	Substance and mixtures corrosive to metals	none	N/A	none	not evaluated
3.1.	Acute toxicity - oral, dermal, inhalation	none	N/A	none	not evaluated
3.2.	Skin corrosion / irritation	N/A	N/A	Skin Irrit. 2	N/A
3.3.	Serious eye damage / eye irritation	N/A	N/A	Eye Dam. 1	N/A
3.4.	Respiratory sensitisation	none	N/A	none	not evaluated
3.4.	Skin sensitisation	none	N/A	none	not evaluated
3.5.	Germ cell mutagenicity	none	N/A	none	not evaluated
3.6.	Carcinogenicity	none	N/A	none	not evaluated
3.7.	Reproductive toxicity	N/A	N/A	Repr. 1B	N/A
3.8.	Specific target organ toxicity –single exposure	none	N/A	none	not evaluated
3.9.	Specific target organ toxicity – repeated exposure	none	N/A	none	not evaluated
3.10.	Aspiration hazard	none	N/A	none	not evaluated
4.1.	Hazardous to the aquatic environment	Aquatic Chronic 1	M-factor = 1	none	
5.1.	Hazardous to the ozone layer	none	N/A	none	not evaluated

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling:

Signal word: Danger

Hazard pictogram: GHS08, GHS05, GHS09

Hazard statements:

H361f: Suspected of damaging fertility

H315: Causes skin irritation.

H318: Causes serious eye damage.

H410: Very toxic to aquatic life with long lasting effects.

Proposed notes assigned to an entry: None

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

4-tert-butylphenol (ptBP) was on the 4th priority list of the Existing Substances Regulation and its classification was reviewed in the context of the Risk Assessment procedure as it was a requirement to harmonize the classification for all endpoints.

In September 2005 TC C&L agreed to classify ptBP with N; R 51/53 (see Annex I). In March 2006 TC C&L agreed to classify ptBP with Xi; R 37/38 - R 41. In September 2007 TC C&L further agreed to classify the substance with Rep. Cat.3; R62. However, this classification was not included in the old legislation. Norway therefore proposed harmonized classification for the health hazards according to CLP on 11 June 2010. The proposal was discussed in RAC and new harmonized classification for the health hazards was included in Regulation (EU) No 605/2014.

2.2 Short summary of the scientific justification for the CLH proposal

The published information on the toxicity of ptBP indicates chronic effects on aquatic organisms (fish) of serious concern (reduced growth rate, reduction in secondary male sexual characteristics and a delay in the time to hatch) with a NOEC at 10 µg/L. Furthermore feminization of gonadal ducts of male fish and elevated levels of plasma VTG in females with a NOEC at 100 µg/L. ptBP is considered rapidly biodegradable without meeting the 10-day window. There is sufficient data to propose harmonised classification and labelling for environmental hazard.

2.2.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

Repr. 2; H361f
Skin Irrit. 2; H315
Eye Dam. 1; H318
GHS08, GHS05, Danger

2.2.2 Current classification and labelling in Annex VI, Table 3.2 in the CLP Regulation

Repr. Cat. 3; R62
Xi; R38-41

2.3 Current self-classification and labelling

2.3.1 Current self-classification and labelling based on the CLP Regulation criteria

Table 4: The following classifications for environmental hazard have been notified by Industry to ECHA and are published in the C&L inventory (15.09.2015)

Hazard classes:	**H-statements/M-factor:**	**Notifications relevant for this dossier:**
Aquatic Chronic 1	H410, M (chronic) = 1	127
Aquatic Chronic 2	H411	1382
Aquatic Chronic 3	H412	10
No environmental classification	-	981
Total number of notifications for environmental hazard	-	2500

2.3.2 Current self-classification and labelling based on DSD criteria

N/A

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

There are two main arguments according to the guidance on the preparation of dossiers for harmonised classification and labelling that justifies a harmonized classification and labelling for environmental effects of ptBP. Firstly, a change in an existing entry is justified due to changes in the CLP classification criteria. Secondly, there are differences in self-classification between different notifiers in the C&L Inventory and/or between different registration dossiers.

Norway was rapporteur for the EU Risk Assessment (RAR) and in that context a classification for environment was submitted to TC C&L. In September 2005 TC C&L agreed to classify ptBP with N; R 51/53. This classification is not included in CLP, annex VI. The classification could not be justified according to CLP when Norway proposed harmonized classification for the health hazards in June 2010. However, with the revision of the environmental criteria in Regulation (EU) No 286/2011 (2. ATP) a classification can now be justified. In addition, the RAR conclusion concerning fish resulted in new data, which is the basis for the current proposal.

Chronic effects on aquatic organisms (fish) are of serious concern (reduced growth rate, reduction in secondary male sexual characteristics and a delay in the time to hatch) with a NOEC at 10 µg/L. Clearly defined estrogenic effects evidenced by feminization of gonadal ducts of male fish and elevated levels of plasma VTG in females were present at 300 µg/L (NOEC = 100 µg/L). ptBP is registered in a high tonnage band (10.000-100.000 tonnes per annum) in EU.

The self-classifications notified by Industry and published in the C&L Inventory shows a great degree of variety for the environmental hazard of the substance. Only 5% have classified ptBP with Aquatic Chronic 1.

This justifies a classification for ptBP.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

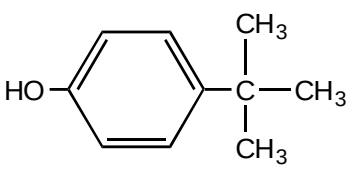
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 5: Substance identity

EC number:	202-679-0
EC name:	4-tert-butylphenol
CAS number (EC inventory):	98-54-4
CAS number:	98-54-4
CAS name:	Phenol, 4-(1,1-dimethylethyl)-
IUPAC name:	4-(1,1-Dimethylethyl)phenol
CLP Annex VI Index number:	604-090-00-8
Molecular formula:	$C_{10}H_{14}0$
Molecular weight range:	150.22

Structural formula:



1.2 Composition of the substance

Table 6: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
4-tert-butylphenol (98-54-4)	>= 96% w/w		

Current Annex VI entry:
Repr. 2; H361f
Skin Irrit. 2; H315
Eye Dam. 1; H318
GHS08, GHS05, Danger

Table 7: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks
Not relevant			Formation of 2,4,6-tri-tert-butylphenol during the production of 4-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 (4-tert-butylphenol) is below 2 ppm. The situation for 2,4-di-tert-butylphenol is similar.

Current Annex VI entry: N/A

Table 8: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
No data available				

Current Annex VI entry: N/A

1.2.1 Composition of test material

The purity of ptBP tested in the studies is above 96% w/w where reported. Information on the actual composition used is provided in the relevant tables in this report, if available, and also in the associated IUCLID summaries (where provided).

1.3 Physico-chemical properties

Table 9: Summary of physico - chemical properties

Property	**Value**	**Reference**	**Comment (e.g. measured or estimated)**
State of the substance at 20°C and 101,3 kPa	White flakes at 20 °C		
Melting/freezing point	Ca 100 °C	Huels AG, Marl (A), 1992	
Boiling point	237.5 °C at 1,013 hPa,	Huels AG Marl (A), 1992	
Relative density	0.92 g/cm^3 at 110 °C, however at this high temperature, ptBP is in the liquid state.	Huels AG Marl (A), 1992	
Vapour pressure	0.5 Pa at 20 °C, 1.3 x10^2 Pa at 60 °C	Huels AG Marl (B), 1994 SIDS	
Surface tension	-		
Water solubility	**Conc. at sat. (g/l)** 0.5 (at 25 °C) 0.61 (at 25 °C) 0.8 (at 25 °C)	 (Huels AG Marl (A), 1992) (SIDS, SIAP, 2000) (Boddeker et al., 1990)	
Partition coefficient n-octanol/water	2.44 and 3.31 3.29 at 25 °C 3.42 QSAR	Method: Flask shaking, Huels AG Marl (C) and (D), 1972 Method: OECD 107, SIDS, SIAP Epiwinsuite v3.1	Measured Measured Calculated
Flash point	**Open cup:** About 115 °C	Huels AG Marl (C)	
Flammability	Flammability upon ignition (solids): no data available Flammability-on contact with water: The classification procedure needs not to be applied because the organic substance does not contain metals or metalloids. Pyrophoric properties of solids: The classification procedure needs not to be applied because the organic substance is known to be stable into contact with air at room temperature for prolonged periods of time (days).		
Explosive properties	The classification procedure needs not to be applied		

Property	Value	Reference	Comment (e.g. measured or estimated)
	because there are no chemical groups present in the molecule which are associated with explosive properties.		
Self-ignition temperature	The study does not need to be conducted for solids, because the substance has a melting point < 160°C.		
Oxidising properties	The classification procedure needs not to be applied because the organic substance contains oxygen, which is chemically bonded only to carbon.		
Granulometry			
Stability in organic solvents and identity of relevant degradation products			
Dissociation constant			
Viscosity	2.4 mPa s at 100 °C	Huels AG Marl (A, 1992)	

2 MANUFACTURE AND USES

2.1 Manufacture

The total tonnage band is 10.000-100.000 tonnes per annum (ECHA dissemination web site. Information as accessed October 2015).

2.2 Identified uses

The major use is as a monomer in chemical synthesis, e.g. for the production of polycarbonates, phenolic resins, epoxy resins etc. The material is also hydrogenated to the corresponding cyclic alcohol. Minor amounts are used for the production of oilfield chemicals and as an intermediate for the production of an active ingredient in agrochemicals.

According to the registration (ECHA dissemination web site, information as accessed in October 2015) typical products are adhesives, sealants, coatings and paints, thinners and paint removers.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Not evaluated in this dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

Not evaluated in this dossier.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.1 Degradation

ptBP is rapidly degradable, but fails to pass the 10-day window according to the OECD 301 F (EC C.4-D Part V.) Manometric Respirometry test. The substance is stable to visible light irradiation.

5.1.1 Stability

Xiao et al. (2014) showed that ptBP was hardly degraded under visible light irradiation.

5.1.2 Biodegradation

5.1.2.1 Screening tests

Aerobic biodegradation performed according to OECD 301 F, "Manometric Respirometry Test" was carried out with two levels of ptBP, 15 mg/l and 25 mg/l (NIVA, 2001b. Unpublished results. NIVA has confirmed that we could use the study for this proposal). The study was conducted according to GLP. The inoculum used was micro-organisms cultivated in an in-house activated sludge simulation unit and adaptation to ptBP had not taken place.

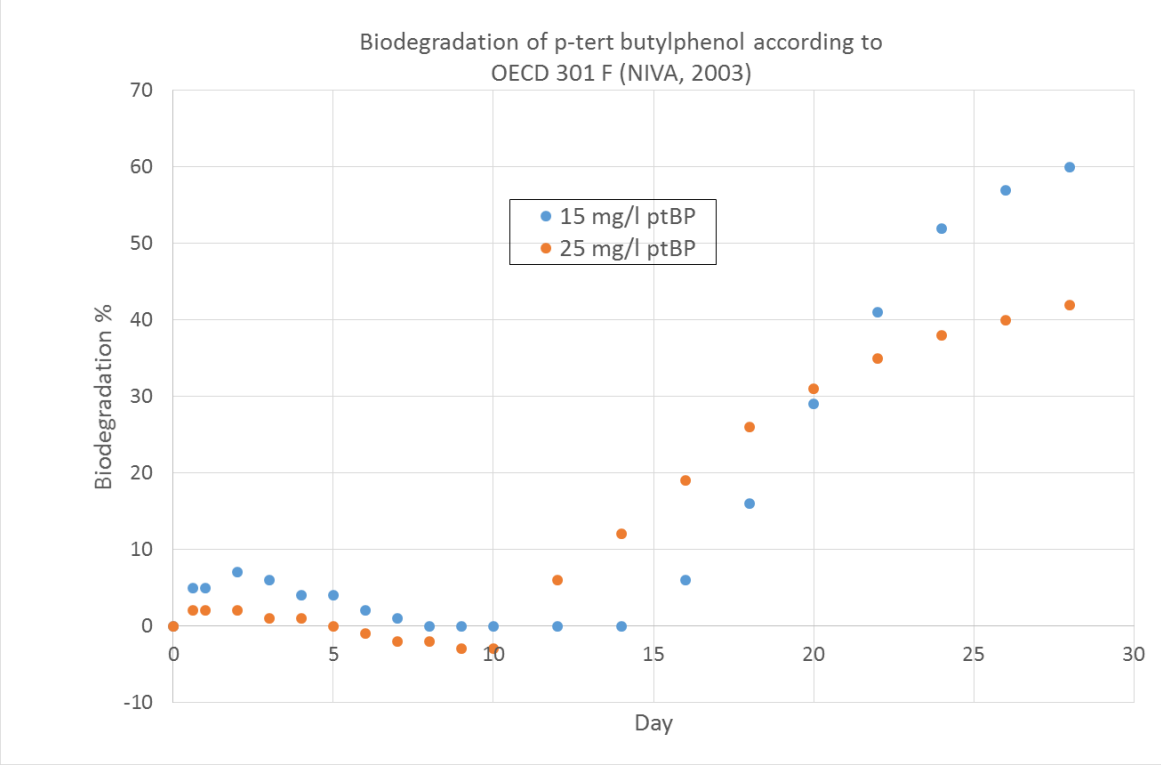


Figure 1: Aerobic biodegradation of ptBP performed according to OECD 301 F carried out with two levels of ptBP; 15 mg/l and 25 mg/l (NIVA, 2001b).

Figure 1 shows that there was a lag phase at both exposure concentrations before the degradation of the test compound started. The biodegradation after 28 days was 60 % for 15 mg/l ptBP and 42 % for 25 mg/l ptBP. The observed lag phase is longer at 15 mg/l (16 days) than at 25 mg/l (12 days). This indicates that the lag phase may not be related to toxicity but rather to adaptation. At 15 mg/l

10 % degradation is achieved between sample point day 16 and day 18. At this dose, 60% degradation was achieved on day 28. At 25 mg/l, 10% degradation was achieved between day 12 and 14. However, only 42% biodegradation was achieved on day 28 at this dose. Substances are considered rapidly degradable studies based on oxygen depletion if 60 % of theoretical maximum biodegradation is reached on day 28. This levels of biodegradation must be achieved within 10 days of the start of degradation which point is taken as the time when 10 % of the substance has been degraded.

According to the test results of this study, ptBP should be regarded as rapidly biodegradable but failing the 10 day window criterion, although this has to be considered as a borderline case. The study shows that municipal sludge microorganisms need an adaptation period in order to be able to degrade ptBP rapidly.

According to a MITI II test (MITI, 1992), no biodegradation was observed in a test system inoculated with 100 mg/l of mixed sludge and 30 mg/l of ptBP after 14 days. No biodegradation is probably due to an inhibitory concentration of ptBP in this study combined with a long lag phase.

Other results from tests of biodegradation according to OECD 301 B and 302 C presented on ECHAs dissemination page suggests that ptBP is not rapidly degradable and/or does not meet 10 day window. However, the fact that ptBP is toxic to microbial organisms at concentrations ≥ 25 mg/l should be taken into consideration when assessing these results. Furthermore, a test of biodegradation according to EU Method C.4.A (Determination of the "Ready" Biodegradabililty – Dissoved Organic Carbon (DOC) Die-Away Test) shows that ptBP is rapidly biodegradable.

5.1.2.2 Simulation tests

In a report by Scharf & Sattelberger (1999) from 17 Sewage treatment plants (STP), the concentration of alkylphenols (4- tert-butylphenol, 4-sec-butylphenol, 4-tert-octylphenol, 4-tert-amylphenol and 4- nonylphenol), nonylphenolethoxylates, phthalates and organotin compounds were determined in the inflow and outflow of STPs. 24-hours integrated samples from in- and outflow of the STPs were collected at the same day. The sampled STPs were mostly municipal. The concentrations in the outflow show a removal of ptBP between 3 and 53 %. In two of the STPs there was a significant increase in the concentration through the plant.

Monitoring of WWTP presented in the EU Risk Assessment Report for ptBP (2008) under Regulation (EC) 793/93 indicate 35-45% degradation of ptBP under normal conditions.

5.1.3 Summary and discussion of degradation

Concerning biodegradability there are conflicting results available. According to the CLP regulation, Annex I section 4.1.2.9, substances are considered rapidly degradable in the environment if, in 28-day ready biodegradation studies, at least the following levels of degradation are achieved: (i) tests based on dissolved organic carbon: 70%, (ii) tests based on oxygen depletion or carbon dioxide generation: 60% of theoretical maximum. These levels of biodegradation must be achieved within 10 days of the start of degradation. The start of degradation is the time when 10 % of the substance has been degraded.

The results from the Manometric Respirometry Test (NIVA, 2001b) show that ptBP is rapidly biodegradable but failing the 10 day window.

Some results from the testing of rapidly biodegradability of ptBP presented on ECHAs dissemination page by registrants also shows that the substance is rapidly biodegradable. However,

there are also other data presented by registrants showing that the substance does not meet the criteria of rapidly biodegradability.

MITI (1992) observed no biodegradation of ptBP in a 14 days-test. The lack of biodegradation in this test is probably caused by the long lag phase that is observed by NIVA (2001b).

Monitoring values from different STPs in Austria (Scharf & Sattelberger, 1999), which are above the detection limit, support the conservative approach characterizing ptBP as rapidly biodegradable, but not fulfilling the 10 day window criterion.

The TC C&L meeting in 2005 concluded that ptBP should be characterized as 'readily biodegradable not meeting the 10 day window criterion' for risk assessment purposes.

In conclusion, ptBP is considered as rapidly biodegradable without meeting the 10-day window.

5.2 Environmental distribution

5.2.1 Adsorption/Desorption

No direct information is available. QSAR estimations (Episuite v3.1) give a Koc of 1912. In Freitag (1984) a partition coefficient of 240 in sludge was found and this agrees well with estimated Kp for sludge using a Koc of 1912 and Foc-susp of 0.1 giving Kpsusp=192.

EUSES gives a Koc of 582 based on a Log Kow of 3.29.

Experimental data and calculated partition coefficients indicate that ptBP will have a low mobility in soil.

5.2.2 Volatilisation

The volatilisation of ptBP from surface water to air may be estimated by the Henry's Law constant. This is calculated as 0.123 $Pa.m^3 * mol^{-1}$ for ptBP. The air-water partitioning coefficient ($K_{air\text{-}water}$) may be derived from the Henry's law constant and is calculated as 5.19×10^{-5} (European Union Risk Assessment Report, P-TERT-BUTYLPHENOL, 2008).

5.2.3 Distribution modelling

The potential environmental distribution of ptBP was obtained from a generic fugacity model (Mackay level III). The fugacity model indicates a high proportion of ptBP in the air compartment when all ptBP is released to air. However, this is probably not entirely realistic as the model does not incorporate degradation processes. The half life of ptBP in the atmosphere is 0.4 days and would rapidly reduce the amount in the atmosphere. Similar reservations should be applied with respect to levels in soil and water which in part is determined by biodegradation rates (European Union Risk Assessment Report, P-TERT-BUTYLPHENOL, 2008).

5.3 Aquatic Bioaccumulation

The question of bioaccumulation was discussed at the TC C&L meeting in 2005, and a BCF=120 was accepted. According to the Risk assessment profile for ptBP (EU 2008), the data suggest that ptBP does not bioaccumulate in the food chain.

5.3.1 Aquatic bioaccumulation

5.3.1.1 Bioaccumulation estimation.

Not applicable.

5.3.1.2 Measured bioaccumulation data

Freitag et al. (1984) studied the bioaccumulation of ptBP in golden orfe (*Leuciscus idus melanotus*) by exposure for three days to ptBP. The measured bioconcentration factor from this study was 120. The same team also tested bioaccumulation of ptBP in algae (*Chlorella fusca var. vacuolated*) by exposure to ptBP for 24 hours. The measured bioaccumulation factor in this study was 34. Furthermore, the same authors found that the administered dose of ptBP was mainly excreted via urine (26.7 %) and feces (72.9%) after oral exposure.

5.3.2 Calculated bioaccumulation data

Hu and Aizawa (2003) estimated that the log Pow for ptBP is 3.17 by using ACD/log Pow Ver.1.0 (Advanced Chemistry Development Inc.). ptBP is therefore not expected to bioaccumulate.

5.3.3 Summary and discussion of aquatic bioaccumulation

The bioaccumulation of ptBP has been studied in algae and fish. Furthermore, data modelling of the bioaccumulation of ptBP was performed. In summary, the data indicate that ptBP does not bioaccumulate.

5.4 Aquatic toxicity

Table 10: Summary of relevant information on aquatic toxicity

Method	Results	Reference
Deformities in fathead minnow (*Pimepales promelas*)	96h EC_{50}: 5,1 mg/l	Holcombe et al (1984)
Toxicity in common carp (*Cyprinus carpio*)	96h LC_{50}: 6.9 mg/l	Barse et al. (2006)
The test method was equivalent or similar to OECD Guideline 210 (Fish, Early-Life Stage Toxicity Test), but more extended. The test was performed on fathead minnow (*Pimephales promelas)*	Growth rate: 128 days NOEC: 10 ug/l Secondary sexual characteristics: 128 days NOEC 10 ug/l Time to hatch: 128 days NOEC 10 ug/l.	Krueger et al. (2008)
Endocrine disruption and metabolic change in common carp (*Cyprinus carpio*)	28-days EC_{50}: 0.69 mg/L	Barse et al. (2006)
Acute toxicity for *Daphnia magna*	48h EC_{50}: 3,9 mg/l	Kühn R et al (1989)
Toxicity of algae (*Selenastrum capricornutum*)	72h IC50: 14 mg/l 72 h NOEC: 0,32 mg/l	NIVA (2001a)

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

Type of study:	Deformities in fathead minnow (*Pimepales promelas*)
Reference:	Holcombe et al (1984)
Animal species:	Fathead minnow (*Pimepales promelas*)
Test substance:	4-tert-butylphenol, > 99% purity
Doses:	1.16, 1.87, 3.1, 5.44, 9.47 and 99.8 mg/L
Group sizes:	Fifty fathead minnows (25 per duplicate tank) were exposed in each concentration and in controls.
Results:	The 24h LC50 for ptBP was 6.21 mg/L, 48h LC50 was 5.69 mg/L, 72h LC50 was 5.26 mg/L and 96h LC50 was 5.14 mg/L. After exposure to pbBP for 96 hours, the fish were unreactive to outside stimuli at a dose of 3.1 mg/L, and deformities were observed at the dose of 5.44 mg/L.
Type of study:	Acute toxicity test performed according to American Public Health Association, American Water Works Association, and Water pollution Control Federation, Standard Methods for the Examination of Water and Wastewater, sixteenth ed. American Public health Association, Washington DC, 1985.
Reference:	Barse et al. 2006
Animal species:	Common carp (*Cyprinus carpio*)
Test substance:	4-tert butylphenol
Group sizes:	Ten fish per aquarium
Results:	Initial range finding tests were performed to select the maximum exposure level. The 96h LC_{50} of 4-tert butylphenol was found to be 6.9 mg/L.

5.4.1.2 Long-term toxicity to fish

Type of study:	OECD Guideline 210 (Fish, Early-Life Stage Toxicity Test), extended.
Reference:	Krueger et al. (2008). Unpublished results (the registrant has confirmed that we could use the study for this proposal).
Animal species:	Fathead minnow *(Pimephales promelas)*, newly fertilized embryos
Test substance:	Para-Tertiary Butyl Phenol
Doses, vehicle, duration:	Measured water concentrations were (2, 25, 82, 413 ug/l), deviated from the nominal concentrations (1, 30, 100, 500 ug/l). Water. 128

	days
Group sizes:	Two incubation cups, each containing 25 embryos, were placed in each of five replicate test chambers (tanks) per treatment (50 embryos per tank, a total of 250 embryos per treatment). The control group had ten tanks with a total of 500 embryos. After hatching, 200 larvae per treatment (400 larvae in the control) were released from the incubation cups into larger test chambers (40 per tank) where exposure continued and observations of condition and mortality were conducted. On day 28 post-hatch (study day 33), the fish were thinned to 32 fish per tank, for a total of 160 fish per treatment group and 320 fish in the control group, and exposure to test concentrations continued for the duration of the study. The embryos originated from 25 different spawnings.
Results:	Exposure to ptBP at the test concentrations did not affect sex ratio or male serum VTG concentrations in any of the treatment groups. Increased concentrations of VTG in females that were observed in the 300 ug/L treatment group were considered treatment related, and suggest a slight estrogenic effect at this ptBP concentration. Almost all of the males evaluated in the 300 ug/L treatment group (42 of 45) exhibited feminization of gonadal ducts (minimal to mild). These results suggest that ptBP caused estrogenic effects only in the 300 ug/L treatment group. Small, but statistically significant, treatment-related effects on growth and secondary sex characteristics were observed in the 30, 100 and 300 ug/L treatment groups. However, the effects in the 30 and 100 ug/L treatment groups were attributed to slight delays in development as opposed to estrogenic effects. It is important to note that minor delays in the onset of secondary sex characteristics may be transient, short lived and may no longer appear at a later stage of development. From a biological point of view, it is considered questionable whether these small differences could have any relevance at the fish population level. It is concluded that the induction of VTG in females, complete feminization of male gonads are clear indicators of endocrine disruption. Observations such as delayed onset of male sex characteristics, pigmentation of fin or nose/lip, reduction in fatpads and/or fatpad scores, and reduction in tubercles, tubercle count and score, were all considered to provide supportive evidence for an ED mode of action. It was noted by the contract laboratory that these endpoints showed treatment-related effects that potentially could be related to small delays in development, where the overall effect on the fish population level was uncertain. Taking all available information into account, the most sensitive endpoints were reduced growth, reduction in secondary male sex characteristics, and the delay in the time to hatch. Overall statistical LOEC and NOEC values were 30 µg/L and 10 µg/L, respectively. Clearly defined estrogenic effects were clearly present in the 300 µg/L treatment group as evidenced by feminization of gonadal ducts of male fish and elevated levels of plasma VTG in females.

Type of study:	Endocrine disruption and metabolic change
Reference:	Barse et al. 2006
Animal species:	Common carp (*Cyprinus carpio*)
Test substance:	4-tert butylphenol
Doses, vehicle, duration:	0, 0.69 mg/L, 1.38 mg/L and 2.3 mg/L. Stock solutions were prepared in acetone. The experiment lasted for 28 days.
Group sizes:	12 per dose
Results:	The mass of the testicles was significantly decreased ($P<0.01$), whereas the mass of the liver and kidney was significantly increased ($P<0.01$) after exposure to 0.69 mg/L 4-tert butylphenol. No significant changes in the mass of the brain was observed. Significant changes in the histo-morphology were observed after exposure to 0.69 mg/L 4-tert butylphenol. Furthermore, a significant decrease in the size, number of germ cells of the carp testis was observed at the same dose. A significant ($P<0.01$) change in the quantity of vitellogenin in muscle homogenates was also observed at exposure to 0.69 mg/L 4-tert butylphenol. An overall elevated alanine amino transferase (ALT) and lowered aspartate amino transferase (AST) in muscle tissue was also observed at exposure to 0.69 mg/L 4-tert butylphenol.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

Type of study:	Acute daphnia immobilisation test, according to DIN 38412, Part II
Reference:	Kuhn et al. 1989
Animal species:	*Dapnia magna*, 6-24h old
Test substance:	4-tert butylphenol
Group sizes	No information
Results:	The results of the effects was assessed by testing the animals ability to swim after 24 and 48 hours of exposure to 4-tert butylphenol. The EC_{50} after 24 hours of exposure was 4.2 mg/L and after 48 hours of exposure it was 3.9 mg/L. The EC_0 was 2.6 mg/L and the EC_{100} was 7.1 mg/L after both 24 and hours of exposure.

5.4.2.2 Long-term toxicity to aquatic invertebrates

None available. However, there is information on this from the lead registrant on ECHAs dissemination page.

5.4.3 Algae and aquatic plants

Type of study:	OECD Guideline 201 (Alga, Growth Inhibition Test).
Reference:	NIVA, 2001a. Unpublished results (NIVA has confirmed that we could use the study for this proposal).
Species:	Green algae, *Selenastrum capricornutum*
Test substance:	CAS no. 98-54-4 dissolved in acetone
Results:	4-tert butylphenol inhibited the growth of *Selenastrum capricornutum*. The growth inhibiting effect increased gradually over a large range of concentrations. Significant effects on the growth rate were observed above 0.32 mg/L (NOEC) and the EC_{50} was 14 mg/L. Growth inhibition was not complete at 18 mg/L, which was the highest tested concentration. The EC_{50} was estimated at 2.4 mg/L. NOEC for effect on area under growth curve could not be determined since significant reduction was observed at the lowest test concentration (0.32 mg(L)).

5.4.4 Other aquatic organisms (including sediment)

None available. However, there is information on this on ECHAs dissemination page.

5.5 Comparison with criteria for environmental hazards (sections 5.1 – 5.4)

In the long-term toxicity test to fish a NOEC value of 10 µg/l was obtained. In acute toxicity tests the LC_{50} and EC_{50} values in the range 3.9 mg/l to 6.7 mg/l were obtained and ptBP is not considered as rapidly biodegradable without meeting the 10 day window.

These results fulfil the criterion of Aquatic chronic 1 (NOEC ≤ 0,01 mg/l) in the 2. ATP to CLP.

5.6 Conclusions on classification and labelling for environmental hazards (sections 5.1 – 5.4)

Based on the data from the long-term toxicity to fish ptBP should be classified hazardous to the aquatic environment according to criteria in Commision Regulation (EU) No 286/2011 (2. ATP to CLP) with Aquatic Chronic 1; H 410 and M-factor = 1.

Classification Aquatic Chronic 1; H 410 is registered by the Industry to ECHA and published at the ECHA website.

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

4-*tert*-Butylphenol (ptBP) is currently listed in Annex VI of the CLP Regulation (EC) 1272/2008 but without any classification for environmental hazards. The Dossier Submitter (DS) proposed to classify the substance as Aquatic Chronic 1 - H410 (M=1) based on rapid degradation and a chronic NOEC of 0.01 mg/L in fish.

Degradation

ptBP is stable under visible light irradiation (Xiao *et al.*, 2014). No further information about abiotic degradation is provided by the DS.

Conflicting biodegradability results are available. An inherent MITI II test (MITI, 1992) (equivalent to OECD TG 302C) reported no biodegradation after 14 days in a test system inoculated with 100 mg/L of mixed sludge and 30 mg/L of ptBP. A ready biodegradation study conducted according to OECD TG 301F (Manometric Respirometry Test) (NIVA, 2003b) using non-adapted inoculum from an in-house activated sludge simulation unit indicated 60 % and 42 % degradation after 28 days for 15 and 25 mg/L ptBP, respectively. Failure to meet the 10-day window criterion means that ptBP was not readily biodegradable in this study. However, ptBP is toxic to micro-organisms at concentrations ≥ 25 mg/L, so the slower rates of degradation in these two studies can be ignored. A lag phase was also evident in the Niva (2003b) study, implying that for the lower test concentration of 15 mg/L micro-organisms need an adaptation period in order to be able to degrade ptBP rapidly.

The DS refers to additional studies on ECHA's dissemination page by the REACH Registrants but does not provide any details. For completeness, they are:

- A second ready test conducted according to OECD TG 301B (CO_2 Evolution Test), showing around 60% degradation after 28 days at 5 and 10 mg C/L. Failure to meet the 10-day window criterion indicates that ptBP was not readily biodegradable in this study.
- A third ready test conducted according to OECD TG 301A (Dissolved Organic Carbon (DOC) Die-Away test) used non-adapted inoculum derived from activated sludge from a domestic sewage plant. The DOC removal was found to be 98 % after 28 days at 13 mg/L ptBP (corresponding to 10.4 mg DOC/L). The robust study summary (RSS) states that ptBP was readily biodegradable, meeting the 10-day window criterion, although this cannot be explicitly determined from the information presented. Further details of this study are given under Supplemental Information.

The DS also summarised monitoring evidence from sewage treatment plants (STPs). Scharf and Sattelberger (1999) reported ptBP removal rates of between 3 and 53 % in 17 Austrian STPs. STP monitoring data presented in the EU Risk Assessment Report for ptBP (EC, 2008) under Regulation (EC) 793/93 were also claimed to have indicated 35-45 % degradation of ptBP under 'normal conditions' (although RAC cannot find this information in the original source). Further consideration of these data is given under Supplemental Information.

The DS concluded that the weight of evidence supports characterization of ptBP as »rapidly

biodegradable, but not fulfilling the 10 day window criterion«.

Bioaccumulation

The measured octanol-water partition coefficient (log Kow) of ptBP is in the range 2.4 – 3.3. Freitag *et al.* (1984) studied the bioaccumulation of ptBP in golden orfe (*Leuciscus idus melanotus*) after three days of exposure. The measured bioconcentration factor from this study was 120 L/kg. No information is provided about the time to steady state or lipid content of the fish.

Aquatic toxicity

Aquatic toxicity data are available for all three trophic levels. In the following table, a summary of the relevant information from aquatic toxicity studies is reported (the key endpoint used in long-term hazard classification is highlighted in bold).

Table 1: Summary of relevant information on aquatic toxicity

Method	**Test organism**	**Endpoint**	**Toxicity values in mg a.s./L**	**Reference**
Short-term toxicity to fish				
Standard Methods for the Examination of Water and Wastewater, 16th ed. American Public health Association, Washington DC, 1985	*Pimephales promelas*	96-h EC_{50} (deformities)	5.14	Holcombe *et al.*, 1984
n.a.	*Cyprinus carpio*	96-h LC_{50}	6.9	Barse *et al.*, 2006
Long-term toxicity to fish				
OECD TG 210, extended	*Pimephales promelas*	**128-d NOEC** (growth rate, secondary sexual characteristics and time to hatch)	**0.0096**	Krueger *et al.*, 2008
n.a.	*Cyprinus carpio*	28-d EC_{50} (endocrine disruption, metabolic change)	0.69	Barse *et al.*, 2006
Toxicity to aquatic invertebrates				
DIN 38412, Part II	*Daphnia magna*	48-h EC_{50} (immobilisation)	3.9	Kühn *et al.*, 1989
Toxicity to algae				
OECD TG 201	*Selenastrum capricornutum* (now known as *Raphidocelis* (or *Pseudokirchneriella*) *subcapitata*)	72-h IC_{50} 72-h NOEC (growth inhibition)	14 0.32	NIVA, 2001a
n.a. – data not available				

Two acute and two chronic aquatic toxicity tests on fish are available, the lowest values being obtained in fathead minnow (*Pimephales promelas*). In the acute toxicity study, the 96-h LC_{50} was 5.14 mg a.s./L. The long-term OECD TG 210 (extended) fish toxicity study provided a 128-day NOEC of 0.01 mg/L (nominal), based on growth rate, secondary sexual characteristics and time to hatch. The 128-d LOEC was 0.03 mg/L (nominal). According to the RSS from the registration dossier on ECHA's dissemination page, the NOEC would be 0.0096 mg/L based on mean measured concentrations. The DS reports different measured concentrations, citing 0.002 mg/L for the NOEC (but incorrectly reporting the equivalent nominal concentration as 0.001 mg/L). RAC prefers to use the information from the registration dossier, so the NOEC is taken to be 0.0096 mg/L.

Comments received during public consultation

Four Member State Competent Authorities (MSCAs), one individual and one company commented on the proposed environmental hazard classification. Three MSCAs and the company agreed with the classification proposal, with it also being indicated that the proposed environmental hazard classification was also agreed upon in the REACH consortium.

Two MSCAs asked for clarifications about the degradability conclusion, one of these MSCAs also requested further details about the chronic aquatic toxicity.

One individual proposed classification as Aquatic Chronic 2 based on multiple acute studies available in the CLH report and the fact that the chronic fish study produced a nominal NOEC that is borderline between classification categories (concerns about wide concentration intervals in this study were misplaced because of a typographical error in the original dossier). They were also concerned about the lack of detail in the unpublished chronic fathead minnow study, although the DS pointed out that the information was already included in the REACH registrations with a reliability score of 1 (reliable without restriction).

Assessment and comparison with the classification criteria

Degradation

The DOC Die-Away Test (equivalent to OECD TG 301A) shows degradation of 98 % (DOC decrease) after 28 days and > 70 % within 10 days after the time at which the degradation reached 10 %. ptBP is readily biodegradable based on these results. RAC reviewed the available information for this test (see Supplemental information) and considered it reliable for the purposes of classification. ptBP was significantly degraded (60 % after 28 days) in two additional ready biodegradation tests (OECD TG 301B and OECD TG 301F) but failed to meet the 10-day window (i.e. there was a lag phase). As a result, ready biodegradability cannot be determined from those studies. Nevertheless, these studies indicate that ptBP has the potential to mineralise, with the more extensive degradation measured in the OECD TG 301A study (98% after 28 days) presumably reflecting the presence of competent degraders in this particular test (it is well known that the outcome of ready tests can be limited by compromised microbial diversity (see for example Kowalczyk *et al*., 2015)).

The OECD TG 301A study reportedly used an unusually high level of ammonium chloride (NH_4Cl) in the mineral medium. No explanation is provided in the RSS, but although this might be a transcription error, RAC cannot check because the original study report is not available for

review. As NH_4Cl is also a nutrient, a high level could have influenced microbial growth, although it is not known whether this would have affected the biodegradability of the substance. There might possibly have been an effect on pH, but this was not measured (the pH was not intentionally adjusted according to the RSS). The pKa of ptBP is estimated to be above 10 in the REACH registration dossier, indicating that it is not ionised in the normal envirnmental pH range. Changes in pH might therefore affect microbial growth but are unlikely to affect the bioavailability of the substance. For comparison, the pH in the OECD TG 301B and 301F studies was 7.5-7.6 (determined at test termination) and not measured, respectively.

On balance, the influence of the ammonium chloride concentration remains uncertain but is not considered to invalidate the study.

RAC has decided that no firm conclusions regarding biodegradability can be drawn from WWTP (Waste Water Treatment Plant) monitoring studies (see Supplemental information). The results of QSAR modelling performed by RAC are borderline with respect to ready biodegradation (see Supplemental information).

The Guidance on the Application of the CLP Criteria Version 4.1, June 2015, paragraph II.3.5., page 568 gives the following advice: "In general, conflicting results for a substance which has been tested several times with an appropriate biodegradability test could be interpreted by a 'weight of evidence approach'. This implies that if both positive (i.e. higher degradation than the pass level) and negative results have been obtained for a substance in ready biodegradability tests, then the data of the highest quality and the best documentation should be used for determining the ready biodegradability of the substance. However, positive results in ready biodegradability tests could be considered valid, irrespective of negative results, when the scientific quality is good and the test conditions are well documented, i.e. guideline criteria are fulfilled, including the use of non-pre-exposed (non-adapted) inoculum."

Taking into account all available data on degradability (including the result of the DOC Die-Away test) and the CLP guidance, ptBP can be considered as a rapidly degradable substance in the environment.

Bioaccumulation

RAC agrees that ptBP has a low potential to bioaccumulate based on a log K_{ow} value of <4 and measured fish BCF value of 120 L/kg. The measured BCF value is less than the threshold of 500 L/kg in the CLP Regulation.

Aquatic toxicity

Acute*:*

Short-term aquatic toxicity data are available for all three trophic levels, and the L(E)C_{50}s are all above 1 mg/L. The substance therefore **does not require classification for acute aquatic toxicity**.

Chronic:

Long-term aquatic toxicity data are available for fish and algae. There are no long-term data for aquatic invertebrates, but the conclusion about rapid degradability and bioaccumulation potential mean that the surrogate method does not need to be applied for this trophic group. The lowest result is a 128-d NOEC of 0.0096 mg/L (mean measured concentration) for the fathead minnow *Pimephales promelas*. As this concentration is below the threshold value of 0.01 mg/L for rapidly degradable substances, RAC concludes that classification as **Aquatic Chronic 1 (H410)** is warrented. As the NOEC value is in the range 0.001 < NOEC ≤ 0.01 mg/L, the

chronic **M-factor is 1** for rapidly degradable substances (CLP, Annex I, Table 4.1.3), as proposed by the DS and agreed on by the REACH registrants.

Note: Following the public consultation, RAC became aware of a 28-d semi-static ecotoxicity study with juvenile fish (Pikeperch or Zander *Sander lucioperca*) (Demska-Zakęs. 2005). Significant (irreversible) changes in sex ratio were reported at the lowest test concentration of 0.001 mg/L (nominal). RAC has not evaluated this study, but notes that it supports classification as Aquatic Chronic 1 (see Supplemental Information in the Background Document). If the study were satisfactorily validated, it might influence the M-factor (increasing it by a factor of 10, since it implies a NOEC below 0.001 mg/L).

Supplemental information - In depth analyses by RAC

Due to uncertainties in the degradation data set and comments from RAC members, the Rapporteurs have analysed the following additional information.

Degradability

a) Biodegradation predictions

Using the CAS number as the input, BIOWIN v4.10 gave the following results:

Model component	Probability	Cut-off point between ready & non-ready biodegradability
Biowin1 (Linear Model)	0.6079	0.5
Biowin2 (Non-Linear Model)	0.5152	0.5
Biowin3 (Ultimate Survey Model)	2.7115 (weeks-months)	2.75
Biowin4 (Primary Survey Model)	3.5173 (days-weeks)	-
Biowin5 (MITI Linear Model)	0.4312	0.5
Biowin6 (MITI Non-Linear Model)	0.4050	0.5

ptBP is within the model domain. The REACH Guidance on information requirements for specific endpoints (Chapter R.7b) indicates that the Biowin1, 2, 3 and 4 models were based on the conclusions of a US EPA expert panel. Biowin 5 and 6 are mainly based on MITI I data, which uses a uniquely derived inoculum. The guidance suggests that an overall prediction of ready biodegradability can be drawn if the Biowin3 result is ≥2.75 and the Biowin5 result is ≥0.5, but cautions that this had not been accepted for hazard assessment in the EU yet. In this case, the results are 2.7115 and 0.4312, respectively. The models therefore do not give a clear indication that ptBP is readily biodegradable. However, the REACH Guidance indicates that, due to differences in model performance, it may not be appropriate to draw conclusions when predictions are close to the cut-off point, i.e. a biodegradability probability score between 0.4 and 0.6 for Biowin1, 2, 5 or 6. In this case, with the exception of the Biowin1 result (which is marginally above 0.6), the predictions fall within this range. The Biowin3 result is also very close to the cut-off. RAC therefore considers the predictions to be borderline.

b) Implications of WWTP data

Using the physico-chemical properties provided in the CLH report, removal rates for ptBP in a

WWTP (using the SimpleTreat model in EUSES) can be predicted as follows:

- 88 % if the substance is readily biodegradable,
- 69 % if the substance is "readily biodegradable not meeting the 10-d window",
- 44 % if the substance is inherently degradable.

Removal rates estimated from WWTP monitoring data might therefore provide support for a decision on rapid degradability. The DS provides only a partial description of the study by Scharf and Sattelberger (1999) on removal rates at municipal WWTPs in Austria, but a more detailed description is provided in EC (2008). The effluent concentration was below the detection limit at half the sites (7 of 14); removal was above 77 and 94 % at two of these sites. Removal rates were in the range 3–53 % for five sites with effluent concentrations above the detection limit. The ptBP concentration was higher in effluent than influent at the remaining two sites. This finding implies either ptBP formation *in situ* (e.g. from derivatives or other alkylphenols) or a mis-match between samples (e.g. if effluent samples were collected within the hydraulic retention time of the WWTP). If *in situ* formation occurred, then the level of removal could be higher than suggested. If the effluents were not properly matched to the influents, these data cannot be used. Either way, this study is insufficient to provide a clear picture of actual removal. It is, however, notable that ptBP was detected in the influent at all 16 sites in the range 63–887 ng/L.

EC (2008) also provides data for three Swedish WWTPs. The removal level was 2 and 40 % at two sites but the ptBP concentration in effluent was higher than in influent at the third site. ptBP was detected in the influent at all sites in the range 46 – 98 ng/L.

RAC has decided that it is not appropriate to draw conclusions onthe implications for degradability from these data.

c) DOC Die-Away test

The CLH report states that the REACH registration dossier includes a test of biodegradation according to EU Method C.4.A (Determination of the "Ready" Biodegradability – Dissolved Organic Carbon (DOC) Die-Away Test) [equivalent to OECD TG 301A], which shows that ptBP is rapidly biodegradable. No further details are provided. RAC does not have access to the original study, but EU RAR (EC, 2008) includes the following description:

> "The aerobic biodegradation was tested in a DOC-Die-Away test according to OECD TG 301A (Hüls AG, 1994). The study was conducted according to GLP. The test substance concentration used was 13 mg/L ptBP corresponding to 10.4 mg DOC/L. Inoculum from a predominantly municipal WWTP was used. The DOC removal was found to be 98 % after 28 days. According to this test results the substance can be regarded as readily biodegradable meeting the 10-day window criterion. Adsorption can be ruled out as a removal path as shown by DOC measurements after 3 hours. Sodium benzoate was used as a reference control and achieved 99 % removal after 28 days, fulfilling the 10-day criterion. However, it cannot be excluded that the inoculum might have been adapted to ptBP as it was taken from a municipal WWTP in a heavily industrialised area where industry might be located using ptBP."

RAC notes that the final sentence is somewhat speculative. In fact, the RSS on the ECHA dissemination site states that a non-adapted inoculum was used. The WWTP data mentioned above suggest that ptBP can often be detected in WWTP influent at low concentrations, so it might be difficult to collect WWTP inocula that have not been pre-adapted to some extent.

The following details are provided in the RSS:

Year: 1993

Report Date: 1994

Guideline: EU Method C.4-A (Determination of the "Ready" Biodegradability - Dissolved Organic Carbon (DOC) Die-Away Test)

GLP compliance: yes

Inoculum or test system: activated sludge, domestic, non-adapted

Details on inoculum:
- Source of inoculum/activated sludge: domestic sewage plant (Marl-East, Germany)
- Laboratory culture: no
- Storage conditions: aeration
- Storage length: not mentioned
- Preparation of inoculum for exposure: 15 min centrifugation at 3000 rpm, decantation of supernatant, resuspension of sludge in mineral medium, this procedure done twice, determination of dry weight
- Pretreatment: no further pretreatment mentioned
- Concentration of sludge: 27.0 mg/L suspended solids; dry weight of inoculum: 3.38 g/L
- Initial cell/biomass concentration: no data
- Water filtered: no

Duration of test (contact time): 28 d

Initial test substance concentration: 10.4 mg/L based on DOC

Parameter followed for biodegradation estimation: DOC removal

Details on study design:
TEST CONDITIONS
- Composition of medium: 10 mL stock solution a and 1 mL stock solutions b - d each made up to 1 L deionised water
  stock solution a: 8.5 g/L KH_2PO_4, 21.75 g/L K_2HPO_4, 33.3 g/L Na_2HPO_4 x 2 H_2O, 20.0 g/L NH_4Cl
  stock solution b: 22.5 g/L $MgSO_4$ x 7 H_2O
  stock solution c: 27.7 g/L $CaCl_2$
  stock solution d: 0.25 g/L $FeCl_3$ x 6 H_2O
- Additional substrate: none
- Solubilising agent (type and concentration if used): not used
- Test temperature: 21.8 - 22.3 °C
- pH: no data
- pH adjusted: no
- Aeration of dilution water: not mentioned
- Suspended solids concentration: 27.0 mg/L
- Continuous darkness: yes

TEST SYSTEM
- Culturing apparatus: 2000 mL Erlenmeyer flasks, loosely closed with aluminium foil, on a shaking machine
- Number of culture flasks/concentration: 2
- Method used to create aerobic conditions: aeration through a frit

- Method used to create anaerobic conditions: not applicable
- Measuring equipment: infrared carbon analyser (Shimadzu T 500)
- Test performed in an open system: yes

SAMPLING
- Sampling frequency: after 0 and 3 hours, and on days 7, 14, 21, 27 and 28
- Sampling method: not mentioned
- Sample storage before analysis: not mentioned

CONTROL AND BLANK SYSTEM
- Inoculum blank: yes (2 vessels with inoculum without test substance)
- Abiotic sterile control: not performed
- Toxicity control: not performed

STATISTICAL METHODS: no statistics performed

Reference substance: benzoic acid, sodium salt

Remarks: 10.7 mg DOC/L

Results and discussion

Test performance: Inoculum corresponding to 27.0 mg/L was given in 3 vessels (volume 3 L), filled up with about 2 L mineral medium. 50 mL test substance stock solution (520 mg/L DOC), resp. 44 mL control substance stock solution (608 mg/L DOC) were given into each vessel and filled up to 2.5 L with mineral medium. From these batches two times 1000 mL were given into 2000 mL Erlenmeyer flasks. The loosely covered flasks were incubated in the dark on a shaking machine for 28 days.

% Degradation of test substance: ca. 98 after 28 d (DOC removal)

% Degradation of reference substance: >70 after 7 d

Table: Degradation kinetic

sampling time	degradation [%]			
	test substance			reference substance
	vessel 1	vessel 2	**mean**	
3 h	0	0	**0**	0
7 d	17.7	12.3	**15**	99
14 d	77.3	82.5	**80**	99
21 d	100.4	99.8	**100**	100
27 d	99.4	98.7	**99**	100
28 d	97.6	97.6	**98**	99

Conclusions: The test substance reached 98 % degradation (DOC decrease) after 28 days and > 70 % within 10 days after the time at which the degradation had reached 10 %. The test substance was therefore considered to be readily biodegradable.

Validity criteria fulfilled: yes

***RAC opinion**:* The study is considered reliable with restrictions by the REACH Registrant(s) although no reason is provided as to why it is not fully reliable. RAC notes that no information is available on pH, and the amount of nitrogen in the mineral medium was higher than recommended in the test guideline by a factor of about 40 (20 g/L of ammonium chloride was used rather than 0.5 g/L). This could perhaps be a typographical error but the original study report would need to be checked. Otherwise, all validity criteria are fulfilled, and ptBP is not a

difficult substance to test. The study used non-adapted inoculum, as well as a non-inhibitory test concentration. Based on DOC removal and the fact that the substance is not highly adsorptive (the organic carbon-water partition coefficient is estimated to be in the range 500 – 2 000), the substance can be considered readily biodegradable, achieving almost complete removal by 21 days. Although the RSS does not include all of the data to demonstrate that ptBP met the 10-day window, it did achieve 80% degradation after 14 days. The 10-day window would therefore have been met provided that 10% degradation was achieved on or after day 4 of incubation. Subsequently, the conclusion of the RSS is that the 10-day window was met, and RAC has no reason to challenge it.

There is no simple or clear explanation for the difference in the result of this test compared to the others presented in the CLH report, other than the possibility of microbial inhibition (with lag phases) at higher concentrations than those used in this test. However, both the REACH and CLP Guidance indicate that, due to the stringency of ready biodegradation tests, a positive result obtained in a valid, well documented standard study (including assurance of the use of non-pre-exposed (non-adapted) inoculum) is used to indicate rapid degradation for classification, irrespective of other negative results (unless there are strong weight of evidence or structural reasons to question this result, which is not the case here).

Additional long-term fish study (Demska-Zakęś, 2005)

The Austrian Competent Authority (CA) has provided the following information.

A long-term study has been performed with juvenile Pikeperch [Zander] (*Sander lucioperca*) to investigate the effects of ptBP on mortality, development (weight, length, condition factor, gonads) and sex ratio (based on histological examination).

Materials and Methods

Sexually undifferentiated fish from artificial spawning were exposed to ptBP from 60 days post hatching (dph) until 88 dph. These 28 days of exposure were followed by 56 days of rearing without the test substance (until 144 dph). The test included a dilution water control, a solvent control (ethanol, 10 µL/L) and four treatment concentrations of 1, 10, 100, 200 µg/L (nominal) for ptBP and as well for the positive control (17ß-estradiol). 80 fish per tank were tested in three replicates/treatment. The fish were kept in tanks with a water volume of 80 L under semi-static conditions (approximately 50 % water exchange per 24 h) and permanent lighting (50-60 lux). Each tank was separately filtered by a biological filter (filter performance was 4 L/min corresponding to the 3-fold tank volume per hour). The test temperature was 22.0±0.5 °C.

The adaptations made were in accordance with aquaculture practices rather than OECD TG 234. The fish were held under constant light of weak intensity in a recirculation-system under semi-static conditions, with 50 % volume exchange per day and biological filtration of the tank water.

Despite some weaknesses in the test design, along with modifications compared to OECD TG 234, the study is considered valid and rated with Klimisch 2 [by the Austrian CA], as nominal concentrations in semi-static conditions are considered worst case assumptions of real concentrations due to possible degradation and adsorption during the test.

The fish were examined for an effects assessment on 88 dph (after 28 days exposure) and on 144 dph at the test end.

Results

No statistically significant effects of ptBP on mortality, total length, body weight, or condition factor of the fish were observed. However, ptBP had significant dose-dependent effects on the gonads, starting from the lowest test concentration (Table 1 + 2). In neither of the investigated endpoints was a statistically significant difference between the dilution water control and the solvent control encountered.

Table 1: NOECs and LOECs for 4-tert-butylphenol

Effects on sex ratio (histological)	28-d NOEC	28-d LOEC
Decrease in male fish	<0.001 mg/L (nom.)	0.001 mg/L (nom.)
Increase in female fish	<0.001 mg/L (nom.)	0.001 mg/L (nom)
Occurrence of Intersex fish (histological analysis)	<0.001 mg/L (nom.)	0.001 mg/L (nom.)

Table 2: Sex structure of pikeperch after 28 days of exposure to 4-tert-butylphenol (D88) and after a subsequent rearing of 56 days without the test substance (D144). These values refer to mean numbers of fish in percent and were extrapolated from a graph (Fig. 21 in Demska-Zakes, 2005).

Treatment (µg/L)	Female	Male	Intersex	Sterile
D88				
Dilution water control	52^{ab}	48^{a}	0^{a}	0^{a}
Solvent control	47^{a}	53^{a}	0^{a}	0^{a}
1	58.5^{bc}	31.5^{b}	10^{ab}	0^{a}
10	68^{c}	15^{c}	17^{b}	0^{a}
100	80^{d}	0^{d}	20^{b}	0^{a}
200	98^{e}	0^{d}	2^{a}	0^{a}
D144				
Dilution water control	48^{a}	52^{a}	0^{a}	0^{a}
Solvent control	52^{ab}	48^{a}	0^{a}	0^{a}
1	57.5^{b}	32^{b}	10.5^{b}	0^{a}
10	68^{c}	16.5^{c}	15.5^{b}	0^{a}
100	78^{d}	0^{d}	22^{c}	0^{a}
200	100^{e}	0^{d}	0^{a}	0^{a}

Values with the same superscript in the same column are not significantly different (P>0.05).

After 28 days of exposure, the ratio of male fish (according to histological determination) was significantly decreased at the lowest test concentration (0.001 mg/L). Compared to the solvent control, the ratio of female fish increased in the lowest test concentration. The appearance of intersex species (comprising sex characteristics from both sexes e.g. testis-ova/ ovo-testis, formation of an oviduct with regressed spermatogenic lobules in the same fish) increased significantly from 1 µg/L at 144 dph and was not observed in the controls. The sex ratio shifted in a dose-dependent manner, leading to 98 and 100 % fish with female sex characteristics at the two sample points, 88 dph (Figure 1a) and 144 dph (Figure 2a), respectively. The observed effects on the sex characteristics were irreversible during the duration of the test (including 56 days of rearing without exposure to the test substance).

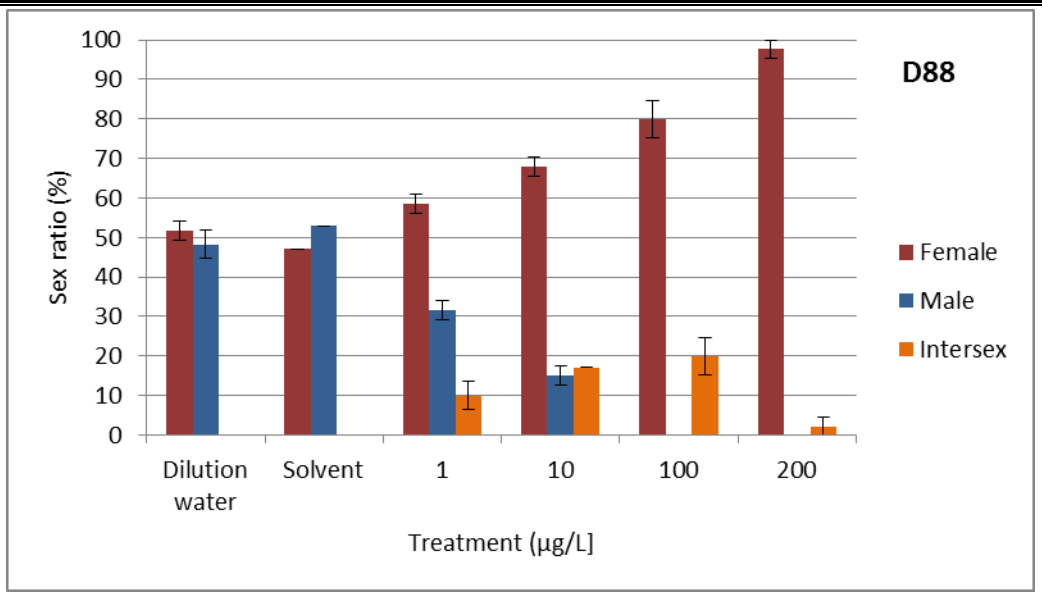


Figure 1: Sex structure of pikeperch (*Sander lucioperca*) after 28 days of exposure to 4-tert-butylphenol (D88). The bars represent the mean number of individuals of each sex (± standard deviation), derived from the replicate tanks (n=3) within each treatment, expressed in percent. Values were extrapolated from Fig. 21 in Demska-Zakes (2005).

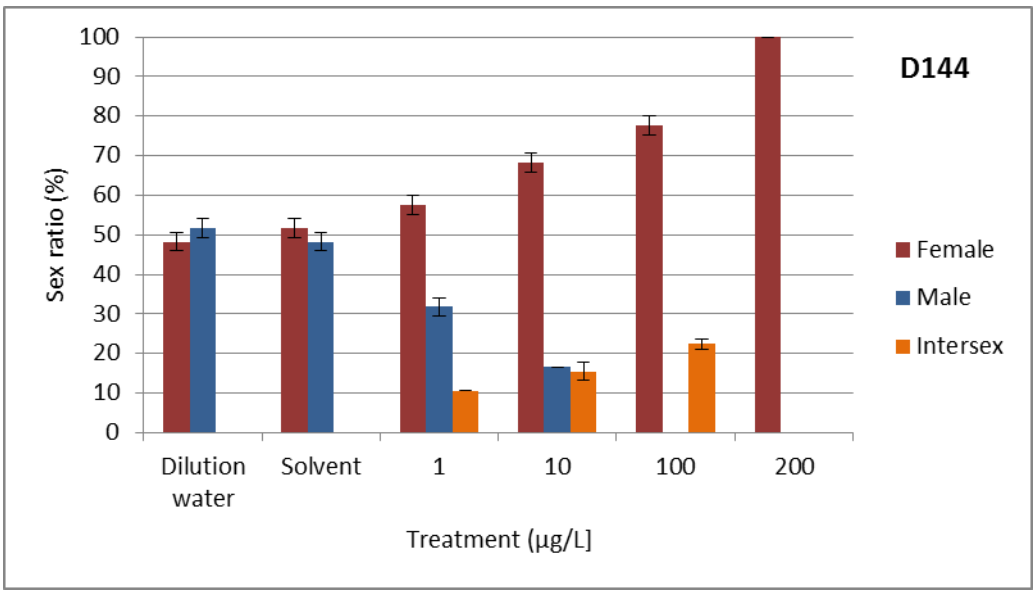


Figure 2: Sex structure of pikeperch (*Sander lucioperca*) after 28 days of exposure to 4-tert-butylphenol and a subsequent rearing of 56 days without the test substance (D144). The bars represent the mean number of individuals of each sex (± standard deviation), derived from the replicate tanks (n=3) within each treatment, expressed in percent. Values were extrapolated from Fig. 21 in Demska-Zakes (2005).

In Table 3, an overview regarding the effect concentrations for all investigated endpoints is provided.

Table 3: Effect concentrations for the investigated endpoints in juvenile pikeperch (*Sander lucioperca*) after 28 days of exposure to 4-tert-butylphenol. Concerning these effect concentrations, the results of 88 dph and 144 dph were combined to an overall conclusion based on the most reliable findings.

	Mortality	TL	BW	CF	Female ↑	Male ↓	Intersex ↑	Sterile ↑
NOEC (µg/L)	>200	>200	>200	>200	<1	<1	<1	>200
LOEC (µg/L)	>200	>200	>200	>200	1	1	1	>200

BW body weight, CF condition factor, female ↑ increase of female sex characteristics, Intersex ↑ appearance of intersex species, Male ↓ decrease of male sex characteristics, Sterile ↑ appearance of sterile species, TL total length

RAC opinion: This information was received very late in the evaluation process and has not been subject to public consultation. A full study report in English is not available, and the information has not yet been published in peer-reviewed scientific literature. Whilst the study appears to be convincing, RAC notes the following:

- There is no information about the positive control response.
- The study was not performed according to a validated standard test guideline or GLP. Its reliability needs to be confirmed, and a full RSS is required with details of deviationsfrom OECD methodology together with their potential influence on the results.
- Confirmation that the histopathology is credible, independently verified and included enough indidviduals at each concentration, is required.
- Information is needed on any historical variation in the tested parameters with this species and what factors influence sex differentiation.
- RAC is aware that other alkylphenols were tested as part of the same study, although this is not mentioned in the information supplied. There should be some comparison between the responses in this species and standard test guideline species for these substances in order to provide information on its relative sensitivity.

On this basis, RAC considers that it is premature to include it in the opinion as being of suitable reliability as the key study. RAC notes that it supports classification as Aquatic Chronic 1. If satisfactorily validated, it might influence the M-factor (increasing it by a factor of 10, since it implies a NOEC below 0.001 mg/L).

6 OTHER INFORMATION

None

7 REFERENCES

Barse AV, Chakrabarti T, Ghosh TK, Pal AK and Jadhao SB. One-tenth dose of PC_{50} of 4-tert butylphenol causes endocrine disruption and metabolic changes in *Cyprinus carpio.* Pesticide biocehm and Physiol. 86 (2006) 172-179.

Böddeker KW, Bengtson G and Bode E. Pervaporation of low volatility aromatics from water. J. Membr. Sci. 53; 143-158. 1990.

EU Risk Assessment Report for p-tert butylphenol, CAS No: 98-54-4, EINECS No: 202-679-0 Final approved version, 2008

ECHA dissemination web site. Information as accessed September and October 2015. European Chemicals Agency (2014): http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d8bb7ca-18a5-44ef-e044-00144f67d249/DISS-9d8bb7ca-18a5-44ef-e044-00144f67d249_DISS-9d8bb7ca-18a5-44ef-e044-00144f67d249.html

Freitag D, Lay JP, Korte F. Environmental hazard profile – test results as related to structures and translation into the environment. Environmental Toxicol 1984;111-36.

Holcombe GW, Phipps GL, Knuth ML, Felhaber T. The acute toxicity of selected substituted phenols, benzenes and benzoic acid esters to fathead minnows *pimephales promelas.* Environmental Pollution (Series A) 1984;35:367-81.

Hu JY, Aizawa T. Quantitative structure–activity relationships for estrogen receptor binding affinity of phenolic chemicals. Water Res., 37 (2003), pp. 1213–1222

Huels AG Marl 1992. (A): Sicherheitsdatenblatt Huels AG, 28.04.

Huels AG Marl (B) 1994: Productinformation “p-tert-butylphenol”, Art.-Nr.: 001786; Ausgabe 01.08.

Huels AG Marl (C): Huels-Untersuchung (unpublished).

Huels AG Marl 1972 (D): Church C, Hansch C: unpublished results, cited in Leo A et al., Chem. Rev., 71; 531, 537-538.

Krueger HO, Kendal TZ, Martin KH and Nixon WB. Final report Para-Tertiary Butyl Phenol (PTBP): A partial Life Cycle Test with the Fathead Minnow (Pimephales promelas). Wildlife International Ltd. Project number: 583A-109. 2008. Unpublished.

Kühn R, Pattard M, Pernak KD, Winter A. Results of the harmful effects of selected water pollutants (anilines, phenols, aliphatic compounds) to *Daphnia magna.* Wat Res 1989;23(4):495-9.

MITI (1992) Biodegradation and Bioaccumulation Data of Existing Chemicals. Based on the CSCL Japan. Ministry of Trade and Industry, Japan.

NIVA: Test report for 4- tert butylphenol, growth inhibition of green alga *Selenastrum capricornutum,* Study number G023/2, (2001 a). Unpublished.

NIVA: Test report, biodegradation of 4- tert butylphenol. Ready biodegradability –evaluation of the aerobic biodegradability in aqueous medium, manometric respirometry test, OECD 301F, Study number G023/3, (2001b). Unpublished.

Scharf S., Sattelberger R.: Hormonell wirksame Substanzen im Zu- und Ablauf von Klaeranlagen.Wien, März 1999. (Berichte; BE-151), ISBN: 3-85457-501-7.

SIDS Initial assessment profile. p-tert-butylphenol Cas No. 98-54-4. 2000

Xiao X, Xing C, He G, Zuo X, Nan J and Wang L. Solvethermal synthesis of novel hierarchical $Bi_4O_5I_2$ nanoflakes with highly visible light photocatalytic performance for the degradation of 4-tert-butylphenol. Applied Catalisis B. Environmental Vol. 148-149, 27 April 2014 (14-163)

Additional references
Additional references not included in the CLH report Demska-Zakęs K. (2005). Effect of select xenobiotics on the development of the fish reproductive system. Dissertations and monographs UWM Olsztyn 103: 1–61 [in Polish]. Hüls AG (1994): EITHER Report No. DDA-59, unpublished OR Report No. SK-94/14, unpublished, as cited in the Reference List for EC (2008). Kowalczyk A, Martin T J, Price O R, Snape J R, van Egmond R A, Finnegan C J, Schäfer H, Davenport R J & Bending G D (2015). Refinement of biodegradation tests methodologies and the proposed utility of new microbial ecology techniques. Ecotoxicology and Environmental Safety, 111, 9–22.

8 ANNEXES

Annex I: Final follow-up from Meeting on Environmental Effects of Existing Chemicals, Pesticides & New Chemicals, Pesticides. Ispra 28-30 September 2005.

EUROPEAN COMMISSION
DIRECTORATE GENERAL JRC
JOINT RESEARCH CENTRE
Institute for Health and Consumer Protection
Unit: Toxicology and Chemical Substances
European Chemicals Bureau

Ispra, December 20, 2005

Follow-up III (Final Follow-up)

Meeting on Environmental Effects of Existing Chemicals, Pesticides & New Chemicals, Pesticides

Ispra, 28-30 September 2005

1. Environmental Classification of Metals and Metal Compounds (Working Group Meeting, September 27)

The report back from the working group meeting on metals was limited. Due to the sudden loss of a colleague at the ECB who had been in charge for the preparations of that meeting, the working group had interrupted their work the day prior to the meeting of the TC C&L as they got the news about this tragic event.

The work of the metals working group will be continued in 2006 if possible, depending on to resources available at the ECB.

2. Classification of New Substances

Follow-up of the session on New Substances is sent out separately.

3. Group Entry for Nickel Compounds

The TC C&L agreed in principle to the DK proposal on group entries for nickel compounds to be included or revised in Annex I. Member States were invited to send their detailed comments/questions on the entries presented in ECBI/96/04 Add. 2 directly to Denmark with copy to the ECB at the latest 7 November.

This would give DK the possibility to inform at the TC C&L Health meeting in November on the comments and extent of the comments concerning environment. The intention of DK was then to collect comments also from the TC C&L on health and present a revised proposal for the group entries for nickel compounds prior the end of the year.

FU II: Spain has sent in a note expressing agreement with the Danish proposal on the nickel compounds (grouping of categories based on their water solubilities).

4. Classification of Existing substances

4. 1. Existing substances concluded

PGMA; 2-methoxy-1-methyl ethyl acetate (F) Index : 607-195-00-7CAS: 108-65-6

EC: 203-603-9 *HH: agreed 03/2005.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No	L(E)C_{50} > 100	Readily degradable	log Kow ≥ 3	Not relevant

classification		(based on data)		
Specific concentration limits:				

PGME; 1-methoxy propan-2-ol (F) Index: 603-064-00-3 CAS: 107-98-2

EC: 203-539-1 *HH: agreed 03/2005*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	$L(E)C_{50} > 100$	Readily degradable (based on data)	log Kow ≥ 3	Not relevant
Specific concentration limits:				

TCPP; Tris(2-chloro-1-methylethyl) phosphate (IRL/UK) Not in Annex I

CAS: 13674-84-5 EC: 237-158-7 *HH: within ESR further testing is carried out.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	$10 < L(E)C_{50} \leq 100$	Not readily degradable (based on data)	log $K_{ow} < 3$	NOEC > 1 mg/l
Specific concentration limits:				

TDCP; Tris[2-chloro-1-(chloro methyl) ethyl] phosphate (IRL/UK)

Not in Annex I CAS: 13674-87-8 EC: 237-159-2 *HH: Within ESR further testing is carried out.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause

N, R51-53 **S61**	1 < L(E)C_{50} ≤ 10	Not readily degradable (based on data)	log K_{ow} > 3	Not relevant
Specific concentration limits:				

V6; 2,2-bis(chloromethyl) tri methylene bis [bis(2-chloro ethyl) phosphate (IRL/UK) Not in Annex I CAS: 38051-10-4 EC: 253-760-2 *HH: Within ESR further testing is carried out.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	10 < L(E)C_{50} ≤ 100	Not readily degradable (based on data)	log K_{ow} < 3	NOEC > 1 mg/l
Specific concentration limits:				

4-tert-butylbenzoic acid (D) Not in Annex I CAS: 98-73-7 EC: 202-696-3

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R51-53 **S 61**	1 < L(E)C_{50} ≤ 10	Not readily degradable (based on data)	log K_{ow} > 3 BCF < 100	Not relevant
Specific concentration limits:				

EPTAC; 2,3-epoxy propyl trimethyl ammonium chloride (FIN) Not in Annex I

CAS: 3033-77-0 EC: 221-221-0 *HH: agreed 03/2005*.

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
R52-53 **S61**	10 < L(E)C_{50} ≤ 100	Not readily degradable (based on data)	log K_{ow} < 3	NOEC ≤ 1 mg/l
Specific concentration limits:				

CHPTAC; (3-Chloro-2-hydroxy propyl) trimethyl ammonium chloride (FIN) Not in Annex I
CAS : 3327-22-8 EC: 222-048-3 *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
R52-53 **S61**	10 < L(E)C_{50} ≤ 100	Not readily degradable (based on data)	log K_{ow} < 3	NOEC ≤ 1 mg/l
Specific concentration limits:				

CBS; N-cyclohexylbenzo-thiazole-2-sulphenamide (D) Index: 613-136-00-6

CAS: 95-33-0 EC: 202-411-2 *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	0.1 < L(E)C_{50} ≤ 1	Not readily degradable (based on data)	log K_{ow} > 3 BCF >100	Not relevant
Specific concentration limits:				

The current Annex I classification for ENV was confirmed.

Methenamine (D) Index: 612-101-00-2 CAS:100-97-0 EC: 202-905-8

HH: to be discussed.

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	L(E)C_{50} > 100 (mg/l)	Not readily degradable (based on data)	log K_{ow} < 3	Not relevant
Specific concentration limits:				

The current Annex I classification for ENV was confirmed.

Chlorine (IT) Index: 017-001-00-7 CAS:7782-50-5 EC: 231-959-5 *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50 **S61**	0.001 < L(E)C_{50} ≤ 0.01			Not relevant
Specific concentration limits:	C_n ≥ 0.25% : **N, R50** (S61)			

4-Tert butyl phenol; 4-(1,1-Dimethyl -ethyl) phenol (NO) Not in Annex I

CAS: 98-54-4 EC: 202-679-0 *HH: to be discussed..*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R51-53	1 < L(E)C_{50} ≤ 10	Readily degradable (based on data)	log K_{ow} > 3 BCF >100	Not relevant.

S61				
Specific concentration limits:				

IND has submitted document ECBI/20/05 Add. 1 on the substance in time for the meeting. However, ECB failed to post the document on the agenda. It was then distributed as a room document and then again in FU I. MS are invited to react to the document in the FU period.

FU II: NO has sent in the relevant part of the RAR (ECBI/20/05 Add. 2).

FU III: Sweden has reacted to document ECBI/20/05 Add.1. Sweden, referring to the bioaccumulation of ptBP noted that IND in its letter questioned the use of the Freitag et al. 1984 study in determination of the BCF of the substance. Sweden believed that the question of bioaccumulation had been thoroughly discussed by the TC NES and the value of BCF (i.e. 120) had been accepted and therefore they did see no reason for rejecting the study for classification purposes.

The substance will be classified as outlined in the box.

AEEA; 2-(2-amin ethylamino)ethanol Index: 603-194-00-0 (not yet in Annex I, but in draft list for 30th ATP) CAS:111-41-1 EC: 203-867-5 *HH: agreed 09/04*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	$10 < L(E)C_{50} \leq 100$	Readily degradable (based on data)	$\log K_{ow} < 3$	Not relevant
Specific concentration limits:				

F has sent in a revised classification proposal for the substance (ECBI/62/04 Add. 3).

FU II: Spain sent in a note in which they express agreement with not classifying this substance for the environment, and that furthermore EPIWIN calculations are in agreement with the experimental data.

2-Ethylhexyl-2-ethylhexanoate Not in Annex I CAS: 7425-14-1 EC: 231-057-1 *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification	L(E)C_{50} > 100	Readily degradable (based on data)		Not relevant
Specific concentration limits:				

PFOS; Perfluorooctane sulfonate [1]and its Salts Not in Annex I CAS: 1763-21-1[1] Not in EINECS *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R51-53 **S61**	1 < L(E)C_{50} ≤ 10	Not readily degradable (based on data)	BCF >100	Not relevant.
Specific concentration limits:				

The final entry still has to be defined at the HH meeting.

Ketoconazole Not in Annex I CAS: 65277-42-1 EC: 265-667-4 *HH: to be discussed*

Classification S -phrases	Toxicity	Degradation	Bio accumulation	Escape clause
N, R50-53 **S60-61**	0.1 < L(E)C_{50} ≤ 1	Not readily degradable (default in absence of information). According to QSAR (Episuite 3.1) substance is not biodegradable	BCF >100 log K_{ow} > 3	Not relevant

Specific concentration limits:	

FU II: Norway has sent in a complemented classification proposal (ECBI/42/05 Rev. 1) that contains the requested information on the applied QSAR.

FU III: Sweden has sent in a note saying that the classification proposal was based on QSAR values. Norway, the rapporteur country provided the QSAR models that had been applied (ECBI/42/05 Rev.1). According to their judgement the QSAR models had been correctly applied and the results give a firm picture of the toxicity of the substance. Therefore, in absence of experimental data, they would like to support the proposed classification based on QSAR.

Phenolphthalein Not in Annex I CAS: 77-09-8 EC: 201-004-7

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification (lack of data)	No relevant information	No relevant information	No relevant information	Not relevant
Specific concentration limits:				

Leucomalachite green Not in Annex I CAS: 91-95-2 EC: 202-110-6 *HH: to be discussed*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	$0.1 < L(E)C_{50} \leq 1$	Not readily degradable (based on data)	log $K_{ow} < 3$	Not relevant.
Specific concentration limits:				

No data was available on the substance. Classification is based on read-across to malachite green.

Diaminobenzidine Not in Annex I CAS: 91-95-2 EC: 202-110-6 *HH: concluded 05/2004*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
No classification (lack of data)	No relevant information	No relevant information	No relevant information	Not relevant
Specific concentration limits:				

4. 2. Existing substances to be concluded in the follow-up period

4. 3. Existing substances <u>not</u> concluded

Nickel powder CAS: 7440-02-0 EC: 231-111-4

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[R52-53] **[S61]**				
Specific concentration limits:				

The discussion was postponed to the next meeting.

TNPP; Tris (nonylphenyl) phosphate (F) Not in Annex I CAS: 26523-78-4

EC: 247-759-6 *HH: to be discussed 11/2005.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**				
Specific concentration limits:				

Discussion was postponed since the substance is still evaluated under the ESR program**.**

PFOA; Perfluorooctane acetate Not in Annex I CAS: 335-67-1 EC: 206-397-9 *HH: to be discussed*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[No classification]				
Specific concentration limits:				

The discussion was postponed. IND will provide new data.

4-chlorophenylisocyanate Index: 615-033-00-1(not yet in Annex I) CAS: 104-12-1

EC: 203-176-9 *HH : agreed 01/2003.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[No classification]				
Specific concentration limits:				

The discussion of the substance was postponed. UK will prepare a revision of the proposal.

2,4-Dinitrotoluene (E) Index: 609-007-00-9 CAS: 121-14-2 EC: 204-450-0

HH: to be discussed.

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.1 < L(E)C_{50} \leq 1$	Not readily degradable (based on data)	log K_{ow} < 3 BCF < 100	Not relevant.
Specific concentration limits:				

The substance was provisionally agreed. B, F and SK will have a look at the RAR and react in the FU if they disagree with the provisional classification.

FU III: Spain has sent in document ECBI/17/05 Add. 6 containing the correct values for bioaccumulation. The box has been revised accordingly.

IND has sent in document ECBI/17/05 Add. 7 contesting the proposed classification and outlining why further debate was needed. Spain (the rapporteur for this substance) also had severe reservations against the classification as listed in the box. The substance will be discussed at the next meeting.

Diisobutyl phthalate Not in Annex I CAS: 84-69-5 EC: 201-553-2 *HH: to be discussed*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[No classification]	$1 < L(E)C_{50} \leq 10$	Readily degradable (based on data)	log K_{ow} > 3 BCF < 100	Not relevant
Specific concentration limits:				

F has sent in a revised proposal (ECBI/116/04 Add. 3). IND has sent in a report on a fish LC50 test (ECBI/116/04 Add. 4). If there is no disagreement from MS in the follow-up, the substance will be classified as outlined in the box.

FU II: Spain has sent in a note expressing disagreement with the argumentation not to classify for the environment that was included in the French proposal; the measured BCF's vary from 125 to 2937 and the aquatic acute toxicities are into R51 range in the three trophic levels, besides EPIWIN

calculations are in agreement with the experimental data. The Spanish proposal is to classify this substance as N R51/53.

FU II: Sweden has sent in a note saying that they would very much appreciate a summary of the results from one of the references cited in the French classification proposal for the substance (i.e. Wiegand, H.J. and N.Scholz, 1997) before they can make any comments on the new classification.

FU III: The substance will be discussed at the next meeting based on the comments from Spain and Sweden submitted in FU II.

Alkyl Amines (text is relevant for boxes numbered 1-5):

FU I + II: Bioaccumulation of the substance will be discussed at TCNES IV. MS can react in the FU if the discussions there should challenge the recommendation made at the TC C&L.

FU III: DK has sent in documents ECBI/04/05 Adds. 14 and 15 in which they confirm that all five alkyl amines (fatty acids) should be classified as outlined in the boxes. At the TCNES IV IND has promised to submit new information relevant also for classification.

At the next meeting MS might re-discuss the substances(s) if new relevant information will be available or agree with the provisional classification as outlined in the boxes.

1. Tallow alkyl amine (D) Not in Annex I CAS: 61790-33-8 EC: 263-125-1 *HH: To be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.01 < L(E)C_{50} \leq 0.1$	Readily degradable (based on data)	$\log K_{ow} > 3$ BCF >100	Not relevant
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

2. 1-Octadecanamine (D) Not in Annex I CAS: 124-30-1 EC: 204-695-3 *HH: To be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.01 < L(E)C_{50} \leq 0.1$	Readily degradable (based on data)	log K_{ow} > 3 BCF >100	Not relevant
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

3. Cocos alkyl amine (D) Not in Annex I CAS: 61788-46-3 EC: 262-977-1

HH: To be discussed.

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.01 < L(E)C_{50} \leq 0.1$	Readily degradable (based on data)	log K_{ow} > 3 BCF >100	Not relevant
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

4. Hydrogenated tallow alkyl amine (D) **Not in Annex I CAS: 61788-45-2 EC: 262-976-6** ***HH: To be discussed.***

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.01 < L(E)C_{50} \leq 0.1$	Readily degradable (based on data)	log K_{ow} > 3 BCF >100	Not relevant
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

5. (Z)-Octadec-9-enylamine (D) Not in Annex I CAS: 112-90-3 EC: 204-015-5 *HH: To be discussed*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**	$0.01 < L(E)C_{50} \leq 0.1$	Readily degradable (based on data)	$\log K_{ow} > 3$ BCF >100	Not relevant
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

5. General Issues

ECB will send out ECBI/13/05 Rev. 1 (revised procedure for classification of biocides) in the follow-up period.

FU III: IND has submitted document ECBI/61/05 concerning the use of non-standard species for determination of aquatic toxicity.

6. Setting of Specific Concentration Limits for Substances Very Toxic to the Environment

The conclusions from this agenda point can be found in document ECBI/88/04 Add. 1 Rev. 5.

7. Pesticides

7. 1. Pesticides concluded

Cyprodinil (F) Not in Annex I CAS:121552-61-2 Not in EINECS *HH: concluded 09/2004.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	$0.01 < L(E)C_{50} \leq 0.1$	Not readily degradable (based on data)	$\log K_{ow} > 3$ BCF >100	Not relevant
Specific concentration limits:	$C_n \geq 2.5\%$: **N, R50-53** (S60-61) $0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61) $0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)			

Mancozeb Index: 006-076-00-1 CAS: 8018-01-7 Not in EINECS *HH: to be discussed*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50 **S61**	$0.01 < L(E)C_{50} \leq 0.1$	No classifiable degradation products	$\log K_{ow} < 3$	Not relevant
Specific concentration limits:	$C_n \geq 2.5\%$: **N, R50** (S61)			

MS are given the possibility to react in the follow-up period if they still want to apply R53.

FUII: Please note that in follow-up I the substance was listed erroneously with N; R50-53 (SCLs M-factor 10). This is now corrected.

FU III: Norway has sent in a note saying that after further review of the documentation and discussions with the Norwegian Food Safety Authority they can support the classification as listed in the box. The substance will be classified as outlined in the box.

MCPA (ISO); 4-chloro-*o*-tolyloxyacetic acid (I) Index: 607-051-00-3

CAS: 94-74-6 EC: 202-360-6 *HH: Concluded 09/2003***.**

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	$0.1 < L(E)C_{50} \leq 1$	Not readily degradable (based on data)	log $K_{ow} < 3$	Not relevant
Specific concentration limits:				

IT has the possibility to come back in the follow-up period with a revised proposal. If that is not the case the substance will be classified as outlined in the box.

FU III: IT did not submit a revised proposal. The substance will be classified as outlined in the box.

Salts of MCPA (I) Index: 607-052-00-9 *HH: to be re-reviewed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	$0.1 < L(E)C_{50} \leq 1$	Not readily degradable (based on data)	log $K_{ow} < 3$	Not relevant
Specific concentration limits:				

The substance was classified in analogy to the acid (MCPA). IT has the possibility to come back in the follow-up period with a revised proposal. If that is not the case the substance will be classified as outlined in the box.

FU III: IT did not submit a revised proposal. The substance will be classified as outlined in the box.

Esters of MCPA (I) Index: 607-052-00-9 *HH: to be re-reviewed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
N, R50-53 **S60-61**	$0.1 < L(E)C_{50} \leq 1$	Not readily degradable (based on data)	log $K_{ow} < 3$	Not relevant
Specific concentration limits:				

IT has the possibility to come back in the follow-up period with a revised proposal. If that is not the case the substance will be classified as outlined in the box.

FU III: IT did not submit a revised proposal. The substance will be classified as outlined in the box.

7. 3. Pesticides <u>not</u> concluded

Difenacoum (FIN) Index: 607-157-00-X CAS: 56073-07-5 EC: 259-978-4 *HH: to be discussed.*

Classification S -phrases	Toxicity	Degradation	Bioaccumulation	Escape clause
[N, R50-53] **[S60-61]**				
Specific concentration limits:	**[**$C_n \geq 2.5\%$: **N, R50-53** (S60-61)**]** **[**$0.25\% \leq C_n < 2.5\%$: **N, R51-53** (S61)**]** **[**$0.025\% \leq C_n < 0.25\%$: **R52-53** (S61)**]**			

The discussion of the substance was postponed since it will be discussed at the TM of the Biocides Group. The substance still has to be discussed for HH.

8. Planning of further meetings

Next TC C&L for Environmental Effects :

Wednesday April 26 – Thursday April 27, 2006 , JRC Ispra.

Please note that a session on New Substances cannot be confirmed since ECB will try to cover classification of New Substances entirely in a written form.