Substance name: Bis(tributyltin) oxide
EC number: 200-268-0
CAS number: 56-35-9

MEMBER STATE COMMITTEE SUPPORT DOCUMENT FOR IDENTIFICATION OF BIS(TRIBUTYLTIN) OXIDE AS A SUBSTANCE OF VERY HIGH CONCERN

Adopted on 1 October 2008

CONTENTS

Substance Name: **Bis(tributyltin) oxide**

EC Number: **200-268-0**

CAS number: **56-35-9**

- *The substance is identified as a PBT substance according to Article 57 (d) of Regulation (EC) No 1907/2006 (REACH).*

Summary of the evaluation:

Bis(tributyltin) oxide is considered as a PBT substance. Tributyltin, to which the substance transforms in the aqueous environment, fulfils the P, B and T criteria. Bis (tributyltin) oxide has been discussed in the TC-NES PBT working group and the subgroup concluded (November 2004) that the substance fulfils the PBT criteria, see http://ecb.jrc.it/esis/index.php?PGM=pbt.

Half-lives of > 1- 15 years have been observed in sediment degradation experiments. In a soil degradation study an aerobic half-life of 114 d at 25 ºC was estimated corresponding to 323 d at 12 ºC. (P/vP). Experimental reliable BCFs are available for four marine fish species and they all are > 2000 (B). The lowest reliable chronic NOEC for TBT was identified to be 0.06 µg Sn l^{-1}, corresponding to ca. 0.15 µg TBT l^{-1}, for *Daphnia magna* (T criterion for environment). In addition to the very high toxicity in relation to conventional toxicity end-points, TBT compounds elicit effects in the endocrine systems of aquatic organisms. The mollusc species *Nucella lapillus* (dog whelk) is the most sensitive species to tributyltin compounds. A LOEC of 0.002 µg l^{-1} was obtained in a 360-d study looking at imposex (NOEC < 0.002 µg l^{-1}). Moreover, tributyltin compounds are classified as toxic; danger of serious damage to health by prolonged exposure through inhalation and if swallowed (T; 48/23/25) and TBTO therefore fulfils also the T criterion for human health.

Registration number(s) of the substance or of substances containing the substance:

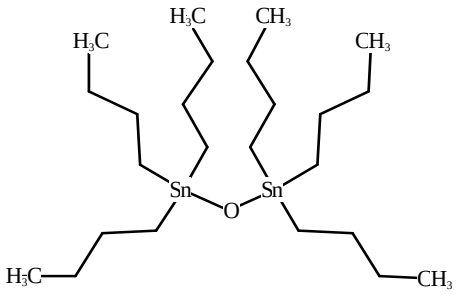
Not available.

JUSTIFICATION

1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Name: Bis(tributyltin) oxide
EC Number: 200-268-0
CAS Number: 56-35-9
IUPAC Name:
Molecular Formula: C24H54OSn2
Structural Formula:



Molecular Weight: 596.12
Synonyms: TBTO; Hexa-n-butyldistannoxan; Bis(tri-n-butylzinn)oxid; Tri-n-butylzinnoxid

1.2 Composition of the substance

Impurities as reported by GDCh (2003) are:

Di-n-butyltin oxide ca. 0.5 % w/w

Tetra-n-butyltin ca. 1.2 % w/w

Tetra-n-butyl-1,3-di-(2-ethyl-hexyl)-di-stannoxane ca. 1.3 % w/w

1.3 Physico-chemical properties

Table 1 Summary of physico-chemical properties

REACH ref Annex, §	Property	Value	Comments
VII, 7.1	Physical state at 20 C and 101.3 Kpa	liquid, metallic, organometallic	European Commission (2000)
VII, 7.2	Melting / freezing point	< - 45 °C	Chapman and Hall (1984) as cited in GDCh (2003)
VII, 7.3	Boiling point	220-230 °C at 13 hPa	Chapman and Hall (1984) as cited in GDCh (2003)
VII, 7.5	Vapour pressure	0.00000085 – 0.00016 hPa at 20 °C	Blunden et al. (1984) as cited in GDCh (2003)
VII, 7.7	Water solubility	0.73 mg l^{-1} (at pH 6.0-6.6; distilled water)	Maguire et al. (1983) as cited in GDCh (2003)
		4.0 mg l^{-1} (at pH 7.0; 20 °C; distilled water)	Maguire et al. (1983) as cited in GDCh (2003)
		18-71.2 mg l^{-1}	The range of several sources as cited in GDCh (2003)
		3-10 mg l^{-1} (artificial seawater)	Blunden et al. (1984) as cited in GDCh (2003)
VII, 7.8	Partition coefficient n-octanol/water (log value)	4.05 (estimated)	KOWWIN v1.67
		3.31	CITI (1992) as cited in GDCh (2003)
		3.2 (pH 6.0, at 20 °C)	Maquire et al. (1982) as cited in GDCh (2003)
		3.8	Laughlin et al. (1986) as cited in GDCh (2003)
	Dissociation constant	6.25	GDCh (2003); for tributyltin cation
		6.51	OECD (2007); for unspecified tributyltin compound

It is noted that the results of water solubility and logKow tests are significantly dependent on the pH where the tests have been conducted.

2 CLASSIFICATION AND LABELLING

2.1 Classification in Annex I of Directive 67/548/EEC

The hazard classification of "tributyltin compounds, with the exception of those specified elsewhere in this Annex", Index No. 050-008-00-3, according to the 19th ATP, updated in the 29th ATP of Directive 67/548/EEC, applies for TBTO and is as follows:

Classification:

T; R25-48/23/25

Xn; R21

Xi; R36/38

N; R50-53

Risk phrases:

R21	Harmful in contact with skin
R25	Toxic if swallowed
48/23/25	Toxic; danger of serious damage to health by prolonged exposure through inhalation and if swallowed
R36/R38	Irritating to eyes and skin
R50-53	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment

Safety phrases:

S1/2	Keep locked up and out of the reach of children
S35	This material and its container must be disposed of in a safe way
S36/37/39	Wear suitable protective clothing, gloves and eye/face protection
S45	In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
S60	This material and its container must be disposed of as hazardous waste
S61	Avoid release to the environment. Refer to special instructions/Safety data sheets

Specific concentration limits are given in Annex I of Directive 67/548/EEC.

2.2 Self classification(s)

Not available.

3 ENVIRONMENTAL FATE PROPERTIES

3.1 Degradation

3.1.1 Abiotic degradation

Maguire et al. (1984 as cited in GDCh, 2003) and Laughlin et al. (1986 as cited in GDCh, 2003) expect that TBTO dissociates in aqueous solution forming a hydrated tributyltin (TBT) cation. TBT will form complexes with organic compounds such as chlorides, hydroxide and nitrate. In oxic waters the proportions of these various complexes are controlled mainly by pH. When the pH of water is equal to the acidity constant (approx. 6.25), half of the TBT occurs in the cationic form (TBT^+). As pH increases less will be found as free ions and more will occur as a complex (Meador 2000). WHO (1990) reports, that tributyltins remain in equilibrium in seawater under normal conditions as three species (hydroxide, chloride and carbonate). The predominant forms in seawater are $Bu_3SnOH_2^+$ and Bu_3SnCl at pH < 7, Bu_3SnCl, Bu_3SnOH, and $Bu_3SnCO_3^-$ at pH 8, and Bu_3SnOH and $Bu_3SnCO_3^-$ at pH > 10.

The C-Sn bonds of TBTO are stabile against hydrolysis under environmental conditions (CDCh, 2003), but this bond can be cleaved under UV-radiation at 290 nm according to Navio et al. (1993 as cited in GDCh, 2003). WHO (1990) reviewed similar study results on photodegradation in water under various conditions. Photodegradation of TBT can be expected to be a relevant removal pathway in the environment only in very shallow clear waters and in the first few centimeters layer of the water column. Aquatic photodegradation is not considered to have relevant impact on the overall persistency of TBT in the environment.

Indirect photochemical degradation in the atmosphere is considered to be fast based on the estimated half-life of 4.5 hours for the reaction with OH-radicals using AOP v1.91 (24 h day^{-1}; $5*10^5$ OH^- cm^{-3}). It is noted, however, that due to the very low volatility of TBTO, atmospheric degradation is not a relevant route of degradation for this substance.

3.1.2 Biodegradation

Degradation half-lives from experiments with natural micro-organism populations under aerobic conditions in aquatic systems are between 4 and 225 days and describe mainly primary degradation and not complete mineralisation (GDCh, 1988). In the studies reviewed by WHO (1990), half-lives from several days to several months in water have been determined for different test temperatures and including both pre-adapted (polluted) and non-adapted water samples. Slesinger & Dresser (1978 as cited by WHO, 1990) conducted studies in a Warburg respirometer under aerobic conditions and showed that microflora derived from activated sludge and soil were capable of partially degrading TBTO. The half-life was 70 days, whereas under anaerobic conditions it was 200 days. Seligman et al. (1986 as cited by WHO, 1990) also showed evidence for biodegradation; in medium polluted by TBTO at 0.5 µg/litre, the TBTO half-life was 7 days in the dark and 6 days in the light. In water containing 0.03 µg TBTO/litre, the half-life was 19 days in the dark and 9 days in the light. In all cases, dibutyl derivatives were formed and, to a lesser extent, monobutyl derivatives. In studies with 14C-labelled TBTO, the measurement of 14CO2 production suggested a half-life of between 50 and 75 days.

Only few studies are available on sediment; the degradation half-life in these studies is > 1-15 years. Studies in highly polluted areas show, that after a certain concentration has been reached, no further TBT degradation occurs (GDCh, 2003). Sarradin et al. (1995) estimated the biodegradation

rate of TBT from the vertical distribution of butyltin compounds in marine sediments. For the transformation of TBT to DBT a half-life of 2.1 years was calculated.

Springborn Laboratories (1995b, as cited in GDCh, 2003) has reported on an aerobic degradation test with ^{14}C-TBTO and sandy loam soil. A nominal test concentration of 1.15 mg TBTO kg^{-1} dw and a test temperature of 25 ºC were employed. Half-life for primary degradation was estimated to be 114 days (323 days corrected to 12 ºC according to the TGD), whereas the main degradation product was identified as dibutyltin and monobutyltin as a minor product. The recovery at day 365 of the experiment was still 80 % (at the start 100 %). Springborn Laboratories (1994 as cited in GDCh, 2003) determined a half-live of 130 days (368 days corrected to 12 ºC according to the TGD) for primary degradation of ^{14}C-TBTO in anaerobic conditions in a test similar to the aerobic soil test. Huang and Matzner (2004) studied the degradation of various organotin compounds in three acid forest soil types. The soils were spiked with organotin compounds corresponding to 50-5 ng Sn/g of soil. All incubations were carried out at 20 °C in the dark. The half-life of TBT was 0.5 years in the lower organic (Oa) horizon and 1.6 years in the mineral soil. In a wetland soil, the half-life under anoxic conditions was 4.4 years. A stepwise dealkylation of TBT was observed. The half-lives for DBT and MBT in this soil were 0.8 and 1.0 years respectively.

3.1.3 Summary and discussion of persistence

A substance is considered to be persistent (P) if it has a half-life >60 days in marine water or > 40 days in fresh- or estuarine water, or >180 days in marine sediment or >120 days in freshwater or estuarine sediment or soil. A substance is considered to be very persistent (vP) if it has a half-life > 60 days in marine, fresh- or estuarine water or >180 days in marine sediment, freshwater or estuarine sediment or soil.

TBTO is subject to transformation when dissolved to aqueous solution. Different tributyltin (TBT) species form as dissolution products, whereas the species formed depend mainly on the pH but also on other abiotic conditions. TBT is expected to be stabile to abiotic degradation in the normal environmental conditions.

Experimental half-lives of tributyltin compounds in water between 4 and 225 days have been reported by GDCh (1988) and between several days to several months by WHO (1990). According to GDCh (2003), the few studies available on degradation in sediment showed degradation half-lives of > 1-15 years.

In a soil degradation study an aerobic half-life of 114 d at 25 ºC was estimated corresponding to 323 d at 12 ºC. Biodegradation studies in forest soils have shown half-lives of primary degradation of TBT between 0.5 and 4.4 years at 20 °C.

Based on the available data it is concluded that TBT meets the P/vP criterion.

3.2 Environmental distribution

3.2.1 Adsorption/desorption

Sorption behaviour of TBTO was investigated by Springborn laboratories (1995a as cited in GDCh, 2003) in a system consisting of seawater and sandy sediment (OC of 1.8 %) in volume ratio of 10:1. The partitioning coefficient between water and sediment was determined to be 28 after the establishment of the equilibrium within 48 hours. A Koc was estimated to be 2650. As the test was conducted in seawater (pH > 7 assumed), TBTO has been mainly present in non-dissociated form of

tributyltin (e.g., TBTOH). The Koc at pH < ca. 6.5 can be assumed to be lower than at pH around 7 to 8 due to the predominance of the cationic, more hydrophilic form of tributyltin at pH ca. < 6.5.

The partitioning coefficient can be expected to vary along the whole range of environmentally relevant pH due to the speciation behaviour of TBT. Ma et al. (2000 as cited in GDCh, 2003) observed partitioning in water-sediment sorption tests using tributyltin chloride as test substance and adjusting individual test systems to a pH between 1.5 and 11.5. Partitioning between porewater and water was highest within pH of 7.5 – 8 decreasing below and beyond this range.

For the comparison, Koc for predominantly hydrophobics is predicted at 2400 based on the logKow of 4.05 according to the TGD. PCKOWIN v1.66 predicts a Koc of 3.7×10^7 for TBTO, but it is likely, that this program does not take into account the transformation of TBTO to TBT in water. PCKOWIN v1.66 predicts for tributyltin (CAS 20763-88-6) a Koc of 9950 and for tributyltin chloride (CAS 56573-85-4) and tributyltin hydroxide (CAS 1067-97-6) a Koc of 15 010.

Based on the information described above, TBTO (more precisely its aqueous transformation product TBT) is expected to be very slightly mobile in sediment and soil in the pH-range of ca. 6.5 to 8 based on the experimental and estimated adsorption coefficients and its dissociation behaviour. The adsorption potential to sediment and soil can be expected to be significantly lower at pH < 6.5 and pH > 8.

3.2.2 Volatilisation

Based on the vapour pressure provided in Table 1, TBTO has a very low volatility. An estimated Henry's Law coefficient has been reported to be 2×10^{-5} kPa mol^{-1} (GDCh, 1988) indicating that the substance is only slightly volatile from aqueous surfaces. Volatilisation to air is therefore assumed to be not a relevant route of distribution for TBTO.

3.2.3 Long-range environmental transport

Due to the fast estimated atmospheric degradation and the very low volatility, TBTO is not expected to be susceptible to long-range transport via air in vapour phase.

3.3 Bioaccumulation

It is noted that due to the transformation of TBTO in aqueous solution to TBT species, and as TBTO cannot be analysed in aqueous solution (GDCh, 2003; WHO, 1990), the experimental results presented generally refer to TBT.

3.3.1 Aquatic bioaccumulation

3.3.1.1 Bioaccumulation estimation

Due to the dissociation behaviour of tributyltin cation, it can be expected that its bioaccumulation potential is lower at pH –range below its pKa (ca. 6.5), whereas its undissociated, more hydrophobic forms (TBTOH and TBTCl) predominate at a pH-range above this value up to the point where an anionic species is formed. Laughlin et al. (1986) found that the octanol-water partitioning coefficient (K_{OW}) for TBT varies as a function of salinity. The lowest value 5500 was measured in 25 ‰ and increased in higher and lower salinities to a maximum of 7000 in deionized water. A review of available data (Meador 2000) indicates, however, that species-specific

toxicokinetics rather than environmental partitioning determines the bioaccumulation of TBT. The KOW is therefore of limited value for predictions of bioconcentration factors of TBT.

3.3.1.2 Measured bioaccumulation data

Experimental bioaccumulation data of various aquatic species have been reviewed by, e.g., WHO (1990) and GDCh (2003 and 1988) and US EPA (2003). Measured BCFs vary considerably between species and are also affected by differences in availability of TBT in various aquatic environments. The bioconcentration of TBT is expected to increase with increasing pH in the range 6-8 due to increasing dominance of non-ionic complexes. Tsuda et al. (1990) showed that BCF in the freshwater carp (*Cyprinus carpio*) increased from 1190 at pH 6.0 to 2250 at pH 7.8. BCFs for whole marine fish in experiments using TBTO as test substance at levels below its water solubility and an appropriately long exposure time (8 weeks) have been reported by Yamada and Takayanagi (1992, as cited in GDCh, 2003) for *Pargus major* (9 400 - 11 000), *Mugil cephalus* (2 300 - 3 000) and *Rudarius ercodes* (3 200 - 3 600) and by Ward et al. (1981 as cited in WHO, 1990) for *Cyprinodon variegatus* (2 600). The study by Yamada and Takayanagi (1992) was carried out in a continuos flow-trough system with exposure concentrations ranging from 38-659 µg/l of TBTO in natural sea water. The fish were exposed to TBTO for 8 weeks followed by 2-4 weeks in TBTO-free water to study depuration. The concentration of TBT in fish was measured every two weeks during the uptake phase and every week during the depuration phase. Bioconcentration factors were calculated from the measured concentrations of TBT in fish and water at the end of the uptake phase. TBT concentrations were highest in the skin and gill and lowest in the muscle. The distribution of TBT within the fish was not correlated to the lipid concentrations of various tissues.

Metabolism seems to take place in fish according to several studies, where additional butyltin compounds have been analysed (e.g., Ward et al., 1981 as cited in WHO, 1990). Depuration half-lives determined for three fish species by Yamada and Takayanagi (1992) were between 7 and 29 days. The differences in the elimination rate constants could explain the difference in BCF between the three species.

Among invertebrates, annelids and crustaceans exhibit bioaccumulation factors around 1000, while molluscs and particularly predatory prosobranchs have had concentration factors of 10 000 to 100 000 in a variety of laboratory and field studies (GDCh, 2003, US EPA 2003).

3.3.2 Summary and discussion of bioaccumulation

Due to the dissociation behaviour, high bioaccumulation potential is generally expected at pH > 6.5, whereas in the acidic range a lower bioaccumulation potential can be anticipated due to the predominance of the ionised, more hydrophilic form of tributyltin.

A substance fulfils the bioaccumulation criterion (B) when the bioconcentration factor (BCF) is higher than 2 000 and the very bioaccumulative criterion (vB) when the bioconcentration factor is greater than 5 000. Experimental BCFs in whole fish > 2000 were determined in studies with appropriately low test concentrations and long exposure periods in several marine fish species. Bioaccumulation potential of molluscs and prosobranchs seems to be even higher (BCF 10 000 to 100 000) based on various field and laboratory studies. Experimental reliable BCFs are available for four marine fish species and they all are > 2000; TBT meets therefore the bioaccumulation criterion (B).

4 HUMAN HEALTH HAZARD ASSESSMENT

Tributyltin compounds fulfil the criteria for the identification of a toxic substance according to Annex XIII (1.3). Tributyltin compounds are classified and labelled as T (Toxic), R48/23/25 (Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed), due to the hazard classification of “tributyltin compounds, with the exception of those specified elsewhere in this Annex”, Index No. 050-008-00-3, according to the 19th ATP, updated in the 29th ATP of Directive 67/548/EEC.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.1 Aquatic compartment (including sediment)

Endocrine effects have been observed amongst various aquatic species, the review of which has been provided, e.g., in GDCh (2003), RPA (2003) and Vos et al. (2000).

A large dataset exists for TBT with standard acute and chronic studies at three trophic levels. The lowest reliable chronic NOEC for TBT was identified in the risk assessment of organotin compounds (RPA, 2003 and 2005) to be 0.06 µg Sn l^{-1} for *Daphnia magna* (Kühn et al., 1989 as cited in RPA, 2003). This corresponds to ca. 0.15 µg TBT l^{-1}.

Based on the review of European Commission (2005), the mollusc species *Nucella lapillus* (dog whelk) is the most sensitive species to tributyltin compounds. A LOEC of 0.002 µg l^{-1} was obtained in a 360-d study looking at imposex (NOEC < 0.002 µg l^{-1}). European Commission (2005) derived a SSD curve using 24 NOECs in total from several species of fish, crustaceans, molluscs, insects and echinoderms. A 5th percentile of the SSD was calculated to be 0.00083 µg TBT l^{-1}. The highest NOEC-value of the data used for the SSD was 18 µg TBT l^{-1} from a 4-day test with *Chlorella pyrenoidosa*.

5.1.1 Endocrine disrupting effects of exposure to TBT

5.1.1.1 Aquatic invertebrates

The endocrine disrupting effects of TBT results in the masculinisation of females within a species. In invertebrates, or more specifically molluscs, this is manifested as two distinct phenomena, ‘imposex’ and ‘intersex’, both of which have been strongly correlated to TBT exposure. The prevalence of imposex and intersex has been well documented in the scientific literature with responses occurring following exposure to environmentally relevant concentrations of TBT (reviewed in Oehlmann et al. 2007; Sumpter, 2005). Both biological effects endpoints have been found to show significant correlations with TBT concentrations in ambient seawater. For this reason, imposex and intersex have been used as combined biological markers for TBT effect monitoring for more than a decade (OSPAR, 1996).

Imposex

Imposex is characterised by the formation of male sexual organs in females ultimately resulting in the sterilisation of the population. An imposex classification scheme has been developed, which enables the severity of the imposex condition to be graded from stages 0 to 6 (Fioroni et al. 1991; Gibbs et al. 1987). Stage 0 indicating that a female shows no signs of male characteristics (i.e. no development of the vas deferens and absence of a penis) to stage 6 where the vas deferens is fully developed and blocks the vulva resulting in retention of egg capsules and eventual death.

The imposex phenomenon has so far been reported in over 150 molluscs from field observations (DeFur et al., 1999). Examples of field studies where imposex measurements have been used for TBT contamination assessment, with particular emphasis on European waters, is seen in Table 2. The dog whelk, *Nucella lapillus* is by far the most common species used for the biological assessment of TBT contamination in environmental monitoring programs.

Table 2. Examples of species used to measure imposex in environmental monitoring programs

Species	Common name	Location	Reference
Buccinum undatum	Common whelk	North Sea coast	Ten Hallers-Tjabbes et al 1994; Idel et al 1997
		Scottish coast	Nicholson et al 1998
Nucella lapillus	Dog whelk	Scottish North Sea coast	Bailey et al 1995
		Irish coasts	Minichin et al 1995
		North Sea coast	Evans et al 1995
		British coast	Evans et al 1998
		French Atlantic coast	Oehlmann et al 1996b
		Scottish coast	Nicholson et al 1998
		Tyne river, UK	Smith et al 2006
Ocinebrina aciculata	Gastropod	French Atlantic coast	Oehlmann et al 1996a
Hydrobia ulva		North & Baltic sea	Oehlmann et al 1996b
Neptunea antiqua	Red whelk	North sea coast	Idel et al 1997
Hinia reticulata	Netted dog whelk	French Atlantic coast	Oehlmann et al 1996b
Bolinus brandaris	Snail	Spanish Med coast	Morcillo & Porte 1998

Despite the fact that imposex has been reported in many molluscs, the sensitivity of the imposex response to known concentrations of TBT in controlled laboratory exposures is limited to a few species (Table 3).

From the chronic toxicity data in table 3, differences in the imposex response between the species measured can be seen. *Nucella lapillus* is the most sensitive species to TBT and also the most widely used in environmental monitoring programs. A lowest observable effect concentration (LOEC) of 0.002 µg l^{-1} was reported for *N. lapillus* (Davies et al. 1997). Similar levels of sensitivity were found in the closely related species *Hinia reticulate* and *Buccinum undatum* with LOECs of 0.012 µg l^{-1} and 0.017 µg l^{-1} TBT, respectively. In contrast, the imposex response of the freshwater snail (*Marisa cornuarietis*) to TBT exposure was much less sensitive with a NOEC of 0.125 µg l^{-1} (Schulte-Oehlmann et al. 1995).

Table 3. Sensitivity of imposex to TBT exposure: laboratory based studies with molluscs.

FW SW	Species	Common name	Test duration (days)	endpoint	Value (µg/L) (*mg/kg)	Reference
FW	*Marisa cornuarietis*	Giant ramshorn snail	180	NOEC	0.125	Schulte-Oehlmann et al., 1995
SW	*Hinia reticulate*	Netted dog whelk	150	LOEC	0.012	Stroben et al 1992
SW	*Nucella lapillus*	Dog whelk	365	NOEC	<0.002	Davies et al 1997
				LOEC	0.002	
SW	*Nassarius reticulatus*	Netted whelk		EC50	*16.9	Tilmann 2004
SW	*Buccinum undatum*	Common Whelk	240	NOEC	0.01	Mensink et al 1998
				LOEC	0.017	
				LOEC	0.07	Mensink et al 2002

Intersex

The intersex response is closely related to imposex in that they are both a biological response to TBT exposure that results in the masculinisation of the female gonad. However, unlike imposex, which has been identified in over 150 molluscs, the intersex response is almost entirely specific to the common periwinkle *Littorina littorea* (Bauer et al. 1995). Intersex females are characterized by male features on female sex organs. It is a gradual transformation of the female pallial tract, which can be described by a scheme with four stages, increasing severity from 1 to 4.

The sensitivity of the intersex response in *L. littorea* to TBT exposure was measured as LOEC 0.24 $\mu g\ l^{-1}$ (Bauer et al. 1997). This is approximately 100 fold less sensitive than the imposex response in *N. lapillus.*

The intersex response in *L. littorea*, is often used in areas of high TBT exposure. This is mainly due to the absence of *N. lapillus* in these areas and the higher tolerance of *L. littorea* to TBT exposure. Examples of monitoring studies where the intersex response was used are listed in table 4. The intersex response in the clam (measured as ovotestis) has been recently developed to assess TBT exposure in UK estuaries. Different severities of intersex in *S. plana* were found between the estuaries suggesting its suitability for environmental monitoring programs, although the sensitivity of the biological response to known concentrations of TBT have not been reported.

Table 4. Examples of species used to measure intersex in environmental monitoring programs

Species	Common name	Method	Location	Reference
Littorina littorea	Common periwinkle	Intersex	North sea	Bauer et al 1995; Oehlmann et al 1996a
			Dutch marine & brackish	Schipper et al 2008
			Scheldt	De Wolf et al 2001; 2004
			Cork Ireland	Casey et al 1998
Scrobicularia plana	Clam	Intersex (ovotestis)	UK estuaries	Chesman & Langston, 2006; Langston et al 2007;

Overall, the imposex response, particularly in the dog whelk is a more sensitive biomarker of TBT exposure than the intersex response and is often used in areas that are only slightly contaminated with TBT. Measurements of intersex response in *L. littorea* populations are beneficial for biological TBT-effect monitoring in areas where *N. lapillus* are absent (Bauer et al. 1997; Oehlmann et al. 1998).

5.1.1.2 Fish

The endocrine effects of TBT exposure in fish have been less well documented in the scientific literature. Studies that have been identified are listed in table 5.

In the Japanese medaka (*Oryzias latipes*), TBT exposure was found to cause changes in morphology, hatching, histopathology, embryonic development as well as changes in sexual behaviour and reproduction with lowest effects as 0.5 µg l^{-1} and 0.16 µg g^{-1}. Changes in sexual differentiation were found in the Japanese flounder (*Paralichthys olivaceus*) when exposed to 1 µg l^{-1} TBT and greater (Shimasaki et al 2003). These responses were approximately 1000 fold less sensitivity to TBT exposure than *N. lapillus.* However, the most sensitive response to TBT exposure was reported in the zebra fish (*Danio rerio*), with an altered sex ratio in favour of males when exposed to 0.1 ng l^{-1} TBT and greater (McAllister & Kine, 2003).

Table 5. Sensitivity of endocrine responses in fish as a result of TBT exposure.

FW SW	Species	Common name	Method	Test Duration (days)	Endpoint	[TBT] (µg/L) (*µg/g)	Reference
FW	*Oryzias latipes*	Japanese Medaka	morphological changes, hatching	9	NOEC	<12.5	Bentivegna & Piatkowski, 1998
					LOEC	12.5	
			histopathology	28	NOEC	0.15	Wester et al., 1989
					LOEC	0.5	
			abnormal embryonic development		LOEC	*0.16	Hano et al. 2007
			Alter sexual behaviour and reproduction		LOEC	*1	Nakayama et al. 2004
FW	Danio rerio	Zebra fish	altered sex ratio towards males	70	LOEC	0.0001	McAllister & Kime 2003
SW	*Paralichthys olivaceus*	Japanese flounder	sex differentiation - histology		LOEC	*1	Shimasaki et al 2003

5.1.1.3 Conclusion

The endocrine disruption effects of TBT, to which TBTO transforms in the aqueous environment, are extensively studied and well documented. Based on the existing literature (reviewed above), endocrine disruption measured as either imposex or intersex is well documented for TBT in molluscs at concentrations as low as 2-10 ng l^{-1}. Examples of alterations in morphology, histopathology, embryonic and sexual development, and altered sex ratios have also been reported in freshwater and marine fish species, with endocrine disrupting effects reported at higher concentrations than that found in molluscs. However, a skewed sex ratio towards male fish was observed at low levels of exposure to TBT (0.1 ng l^{-1}) in zebra fish. The low effect concentrations were not supported by other studies in fish, however.

5.1.2 Summary and discussion of toxicity

A substance fulfils the toxicity criterion (T-) when the long-term no-observed effect concentration (NOEC) for marine or freshwater organisms is less than 0,01 mg/l, or the substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic for reproduction (category 1, 2, or 3), or there is other evidence of chronic toxicity, as identified by the classifications: T, R48, or Xn, R48 according to Directive 67/548/EEC.

A large data set on standard and non-standard long-term effect studies is available for TBT compounds. NOECs are generally in the range of < 1 to several ten µg TBT l^{1}. The lowest reliable

chronic NOEC for TBT was identified to be 0.06 µg Sn l^{-1}, corresponding to ca. 0.15 µg TBT l^{-1}, for *Daphnia magna*.

In addition to the very high toxicity in relation to conventional toxicity end-points, TBT compounds elicit effects in the endocrine systems of aquatic organisms. The mollusc species *Nucella lapillus* (dog whelk) is the most sensitive species to tributyltin compounds. A LOEC of 0.002 µg l^{-1} was obtained in a 360-d study looking at imposex (NOEC < 0.002 µg l^{-1}). TBT compounds are considered to fulfil the T criterion for ecotoxicity.

6 PBT, VPVB AND EQUIVALENT LEVEL OF CONCERN ASSESSMENT

6.1 PBT/vPvB Assessment

Persistence: Bis(tributyltin) oxide (TBTO) transforms in aqueous solution to tributyltin (TBT). The form in which TBT is present in the environment, depends much on pH, but also on other abiotic conditions. Various degradation studies in water show half-lives between few days to several months. Half-lives of > 1- 15 years have been observed in sediment degradation experiments. In a soil degradation study an aerobic half-life of 114 d at 25 ºC was estimated corresponding to 323 d at 12 ºC. Based on the available data it is concluded that TBT meets the P/vP criterion.

Bioaccumulation:.The bioaccumulation potential is expected to be dependent on the pH of the exposure medium. Due to the dissociation behaviour, high bioaccumulation potential is generally expected at pH > 6.5, whereas in the acidic range a lower bioaccumulation potential can be anticipated due to the predominance of the ionised, more hydrophilic form of tributyltin.

Experimental BCFs in whole fish > 2000 were determined in studies with appropriately low test concentrations and long exposure periods in several marine fish species. Accumulation of TBT compounds to invertebrates has been observed in various studies. The accumulation/concentration factors in certain molluscs have been observed in a range of 10 000 to 100 000. Experimental reliable BCFs are available for four marine fish species and they all are > 2000; TBT meets therefore the bioaccumulation criterion (B).

Toxicity: A large data set on standard and non-standard long-term effect studies is available for TBT compounds. The lowest reliable chronic NOEC for TBT was identified to be 0.06 µg Sn l^{-1}, corresponding to ca. 0.15 µg TBT l^{-1}, for *Daphnia magna*. In addition to the very high toxicity in relation to conventional toxicity end-points, TBT compounds elicit effects in the endocrine systems of aquatic organisms. The mollusc species *Nucella lapillus* (dog whelk) is the most sensitive species to tributyltin compounds. A LOEC of 0.002 µg l^{-1} was obtained in a 360-d study looking at imposex (NOEC < 0.002 µg l^{-1}). TBT compounds are considered to fulfil the T criterion for ecotoxicity.

Moreover tributyltin compounds are classified as toxic; danger of serious damage to health by prolonged exposure through inhalation and if swallowed (T; 48/23/25) and TBTO therefore fulfils also the T criterion for human health.

In the impact Assessment of Potential Restrictions on the Marketing and Use of Certain Organotin Compounds (RPA 2007b) it is concluded (with SCHER agreeing) that, in relation to the marine environment, TBT is likely to be classified as both **PBT** and **vPvB** substance.

6.2 Conclusion of PBT and vPvB assessment

Tributyltin, the aqueous transformation product of bis(tributyltin) oxide, fulfils the P, B and T criteria. Furthermore, bis(tributyltin) oxide fulfils the T criterion for human health due to the hazard classification of tributyltin compounds. Bis(tributyltin) oxide is considered to be a PBT substance.

REFERENCES

Al Bitar F (2004): Hazardous Chemicals in Belgian House Dust, Greenpeace Belgium, dated March 2004.

Aquateam rapport, 2006. Screeningundersøkelse av metaller og organiske forurensninger i slam fra fire norske renseanlegg (rapport nr. 06-031).

BgVV (2000): Tributylzinn (TBT) und andere zinnorganische Verbindungen in Lebensmitteln und verbrau-chernahen Produkten, Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin, 6 March 2000 (with English translation provided by ETINSA).

Borghiand V & Port C (2002): Organotin Pollution in Deep-Sea Fish from the Northwestern Mediterranean, Environmental Science and Technology, Vol 36, No. 20, pp 4224-4228.

Bortoli A et al (2003): Butyltins and Phenyltins in Biota and Sediments from the Lagoon of Venice, Oceanologia, Vol 45(1), 2003, pp 7-23.

BUA (2003): Tributyltin Oxide, Report No 238 by the German Advisory Committee on Existing Chemicals (BUA), Stuttgart, S Hirzel.

EFSA (2004): Opinion of the Scientific Panel on Contamination in the Food Chain on a Request from the Commission to Assess the Health Risks to Consumers associated with Exposure to Organotins in Foodstuffs, adopted on 22 September 2004, The EFSA Journal (2004) 102, 1-119.

ESPA, 2005. European Stabiliser Producers Association, Email of J.P.Donnelly to the Norwegian Rapporteur, 31.01.2005.

European Commission, 2000. IUCLID Dataset, Bis(tributyltin)oxide, CAS 56-35-9, 18.2.2000.

European Commission, 2005. Common Implementation Strategy of the Water framework Directive, Environmental Quality Standards (EQS), Substance Data Sheet, Priority Substance No. 30, Tributyltin compounds. Final version, Brussels, 15 January 2005.

Fent K (1996): Organotin Compounds in Municipal Wastewater and Sewage Sludge, The Science of the Total Environment, Vol 185, pp 151-159.

Fent K and Hunn J (1995): *Organotins in Freshwater Harbors and Rivers: Temporal Distribution, Annual Trends and Fate,* Environ. Toxicol. Chem. 14(7):1123-1132.

Fromme H et al (2005): Occurrence of Organotin Compounds in House Dust in Berlin (Germany), Chemosphere, Vol 58, pp 1377-1383.

Gangl M et al (2001): Hormonell wirksame Substanzen in Klärschlämmen , Monographien Band 136, Umweltbundesamt.

GDCh, 2003. BUA Report 238 (Supplementary Reports IX), Tributyltin oxide (Bis-[tri-n-butyltin]oxide) (No. 36), CDCh-Advisory Committee on Existing Chemicals (BUA).

GDCh, 1988. BUA Report 36, Tributyltin oxide (Bis-[tri-n-butyltin]oxide), GDCh-Advisory Committee on Existing Chemicals (BUA).

Green Norman and Ruus Anders (2008): Joint Assessment and Monitoring Programme (JAMP). Overvåking av miljøgifter i marine sedimenter og organismer 1981-2006. SFT Rapport 1018/2008 unpublished.

Hall LW et al (2000): A Probabilistic Ecological Risk Assessment of Tributyltin in Surface Waters of the Chesapeake Bay Watershed, Human Ecol. Risk Assess. 6(1):141-179.

Harino H et al (2005): Accumulation of Butyltin Compounds in Benthic Biota of the Mersey Estuary, Marine Pollution Bulletin, Vol 50, pp 208-236.

Hillenbrand et al.2006: ftp://udis.uba.de/pub/prioritaere_Stoffe/Tributylzinn_final.pdf)

Hillebrand et al (2006): Emissionsminderung für prioritäre und prioritäre gefährliche Stoffe der Wasserrahmenrichtlinie – Stoffdatenblätter, Forschungsbericht 203 21 280, Umweltbundesamt.

Hoch M (2001): Organotin Compounds in the Environment - An Overview, Applied Geochemistry 16, 2001, pp 719-743.

Huang J-H et al (2004): Organotin Compounds in Precipitation, Fog and Soil of a Forested Ecosytem in Germany, Environmental Pollution, Vol 130, pp 177-186.

Huang J-H and Matzner E (2004): Degradation of organotin compounds in organic and mineral forest soils. J. Plant Nutr. Soil Sci. 167, pp. 33-38.

Japanese Ministry of Environment (2001): Report on the Test Results of Endocrine Effects of Tributyltin (TBT) on Fish, draft report by the Environment Health Department, Ministry of Environment, Japan, dated August 2001.

Kannan K et al (1999): Occurrence of Butyltin Compounds in Human Blood, Environmental Science and Technology, Vol. 33, No. 10, pp 1776-1779.

Klingmüller D, Watermann B (2000): TBT-zinnorganische Verbindungen- eine wissenschaftliche Bestandsaufnahme, Berichtsnummer UBA-FB, Umweltbundesamt.
http://www.umweltdaten.de/publikationen/fpdf-l/2245.pdf

Laughlin RB Jr, Guard HE and Coleman, WM (1986): Tributyltin in seawater: Speciation and octanol-water partitioning coefficient. Environ. Sci. Technol. 20, pp 201-204.

Lo S et al (2003): Dithioerythritol (DTE) Prevents Inhibitory Effects of Triphenyltin (TPT) on the Key Enzymes of the Human Sex Steroid Hormone Metabolism, J. Steroid Biochemistry and Molecular Biology, Vol 84, pp 569-576.

Lytle et al. 2003. Life-cycle toxicity of dibutyltin to sheepshead minoww and implications of the ubiquitous tributyltin impurity in test material. Appl. Organometal. hem. 17, 653-661.

Meador JP (2000): Predicting the fate and effects of tributyltin in marine systems. Rev. Env. Comtam. Toxicol. 166, pp. 1-48.

Meijer L et al (2004): Man-Made Chemicals in Human Blood - Levels of Forty-Six Chemicals in a Dutch Cohort, report issued by Greenpeace (Netherlands), dated November 2004.

Neumann WP(1970): The Organic Chemistry of Tin. Interscience: New York, 1970; 53.

Nielsen JB & Strand J (2002): Butyltin Compounds in Human Liver, Environmental Research Section A, Vol 88, pp 129-133.

OECD, 2007. SIDS Initial Assessment Profile for SIAM 24, 19-20 April, 2007. Tributyltin chloride, CAS No. 1461-22-9.

RPA, 2003. Revised assessment of risks to health and the environment associated with the use of organostannic compounds (excluding use in antifouling paints). Final Report (Draft) – December 2003. Prepared for the European Commission by Risk & Policy Analysts Limited (RPA).

RPA, 2005. Risk assessment studies on targeted consumer applications of certain organotin compounds. Final Report – September 2005. Prepared for the European Commission by Risk & Policy Analysts Limited (RPA).

RPA, 2007a. Impact assessement of potential restrictions on the marketing and use of certain organotin compounds. Interim Report, April 2007. Prepared for the European Commission by Risk & Policy Analysts Limited (RPA).

RPA, 2007b. Impact assessement of potential restrictions on the marketing and use of certain organotin compounds. Final Report, October 2007. Prepared for the European Commission by Risk & Policy Analysts Limited (RPA).

Santillo D et al (2003): Consuming Chemicals: Hazardous Chemicals in House Dust as an Indicator of Chemical Exposure in the Home, Greenpeace Research Laboratories, dated January 2003.

Sarradin PM, Lapaquellerie Y, Astruc A, Latouce C and Astruc M (1995): Long –term behaviour and degradation kinetics of tributyltin in a marina sediment. Sci. Tot. Environ. 170, pp 59-70.

SCOOP (2003): Assessment of the Dietary Exposure to Organotin Compounds of the Population of the EU Member States, Report on Tasks for Scientific Cooperation (SCOOP) prepared for Directorate-General Health and Consumer Protection (DG SANCO), dated October 2003.

Sekizawa J et al (2003): Integrated Human and Ecological Risk Assessment: A Case Study of Tributyltin and Triphenyltin Cimpounds, Human and Ecological Risk Assessment, Vol 9, No. 1, pp 325-342.

Sternbeck, J., Fäldt, J. og Österås, A.H. (2006): Screening of organotin compounds in the Swedish environment. WSP Environment, Stockholm.

Summer KH, Klein D and Greim H (1996): Ecological and Toxicological Aspects of Mono- and Disubstituted Methyl-, Butyl-, Octyl- and Dodecyltin Compounds, "GSF Report" for the ORTEPA, August1996.

Takahashi S et al (1999): Butyltin Residues in Livers of Humans and Wild Terrestrial Mammals and in Plastic Products, Environmental Pollution, Vol 106, pp 213-218.

Tsuda TS, Aoki S Kojima M and Harada H (1990). The influence of pH on the accumulation of tri-n-butyltin chloride and triphenyltin chloride in carp. Comp. Biochem. Physiol. 95C: 151-153.

Uhl M et al (2004): Hausstaub – ein Indikator für Innenraumbelastung, Bericht 258, Umweltbundesamt.

UNEP (2002): Mediterranean Regional Report, one of the UNEP Chemicals Regional Reports on Persistent Toxic Substances, dated December 2002.

US EPA (2003) Ambient aquatic life water quality criteria for tributyltin (TBT)- Final. Office of Water, Office of Science and Technology, Health and Ecological Criteria Division, Washington D.C.

Waldock R et al (1999): Surveys of the Benthic Infauna of the Contamination, J. Mar. Biol. Ass. U.K. 79:225-232.

WHO, 1990. Environmental Health Criteria 116, Tributyltin compounds. International Programme on Chemicals Safety, World Health Organisation, Geneva, 1990.

Yamada H and Takayanagi K (1992): Bioconcentration and elimination of bis(tributyltin)oxide (TBTO) and triphenyltin chloride (TPTC) in several marine fish. Wat. Res. 26(12), pp. 1589-1595.

ANNEX. REFERENCES RELATED TO ENDOCRINE DISRUPTION

Bailey SK, Davies IM, Harding MJC, 1995. Tributyltin contamination and its impacts on Nucella lapillus population. Proc Royal Soc Edinburgh, 1038:113-126.

Bauer B, Fioroni P,.Ide I, Liebe S, Oehlmann J, Stroben E, Watermann 1995. TBT effects on the female genital system of Littorina littorea - A possible indicator of Tributyltin pollution. Hydrobiologia 309:15-27.

Bauer B, Fioroni P, Schulte Oehlmann U, Oehlmann J, Kalbfus W. 1997. The use of Littorina littorea for tributyltin (TBT) effect monitoring results from the German TBT survey 1994/1995 and laboratory experiments. Environmental pollution 96:299-309.

Bentivegna CS, Piatkowski T, 1998. Effects of Tributyltin on medaka (Oryzes latipes) embryos at different stages of development. Aquatic toxicology, 44:117-128.

Casey J, De Grave S, Burnell GM, 1998. Intersex and Littorina littorea in Cork Harbour: results of a medium-term monitoring programme. Hydrobiologia 378:193-197.

Chesman B, Langston W, 2006. Intersex in the clam Scrobicularia plana: a sign of endocrine disruption in estuaries? Biology letters 2:420-422.

Davies IM, Harding MJC, Bailey SK, Shanks AM, Lange R, 1997. Sublethal effects of tributyltin oxide on the dogwhelk Nucella lapillus. Marine ecology progress series, 158:191-204.

DeFur PL, Crane M, Ingersoll C, Tattersfield L, (eds) 1999. Endocrine disruption in invertebrates: endocrinology, testing, and assessment. In: Proceedings of the workshops on endocrine disruption in invertebrates, 12–15 December 1998, Noordwijkerhout, SETAC Press, Pensacola, The Netherlands.

De Wolf H, De Coen W, Backeljau T, Blust R, 2001. Intersex and sterility in the periwinkle Littorina littorea (Mollusca: Gastropoda) along the Western Scheldt estuary, the Netherlands. Marine environmental research 52:249-255.

De Wolf H, Handa C, Backeljau T, Blust R, 2004. A baseline survey of intersex in Littorina littorea along the Scheldt estuary, The Netherlands. Marine pollution bulletin 48:592-596.

Evans S, Leksono S, McKinnel PD, 1995. Tributyltin pollution - A diminishing problem following legislation limiting the use of TBT-based anti-fouling paints. Marine pollution bulletin 30:14-21.

Evans SG, Nicholson GJ, Browning C, Hardman E, Seligman O, Smith R, 1998. An assessment of tributyltin contamination in the North Atlantic using imposex in the dogwhelk Nucella lapillus (L.) as a biological indicator of TBT pollution. Invertebrate reproduction & development 34:277-287.

Fioroni P, Oehlmann J, Stroben E, 1991. The pseudohermaphroditism of prosobranchs – morphological aspects. Zoologischer anzeiger, 226:1-26.

Gibbs PE, Bryan GW, Pascoe PL, Burt GR, 1987. The use of the dogwhelk, Nucella lapillus, as an indicator of Tributyltin (TBT) contamination. Journal of the Marine Biological Association of the United Kingdom. 67:507-523.

Hano TY, Oshima Y, Kim SG, Satone H, Oba Y, Kitano T, Inoue S, Shimasaki Y, Honjo T, 2007. Tributyltin causes abnormal development in embryos of medaka, Oryzias latipes. Chemosphere 69:927-933.

Idel I, Witten EP, Fischer J, Kalbfus W, Zellner A, Stroben E, Watermann B, 1997. Accumulation of organotin compounds in the common whelk Buccinum undatum and the red whelk Neptunea antiqua in association with imposex. Marine ecology progress series 152:197-203.

Langston WJ, Burt GR, Chesman BS, 2007. Feminisation of male clams Scrobicularia plana from estuaries in Southwest UK and its induction by endocrine-disrupting chemicals. Marine ecology progress series, 333:173-184.

McAllister B, Kime D, 2003. Early life exposure to environmental levels of the aromatase inhibitor tributyltin causes masculinisation and irreversible sperm damage in zebrafish (Danio rerio). Aquatic toxicology 65:309-316.

Mensink BP, Krait H, Ten Hallers-Tjabbes CC, Boon JP, 1998. Imposex in juvenile common whelks by Tributyltin and consequences for the supposed mechanism. Marine environmental research, 46:176-177.

Mensink BP, Krait H, Vethaak AD, Ten Hallers-Tjabbes CC, Koeman JH, van Hattum B, Boon JP, 2002. Imposex induction in laboratory reared juvenile Buccinum undatum by tributyltin (TBT). Environmental toxicology and pharmacology 11:49-65.

Minichin D, Oehlmann J, Duggan CB, Stroben E, Keatinge M, 1995. Marine TBT antifouling contamination in Ireland, following legislation in 1987. Marine pollution bulletin 30:633-639.

Morcillo Y, Porte C, 1998. Monitoring of organotin compounds and their effects in marine molluscs. Trac-trends in analytical chemistry 17:109-116.

Nakayama K, Oshima Y, Yamaguchi T, Tsuruda Y, Kang IJ, Kobayashi M, Imada N, Honjo T, 2004. Fertilization success and sexual behaviour in male medaka, Oryzias latipes, exposed to tributyltin. Chemosphere, 55:1331–1337.

Nicholson GJ, Evans SM, Palmer N, Smith R, 1998. The value of imposex in the dogwhelk Nucella lapillus and the common whelk Buccinum undatum as indicators of TBT contamination. Invertebrate reproduction & development, 34:289-300.

Oehlmann J, Fioroni P, Stroben E, Markert B, 1996a. Tributyltin (TBT) effects on Ocinebrina aciculate (Gastropoda: Muricidae): imposex development, sterilization, sex change and population decline. Science of the total environment, 188:205-223.

Oehlmann J, Idel I, Bauer B, Watermann B, Schulte-Oehlmann U, Liebe S, Fioroni P, 1996b. Erfassung morphologischer und histopathologischer effekte von organozinnverbindungen auf marine mollusken und prufungen ihrer verwendbarkeit fur ein zukunftiges biologisches effektmonitoring. Forschungsvorhaben des umweltbundesamt Berlin, 102 40 303/01 p194.

Oehlmann J, Stroben E, Schulte-Oehlmann U, Bauer B, 1998. Imposex development in response to TBT pollution in Hinia incrassata (Strom, 1768) Prosobranchia, Stenoglossa. Aquatic toxicology 43:239-260.

Oehlmann J, Di Benedetto P, Tillmann M, Duft M, Oetken M, Schulte-Oehlmann U, 2007. Endocrine disruption in prosobranch molluscs: evidence and ecological relevance. Ecotoxicology 16:29-43.

Oslo, Paris Commissions (ed) 1996. Agenda item 9 of the environmental assessment and monitoring committee (ASMO). OSPAR, Vila Franca (=ASMO 96/9/8-E).

Schipper CA, Smit MGD, Kaag NHBM, Vethaak AD, 2008. A weight-of-evidence approach to assessing the ecological impact of organotin pollution in Dutch marine and brackish waters; combining risk prognosis and field monitoring using common periwinkles (Littorina littorea). Marine environmental research 66:231-239.

Schulte-Oehlmann U, Bettin C, Fioroni P, Oehlmann J, Stroben E, 1995. Marisa cornuarietis (GASTROPODA, PROSOBRANCHIA) - A potential TBT bioindicator for fresh-water environments. Ecotoxicology 4:372-384.

Shimasaki Y, Kitano T, Oshima Y, Inoue S, Imada N, Honjo T, 2003. Tributyltin causes masculinization in fish. Environmental toxicology and chemistry 22:141-144.

Stroben E, Oehlmann J, Fioroni P, 1992. Hinia reticulate and Nucella lapillus – Comparison of 2 Gastropod tributyltin bioindicators. Marine biology 114:289-296.

Sumpter, J. 2005. Endocrine disrupters in the aquatic environment: An overview. Acta Hydrochimica et Hydrobiologica 33:9-16.

Ten Hallers-Tjabbes CC, Kemp JF, Boon JP, 1994. Imposex in whelks (Buccinum undatum) from the open North sea: relation to shipping traffic. Marine pollution bulletin 28:311-313.

Tilmann M, 2004. Sediment toxicological investigation using gastropods and insects, with special emphasis on endocrine active substances. Cuvillier, Gottingen.

Wester PW, Canton JH, van lersel AAJ, Krajnc EI, Vaessen HAMG, 1989. The toxicity of bis(tri-n-butyltin) oxide (TBTO) and di-n-butyltinchloride (DBTC) in the small fish species Oryzias lapites (medaka) and Poecilia reticulate (guppy). Aquatic toxicology, 16: 53-72.