

GDCh-Advisory Committee
on Existing Chemicals (BUA)

Tetrabromobisphenol A

BUA Report 239

(December 2002)



S. Hirzel

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GDCh-Beratergremium
für Altstoffe (BUA)



S. Hirzel

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Preface

The Advisory Committee on Existing Chemicals of Environmental Relevance, BUA for short, was established in May 1982 to help the German federal government cope with the large task of dealing with existing chemicals. In an agreement between federal government, scientific community, and the chemical industry, it was associated with the German Chemical Society (GDCh, Gesellschaft Deutscher Chemiker) to ensure objective work carried out in accordance with scientific principles. Since the beginning of 2001 the BUA has been composed of scientists from the research areas of chemistry, analytics, monitoring, toxicology, primary and secondary exposition, aquatic and terrestrial toxicology as well as the fate and behaviour of compounds in water, soil, air. The BUA is supported by experts from federal government agencies and the German Chemical Industry Association (Verband der Chemischen Industrie [VCI]).

No other national or international body has dealt with the ecological and health-related effects of as many existing chemicals as the BUA. Upon the recommendation of the federal government, the BUA has participated as a Peer-Review Group in the evaluation of ICCA-compounds (ICCA= International Council of Chemical Associations) since 2000 and also acts as the Contact Point in the OECD-HPV-Chemicals Programme (High Production Volume). The goal of the initiative is on the one hand to complete the data on the HPV chemicals and on the other to undertake an internationally coordinated evaluation of their hazard potential.

The BUA began an additional national project in 1997, which also selects and assesses existing chemicals with a lower production volume in the range of 100 - 1000 tonnes/year. The chemical industry presents about 50 datasets for such substances each year, for which the BUA sets the priority. Comprehensive reports are published on chemicals suspected of having a hazard potential. If the data available for substance assessment are insufficient, the gaps in knowledge are documented and, if necessary, investigations recommended. On the national level, the BUA has produced comprehensive reports on about 330 substances and carried out preliminary evaluation and classification (priority-setting) for approximately 200 more. The processes leading to priority-setting and the BUA reports are published to lend transparency to the Committee's work.

Moreover, BUA is increasingly addressing scientific questions and problems, which apply simultaneously to many compounds, among others: "Marine Risk Assessment: Concept and Criteria" (BUA Report 220), "Biological Impact of Synthetic and Natural Endocrine Active Substances – Effects on Human Health" (BUA Report 228), Risk Assessment of Substances in Soils" (BUA Report 230), Persistent Organic Pollutants (POPs) (BUA Report 232) and "Safety Factors in Toxicological Risk Assessment". For each of these themes an analysis is made of the scientific state of the art, is documented and the results published in reports such as the current volume. The aim of BUA is to develop assessment concepts, determine data gaps, point out the need for further research and, last but not least, also to reduce information deficits in the general population.

Weihenstephan
February, 2002

Helmut Greim
BUA Chairman

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Abbreviations

^{14}C	carbon-14 isotope (radioactive)
λ	lambda (sign for wavelength)
BCF	bioconcentration factor
BAT	biological tolerance value for industrial compounds
BOD	biological oxygen demand
CAS	Chemical Abstracts Service
d	day(s)
DIN	The German national standards body
d.n.g.	details not given
dw	dry weight
EC	effect concentration
EC ₅₀	concentration of the test compound, at which an effect is observed in 50 % of organisms
ECD	electron capture detection
EPA	Environmental Protection Agency (US)
GC	gas chromatography
h	hour(s)
HPLC	high performance liquid chromatography
IUCLID	International Uniform Chemical Information Database
l	litre
K _{OW}	n-octanol / water partition coefficient
LAI	The Committee for Emission Safety of the German Federal States
LAWA	The Working Group of the German Federal States on Water
LC ₅₀	concentration of the test compound, which is lethal for 50 % of organisms
LOEC	lowest observed effect concentration
log	(decadic) logarithm
MAK	German maximum workplace concentration
MS	mass spectroscopy
NOEC	no observed effect concentration
OECD	European Organisation for Economic Cooperation and Development
pK _a	acid constant
PNEC	predicted no effect concentration
QSAR	quantitative structure activity relationship
SD	standard deviation
T	temperature
t	tonne
TGD	Technical Guidance Documents
UBA	German Federal Environmental Agency
WGK	German water hazard class
ww	wet weight

Summary

Ecological Aspects

TBBPA is employed worldwide as a flame retardant for synthetic resins and plastics. The main area of application is as a reactive flame retardant for epoxy resins used in printed circuit boards. In its use as reactive flame retardant, most of the TBBPA is present in the matrix in a covalently bound state. Small portions remain unbound, however, and may cause diffuse emissions into the environment through application and disposal.

The global consumption in 1999 was about 120 000 tonnes, of which about 13 800 tonnes were used in Western Europe. Corresponding figures for 1990 were estimated at 50 000 and 7000 tonnes, respectively.

It is estimated that about 3500 – 4500 t TBBPA/y were used in Germany in 1999.

One processor in Germany used TBBPA as a flame retardant for plastics until mid-2001. According to a worst case estimate, a maximum of 0.26 µg/l TBBPA entered sewage plant receiving waters. On this basis, a maximum TBBPA concentration in receiving waters of 0.00011 µg/l is calculated. The sewage sludge was burned or deposited. The exhaust was purified by a filter system and the filtered material incinerated. Thus, no introduction into the geosphere was to be expected from this processing plant. No other data are available on emissions through processing in Germany. On the grounds of processing plants in the USA, TBBPA concentrations in the air of < 0.01 – 1.80 µg/m³ were detected in 1977.

In Germany (Baden-Württemberg), sampling carried out in 15 different rivers and streams (determination limit 0.0002 µg/l) found TBBPA concentrations of about 0.001 µg/l in three water samples from three different streams. Another sample, collected near a point source according to the authors, contained 0.02 µg/l TBBPA. In 12 of 19 sediment samples, taken downstream from sewage plant outlets in 11 different rivers, TBBPA was detected at concentrations from < 0.2 to 1.83 µg/kg dw. In 11 of 19 sewage plant outlets sampled, TBBPA was found at concentrations of 0.0002 to 0.025 µg/l. The sewage sludge from 8 different sewage plants contained

< 0.2 to 34.45 µg TBBPA/kg dw. A more recent sewage sludge investigation showed TBBPA concentrations of 0.4 to 62.2 µg/kg (dw), with a mean value of 14 µg/kg.

TBBPA is not readily biodegradable (0 % after 14 days).

In the soil TBBPA is degraded slowly, under aerobic and anaerobic conditions, with half-lives of more than two months and maximum mineralisation rates of 6 % within this period.

TBBPA can be almost completely dehalogenated to bisphenol A under anaerobic conditions in sediment. Under anaerobic conditions, no further degradation of bisphenol A occurs, as is observed under aerobic conditions. Bisphenol A is readily biodegradable in degradation tests. In the EU risk assessment for bisphenol A (not yet approved), a half-life of 15 days, with 97 % elimination in 75 days, was given as conservative assumption for aerobic sediments, as well (ECB 2002). In assessing TBBPA, possible effects of the degradation metabolite bisphenol A in anaerobic sediments should be taken into account.

The calculated half-life for indirect photolysis of TBBPA is 43.4 hours. In the presence of UV light TBBPA is degraded with a half-life of a few days.

Due to its physicochemical properties, TBBPA binds strongly to sediments and soils. This is supported by Mackay (level 1) modelling. Accordingly, the target compartments in equilibrium are the soil (51 %) and sediment (49 %).

Studies on the concentration in organisms gave BCF values, based on the original radioactivity, of 30 to 1200 for fish and 243 to 3190 for *Chironomus tentans* larvae. In fish (*Lepomis macrochirus*) the half-life for the elimination of ¹⁴C-TBBPA from muscle and intestines was < 24 hours. The compound was completely eliminated within 7 days. In the tissue of oysters (*Crassostrea virginica*), with a BCF of 720 based on the original radioactivity, more than a third of the radioactivity was still detected after 14 days.

TBBPA is very toxic to various aquatic organisms. Known effect values and concentrations factors for various organisms are compiled in Table 1. The lowest 72-h E_bC₅₀ for aquatic plants (marine algae) is 90 µg/l. For *Selenastrum capricornutum*,

however, no effect was determined up to the highest tested concentration of 5600 µg/l. For *Daphnia magna*, the 48-h EC₅₀ is 960 µg/l, the 21-d NOEC (reproduction) being 300 µg/l. In a 96-h test with the marine American oyster *Crassostrea virginica*, growth was already reduced significantly at the lowest tested concentration (18 µg/l). The EC₁₀ was determined to be 2.6 µg/l and substitute for a NOEC.

The LC₅₀ (96 h) for several fish species is between 400 and 3000 µg/l. In an early-life-stage fish test (35 d) the NOEC for the survival, length and weight of larvae was 160 µg/l. No effects were determined for *Chironomus tentans* in the 14-day sediment test with TBBPA concentrations of 228 000 to 341 000 µg/kg dw sediment, using sediments of various composition.

In the terrestrial area, results are available on the germination and growth of mono- and dicotyledonous plants. The 21-d EC₅₀ values were > 4595 mg/kg dw soil and the 21-d NOECs were between 16 mg/kg (*Cucumis sativa*) and 4595 mg/kg (*Glycine max*). Studies on soil-dwelling invertebrates are lacking. An investigation on embryos of the Japanese quail (*Coturnix japonica*) and the domestic chicken (*Gallus domesticus*) showed no endocrine effects. After intraperitoneal injection, no endocrine effects were detected on the larval development of the African clawed toad (*Xenopus laevis*) or the rainbow trout (*Oncorhynchus mykiss*).

No information is available on the effects of TBBPA in complex systems (e.g. mesocosms).

Taking into account the sublethal effects on the growth of oysters, with an EC₁₀ of 2.6 µg/l in a 96-h test and an assessment factor of 50, the PNEC is considered to be 0.052 µg/l. This PNEC is greater by a factor of 2.6 than the highest measured concentration in a monitoring programme in rivers and streams with a point source (0.02 µg/l).

Table 1: Toxicity and Bioaccumulation Data for TBBPA (for details see 5.3 and 6)

Species	EC ₅₀	LC ₅₀	NOEC	LOEC	BCF
Microorganisms					
<i>Giardia lamblia</i>	82 000 - 163 000 µg/l (72 h)				
Algae/ Plants					
<i>Skeletonema costatum</i>	90 - 890 µg/l (72 h)				
<i>Thalassiosira pseudonana</i>	130 - 1000 µg/l (72 h)				
<i>Chlorella spec.</i>	> 1500 µg/l (96 h)				
<i>Selenastrum capricornutum</i>	> 5600 µg/l (96 h) ¹				
Invertebrates					
<i>Daphnia magna</i>	960 µg/l (48 h) 1000 µg/l (48 h)		300 µg/l (21 d) (reproduction) 980 µg/l (survival)	980 µg/l (21 d) (reproduction)	
<i>Mysidopsis bahia</i>	860 - 1200 µg/l (96 h)				720 (based on radio-activity)
<i>Crassostrea virginica</i>	98 µg/l (96 h) (growth)		2.6 µg/l (EC ₁₀ 96 h) (growth)		243 - 3190 (based on radio-activity)
<i>Chironomus tentans</i>		130 µg/l (14 d)	≥ 228 000 - ≥ 341 000 µg/kg dw (14 d) (growth)	2	
<i>Acartia tonsa</i>	125 µg/l (120 h, larvae)	400 µg/l (48 h)			
<i>Nitocra spinipes</i>		350 µg/l (96 h)	> 35 µg/l (96 h, larvae)		

Table 1 (Cont.): Toxicity and Bioaccumulation Data for TBBPA

Species	EC ₅₀	LC ₅₀	NOEC	LOEC	BCF
<u>Vertebrates</u>					
<i>Lepomis macrochirus</i>		510 µg/l (96 h)			170 (based on radio-activity intestines)
<i>Oncorhynchus mykiss</i>		400 µg/l (96 h)			
<i>Cyprinus carpio</i>					30 - 485
<i>Pimephales promelas</i>		540 µg/l (96 h); 490 µg/l (144 h)	160 µg/l (35 d, ELS) (survival)	310 µg/l (35 d, ELS)	1200 (based on radio-activity)
<i>Oryzias latipes</i>		8200 µg/l (48 h)			
<i>Danio rerio</i>		3000 µg/l (96 h)			
<i>Xenopus laevis</i>			> 500 µg/l (96 h) (teratogenicity)		
<u>Plants</u>					
<i>Lolium perenne</i>		> 4595 mg/kg (21 d)	62 mg/kg (21 d)		
<i>Allium cepa</i>		> 4595 mg/kg (21 d)	250 mg/kg (21 d)		
<i>Zea mays</i>		> 4595 mg/kg (21 d)	250 mg/kg (21 d)		
<i>Glycine max</i>		> 4595 mg/kg (21 d)	4595 mg/kg (21 d)		
<i>Cucumis sativa</i>		> 4595 mg/kg (21 d)	16 mg/kg (21 d)		
<i>Lycopersicon esculentum</i>		> 4595 mg/kg (21 d)	250 mg/kg (21 d)		

¹ Results of only limited value due to high toxicity of solubiliser.

² No LOEC was determined.

Toxicologic Aspects

Based on the systemic effects caused by repeated inhalation exposure of rats to TBBPA, systemic availability may be assumed. TBBPA is absorbed to about 70 % from the gastrointestinal tract. The TBBPA concentration in the blood increases rapidly, then decreases equally fast and is largely normalised within 24 hours. Elimination occurs almost exclusively in the faeces and only to a minor extent in the urine. For all tissues 2.1 % of the applied substance was still detected after 3 days. TBBPA is excreted to 92 – 97 % in unchanged form in the faeces and is detected as mono- or diglucuronide or sulphate ester glucuronide in the bile. The compound appears to be subject to enterohepatic circulation. Depending on the tissue type, half-lives range from 20 to 71 hours.

After acute inhalational, oral or dermal administration, TBBPA is considered to be of low toxicity.

TBBPA does not irritate the skin of rabbits or guinea pigs, but is slightly irritating to the rabbit eye. This effect is reversible. There is no indication of a sensitising effect in animals or humans.

After 2-week inhalation exposure to dust aerosols, rats exhibit massive salivation, lacrimation and a clear to reddish nasal discharge, beginning at a concentration of 6000 mg TBBPA/m³. A reduction of the liver weight is seen after 2-week inhalation exposure at doses of 2000 mg TBBPA/m³ and above. A 4-week administration of TBBPA in the feed, at doses up to 50 mg/kg bw and day, causes no effects with respect to clinical symptoms, macroscopic or microscopic changes of the liver, kidneys or thyroid gland. In a 90-day feeding study, with a dose of 100 mg TBBPA/kg bw and day, slight but statistically significant decreases in the haematocrit value and the ALT activity in the serum of rats are observed. These effects are not considered to be relevant, toxicologically or physiologically, giving a NOAEL of 100 mg/kg bw and day. Repeated oral administration to mice causes retarded body weight development and changes in clinicochemical and haematological parameters, beginning at 2200 mg/kg bw. An increased organ weight was seen in the spleen, as well as blood outside the red pulp. A repeated oral dose of 7100 mg TBBPA/kg bw and day is lethal for all mice; the NOAEL is 700 mg TBBPA/kg bw and day in a

3-month study. In contrast, a NOAEL of 100 mg/kg bw and day is assumed for the mouse, which indicates the rat's greater sensitivity to TBBPA.

Dermal TBBPA treatment of intact rabbit skin for 3 weeks causes no systemic reactions, except a local reaction in the form of slight erythema.

The occasional, weakly positive, effects of TBBPA in bacterial tests cannot be reproduced. Thus, there is no substantial indication of a mutagenic potential; no DNA-damaging or clastogenic effects were determined in *in vitro* test systems.

Studies on prenatal toxicity to rats give no indication, even at maternally toxic doses, of compound-related foeto- or embryotoxicity, teratogenic effects or postnatal developmental disturbances.

Neurotoxic effects are not observed after TBBPA treatment of neonatal mice.

In vitro investigations give no indications of an effect analogous to that of oestrogen.

Investigations on *in vivo* genotoxicity, fertility and carcinogenicity are lacking.