DANISH MINISTRY
OF THE ENVIRONMENT
Environmental
Protection Agency

Health and Environmental Assessment of Alternatives to Deca-BDE in Electrical and Electronic Equipment

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Preface

From 1 July 2006 the Directive 2002/95/EC on the restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS Directive) specifies that new electrical and electronic equipment (EEE) placed on the market are not to contain polybrominated biphenyls (PBB), polybrominated diphenyl ethers (PBDE) and certain metallic constituents for specified equipment categories. The RoHS directive allows exemption from substitution if (quote) "***substitution is not possible from the scientific and technical point of view or if the negative environmental or health impacts caused by substitution are likely to outweigh the human and environmental benefits of the substitution"*** (end quote). With the Commission Decision 2004/717/EC of 13 October 2005, decabromodiphenyl ether (deca-BDE) in polymeric applications has been exempted from substitution.

Denmark has instituted legal proceedings against the Commissions decision to exempt deca-BDE from the ban in the RoHS directive. The Danish Environmental Protection Agency has initiated two studies to form part of the scientific documentation in support of the case before the Court of Justice of the European Communities: 1) A survey to identify and describe suitable alternatives to the brominated flame retardant deca-BDE and 2) a health and environmental assessment of selected alternatives to deca-BDE as proposed by study 1).

It is beyond the scope of the present study to develop a full evaluation of to what extent negative environmental or health impacts caused by substitution are likely to outweigh the human and environmental benefits of the substitution. The scope is primarily to identify the existence of flame retarding alternatives to deca-BDE with less or equal environmental and health impacts.

The study was steered by a group comprising Torben Nørlem and Frank Jensen, both Danish Environmental Protection Agency, and Frank Stuer-Lauridsen, DHI Water and Environment.

The report was prepared by Frank Stuer-Lauridsen (project manager, fate and environmental studies), Karl-Heinz Cohr, Pernille Borling, Brian Svend Nielsen, Helle Buchardt Boyd, Inge Søborg (health studies) and Trine Thorup Andersen, (fate and environmental studies).

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Summary

Alternatives with acceptable environment and health properties are available to substitute the flame retardant decabromodiphenyl ether.

A market analysis presented 26 potential substitute chemicals for decabromodiphenyl ether in electric and electronic equipment. This study shows that commercially available altenatives exists that allows for the substitution of decabromodiphenyl ether (deca-BDE) in a range of flame retardant applications. None of the six substances selected for a health and environmental assessment appear to have more negative impacts on the environmental, health and/or consumer safety than deca-BDE.

The study was initiated by the Danish EPA because a European Commission Decision exempts deca-BDE from substitution as otherwise required under the European Directive on the restriction of the use of certain hazardous substances in electrical and electronic equipment (the RoHS Directive).

The method for screening
The study comprised collection and evaluation of data on the physical-chemical, the environmental and the health properties of a range of possible alternatives to decabromodiphenyl ether as a flame retardant. A long list of alternatives was identified by COWI (2006) based on a preliminary usage pattern in EU combined with the screening of data availability and preliminary evaluation of Carcinogenic, Mutagenic and Reproductive effects (CMR) on humans and Persistance, Bioaccumulative and Toxic properties (PBT) regarding effects on environment.

The assessment method
A list of six compounds was generated and approved by the Danish EPA for a broader evaluation of adverse health and environmental properties:

- Ethylene bistetrabromophthalimide (EBTPI)
- Tetrabromobisphenol A (TBBPA)
- Tetrabromobisphenol A carbonate oligomer
- Triphenyl phosphates (TPP)
- Red phosphorus (RP)
- Diethylphosphinic acid, aluminium salt

The compounds were assessed for a long range of physico-chemical properties, environmental and human health properties, according to the EU TGD. The most import properties are listed in table 1.

Table 1 The key toxicological and environmental properties for assessment of alternatives to decabfromodiphenyl ether

Physical-chemical properties	Environmental effects and fate	Human health Subchronic/chronic toxicity
Molecular weight Solubility (water) Partition coefficient (log Kow) Acid-base constant (pKa)	Persistance Bioaccumulation Chronic Toxicity	Sensibilisation Genotoxicity Carcinogenicity Reproductive toxicity Teratogenic effects Neurotoxicity

The assessment results

Ethylene bistetrabromophthalimide (EBPTI) has a broad application range comparable to that of deca-BDE and it has been marketed as a general purpose alternative to deca-BDE. For most applications EBPTI has superior technical properties (except for colour), but it is more expensive than deca-BDE. Indications are that EBTPI is not biodegradable, does not bioaccumulate and that the aquatic toxicity is low. EBPTI is not considered to have critical effects concerning MR on human health. On carcinogenicity no data is available for EBPTI.

Based on the available data there appear to be no health and environmental properties of EBPTI prohibitive to the substitution of deca-BDE in the assessed applications.

Tetrabromobisphenol A (TBBPA) has a narrow but important application range for HIPS and ABS in enclosures. It is used in higher concentrations (14-22%) than deca-BDE (12-15%). TBBPA is more toxic to aquatic organisms than deca-BDE, but the compound does not meet the T criteria of PBT classification. There are few data on critical effects for humans, but based on chemical structure there is no indications that TBBPA display CMR characteristics. It should be noted that in the actual use TBBPA in Europe is used mainly reactively rather than additively. This entails that TBBPA is bound to the polymer and it is therefore not bioavailable in the products. The toxicological and environmental effects will be related only to a fraction of TBBPA in the polymer, which may be unreacted, and the impact will be dramatically reduced in such cases

Based on the available data there appear to be no health and environmental properties of TBBPA prohibitive to the substitution of deca-BDE in the assessed applications.

Tetrabromobisphenol A carbonate oligomer also has a narrow but important application range for co-polymers like PC/ABS and PPE/HIPS for enclosures. Few data for the TBBPA carbonate oligomer are available and they suggest less effect than TBBPA. As a worst case the assessment is based on the TBBPA monomer (se above). It should be noted that due to the polymeric nature of TBBPA carbonate the vast majority of TBBPA is not bioavailable in the flame retardant product. The toxicological and environmental effects will be related only to a fraction of TBBPA which may be monomeric. The impact of polymers and oligomers is dramatically reduced compared to monomers

Based on the available data there appear to be no health and environmental properties of TBBPA carbonate oligomer prohibitive to the substitution of deca-BDE in the assessed applications.

The non-halogenated flame retardant triphenylphosphate (TPP) is used primarily in enclosures (PC/ABS and PPE/HIPS) in concentrations of e.g. 8-12% in PC/ABS. There is insufficient data for a firm conclusion on TPP, but there is no evidence for concern with respect to CMR of TPP. TPP is not considered persistent or bioaccumulative according to the PBT criteria. Many data are available on toxicity, and one test result possibly meets the T criteria. The validity of this dataset has been questioned and the results should be confirmed.

The use of TPP as a flame retardant in the assessed applications does not appear to infer additional hazard to the environment or human health when compared to deca-BDE.

Red Phosphorus is normally used in flame-retardant-modified polymer compounds in a concentration range between 5 and 15% (w/w), e.g. in polyamide at 7% (comparable deca-BDE percentage 16-18%) or in glass-fiber-reinforced polyamide at 10-13%. There are no studies available on carcinogenicity, mutagenicity, reproduction toxicity, endocrine effects or sensitisation. Based on the available data, red phosphorus is considered to meet the P and vP criteria due to the inorganic nature of the substance. The data are insufficient for evaluation of the B and T criteria. At a screening level, red phosphorus does not meet the T criteria. Red phosphorus has been marketed in the EU for many years and there is no requirement of new data for existing substances according to EU regulation.

Red phosphorus has been used as a flame retardant for a number of years. The available studies are limited, but do not suggest that RP should be more hazardous to man or environment than deca-BDE.

Organic phosphinate can be used as FR in polyamide at 15-20% compared to 16-18% of deca-BDE. Data are not sufficient to conclude on carcinogenic, reproductive or endocrine disruption potential. There are no indications of mutagenic or sensitising potential of diethylphosphinic acid (aluminium salt). Based on the available data, the tested FR product containing is considered to be very persistent (vP), but not to meet the criteria for bioaccumulation. The available data indicate that diethylphosphinic acid, aluminium salt, is not acutely toxic at concentrations up to the water solubility limit, and has a low acute toxicity towards aquatic organisms.

For diethylphosphinic acid, aluminium salt, few data are available from the manufacturer. The available studies but do not suggest that the compound should be more hazardous to man or environment than deca-BDE.

Table 2 The key toxicological and environmental properties of decabfromodiphenyl ether (deca-BDE) and its halogenated and non-halogenated alternatives are expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (E), sensibilisation (S), persistence (P), bioaccumulation (B) and aquatic toxicity (T). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

Halogenated alternatives	CAS No.	Data availability environment/health		CMR; ES	PBT
Decabromodiphenyl ether	1163-19-5		+++	C0/M-/R- ; E0/S-	P+/B-/T-
Ethylene bistetrabromo-phthalimide (EBTPI)	32588-76-4	+	++	C0/M-/R- ; E-/S0	P+/B-/T-
Tetrabromobisphenol A (TBBPA)	79-94-7	++	+++	C0/M-/R- ; E-/S-	P+/B-/T-
Tetrabromobisphenol A carbonate oligomer [A]	94334-64-2 71342-77-3	-	+	C0/M-/R0 ; E0/S0	N.d.
Non halogenated alternatives	CAS No.:	Data availability environment/health		CMR	PBT
Triphenyl phosphates (TPP)	115-86-6	++	++	C0/M-/R- ; E0/S-	P-/B-/T-
Red phosphorus	7723-14-0	++	++	C0/M0/R0 ; Eo/S0	P+/B0/T-
Diethylphosphinic acid, aluminium salt[B]	225789-38-8	+	+	C0/M-/R0 ; Eo/S-	P-/B-/T-

[A] As a worst case polymers are assessed by their monomer, in this case TBBPA.
[B] Only data for test with the product Exolit OP 1230

In conclusion, it does seem likely that the substitution of deca-BDE by one of the alternatives available today is possible in compliance with the requirement of the RoHS Directive article 5(1)(b). Here an exemption to continue using polybrominated diphenyl ethers, including deca-BDE, is granted only if "***the negative environmental, health and/or consumer safety impacts caused by substitution are likely to outweigh the environmental, health and/or consumer safety benefits thereof;"***

Thus, a number of readily available altenatives exists that allows for the substitution of deca-BDE in a range of flame retardant applications

Sammenfatning på dansk

Der findes alternativer til flammehæmmeren decabromobiphenyl ether på markedet, som har acceptable miljø- og sundhedsegenskaber.

En markedsundersøgelse fandt 26 mulige erstatningsstoffer for decabromobiphenyl ether (deca-BDE) i elektrisk og elektronisk udstyr. I miljø- og sundhedsundersøgelsen af seks af disse markedsførte alternativer til deca-BDE dækkes en bred vifte af deca-BDEs anvendelsesområder. Ingen af de seks alternativer vurderes at have ringere miljø- og sundhedseffekter end deca-BDE.

Undersøgelsen er igangsat af Miljøstyrelsen efter en Kommissionsbeslutning om at undtage deca-BDE fra substitution i elektrisk og elektronisk udstyr, som det ellers er krævet i Europa-Parlamentets og Rådets Direktiv 2002/95/EF af 27. januar 2003 om begrænsning af anvendelsen af visse farlige stoffer i elektrisk og elektronisk udstyr (RoHS Direktivet).

Screeningsmetode

Der er indsamlet og vurderet screeningsdata for fysisk-kemiske, miljømæssige og sundsmæssige egenskaber for en vifte af potentielle alternativer til deca-BDE. Fra bruttolisten med 26 alternativer identificeret af COWI (2006) blev 18 screenet for foreløbige anvendelsesdata for EU i kombination med en hurtig undersøgelse af carcinogene, mutagene og reproduktionstoksiske (CMR) effekter og egenskaber knyttet til persistens, bioakkumulation, og toksiske effekter på miljøet (PBT egenskaber).

Vurderingsmetoden

Baseret på datatilgængelighed og anvendelsesområder blev seks stoffer udtaget til en bredere undersøgelse for miljø- og sundhedsegenskaber:

- Ethylen bistetrabromophthalimid (EBTPI)
- Tetrabromobisphenol A (TBBPA)
- Tetrabromobisphenol A karbonatoligomer
- Triphenyl phosphat (TPP)
- Rød phosphor (RP)
- Diethylphosphinsyre, aluminiumsalt

De udvalgte stoffer blev vurderet efter en lang række fysisk-kemiske, miljø- og sundhedsmæssige egenskabe, jfr. EU TGD, hvoraf de væsentligste er vist i tabel 1.

Tabel 1 Nøgleegenskaber for toksikologisk og miljømæssig vurdering af alternativer til decabfromodiphenyl ether.

Fysisk-kemiske egenskaber	Miljømæssig skæbne og effekt	Sundhedsegenskaber Subkronisk/kronisk toksicitet
Molekylvægt Opløselighed i vand Fordelingskoefficient (log Kow) Syre-base konstant (pKa)	Persistens Bioakkumulation Toksiske effekter	Sensibilisering Genotoksicitet Carcinogenicitet Reproduktionseffekter Fosterskadende effekter Neurotoksicitet

Resultater af vurderingen

Ethylen bistetrabromophthalimid (EBPTI) kan anvendes på en lang række områder i lighed med deca-BDE og det er da også markedsført som et bredt anvendeligt erstatningsstof for deca-BDE. EBPTI har overlegne tekniske egenskaber (bortset fra farveskala), men er dyrere end deca-BDE. Data antyder, at EBPTI ikke er nedbrydeligt, at det ikke bioakkumuleres og at dets akvatiske giftighed er lav. EBPTI skønnes ikke at have kritiske effekter med hensyn til MR. Derer ikke data for carcinogenicitet.

Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter af EBPTI, som vil forhindre en substitution af deca-BDE for de anvendelsesområder, der er vurderet.

Tetrabromobisphenol A (TBBPA) har et smalt men vigtigt anvendelsesområde i HIPS og ABS. Det anvendes i højere koncentrationer (14-33%) end deca-BDE (12-15%). TBBPA er giftigere overfor vandlevende organismer end deca-BDE, men ingen af stofferne er så giftige at de møder T kriteriet fra PBT klassificering. Der er kun få data på de kritiske sundhedseffekter, men baseret på kemisk struktur er der ikke indikationer på at TBBPA vil have CMR effekter. Det bemærkes, at brugen af TBBPA i Europa primært er den såkaldt reaktive, imodsætning til additiv anvendelse. Ved reaktiv anvendelse bindes TBBPA kemisk til polymeren og det medfører at TBBPA ikke er biotilgængeligt i produktet. De toksiskologiske og miljømæssige effekter af stoffet er dermed kun knyttet den rest af ureageret TBBPA, som måtte være i polymeren, og påvirkningen vil være væsentlig reduceret ved den anvendelse.

Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter af TBBPA, som vil forhindre en substitution af deca-BDE for de anvendelsesområder, der er vurderet.

Tetrabromobisphenol A karbonatoligomer produceres specifikt for at dække en smal, men vigtig, anvendelse i co-polymerer som PC/ABS og PPE/HIPS. De få data, som er til rådighed for en vurdering af TBBPA karbonatoligomer, antyder at effektniveauer er lavere end for TBBPA. Som en meget forsigtig fremgangsmåde kan TBBPA karbonatoligomeren vurderes som TBBPA monomeren (se ovenfor). Det bør bemærkes, at i den polymeriske anvendelse af TBBPA karbonat er kun en begrænset fraktion af TBBPA biotilgængeligt i produktet. De eventuelle miljø- og sundhedsmæssige effekter forårsages af den monomere TBBPA og vil være kraftigt reduceret i denne situation.

Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter af TBBPA karbonatoligomer, som vil forhindre en substitution af deca-BDE for de anvendelsesområder, der er vurderet.

Triphenylphosphat (TPP) er en ikke-bromeret flammehæmmer som anvendes i PC/ABS og PPE/HIPS i koncentrationer på f.eks. 8-12% i

PC/ABS. Der er ikke data til endelige vurderinger af TPP, men der er ikke forhold som antyder at TPP skulle have CMR effekter. TPP er ikke et persistent eller bioakkumulerende stof efter PBT kriterierne. Der er mange data for toksicitet, og et enkelt datasæt opfylder T kriteriet. Troværdigheden af dette datasæt er draget i tvivl og resultetet bør efterprøves.

Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter af triphenylphosphat (TPP), som vil forhindre en substitution af deca-BDE for de anvendelsesområder, der er vurderet.

Rød phosphor anvendes normalt i flammehæmmer-modificeret polymerer i koncentrationer fra 5 til 15 vægtprocent, f.eks. 7% i polyamid, hvor der anvendes 16-18% deca-BDE, eller i 10-13% i glasfiberforstærket polyamid. Der er ingen data til rådighed for rød phosphor på carcinogene, mutagene og reproduktionstoksiske (CMR), hormonforstyrrende eller sensibiliserende egenskaber. Baseret på de tilgængelige data vurderes rød phosphor at have P eller vP egenskaber på grund af stoffets uorganiske karakter. Der er ikke tilstrækkelige data til at vurdere bioakkumulation, og toksiske effekter, men på screeningsniveau er rød phosphor ikke giftigt på T niveau. Det skal bemærkes, at rød phosphor har været markedsført i mange år og der derfor ikke kræves ny data efter EU's regler om eksisterende stoffer.

Rød phosphor har været anvendt som flammehæmmer i en årrække. Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter, som overstiger deca-BDEs.

Organiske phosphinater kan bruges som flamehæmmere i polyamid i 15-20% sammenlignet med 16-18% deca-BDE. Der er ikke tilstrækkelige data til at vurdere carcinogene, reproduktionstoksiske og hormonforstyrrende egenskaber. Der er ikke fundet mutagene eller sensibiliserende egenskaber ved diethylphosphinsyre (aluminium salt). Baseret på det tilgængelige data for det testede produkt er det persistent, men ikke bioakkumulerbart eller toksisk i akvatiske organismer.

Diethylphosphinsyre (aluminium salt) er der kun få data til rådighed. Baseret på de tilgængelige data vurderes der ikke at være miljø- eller sundhedseffekter som overstiger deca-BDEs.

Table 2 Nøgleegenskaber for toksikologi og miljøeffekter af decabromdiphenyl ether (deca-BDE) og dets bromerede og ikke-bromerede alternativer er udtrykt i de følgende parametre: carcinogenicitet (C), mutagenicitet (M), reproduktionstoksiske effekter (R), homonforstyrrende effekter (E), sensibilisering (S), persistens (P), bioakkumulering (B) og aqvatisk toksicitet (T). Symboler: + en potential fare, - ingen potential fare og n.d. indikerer at ingen data er tilgængelige.

Bromerede alternativer	CAS Nr.	Datatilgengelighed miljø/sundhed		CMR; ES	PBT
Decabromodiphenyl ether	1163-19-5		+++	C0/M-/R- ; E0/S-	P+/B-/T-
Ethylene bistetrabromo-phthalimid (EBTPI)	32588-76-4	+	++	C0/M-/R- ; E-/S0	P+/B-/T-
Tetrabrombisphenol A (TBBPA)	79-94-7	++	+++	C0/M-/R- ; E-/S-	P+/B-/T-
Tetrabrombisphenol A karbonatoligomer [A]	94334-64-2 71342-77-3	-	+	C0/M-/R0 ; E0/S0	N.d.
Ikke-bromerede alternativer	**CAS Nr.**	**Datatilgengelighed miljø/sundhed**		**CMR**	**PBT**
Triphenyl phosphater (TPP)	115-86-6	++	++	C0/M-/R- ; E0/S-	P-/B-/T-
Rød phosphor	7723-14-0	++	++	C0/M0/R0 ; Eo/S0	P+/B0/T-
Diethylphosphinsyre, aluminium salt[B]	225789-38-8	+	+	C0/M-/R0 ; Eo/S-	P-/B-/T-

[A] Med en forsigtig tilgang kan polymer vurderes som deres monomerer, i dette tilfælde TBBPA.
B Der er kun data fra test med produktet Exolit OP 1230

Konklusionen på denne undersøgelse er, at der er sandsynligt, at deca-BDE kan substitueres med en række alternativer jævnfør RoHS Direktivets artikel 5(1)(b). Her tillades en undtagelse fra substitutionskravet kun hvis: "***den e påvirkning af miljø, sundhed og forbrugersikkerhed, som forårsages af substitutionen, overstiger den gavnlige påvirkning af miljø, sundhed og forbrugersikkerhed;"***

Der findes flere umiddelbart tilgængelige altenativer, som muliggør erstatning af deca-BDE i række flammehæmmer applicationer.

Abbreviations and acronyms

ABS	Acrylonitrile-butadiene-styrene
ATO	Antimony trioxide, Sb_2O_3
BCF	Bioconentration factor
CMR	Carcinogenic, Mutagentic and Reprotoxic substances
BFR	Brominated flame retardant
Deca-BDE	Decabromodiphenylether (same as DBDO)
DK EPA	Danish Environmental Protection Agency
EBPTI	Ethylene bis(phenylthalimide)
EC50	Chemical concentration effecting 50% of the test population
EEE	Electrical and electronic equipment
EFRA	European Flame Retardants Association
EU	European Union
FR	Flame retardant or flame retarded
HIPS	High Impact Polystyrene
LC50	Chemical concentration causing lethality in 50% of the test population
LOEC	Lowest Observed Effect Concentration
MATC	Maximum Acceptable Toxicant Concentration
NOEC	No Observed Effect Concentration
Octa-BDE	Octabromodiphenylether
OECD	Organisation for Economic Co-operation and Development
PA	Polyamide; Nylon
PA6	Polyamide 6; Nylon6
PA66	Polyamide 66; Nylon6-6
PBB(s)	Polybrominated biphenyl(s)
PBDE(s)	Polybrominated diphenyl ether(s)
PBT	Concerning plastics: Poly(butylene terephthalate)
PBT	Concerning environment: Persistent, Bioaccumulative and Toxic
PC	Polycarbonate
PC/ABS	Copolymer of PC and ABS
Penta-BDE	Pentabromodiphenylether
PES	Polyethersulfone
PET	Poly(ethylene terephthalate)
PPE	Polyphenylene ether (same as PPO)
PPE/HIPS	Copolymer of HIPS and PPE
QSAR	Quantitative structure activity relationship
RDP	Resorcinol bis(diphenylphosphate)
RoHS	Restriction of the use of certain hazardous substances in electrical and electronic equipment (Directive)
TBBPA	Tetrabromobisphenol A
TGD	Technical Guidance Document
TPP	Triphenyl phosphate
UL 94	Tests for Flammability of Plastic Materials from Underwriters Laboratories Inc.
vPvB	Very Persistent, very Bioaccumulative
V-0	UL 94 Vertical burn test

1 Introduction

Electrical and electronic equipment (EEE) generate heat and in some circumstances excessive heat with a concomitant risk of fire. Flame retardants (FRs) lower the risk for spread of a fire and they extend the escaping time. FRs are therefore a crucial part of the fire safety protection in homes and industry. The Bromine Science and Environment Forum is formed by the largest producers of bromine flame retardants and the following statements are quoted on their webpage:

- 'In terms of fire hazard, the plastics which are contained in a typical TV set are equivalent to 6 litres of petrol in your living room.

- In the United Kingdom alone, government scientists have estimated that over 3,000 lives were saved in the period from 1988 – 2000 as a result of flame retardants.'

It is clear that FRs including brominated flame retardants (BFRs) save many lives every year. Thus, when alternatives to certain FRs are sought the alternatives must provide a similar protection of the user of electronics. The fire protection grading for plastic achieved by the added FR should be the UL 94 vertical flame test V-0 grade. Some electronics producers have already requested their suppliers to phase out deca-BDE in addition to the phase out of penta-BDE and octa-BDE, while maintaining the fire protection level. Consequently, a number of chemical alternatives are already used in EEE on the market in EU. Other producers choose to substitute with non-flammable materials.

A range of brominated and non-brominated alternatives to deca-BDE that allow the plastics to achieve this grading has been identified by COWI (1), and a select number of the possible alternatives are assessed in the present report with respect to their health and environmental properties.

A chemical can be tested for a great number of properties, and for some, e.g. deca-BDE and tetrabromobisphenol A (TBBPA), a wealth of data is available. For others, e.g. the well known existing chemical red phosphorus (RP) or the alkylated phosphinic acid salt (diethyl phosphinic acid, aluminium salt) much fewer data are available. For some substances new data may be generated due to knowledge of concern of structural similar compounds

The methodology for assessing the chemicals are detailed in section 3.1, but an introduction is given here together with a brief outline of the process of selecting the chemicals for the health and environmental assessment (detailed in chapter 2).

Identifying chemical alternatives:

1) A market analysis presented a long list of alternatives to deca-BDE in a range of applications.
2) A screening for data in the open literature and public databases are carried out for substances identified on the long list.

3) A short list was generated based on general data availability, knowledge of prohibitive human and environmental effects, range of applicability, and cost and other market relevant information.

Assessing the short listed chemicals:

4) The properties of the compound are summarised giving the following data priority: Identification data, Physico-chemical characteristics, Health data, Ecotoxicity data and Environmental fate data.
5) An evaluation relative to deca-BDE is given through comparison of critical human health data (carcinogenicity, mutagenicity, reproductive effects, endocrine effects and sensitisation potential) and key environmental data (persistence, bioaccumulation, toxicity).

The data used for the assessment include the data in the public domain with preference to quality data in databases, peer reviewed literature and public reports such as European Union Risk Assessment Reports. Data from the industry and other sources are also used, still with a preference to data generated using standard methods and good laboratory practise.

During the study requests for information was sent to a number of manufacturers of FRs. Some industry organisations (CEFIC, EFRA, BSEF and EBFRIP) had already jointly expressed that they, in view of current legal proceedings, were not in a position to respond to the request, and they were not contacted during the health and environmental assessment.

2 Identification of alternatives to deca-BDE

2.1 List of possible alternatives to deca-bde

A market analysis performed by COWI in January-April 2006 showed that a number of compounds were possible as substitutes for deca-BDE in various polymers (1). A long list of alternative flame retardants was presented for consideration for the health and environmental assessment (Table 2.1).

Table 2.1 Long list of compounds considered for health and environment assessment

Halogen-containing alternative flame retardents	CAS No
Bis(pentabromophenyl) ethane (DBDE)	84852-53-9
Ethylene bistetrabromophthalimide (EBTPI)	32588-76-4
Tetrabromobisphenol A epichlorohydrinpolymer	40039-93-8
Bis(tribromophenoxy)ethane	37853-59-1
Hexabromocyclododecane (HBCD)	3194-55-6; 25637-99-4
Tetrabromobisphenol A (TBBPA)	79-94-7
Tetrabromobisphenol A bis (2,3-dibromopropyl ether)	21850-44-2
Tetrabromobisphenol A carbonate oligomer	94334-64-2; 71342-77-3
Brominated polystyrene	88497-56-7
Poly(dibromostyrene)	148993-99-1
Poly (pentabromobenzyl acrylate) fr 1025	59447-57-3
2,4,6-Tris(2,4,6-tribromophenoxy)-1,3,5 triazine	25713-60-4
Brominated epoxy oligomer	68928-70-1
Chloroparaffins	63449-39-8; 85535-85-9
Dodecachlorododecahydro-dimethanodibenzocyclooctene (Dechlorane Plus)	13560-89-9
Halogen-free alternative flame retardents	
Resorcinol bis(diphenylphosphate) (RDP)	57583-54-7; 125997-21-9
Bisphenol A bis(diphenylphosphate) (BDP, BAPP)	181028-79-5; 5945-33-5
Cresyl diphenyl phosphate (CDP)	26444-49-5
Triphenyl phosphates (TPP): Triaryl phosphates butylated	115-86-6; 68937-40-6
Red phosphorus	7723-14-0
Melamine polyphosphate	218768-84-4
Melamine cyanurate	37640-57-6
Ammonium polyphosphate	14728-39-9; 68333-79-9
Phosphinates: Diethylphosphinic acid, aluminium salt	225789-38-8
Aluminium trihydroxide	21645-51-2
Magnesium dihydroxide	1309-42-8

The use pattern and potential application of alternatives are shown below. Both halogenated and non-halogenated compounds are available as substitutes for deca-BDE. Only two compounds, ethane-1,2-bis(pentabromophenyl) and ethylene bis(tetrabromophthalimide) have the

potential to substitute for deca-BDE in all the listed applications and, as it is shown in Table 2.2, for some applications (PE) as few as three other compounds are presently available for achieving the V-0 classification of the plastics.

Table 2.2 Examples of identified flame retardants for relevant V-0 grade plastics in EEE (1)

Flame retardant	Enclosures				Connectors, etc		Wires	
	HIPS	ABS	PC/ABS	PPE/HIPS	PA	PBT/PET	PP	PE
Halogen-containing FRs								
Deca-BDE / ATO	X	X	X	X	X	X	X	X
Ethane-1,2-bis(pentabromophenyl) / ATO	X	X	X	X	X	X	X	X
Ethylene bis(tetrabromophthalimide) / ATO	X	X	X	X	X	X	X	X
Brominated epoxy polymer / ATO	X	X	X		X	X		
Tetrabromobisphenol-A (TBPPA)/ ATO	X	X						
TBBPA carbonate oligomer / ATO			X	X		X		
TBBPA bis (2,3-dibromopropyl ether) / ATO	X						X	
Tetradecabromodiphenoxybenzene / ATO	X				X	X		X
Tris(tribromophenoxy) triazine / ATO	X	X						
Bis(tribromophenoxy) ethane / ATO		X						
Tris(bromopentyl) phosphate / ATO							X	
Poly(pentabromobenzyl acrylate) / ATO					X		X	
Brominated polystyrene / ATO					X	X		
Poly(dibromostyrene) / ATO						X		
Chloroparaffins / ATO							X	
Dodecachlorododecahydrodi-methanodibenzocyclooctene / ATO or other synergists					X	X		
Non-halogen organo-phosphorus FRs								
Resorcinol bis(diphenylphosphate) (RDP)			X	X				
Bisphenol A bis(diphenylphosphate) (BDP)			X	X				
Triphenyl phosphates (TPP)			X	X				
Other non-halogen FRs								
Intumescent FR systems based on phosphor and nitrogen compounds							X	X
Red phosphorus					X			X
Melamine cyanurate					X		X	
Melamine polyphosphate					X			
Organic phosphinates					X	X		
Magnesium dihydroxide					X		X	

ATO: Antimony trioxide used as synergist

2.2 Screening of data availability for alternative substances

Both halogenated and non-halogenated compounds were selected for a screening of data availability in a series of databases, handbooks, EU Risk Assessments and other reviewed information. A few compounds of the long list and application list were omitted from further assessment due to knowledge of prohibitive human and environmental effects, limited range of applicability, or excessive cost: chloroparaffins, hexabromocyclododecane, aluminium trihydroxide and melamine, triazine and acrylate compounds. The substances chosen for screening were:

<u>Halogenated alternatives</u>

- Bis(pentabromophenyl) ethane (DBDE)
- Ethylene bistetrabromophthalimide (EBTPI)
- Bis(tribromophenoxy)ethane
- Tetrabromobisphenol A (TBBPA)
- Tetrabromobisphenol A bis (2,3-dibromopropyl ether)

- Tetrabromobisphenol A carbonate oligomer
- Brominated epoxy oligomer
- Brominated polystyrene
- Dodecachlorododecahydro-dimethanodibenzocyclooctene (Dechlorane Plus)

Non-halogenated alternatives

- Resorcinol bis(diphenylphosphate) (RDP)
- Bisphenol A bis(diphenylphosphate) (BDP, BAPP)
- Triphenyl phosphates (TPP)
- Red phosphorus
- Ammonium polyphosphate
- Phosphinates
- Diethylphosphinic acid, aluminiumsalt
- Magnesium dihydroxide
- Triaryl phosphates butylated

The data set investigated included assessment of the availability of information on acute and chronic toxicity and ecotoxicity (Table 2.3). Emphasis was given to studies of carcinogenic, mutagenic and reproductive effects in humans and to studies of persistence, bioaccumulation and toxicity in the environment. For these endpoints the information was briefly assessed to allow evaluation of such effects of concern.

Table 2.3 Parameters which were included in the initial data screening for alternatives to deca-BDE

Parameter	Effect
Toxicological data	Acute toxicity - skin irritation - irritation of mucous membranes - allergic reactions
	Subchronic/chronic toxicity - sensibilisation - genotoxicity - carcinogenicity - reproduktive toxicity - teratogenic effects - neurotoxicity
	Toxicokinetics - uptake through skin
Ecotoxicological data	Acute toxicity
	Subchronic/chronic toxicity
	Bioaccumulation
	Fate - biodegradation - abiotic degradation - evaporation/transportation

For several of the long listed compounds very few data were identified in the public domain. A detailed assessment of the data collection was presented to the DK EPA, and summarised below (Table 2.4) with respect to the data availability and the effects on CMR and PBT.

Table 2.4 Evaluation of data availability of halogenated and non-halogenated alternative flame retardants. Symbols: "o" = no data ; "-" = no effect ; "+" = effect ; "( )" = data identified, but not available during screening; "?" = not clear based on screening

Halogenated alternatives	CAS No.	Data availability environment / health		CMR	PBT
Bis(pentabromophenyl) ethane (DBDE)	84852-53-9	-	+	o	o[(2)]
Ethylene bistetrabromo-phthalimide (EBTPI)	32588-76-4	+	++	C0/M-/(R)	P+/B+/T-
Bis(tribromophenoxy)ethane	37853-59-1	++	+	C0/M-/R0	o
Tetrabromobisphenol A (TBBPA)[(3)]	79-94-7	++	+++	C?/M-/R±	P+/B+/T+
Tetrabromobisphenol A bis (2,3-dibromopropyl ether)	21850-44-2	-	+	C0/M?/R0	o
Tetrabromobisphenol A carbonate oligomer	94334-64-2	-	(+)	(-)	o
	71342-77-3	-			o
Brominated epoxy oligomer	68928-70-1	-	(+)	(-)	o
Brominated polystyrene	88497-56-7	-	+	C0/M?/R0	o
Dodecachlorododecahydro-dimethanodibenzocyclooctene (Dechlorane Plus)	13560-89-9	(+)	+	C0/M0/R-	P+/B-/T-
Non halogenated alternatives	**CAS No.:**	**Data availability environment / health**		**CMR**	**PBT**
Resorcinol bis(diphenylphosphate) (RDP)	57583-54-7	-	(+)	?	o
	125997-21-9	-	+	C0/M-/R-	o
Bisphenol A bis(diphenylphosphate) (BDP, BAPP)	181028-79-5	-	(+)	?	o
	5945-33-5	-			o
Triphenyl phosphates (TPP)	115-86-6	+++	+++	C-/M-/R-	P-/B-/T(+)
Red phosphorus	7723-14-0	+++	+++	C0/M-/R+ (1)	P-/B-/T-
Ammonium polyphosphate	68333-79-9	+	+	0	-
Phosphinates		-	-	0	P(-)/B(-)/T-
Diethylphosphinic acid, aluminium salt	225789-38-8	-			o
Magnesium dihydroxide	1309-42-8	-	+++	C-/M0/R-	P-/B-/T-
Triaryl phosphates, butylated	68937-40-6		++	()	o

(1) Shared CAS no. with approx 5 % data on red phosphorus, the rest on white/yellow phosphorus

(2) Debrominated degradation products may not be biodegradable (penta- and hexa-BDE=

(3) TBBPA is also used reactive, and in such applications toxicity is reduced.

2.3 Selection of alternative substances for environmental and health assessment

The long list and the preliminary usage pattern provided by COWI in January 2006 were combined with the screening of data availability and preliminary evaluation of CMR/PBT properties, the following compounds were proposed to the Danish EPA for the detailed assessment of health and environmental properties:

- Ethylene bistetrabromophthalimide (EBTPI)
- Tetrabromobisphenol A (TBBPA)
- Tetrabromobisphenol A carbonate oligomer
- Triphenyl phosphate (TPP)
- Red phosphorus (RP)
- Diethylphosphinic acid, aluminiumsalt

Magnesium dihydroxide was omitted from the assessment in favour of the organic phosphinic acid, because magnesium dihydroxide is widely used and accepted as a FR. The compound cover the main use categories comprising enclosures, connectors and wires as described in Table 2.2.

3 Environmental and health assessment of deca-BDE and selected alternatives

3.1 Methodology

For each of the selected alternatives to deca-BDE, a summary of the key data describing the following parameters is presented in this report:

• Substance identification
• Physico-chemical charateristics
• Environmental assessment (ecotoxicity and environmental fate data)
• Health assessment (toxicological data)

A comprehensive survey of the above properties, from which the key data have been summarised, is presented in Annex A.

3.1.1 Substance identification

The compounds evaluated are identified by the following data:

- CAS No.
- EINECS no.
- EINECS name
- Synonyms
- Molecular formula
- Molecular structure
- SMILES notation
- Major uses
- EU Classification on annex 1 in Directive 67/548/EEC and its updates.

3.1.2 Physical-chemical data

The compounds evaluated are described by the following physical-chemical data:

- Physical form
- Molecular weight
- Melting point/range (°C)
- Boiling point/range (°C)
- Decomposition temperature (°C)
- Flash point (°C)
- Vapour pressure (mm Hg(°C))
- Density
- Solubility (water)
- Partition coefficient (log P_{ow})

- pKa
- Henrys law constant (atm/m^3/mol at °C)

3.1.3 Environmental Assessment

The environmental assessment of the selected alternatives to deca-BDE is based on data for acute and chronic toxicity towards aquatic and terrestrial organisms, bioaccumulation potential and environmental fate. The assessment of the acute ecotoxicological effects is based primarily on standard short-term studies with algae, crustaceans and fish, but also on studies with other species (e.g. microrganisms, sediment living species, terrestrial species) when data are available. Acute effects are typically described by the endpoints mortality, immobilisation or growth inhibition (algae). The assessment of chronic ecotoxicological effects is based primarily on long-term studies with algae, crustaceans and fish, but also on studies with other species when data are available. Chronic or sub-chronic effects are often described by endpoints such as growth inhibition, reproduction, behaviour, hatching and larval development (fish) etc.

The assessment of the potential for bioaccumulation is based on bioaccumulation studies with fish. When data are available, bioaccumulation studies performed with other aquatic organisms are also included in the assessment. When no experimental data are available, the potential for bioaccumulation is evaluated based on QSAR estimates of the octanol-water partition coefficient (log P_{ow}) and other inherent properties of the compounds such as molecular weight. The assessment of the environmental fate of the selected alternatives to deca-BDE is based on data describing the aerobic and anaerobic biodegradability of the compounds and potential for abiotic degradation by hydroloysis and photodegradation. Data regarding mobility/transport in relevant matrices are included when available.

3.1.4 Health Assessment

Based on the retrieved literature a toxicological profile is prepared for each of the selected alternatives of the deca-BDE. The toxicological profile consists of four sections: 1) short-term effects, 2) long-term effects, 3) a summary of the toxicological properties of the substance, and 4) critical effects and dose.

1. Short-term effects are effects which occur at single exposure. This section describes acute effects, i.e. effects in connection with contact or absorption, primarily irritation and temporary systemic effects after absorption into the body, e.g. neurological symptoms such as headache, rumbling in the stomach etc. An allergic reaction is considered short-term effect, whereas development of allergy (sensibilisation) is considered a long-term effect.

2. Long-term effects are effects occurring after exposure for a considerable period. Generally, these effects are systemic. However, it may also be effects on the place of contact, e.g. development of allergy (sensibilisation). Focus is on effects such as cancer, genotoxicity, reproductive effects (including particularly exposed groups such as pregnant women and children), neurotoxicity, development of allergy, and other effects on the organs, e.g. injuries to the liver and kidneys.

3. On the basis of the above a summary is made of the toxicological properties of each substance.

4. Critical effects are the toxicological effects which are the basis of a risk assessment. The critical dose is the highest dose where no adverse effects are observed (also called NOAEL). If a NOAEL is not available the lowest observed dose which causes adverse effects (also called LOAEL) may be used together with a safety factor.

In general flame retardants are practically insoluble, making the bioavailability in the body low. As a consequence the internal body dose may be lower than the dose calculated from the administered amount (exposure dose). The bioavailability depends i.a. on the physical state of the substance, e.g. whether the substance is in solution or it is a suspension of particles, and of the particle size (size distribution). Low bioavailability will cause underestimation of the toxicity, e.g. the estimated NO(A)EL will higher than the "real" NO(A)EL. Only in the case of oral administration of deca-BDE information was available on the bioavailability; the absorption rate (bioavailability) is mentioned as 6% in the Update to RAR on human health (2). For the remainder flame retardants in this report no information was available.

3.1.5 PBT assessment

Based on the above assessment, it is evaluated whether the compounds are expected to meet the criteria for Persistence, Bioaccumulation and Toxicity (PBT criteria) according the EU Technical Guidance Document (TGD) (3).

These criteria are summarised in Table 3.0 below. The table contains two sets of criteria, one for PBT substances and a second category for so-called very persistent and very bioaccumulating substances (vPvB). This second category is developed under the recognition that for substances that are very persistent and bioaccumulate significantly in the food chain, high but unpredictable levels may be reached in wildlife or man over extended time periods. For such substances it is not necessary to demonstrate toxicity in laboratory testing as long-term effects can be anticipated anyway.

Table 3.0 Criteria for identification of PBT and vPvB substances

Criterion	PBT-criteria	vPvB-criteria
P	Half-life > 60 d in marine water or > 40 d in freshwater* or half-life > 180 d in marine sediment or > 120 d in freshwater sediment*	Half-life > 60 d in marine- or freshwater or >180 d in marine or freshwater sediment
B	BCF > 2,000	BCF > 5,000
T	Chronic NOEC < 0.01 mg/l or CMR or endocrine disrupting effects	Not applicable

* For the purpose of marine environmental risk assessment half-life data in freshwater and freshwater sediment can be overruled by data obtained under marine conditions.

For most substances the available data will not allow to come to a definitive answer to the question if the substance must be considered under the PBT assessment. H ence screening data that identify whether the substance has a potential to be a PBT have to be made use of. When it is clear that the P criterion is fulfilled a stepwise approach should be followed to elucidate the B criterion, eventually followed by toxicity testing to clarify the T criterion. In principle, substances are selected when they fulfil the criteria for all three inherent properties P, B and T. However, certain flexibility is required in their

application for instance in cases where one criterion is marginally not fulfilled but the others are exceeded considerably. This may include for example substances that do not fulfil the persistence criteria but bioaccumulate significantly and are measured in marine biota distant from anthropogenic sources (3).

The particular conditions of use and application pattern are not part of the hazard assessment. However, the alternative flame retardants are chemically inserted into the polymer molecule (reactive) or be physically blended in polymers after polymerization (additive) to suppress, reduce, delay or modify the propagation of a flame through a plastic materials. A reactive use will significantly reduce the expression of hazardous toxicological and environmental properties, and this is mentioned where relevant.

3.2 Decabromodiphenyl ether (deca-BDE)

This assessment considers the commercial flame retardant product decabromobiphenyl ether, deca-BDE, and the data given here are excerpts from the final EU Risk Assessment Report (2002) on bis(pentabromophenyl) ether (4). The references are given as found in the EU-RAR. A few data are from the "Update of the Risk Assessment of Bis(pentabromophenyl) ether (Decabromodiphenyl ether)" (2004) (5), the "Addendum to the May 2004 Environmental Risk Assessment of Decabromodiphenyl ether (CAS no. 1163-19-5) (2005) (6) and the human health draft of the "Update of the Risk Assessment Addendum of Bis(pentabromophenyl) ether (Decabromodiphenyl ether) of May 2005 (2).

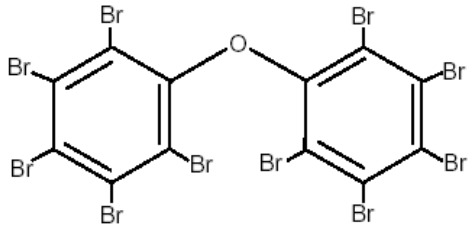
3.2.1 Substance Identification and Physical-Chemical Data

3.2.1.1 Identification

Deca-BDE has the following key identification data:

CAS Number: 1163-19-5
EINECS Number: 214-604-9
IUPAC Name: Bis(pentabromophenyl)ether; (decabromodiphenyl ether)
Molecular formula: $C_{12}Br_{10}O$
Molecular weight: 959.2

Structural formula:



A typical composition for a modern flame retardant product would be 97-98% deca-BDE with 0.3-3.0% of other brominated diphenyl ethers, mainly nonabromodiphenyl ether, and the composition of products supplied in the EU is consistent with these figures.

3.2.1.2 Physical-chemical properties

An experimental value of 4.63×10^{-6} Pa at 21°C was obtained for the vapour pressure; this was just outside of the recommended measurement range of 1×10^{-5} Pa for the instrument. The value can be considered to represent the upper limit to the vapour pressure for deca-BDE and was used in the EU-RAR environmental assessment.

The water solubility of deca-BDE has recently been determined using a generator column method carried out to GLP. In this study a composite sample of deca-BDE from three producers was used (composition was 97.4% deca-BDE, 2.5% nonabromodiphenyl ether and 0.04% octabromodiphenyl ether) and the water solubility was found to be very low at <0.1 µg/l at 25°C (Stenzel and Markley, 1997).

The log K_{ow} value for deca-BDE has recently been determined using a generator column method (MacGregor and Nixon, 1997). The substance tested was a composite sample from three manufacturers and consisted of 97.4% decabromodiphenyl ether, 2.5% nonabromodiphenyl ether and 0.04% octabromodiphenyl ether. The log K_{ow} value was determined as 6.27 at 25°C, and this value was used in the EU-RAR. The experiment was conducted to GLP.

The Henry's Law constant calculated using the estimated solubility of <0.1 µg/l at 25°C the Henry's Law constant is >44.4 Pa m^3/mol (estimated from ratio of vapour pressure and water solubility). Henry's Law constants were estimated by two Structure Activity Relationship methods to be $1.19.10^{-8}$ (bond method) or $4.45.10^{-8}$ atm/m^3/mol (group method).

3.2.2 Environmental assessment

Table 3.1 shows the key ecotoxicity and fate data for deca-BDE.

Table 3.1 Key ecotoxicity and fate data for deca-BDE

Acute toxicity	
Algae	EC50(72-96h) <1 mg/L
Crustaceans	EC50(48h) > the water solubility (QSAR estimate)
Fish	LC50(48h) >500 mg/L (exceeds the water solubility)
Chronic toxicity	
Algae	No data.
Crustaceans	NOEC(21d) for octa-BDE > solubility limit (2 µg/L)
Fish	NOEC(28d) > solubility limit (QSAR estimate)
Bioaccumulation	
BCF (Fish)	Little or no uptake in aquatic organisms
Terrestrial ecosystem	Accumulation found in bird's eggs
Biodegradation	
Aerobic degradation	Not readily biodegradable
Anaerobic degradation	Not biodegradable

3.2.2.1 Acute toxicity

Toxicity to algae

Walsh et al. (1987) studied the toxicity of deca-BDE to the marine unicellular algae ***Skeletonema costatum***, ***Thalassiosira pseudonana*** and ***Chlorella*** sp. The tests were carried out at a salinity of 30o/oo for either 72 hours (***S. costatum***

and ***T. pseudonana***) or 96 hours (***Chlorella*** sp.). The end-point measured was the EC50 for growth based on cell numbers. The exposure concentrations in the test solutions were verified by analysis. In the tests, the deca-BDE was added as a solution in acetone (final acetone concentration around 1 ml/l). Six different growth media were used in the test, one natural sea water and five synthetic sea water formulations. The natural sea water had a salinity of 32‰ and was diluted to give a final test salinity of 30‰ to be comparable with that of the synthetic media. The pHs of the various test media were in the range 7.6-8.2. At the highest concentration tested (1 mg/L) deca-BDE reduced growth of all three species by <50% and so it was not possible to determine the EC50 (it is not clear if any toxic effect were seen at 1 mg/L). The toxicity limit reported is well in excess of the compound's water solubility.

Toxicity to invertebrates
No information is currently available for deca-BDE regarding the acute toxicity towards invertebrates.

Toxicity to fish
A 48h-LC_{50} for orange-red killifish (***Oryzias latipes***) has been determined for deca-BDE as part of a six week bioconcentration study. The LC_{50}(48h) was >500 mg/L (CITI, 1992). The reported toxicity limit is well in excess of the compound's solubility in water. Few other details of this study have been reported.

3.2.2.2 Chronic toxicity
A long-term ***Daphnia*** test has been carried out using octabromodiphenyl ether. No effects on survival, reproduction or growth were seen over 21 days at concentrations up to 2 µg/l (solubility limit) (see the assessment of that substance for further details).

In a recent 120-day feeding experiment with rainbow trout (***Oncorhynchus mykiss***) (Kierkegaard et al., 1997 and 1999), deca-BDE (DOW FR-300-BA; the actual composition of this substance was not given in the paper but the composition of this product has been reported elsewhere as 77.4% deca-, 21.8% nona- and 0.8% octabromodiphenyl ether (Norris et al., 1973 and 1974)) was reported to cause increased liver weights (after 120 days exposure, but not after 16 or 49 days exposure) and lactate levels in blood when administered in food at a dose of 7.5-10 mg/kg body weight/day. No significant effects were reported on the number of lymphocytes or blood haemoglobin levels (a significant decrease in haemoglobin levels occurred at day 16, but this effect had disappeared by day 120) and no effects were seen on Ethoxyresorufin-O-deethylase (EROD), Ethoxycoumarin-O-deethylase (ECOD) or the transketolase activity. In addition no DNA adducts were seen. The effects on the liver occurred late in the exposure period (and also occurred in fish exposed for 49 days, followed by a 41-day depuration period) and may have been related to a build up of more toxic lower brominated congeners in the fish. The substance used in this test had a higher fraction of lower brominated congeners than found in current products, which consist of >97% deca-BDE and <3% nonabromodiphenyl ether. Although the substance was purified on a charcoal column prior to use to remove planar compounds, the significance of these effects to the current commercial product is unknown.

3.2.2.3 Toxicity to micororganisms and terrestrial toxicity
Toxicity to microorganisms

An activated sludge respiration inhibition (OECD 209) test has been carried out with a composite sample of commercial deca-BDE products from three manufacturers (Schaefer and Siddiqui, 2001). The purity of the test substance was given as 97.9% decabromodiphenyl ether. The substance was tested in triplicate at a concentration of 15 mg/L. The inoculum used in the test was activated sludge from a wastewater treatment plant that received predominantly domestic waste. The test was carried out at 20-22°C and the respiration rate of the activated sludge over 3 hours was determined. Two controls and a positive control (3,5-dichlorophenol at concentrations of 5, 15 and 50 mg/L) were also run. The respiration rates in the two controls were both 41.6 mg O_2/L/hour. The mean respiration rate in the deca-BDE treatments was 41.1 mg O_2/L/hour and so no inhibition of respiration was seen at the concentration tested. The EC_{50} for the positive control was determined as 9.8 mg/L, which is within the normal range of 5 to 30 mg/L for this test. The NOEC for deca-BDE from this test is therefore ≥15 mg/L.

Toxicity to plants

The toxicity of deca-BDE to six species of plants has been determined using OECD Guideline 208 (the protocol is based on the 1998 proposal for revision of this test guideline) (Porch and Krueger, 2001). The soil used in the test was an artificial sandy loam soilamd the following six plant species were tested: monocots; corn (***Zea mays***), onion (***Allium cepa***) and ryegrass (***Lolium perenne***); dicots; cucumber (***Cucumis sativa***), soybean (***Glycine max***) and tomato (***Lycopersicon esculentum***). The measured concentrations were 292, 707, 1,177, 2,098 and 5,349 mg/kg dry soil, respectively.

Seedling emergence and growth was measured and the NOEC from these studies was given as ≥6,250 mg/kg dry soil based on nominal values or ≥5,349 mg/kg dry soil based on the mean measured concentration in soil at the start of the test.

Toxicity to earthworms

A 56-day earthworm reproduction study has been carried out with deca-BDE according to the proposed OECD 207 test guideline "Earthworm Reproduction Test (***Eisenia fetida/andrei***)". The test used an artificial soil spiked with mean measured concentrations of 320, 668, 1,240, 2,480 and 4,910 mg/kg dry weight.

After 28 days exposure, the adult worms were removed from the soil and the number of live and dead worms was determined. The soil was then replaced in the test chambers and incubated for a further 28 days to allow any cocoons to hatch. The number of juvenile worms was determined at the end of the second 28-day period.

Overall, no significant adverse effects on survival or reproduction were seen in this study and the NOEC is ≥ 4,910 mg/kg dry weight.

3.2.2.4 Toxicity to sediment living organisms

For sediment, no effects were seen in long-term tests with the oligochaete ***Lumbriculus variegatus*** in two sediment types at concentrations up to 3,841 mg/kg dry weight (equivalent to 1,480 mg/kg on a wet weight basis).

Prolonged sediment toxicity tests using deca-BDE have been carried out with the oligochaete ***Lumbriculus variegatus*** using a flow-through test system with sediments of either 2.4% organic carbon content (Krueger et al., 2001a) or

5.9% organic carbon content (Krueger et al., 2001b). The test protocol was based on the ASTM E 1706-95b Guideline and USEPA Series 850 Ecological Effects Test Guidelines (OPPTS No. 850.1736). The sediment used in the test was an artificial sediment and the test substance was a composite sample from three manufacturers and had a purity of 97.9%. The sediment/test substance mixture was mixed for 24 hours, placed in the flow through the test system and allowed to equilibrate for approximately 44 hours prior to addition of the test organisms. The total exposure period was 28 days.

The nominal concentrations tested in the studies were 313, 625, 1,250, 2,500 and 5,000 mg/kg dry weight, plus a control group. Each treatment and control group was replicated eight times with ten oligochaetes/replicate. Additional replicates were also run in each treatment and control group for analytical sampling of water and sediment. The endpoints investigated in the studies were survival/reproduction (as measured by the total number of organisms present which is a combination of parent survival and reproduction) and growth (as determined by dry weight of organism).

The NOECs from these studies based on measured concentrations are 4,536 mg/kg dry weight for the 2.4% organic carbon sediment and 3,841 mg/kg dry weight for the 5.9% organic carbon sediment.

3.2.2.5 QSAR data

The high octanol-water partition coefficient for deca-BDE (log Kow = 6.27) means that it is not ideally suited for QSAR predictions (generally only valid for substances with log Kow between -1 and 6). Aquatic toxicity predictions have been obtained using the equations for non-polar narcosis in Appendix II of Chapter 4 in the Technical Guidance Document. The results are shown below:

- 96h-LC50 for fish = 1.91.10-7 mol/l = 183 µg/l
- 28d-NOEC for fish = 1.14.10-8 mol/l = 10.9 µg/l
- 48h-EC50 for ***Daphnia*** = 5.29.10-8 mol/l = 50.7 µg/l
- 16d-NOEC for ***Daphnia*** = 3.69.10-9 mol/l = 3.5 µg/l
- 72-96h-EC50 for algae = 3.16.10-9 mol/l = 30.3 µg/l

The predicted NOECs and L(E)C50s are all greater than the water solubility of deca-BDE .

3.2.2.6 Secondary poisoning

The toxicity of deca-BDE to mammalian systems has been extensively reviewed in EU-RAR Section 4 as part of the human health assessment. The lowest long-term NOAEL was 1,120 mg/kg bw/day or 25,000 mg/kg food for systemic effects in a two year chronic study in rats. As this result is from a chronic study, an assessment factor of 10 is appropriate, giving a PNECoral of 2,500 mg/kg food.

Also of concern with regard to secondary poisoning is the possible formation of lower brominated diphenyl ethers as a result of photolysis/degradation of deca-BDE in the environment. It is known that some lower brominated diphenyl ethers (e.g. tetra- and pentabromodiphenyl ether) are potentially much more bioaccumulative and toxic than deca-BDE. The available evidence indicates that the lower brominated diphenyl ethers, if formed, are likely to be only minor products of these reactions, but there is some uncertainty over the actual significance of the process in the environment.

3.2.2.7 Bioaccumulation

A recent study has investigated the uptake of commercial flame retardant (Dow FR-300-BA; presumed 77.4% deca-, 21.8% nona and 0.8% octabromodiphenyl ether) by juvenile rainbow trout from food (Kierkegaard et al., 1997 and 1999). The fish were sampled for biological and chemical investigation after 16, 49 and 120 days. A further group were exposed for 49 days, followed by a 120-day depuration period. Fish were starved for 24-48 hours prior to sampling.

The available data indicates that little or no uptake of deca-BDE occurs in aquatic organisms exposed via the water phase. Some limited uptake of deca-BDE has been seen in experiments with fish exposed via food, but the tissue concentrations reached were much lower than those present in food (it is not clear if steady state had been reached during the 120-day exposure period and so it is possible that uptake could have increased further over extended timescales). Overall, it can be concluded that, although there is some experimental evidence that deca-BDE can be taken up by aquatic organisms via food, only a very small proportion of the total dose was taken up (~0.02-0.13% over 120 days) and so the substance can be considered to have a low bioaccumulation potential. Further evidence for this comes from the fact that there are very few reported occurrences of deca-BDE in biota samples taken from the environment (see Section 3.1.5.2), which contrasts markedly with the situation with penta-BDE.

Although, no bioaccumulation appears in the aquatic food chain, deca-BDE apparently can accumulate in bird's eggs, as demonstrated in biomonitoring studies in terrestrial food chains.

Decabromodiphenyl ether has been found over a wide scale at low (parts per billion) levels in a variety of predatory birds and their eggs, both in the UK and elsewhere, including Arctic regions In bird's eggs several studies have shown an accumulation of deca-BDE. In Peregrine falcons eggs in Sweden deca-BDE was found in 18 of 21 samples analysed and the level found in the egg contents was 28-430 μg/kg lipid. The levels in the wild populations were generally higher than in the captive-bred populations. In two Dutch studies of Common terns deca-BDE was found in eggs in concentrations up to 21 and 70 μg/kg lipid, respectively, but here fewer samples contained deca-BDE and the concentrations found were close to the detection limit of the analytical method (4).

The first studies mentioned above were followed up by a larger study in the UK, and here the substance was detected in 10 species out of the 14 initially sampled. Terrestrial species (especially bird-eating species) appear to have the highest levels in relative terms, though it should be noted that:

- only a very small number of samples were available for several species (limiting the comparison that can be made),
- other species groups (e.g. waterfowl) have not yet been investigated, and
- the substance can also be found in species that are exclusively aquatic (e.g. Great Crested Grebe).

The highest levels were found in Eurasian Sparrowhawk and Peregrine Falcon (5).

In a suite of studies performed in recent years deca-BDE was found in birds eggs in 15-30% of Gull's eggs sampled from Bjørnøya in Svalbard, in all 37 analysed Pergrine falcon eggs sampled 1986-2003 in South Greenland, but in only one sample of eggs of the Little Owl (***Athene noctua***) in Belgium (6).

The new data available to the EU RAR Update do suggest that uptake by organisms in the environment could occur if the organisms are exposed to deca-BDE in a suitable form. The available data also indicate that deca-BDE has a relatively short elimination half-life from organisms (5). Biotransformation has been reported in fish, but no firm conclusions can yet be made on importance of the metabolic pathway (6).

3.2.2.8 Aerobic biodegradability

The biodegradability of deca-BDE has been studied under aerobic conditions using an activated sludge inoculum. Deca-BDE (100 mg/l) was incubated with activated sludge (30 mg/l) from mixed sources in Japan over a 2-week period (equivalent to MITI I test). No degradation (as measured by BOD) was seen, therefore deca-BDE is not readily biodegradable (CITI, 1992). This result indicates that deca-BDE is unlikely to biodegrade rapidly in the environment under aerobic conditions. During 238 days incubation at least 5% of the deca-BDE initially present in the system had degraded to lower brominated congeners (6).

3.2.2.9 Anaerobic biodegradability

From the data generated for other halogenated aromatic substances (see Appendix F), there is a possibility for reductive dehalogenation to occur under some conditions. If such a process occurs for deca-BDE , this could lead to the formation of more toxic and bioaccumulative congeners.

The anaerobic biodegradation of 14C-labelled deca-BDE has been studied in a sediment-water system over 32 weeks (Schaefer and Flaggs, 2001a). The deca-BDE was tested at nominal concentrations of either 5 mg/kg or 500 mg/kg, The test chambers were incubated at ambient room temperature (22^{o}C) in an anaerobic chamber. The test chambers were kept in the dark during the test. The headspaces in the chambers were continually purged with nitrogen and the production of $^{14}CO_2$ and $^{14}CH_4$ as determined over the 32-week incubation period.

Overall, deca-BDE was found to be stable under the conditions used in the test, and so this type of process is not expected to lead to the formation of significant amounts of lower brominated congeners.

3.2.2.10 Abiotic degradation

Several studies have also investigated the degradation of deca-BDE under more environmentally relevant conditions using solid matrices in contact with water and either natural or artificial sunlight, for example Sellström et al. (1998a), Örn (1997), and Jafvert and Hua (2001a). These studies all show that deca-BDE is likely to undergo photodegradation in the environment and that debromination to give lower brominated diphenyl ether congeners does occur, although these are not generally the major degradation products formed. It is also clear that the lower brominated congeners formed can also undergo photodegradation themselves, as seen in the study by Jafvert and Hua (2001c) with 2,2',4,4'-tetrabromodiphenyl ether.

In experiments with zero valent iron, deca-BDE was rapidly transformed to lower brominated congeners. Around 90% of the decabromodiphenyl ether

initially added was converted to mono- to hexabrominated congeners after 40 days and the overall mass balance was around 85-95%. Experiments with iron sulphide and sodium sulphide also showed transformation of deca-BDE to lower brominated congeners but at a slower rate than found with zero valent iron.

3.2.2.11 Conclusion

All available data indicate that the toxic concentrations of deca-BDE towards aquatic organisms exceed the water solubility. NOEC values from long-term studies with both sediment living organisms, terrestrial plants and earthworms likewise indicate a low toxicity of deca-BDE (lowest chronic NOEC value = 3.8 mg/kg dry weight found in a 28 day study with ***Lumbriculus variegates***). Based on the available data, deca-BDE is not expected to bioaccumulate. Taken as a whole, it is clear that the aquatic toxicity and bioaccumulation potential of the polybrominated diphenyl ethers (penta-, octa- and deca-BDE) decreases with increasing bromination and therefore it is unlikely that deca-BDE will show any toxic effects to invertebrates at concentrations below its solubility limit.

Deca-BDE is not readily biodegradable. A 32 week biodegradation study of deca-BDE in sediment and water showed that deca-BDE was stable under anaerobic conditions. Because of the high log Kow and low water solubility, the mobility and availability of deca-BDE in the environment is expected to be limited. Deca-BDE is expected to adsorb strongly to sludge during sewage treatment.

Deca-BDE is likely to undergo photodegradation in the environment and that debromination to give lower brominated diphenyl ether congeners does occur, although these are not generally the major degradation products formed.

Biotransformation has been reported in fish, but no firm conclusions can yet be made on importance of the metabolic pathway (6).

3.2.2.12 Predicted No Effect Concentration (PNEC)

The following PNEC values for deca-BDE are presented in the EU Risk Assessment Report (2002) (4):

$PNEC_{aquatic\ compartment}$	>1.0 µg/L (based on EC_{50} > 1 mg/L for algae)
$PNEC_{aquatic\ compartment}$	>0.2 µg/L (based on long term NOEC for octa-BDE)
$PNEC_{microorganisms}$	≥1.5 mg/L (based on NOEC ≥ 15 mg/L in an activated sludge respiration test
$PNEC_{sediment\text{-}dwelling\ organisms}$	≥384 mg/kg dry weight (based on NOEC for ***Lumbriculus variegates***) ≥148 mg/kg wet weight (based on NOEC for ***Lumbriculus variegates***)
$PNEC_{soil}$	≥ 98 mg/kg dry weight (based on NOEC for earthworms) ≥ 87 mg/kg wet weight (based on NOEC for earthworms)

3.2.2.13 Data sources

The environmental data are excerpts from the final EU Risk Assessment Report (2002) on Bis(pentabromophenyl) ether (4). A few data are from the

"Update of the Risk Assessment of Bis(pentabromophenyl) ether (Decabromodiphenyl ether)" (5) and the "Addendum to the May 2004 Environmental Risk Assessment of Decabromodiphenyl ether (CAS no. 1163-19-5)" (6).

3.2.3 Health assessment

3.2.3.1 Observations in humans

50 Volunteers were exposed to 5% deca-BDE (purity unknown) in petrolatum on the skin. Induction was 3 times a week for 3 weeks and challenge 2 weeks later. No skin sensitisation was seen. 9/50 subjects had skin irritation. 200 Volunteers (80 males and 120 females) were induced with deca-BDE with 9 patches applied to the skin, one every second day. Two batches of unknown purity was used, one as received and one diluted to 2% (w/v) in water. 15/200 showed slight irritation reactions. The subjects were challenged 12 days after the induction period. Neither of two test materials showed sensitisation. Health assessment of workers exposed at least 6 weeks to polybromobiphenyls and polybromobiphenyl oxides, incl. deca-BDE. 4/35 showed higher prevalence of primary hypothyroidism, low serum T4 and free thyroxine (0/80 control subjects). Also a significant reduction in sensory and fibula motor velocities was observed. No deca-BDE was detected in serum. It is unclear whether polybromobiphenyls or deca-BDE is the etiological agent. Thus this study may be indicative only.

Deca-BDE may be slightly irritating to human skin, but does not seem to cause skin sensitisation.

3.2.3.2 Acute toxicity

Groups of 5 male albino Spartan rats were administered orally single doses of 50, 500 or 5,000 mg/kg of deca-BDE in corn oil (Great Lakes DE-83). All rats survived for 14 days and normal weight gain during were observed. Female Sprague-Dawley rats received a single dose of 126, 252, 500, 1,000 or 2,000 mg/kg as a 10% corn oil suspension of deca-BDE dosed by intubation (Dow FR-300-BA: 77.4% deca-BDE, 21.8% nona-BDE and 0.8% octa-BDE). No indications of toxicity after intubation or during the 14-day period were observed. No gross pathological changes were observed at necropsy carried out on one rat/dose level.

Groups of 2 male and 2 female New Zealand White rabbits were administered single doses of 200 or 2,000 mg/kg of deca-BDE (Great Lakes DE-83) to the skin under occlusive wraps for 24 hours. All the animals survived. Animals were observed for 14 days. At the 2,000 mg/kg dosage level all rabbits exhibited normal body weight gains. Local and general signs of toxicity were not reported and necropsies not performed.

Groups of 5 male and 5 female Spartan rats were exposed for one hour to 2 or 48.2 mg/L deca-BDE (Great Lakes DE-83) in air and subsequently observed for 14 days. All rats survived. Dyspnoea and ocular discharge was noted one animal in the 2 mg/L group. In the 48.2 mg/L group, eye squint and increasing motor activity were observed. All rats were normal at the end of 14-day-observation period. Necropsy was not performed.
The usefulness of this assay is dubious since no data on particle size distribution are given.

Deca-BDE appears to be of acute low toxicity by oral, skin and inhalatory exposure with LD_{50} values higher than the limit for classification as dangerous.

3.2.3.3 Irritation

Commercial deca-BDE (74.4% deca-BDE, 21.8% nona-BDE, 0.8% octa-BDE) applied to shaved skin under occlusion as dry solid (500 mg) in 2 groups of 3 New Zealand White rabbits did not cause irritation on intact or abraded skin. No erythematous and oedematous response was observed after a single exposure for 24h or the following observation period of 72h. In another study, deca-BDE (purity unknown) applied as dry solid on shaved skin of New Zealand albino rabbits caused no response on intact skin and a slight erythematous and oedematous response on abraded skin after a single confined exposure of 24 hours. The skin responses after repeated exposures to intact skin for five days/week for two weeks and to abraded skin for three days did not differ from responses following a single administration. No more information is available. Even though the studies were not conducted according to the EU or OECD methods it is concluded in the EU-RAR that deca-BDE is not a skin irritant.

Deca-BDE (93 - 98.5% purity) as dry solid (100 mg) caused transient (reversible in 48h) mild irritation of the conjunctival membranes (grade 1) in New Zealand White rabbits (3 females and 3 males). The cornea, iris and lens were unaffected. This study was carried out under GLP procedures. A single installation of 100 mg deca-BDE (purity unknown) caused mild irritation of the conjunctival membrane in New Zealand White rabbits (3 females and 3 males). Very slight erythema was seen in 3/6 animals and slight erythema in 1/6 animal at 24 hours, and very slight erythema was seen in 1/6 animals at 48 hour. Erythema was reversible in 72 hours. Very slight chemosis was seen in 2/6 animals at 24 and 48 hours, and in 1/6 animals at 72 hours and at day 7. Slight discharge was seen in 1/6 animals at 24 hours and at72 hours, and moderate discharge in 1/6 animals at 48 hours. In the EU-RAR it is concluded that there is no concern about eye irritation.

Spartan rats inhaled aerosols of deca-BDE (Great Lakes DE-83), 2 mg/L and 48.2 mg/L, showed marked dyspnoea in 1/5 and 3/5 animals, respectively.

In the EU-RAR it is evaluated that deca-BDE is not of concern with regard to skin and eye irritation. Data are not sufficient to conclude on respiratory irritation.

3.2.3.4 Sensitisation

No animal data on deca-BDE were available.

Skin irritation was observed in 9/50 persons subjected to repeated application of a suspension of 5% deca-BDE in petrolatum 3 times a week for 3 weeks and challenged two weeks subsequent to the last induction application. None showed skin sensitisation.

Based on the sparse available information it is concluded in the EU-RAR that deca-BDE is not a skin sensitiser. No data are available as to the respiratory sensitising potential of deca-BDE.

3.2.3.5 Repeated dose toxicity

In a 14-day study (NTP), groups of 5 female and 5 male B6C3F1 mice were fed diet containing to up to 100,000 ppm deca-BDE (99% pure). No effects on health, survival or body weights were observed and no compound-related clinical signs or gross pathological effects on major tissues or organs were

reported at the highest dose level, corresponding to approximately 25,000 mg/kg/day for females and 15,000 mg/kg/day for males. In a 13-week study (NTP), groups of 10 female and 10 male B6C3F1 mice were fed diet containing up to 50,000 ppm deca-BDE (99% or 97% pure). Survival, food consumption or final mean body weights were not adversely affected, and no compound related clinical signs or gross or microscopic pathology were observed at the highest dose level, corresponding to approximately 11,000 mg/kg/day for females and 7,000 mg/kg/day for males. In a 14-day study (NTP), groups of 5 female and 5 male F344/N rats were fed diet containing up to 100,000 ppm deca-BDE (99% pure). No effects on health, survival or body weight were observed, and no compound-related clinical signs or gross pathological effects on major tissues and organs were seen at the highest dose level, corresponding to approximately 7,500 mg/kg/day. Both studies were carried out in accordance with GLP procedures. No adverse effects were seen in these tests with mice and rats.

In a 28-day study, groups of 10 female and 10 male rats were fed diet containing up to 1,000 ppm deca-BDE (purity unknown). No compound-related changes were seen in behaviour, appearance, body weights or food consumption. No gross pathologic lesions or variations in organ weights, nor microscopic lesions in the examined tissues (liver, kidneys and thyroid) were observed at the highest dose level, corresponding to80 mg/kg/day for males and 70 mg/kg/day for females. Dose-depending increase in bromine content was seen in liver and fat samples were observed. In a 30-day study, male Sprague Dawley rats (number unspecified) were fed diet containing up to 10,000 ppm deca-BDE (77.4% deca-BDE, 21.8% nona-BDE and 0.8% octa-BDE). No clinical signs of toxicity, no changes in feed consumption, body weight gain, organ weights (heart, testes and kidneys), haematological and urinary values were observed. Enlarged livers were found at the two highest dose levels. Hepatic centrilobular cytoplasmic enlargement and vacuolisation and renal hyaline degenerative cytoplasmic changes were found at the highest dose level. Thyroid hyperplasia was reported at the two highest dose levels. In this study, NOAEL is 8 mg/kg/day and LOAEL is 80 mg/kg/day. In a 13-week study (NTP), groups of 10 female and 10 male F344/N rats were fed diet containing up to 50,000 ppm deca-BDE (97 - 99% pure) were administered in the diet to. No effects on survival, health, body weight or feed consumption were observed and no gross or microscopic effects were reported the highest dose level, corresponding to approximately 3,800 mg/kg/day for females and 2,800 mg/kg/day for males. In the 13-week and 2-year NTP-studies on deca-BDE no immunotoxic properties were found in lymphoid organs. Most studies were carried out in accordance with GLP procedures. In most studies no treatment related effects were seen. In one study using deca-BDE of low purity adverse effects were seen. These were ascribed the impurities of the test substance.

“Chloro”acnegenic activity of deca-BDE studied on rabbit ear (4 New Zealand white male and females). 0.1 ml/day, 5 times/week for 4 weeks. Concentrations of deca-BDE was 0.1, 1, 10 100%, suspension in chloroform. At 10% 1/4 showed slight erythema and exfoliation. No “chloro”acnegenic activity was seen. Mother liquor and still bottom samples from pilot plant production of deca-BDE showed “chloro”acnegenic activity, whereas deca-BDE did not. 0.1 ml/day, 5 days/week for 4 weeks concentration of test substances were 5, 10 or 100%.

Male Sprague Dawley rats (50) were dosed once with deca-BDE dust (20 mg; mean diameter 3.17 µm; 77.4% pure) by intratracheal installation. No untoward effects were observed, except on days 10 and 556 (but not on days 30 and 416). The lungs contained scattered focal aggregates of alveolar macrophages showing clear, angulated, cytoplasmic vacuoles or spaces, which probably represented the location of the dust particles. A very slight focal thickening of the interalveolar septae was noted in 2 rats. Particles were not present in the regional lymph nodes. No evidence of fibrosis or other proliferative response was detected in the lungs or regional lymph nodes. The half-life of deca-BDE in lungs was determined to be 150 days.

Subchronic and chronic oral toxicity of deca-BDE is low. Deca-BDE is believed not to cause chloroacne-like skin problems as a result of repeated contact. No valid information on inhalation is available.

3.2.3.6 Genotoxicity

Deca-BDE (97% pure) was tested in ***S. typhimurium*** TA98, TA100, TA1535 and TA1537 in the presence and absence of S9-mix (100, 333, 1,000, 3,333 or 10,000 µg/plate). The results were negative in TA1535 and TA1537, but equivocal in TA98 and TA100 in the presence of S9-mix. Deca-BDE (98% pure) was tested in ***S. typhimurium*** TA98, TA100, TA1535 and TA1537, and E. coli WP2uvrA in the presence and absence of S9-mix (15, 150, 500, 1,000 1,500 or 5,000 µg/plate). The test results were negative response was found in all strains with and without S9. These studies were performed in accordance with GLP procedures. Two commercial deca-BDE products (unknown purity) were tested in ***S. typhimurium*** TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of S9-mix (50, 150, 500, 1,500 or 5,000 µg/plate). The substances tested positive in TA98, TA100 and TA 1535 in the presence and absence of S9-mix, but were negative in TA1537 and TA1538. The positive results may be due to impurities of the test substances. The study was not carried out in accordance with GLP procedures.

Deca-BDE (unknown purity) was not mutagenic in mouse lymphoma cells (L 5178 Y/TK$^{+/-}$) in the presence and absence of S9-mix (7, 8, 9 or 10 µg/plate). The concentration range in this study was narrow. Deca-BDE (unknown purity) did not induce sister chromatid exchange nor chromosomal aberrations in CHO cells in the presence or absence of S9-mix (50, 100, 200 or 500 µg/ml). The study was carried out in accordance with GLP procedures.

In an ***in vivo*** cytogenetic study on bone marrow cells from rat femur (parental and neonate animals in a reproduction study; 3, 30 or 100 mg/kg bw/day in maternal diet) chromosomal aberrations were not induced. No positive control was included in the study, which furthermore was not performed in accordance with GLP procedures.

In the EU-RAR, the mutagenicity tests with deca-BDE in bacteria are considered as negative. Furthermore, it is evaluated that deca-BDE does not exhibit cytogenetic effects. The overall conclusion is that deca-BDE does not pose a mutagenic risk.

3.2.3.7 Long-term toxicity

Carcinogenicity

In a two-year study (NTP), groups of 50 female and 50 male B6C3F1 mice were fed diet containing 0, 25,000 or 50,000 ppm deca-BDE (97% pure).

Body weights and food consumption were comparable with controls. No compound-related clinical signs of toxicity were reported. No significant differences in survival were observed. Increased incidences of non-neoplastic lesions were observed in several tissues (liver, thyroid gland, stomach). In this study a NOAEL was not established, but LOAEL was 25,000 ppm, corresponding to approximately 3,700 mg/kg/day for females and 3,200 mg/kg/day for males. The frequency of liver neoplasia was significant in males at the low dose, but not at the high dose. The frequency of thyroid follicular cell neoplasia was marginally increased in males, whereas hyperplasia was significant. The study was performed in compliance with GLP procedures.

In a two year study (NTP), groups of 50 female and 50 male Fisher 344/N rats were fed diet containing 0, 25,000 or 50,000 ppm deca-BDE (94 - 97% pure). No clinical signs of toxicity or differences in survival rates were reported. Several non-neoplastic lesions were observed: high dose males exhibited increased incidence of thrombosis and degeneration in the liver without foci of necrosis associated, fibrosis of the spleen and lymphoid hyperplasia of the mandibular lymph nodes. Haematopoiesis in spleens of females and acanthosis of the forestomach in dosed males were slightly increased. Dose dependent decreased incidence of C-cell hyperplasia of the thyroid gland in males was also seen. In this study, a NOAEL for systemic toxicity was 25,000 ppm (1,120 mg/kg/day for males. For local effects, a LOAEL of 25,000 ppm (forestomach acanthosis) was found. Neoplastic nodules were observed in the livers. Tumours were observed in other organs and glands (zymbal gland, osteosarcoma and thyroid gland) as well as a high incidence of mononuclear cell leukaemia. The latter was hampered by a high incidence in control animals. The study was performed in accordance with GLP procedures.

In a two-year study, groups of 25 female and 25 male Sprague-Dawley rats were fed diet containing deca-BDE (purity: 77.4% deca-BDE; 21.8% deca-BDE; 0.8%deca-BDE) corresponding to 0, 0.01, 0.1 or 1 mg/kg bw/day. No effects were seen on survival rates, appearance, mean body weights, feed consumption, haematology, urinalysis, clinical chemistry and organ weights, and no gross and microscopic findings were seen. The maximum dose tested was very low.

In the EU-RAR, it is concluded that a classification for carcinogenicity cannot be made from the available data, but a cautious approach leads to proposal of a LOAEL for carcinogenicity based on the incidence of liver neoplastic nodules.

Reproduction toxicity

Sprague-Dawley rats exposed to commercial deca-BDE (77.4% deca-BDE, 21.8% nona-BDE, 0.8% octa-BDE) in the feed corresponding to 3, 30 (10 males and 20 females) or 100 mg/kg bw/day (15 males and 30 females). 60 days prior to mating, 15 days during mating, through gestation and lactation. No macroscopic signs of toxicity were seen in adults or in neonates. Minor developmental variations in soft tissues and skeleton were observed, the incidences being comparable to controls, no dose-response relationship. The highest tested dose did not produce parental toxicity. Rats and mice were treated with feed containing up to 50,000 ppm deca-BDE (purity >94%) for 13 weeks or 2 years. No macroscopic or microscopic effects were seen on testes, prostate, ovaries or uterus. These studies were not carried out in accordance with GLP procedures.

20 pregnant Sprague-Dawley rats exposed to commercial deca-BDE (77.4% deca-BDE, 21.8% nona-BDE, 0.8% octa-BDE) by gavage, 10, 100 or 1000 mg/kg bw/day on GD 6-15. No effects seen on the dams except higher liver bromine content at 1000 mg/kg. Increased, but not dose-dependent incidence of resorptions from 10 mg/kg and delayed ossification of the skull and subcutaneous oedema at 1000 mg/kg in the foetuses. The data do not allow concluding that these observations are without toxicological relevance.

Pregnant rats (Crl:CD(SD)IGS BR) exposed on GD 0-19 to deca-BDE in corn oil (purity 97.34%) by gavage, 100, 300 or 1000 mg/kg bw/day. No macroscopic or microscopic effects were seen in the dams. In the foetuses low incidences of vascular and heart defects were observed. Early resorptions were statistically significant but within the upper limit of the historic control. This study was well conducted and carried out in compliance with GLP procedures.

A recent study on developmental neurotoxicity studied spontaneous behaviour and habituation capability. The purity of deca-BDE was >98%. Neonate NMRI mice were exposed on postnatal days (PD) 3 or PD 19 (2.22 or 20.1 mg/kg bw), or PD 10 (1.34, 13.4 or 20.1 mg/kg bw). The animals were tested 2, 4 and 6 months after exposure. Effects were seen in animals exposed on PD 3. The effect was marginal at 2.22 mg/kg but significant at 20.1 mg/kg. No treatment related effects were seen at the other exposure days. This study is not performed in accordance with GLP procedures but it points at deca-BDE as a possible developmental neurotoxicant (2).

Deca-BDE is not toxic to the reproduction. Deca-BDE may possibly cause minor developmental defects and resorptions (i.e. abortions). Based on the newest study, EU experts raise concern about the potential of deca-BDE to cause developmental neurotoxicity. It was advised that a new developmental neurotoxicity study be carried out.

3.2.3.8 Toxicokinetics

No data were available on percutaneous absorption of deca-BDE or congeners. It is estimated to be very low based on the high logKow, very low water solubility and high molecular weight.

Male F344/N rats were exposed by feeding to up to 50.000 ppm deca-BDE (purity 97.9-99.2%) for 11 days, corresponding to 3,718 mg/kg bw/day. On day 8 radiolabelled deca-BDE (^{14}C-deca-BDE) was fed. 91.3-101% of the radioactivity was recovered in the faeces within 72 hours. Recovery was not dose-related. Small amounts were found in the liver (0.008-0.064%) and in fatty tissue (0.09-0.157%), highest relative amounts at the lowest dose level (238 ppm).

Rats exposed by feeding to 227 ppm (22-25 mg/kg bw/day) or 48.000 ppm (4.5-5 g/kg bw/day) deca-BDE for 9-11 days. On day 8 radiolabelled deca-BDE (^{14}C-deca-BDE) was fed. 82.5-86.4% of the radioactivity was recovered in the faeces independent of time of sacrifice (24, 48 or 72 hours). Recovery was not dose-related. Small amounts were found in the liver: 0.45, 0.21 and 0.11% at 24, 48 and 72 hours after the radioactive dose, respectively. After 10 days only deca-BDE was identified in the liver. Approximately 0.01% was excreted in the urine. 3 main metabolites (not mentioned) were found in faeces in increasing amounts with increasing dose.

72 hours after intravenous injection of ^{14}C-deca-BDE to rats (F344/N) 74% of the dose was found in the faeces, indicating biliary excretion. The remainder radioactivity was found mainly in muscles, skin, liver and fat. Only traces were found in urine, spleen and brain. Three metabolites were also detected in the faeces, but not identified.

Biliary excretion was studied after intravenous injection of ^{14}C-deca-BDE to F344/N rats. Bile was collected over 4 hours showing an excretion rate of 2.2%/hour of the dose. One metabolite detected, but not identified. Neonate NMRI mice were dosed with 2.22 mg/kg bw ^{14}C-labelled deca-BDE (purity <98%) on PD 3, 10 or 19. Radioactivity was measured 1 and 7 days after dosing in brain, heart and liver. Minor concentrations were found in brain and heart. The concentration in the brain doubled from day 1 to day 7. The concentration in the heart remained at the same level from day 1 to day 7. The concentration in the liver was considerably higher at day 1 and approximately the half at day 7.

In the draft update to the RAR on human health, an oral absorption rate (bioavailability) of 6% is mentioned (2).

No data were available on percutaneous absorption of deca-BDE, but based on its physico-chemical properties deca-BDE is expected not to be absorbed into the body percutaneously. Deca-BDE is only absorbed to a minor extent, approximately 6%, from the gastro-intestinal tract as evaluated from to content in liver and fat as compared with intravenous injection. After intravenous injection approximately 75% of the dose is recovered from faeces indicating large biliary excretion. The remainder of the dose was found in muscles, skin, liver and fat. Only trace amounts were found in urine, spleen, brain and heart. Three metabolites were found in faeces but not identified.

3.2.3.9 Conclusion

Deca-BDE is expected not to be absorbed into the body through the skin and is only absorbed to a little extent from the gastro-intestinal tract. After uptake deca-BDE is excreted with the bile to faeces and subsequently eliminated from the body. Urinary excretion is low. Deca-BDE may accumulate in muscles, skin, liver and fat, but only in trace spleen, brain and heart. Three metabolites of deca-BDE were found in faeces but not identified.

Deca-BDE may be slightly irritating to human skin, but does not seem to cause skin sensitisation. Deca-BDE has low acute toxicity by oral, skin and inhalatory exposure. LD_{50}-values are higher than the limits for classification as dangerous. It is evaluated that deca-BDE is of no concern with regard to skin and eye irritation. Data were not sufficient to conclude on respiratory irritation. Based on the sparse available information it is concluded that deca-BDE is not a skin sensitiser. No data are available as to the respiratory sensitising potential of deca-BDE.

Subchronic and chronic oral toxicity of deca-BDE is low. Deca-BDE is believed not to cause chloroacne-like skin problems as a result of repeated contact. No valid information on inhalation is available.

In the EU-RAR, the mutagenicity tests with deca-BDE in bacteria are considered as negative. Furthermore, it is evaluated that deca-BDE does not exhibit cytogenetic effects. The overall conclusion is that deca-BDE does not pose a mutagenic risk. In the EU-RAR, it is concluded that a classification for carcinogenicity cannot be made from the available data But a cautious

approach has lead EU to propose the use of a NOAEL of 1,120 mg/kg bw/day for the purpose of risk characterisation based on the incidence of liver neoplastic nodules. Taken into account the oral bioavailability of 6%, the NOAEL value may be recalculated to 67 mg/kg bw/day. Deca-BDE is not toxic to the reproduction. Deca-BDE may possibly cause minor developmental defects and resorptions (i.e. abortions). Based on the newest study, EU experts raise concern about the potential of deca-BDE to cause developmental neurotoxicity. It was advised that a new developmental neurotoxicity study be carried out. No studies have been carried out to assess a possible transthyretin-T_4 competition of deca-BDE.

3.2.3.10 Data sources

The health assessment data are excerpts from the final EU RAR on deca-BDE from 2002 (4). A few data are from the draft for the update of the risk assessment (2).

3.2.4 Critical effects

3.2.4.1 CMR

In the EU-RAR, it is concluded that a classification for carcinogenicity cannot be made from the available data, but a cautious approach leads to proposal of a NOAEL of 1,120 mg/kg bw/day for carcinogenicity based on the incidence of liver neoplastic nodules. Taken into account the oral bioavailability of 6%, the NOAEL value may be recalculated to 67 mg/kg bw/day. This value was suggested for the EU risk characterisation.

In the EU-RAR, the mutagenicity tests with deca-BDE in bacteria are considered as negative with and without metabolic activation. Furthermore, it is evaluated that deca-BDE does not exhibit cytogenetic effects. The overall conclusion is that deca-BDE does not present a mutagenic risk.

Deca-BDE is not toxic to the reproduction. Deca-BDE may possibly cause minor developmental defects and resorptions (i.e. abortions). Based on the newest study, EU experts raise concern about the potential of deca-BDE to cause developmental neurotoxicity. It was advised that a new developmental neurotoxicity study be carried out.

3.2.4.2 Endocrine disruption

No studies have been carried out to assess a possible transthyretin-T_4 competition of deca-BDE.

3.2.4.3 Sensitisation

Deca-BDE may be slightly irritating to human skin, but does not seem to cause skin sensitisation in humans. This is supported by sparse available information. In the EU-RAR it is concluded that deca-BDE is not a skin sensitiser. No data are available as to the respiratory sensitising potential of deca-BDE.

3.2.4.4 Summary of critical effects

Based on the available data cited above it may be concluded that deca-BDE may be a weak carcinogen; that deca-BDE is not genotoxic neither in ***in vitro*** mutagenicity studies with bacteria and mammalian cells nor ***in vivo*** in mammals; that deca-BDE may cause minor developmental defects and resorptions and that deca-BDE may cause developmental neurotoxicity, and that deca-BDE is not a skin sensitiser. No data were available on the respiratory sensitising potential of deca-BDE and no studies have been carried

out to assess the endocrine disrupting potential of deca-BDE to mammals including humans.

3.2.5 PBT Assessment

3.2.5.1 Persistence

Deca-BDE is not readily biodegradable based on the results of a single test. In such cases, the TGD recommends that a simulation test for environmental degradation should be performed, but no such data are available. At the present level of information, deca-BDE is thus considered to meet the persistent (P) and very persistent (vP) criteria until otherwise proved.

The potential for formation of recalcitrant lower brominated diphenyl ethers from the (slow) degradation of deca-BDE has been the subject of particular scrutinisation as reported in several reports (3,4). The latter and latest report of August 2005 concludes:

'Decabromodiphenyl ether contines to be a potential, though not proven, source of lower PBDE congeners that are considered to be PBT or vPvB substances.'

Inclusion of the degradation products in existing monitoring programmes, especially in sediment of high sulphide content is proposed.

3.2.5.2 Bioaccumulation

The available data indicates that little or no uptake of deca-BDE occurs in aquatic organisms exposed via the water phase. Some limited uptake of deca-BDE has been seen in fish exposed via food, but the tissue concentrations reached were much lower than those present in food. In support of the results from the bioaccumulation studies, the high molecular weight of deca-BDE (959.2 g/mol) indicates that deca-BDE is unlikely to bioaccumulate significantly (regardless of the log K_{ow} value) due to possible steric hindrance of passage of gill membranes or cell membranes of respiratory organs. Regarding molecular size the EU TGD states that certain classes of chemicals with a molecular mass >700 do not readily bioaccumulate in fish.

Although, no bioaccumulation appear in the aquatic food chain, deca-BDE apparently can accumulate in bird's eggs, as demonstrated in biomonitoring studies in terrestrial food chains (6).

3.2.5.3 Toxicity

The available data (both experimental and QSAR data) suggest that acute and chronic toxic effects occur at levels exceeding the water solubility. Deca-BDE is not expected to meet the (T) criterion.

3.2.5.4 Summary of PBT assessment

Based on the available data, deca-BDE is considered to meet the very persistent (vP) criteria. Deca-BDE is not considered to meet the B or vB criteria on the basis of aquatic tests, but bioaccumulation has been found in the terrestrial food chain in bird's eggs. The available data suggests that deca-BDE is not acutely toxic at concentrations up to the water solubility limit, and that deca-BDE does not meet the T criterion.

3.3 Ethylene bistetrabromophthalimide (EBTPI)

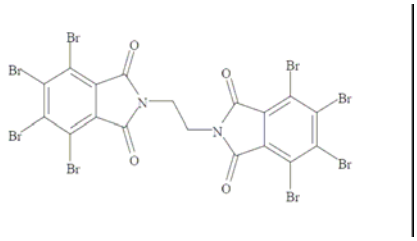
This assessment considers the commercial flame retardant product ethylene bis(tetrabromophthalimide), EBTPI, and the data given here are excerpts from the IUCLID dataset (7) and from a review report on toxicological literature (8).

3.3.1 Substance Identification and Physical-Chemical Data

3.3.1.1 Identification

EBTPI has the following key identification data:

CAS number: 32588-76-4
EINECS Number: 251-118-6
IUPAC Name: N,N'–ethylene bis(3,4,5,6–tetrabromophthalimide)
Molecular formula: $C_{18}H_4Br_8N_2O_4$
Molecular weight: 951.5
Structural formula:



3.3.1.2 Physical-chemical properties

EBTPI is insoluble in water with an estimated solubility of $3.029 \cdot 10^{-9}$ at 25°C (EPIwin, V.3.04) (9,10). Experimental data for determination of the water solubility are not available, but in bioaccumulation study the water solubility was reported to be < 1.63 mg/L (7). EBTPI has an estimated vapour pressure of $2.54 \cdot 10^{-22}$ mmHg at 25°C. The estimated log K_{ow} value is 9.80 (EPIwin V.3.04) (9,10), and EBTPI is thus regarded as being highly hydrophobic. The estimated soil K_{oc} is 800,000 (EPIwin V.3.04) (9,10).

3.3.2 Environmental Assessment

Only limited data describing the environmental properties of EBTPI are available. Table 3.2 shows the key ecotoxicity and fate data for EBTPI.

Table 3.2 Key ecotoxicity and fate data for EBTPI

Acute toxicity	
Algae	No data.
Crustaceans	No data.
Fish	LC50(48h) >500 mg/L
Chronic toxicity	
Algae	No data.
Crustaceans	No data.
Fish	No data.
Bioaccumulation	
BCF (Fish)	<3.3
Biodegradation	
Aerobic degradation	Not readily biodegradable
Anaerobic degradation	No data.

3.3.2.1 Acute toxicity

No data are available regarding the acute toxicity of EBTPI towards algae and crustaceans.

The acute LC_{50} (48h) in orange-red killifish (***Oryzias latipes***) was >500 mg/L in a range finding study (MITI Guideline) performed prior to a bioconcentration study in carp (7,9,10). This level exceeds the estimated water solubility by several magnitudes.

3.3.2.2 Chronic toxicity

No data available.

3.3.2.3 Microorganisms and terrestrial toxicity

No data available.

3.3.2.4 Bioaccumulation

EBTPI did not bioaccumulate in carp (***Cyprinus carpio***) during 56 days in a continuous flow-though system. The measured BCF values were <0.3- 1.3 at a test conc. of 2 mg/L and <3.3 at a test conc. of 0.2 mg/L. The test was conducted according to Japanese MITI Guidelines as a GLP study. (7,9,10). Both test concentrations exceeded the estimated water solubility of EBTPI.

3.3.2.5 Aerobic biodegradability

EBPTA did not biodegrade in a 28 day test for ready biodegradability (OECD 301C Modified MITI Test). The test was conducted as a GLP study with a test concentration of 100 mg/L, using activated sewage sludge as inoculum (7,9,10).

3.3.2.6 Anaerobic biodegradability

No data available.

3.3.2.7 Abiotic degradation

No data available.

3.3.2.8 QSAR data

The high octanol-water partition coefficient for EBTPI (estimated log K_{ow} = 9.8) means that it is not ideally suited for QSAR predictions (generally only valid for substances with log K_{ow} between -1 and 6). QSAR predictions have been obtained using EPIwin, V.3.04 and through the Danish EPA QSAR database available at ECB homepage.

- 96h-LC_{50} for fish = 0.000612 – 0.0032 mg/L (not expected to be soluble at this level)
- Chronic toxicity value for fish = 0.0002 mg/L (not expected to be soluble at this level)
- BCF = 9.5
- Ultimate biodegradation: recalcitrant

3.3.2.9 Conclusion

The available data material is insufficient for a comprehensive environmental assessment of EBTPI. The few studies reported indicate that EBTPI is not readily biodegradable, does not bioaccumulate and has a low aquatic toxicity. The only reported experimental LC_{50} value for fish (>500 mg/L) exceeds the estimated solubility of EBTPI by several orders of magnitude, and the exposure concentrations were not verified by chemical analysis. QSAR

predictions likewise indicate that EBTPI is not biodegradable, does not bioaccumulate and that the aquatic toxicity exceeds the estimated solubility of EBTPI. The estimated log K_{ow} and K_{oc} values indicate that the availability and the mobility of EBTPI in the environment are very limited. Further data describing the ecotoxicological properties of EBTPI are required for an adequate environmental assessment.

3.3.2.10 Predicted No Effect Concentration (PNEC)

No calculations of the PNEC have been found in the literature.

3.3.2.11 Data sources

The data for EBTPI are based on standardised test guidelines (MITI, OECD) and QSAR predictions (EPIwin V. 3.04). The experiments were performed according to GLP and are all > 20 years old.

3.3.3 Health Assessment

3.3.3.1 Observations in humans

Two cases of respiratory problems were reported by workers at a plant in Arkansas which manufactured EBTPI as well as tetrabromophthalic anhydride. Since the two processes were located in close proximity to each other it was difficult to determine which chemical, or a combination of the two, may have been responsible for the respiratory effects (11).

No clear conclusion regarding health effect of EBTPI in humans can be taken from these data.

3.3.3.2 Acute toxicity

Acute oral toxicity was determined by gavage in 5 male and 5 female Sherman-Wistar Rats, which received a single dose of 7500 mg/kg. The rats were observed for 14 days and no mortality was observed. It was thus concluded that the oral LD_{50} was greater than 7500 mg/kg. No information on guideline and GLP, but the study was in compliance with OECD 401(12).

Acute Inhalation toxicity was determined in 5 female and 5 male albino Sprague-Dawley rats, exposed to a dust atmosphere of EBTPI for 1 hour (4,50 ± 3,00 mg/l). Dyspnea was observed in all rats during and up to 5 days after the exposure. 1-mm red foci in the lungs of 2 male and 2 female rats was observed at necropsy. It was concluded that the LD_{50} was greater than 4,50 ± 3,00 mg/l. No information on guideline but in accordance with GLP and in compliance with OECD 403(13).

In an acute dermal toxicity test, 6 albino rabbits were exposed to EBTPI at a dose of 2000 mg/kg with occlusion for 14 days. No mortalities were observed during the 14-day period. Based on the results the dermal LD_{50} was determined to be > 2000 mg/kg. No information on guideline and GLP, but in compliance with OECD 402(14).

The acute toxicity EBTPI is low by oral and dermal exposure but EBTPI is mildly toxic when inhaled.

3.3.3.3 Irritation

Dermal irritation was investigated in albino rabbits. A dose of 0.5 g of EBTPI was applied to the abraded and intact skin under occlusive conditions. Skin readings were made at 24 hours and 72 hours post-application, and a primary irritation score of 0 was assigned to the compound based on no erythema,

eschar, or edema formation (Draize). No information on GLP but the study was similar to description in Federal register, Vol. 38, No.187, P.27019, 27 September 1973 (15).

Eye irritation was investigated in male and female albino New Zealand rabbits. A dose of 100 mg (BT93D) was applied once to the right eye. Observations were made at 1, 24, 48, and 72 hours and finally at day 7. At 1 hour observation all six rabbits showed positive responses, 2 rabbits at 24 hours, and none from 48 hours to the end of the study. Only the conjunctivae were affected. A Draize score of 3.0 (1 hr) indicating that it is considered to be a mild eye irritant. The Draize score was 0.3 at 72 hours and at 7 days after exposure. No information on guideline but in compliance with OECD 405. The study was in compliance with GLP regulations (16).

EBTPI does seem not to be of concern with regard to skin irritation, but eye irritation was observed at a dose of 100 mg. No information on respiratory irritation.

3.3.3.4 Sensitisation

No data.

3.3.3.5 Repeated dose toxicity (e.g. 4w and 13w studies)

A 28-day dietary feeding study was conducted with 40 weanling Sprague-Dawley male rats (0, 0.01, 0.1 and 1.0% EBTPI in the diet). No treatment-related abnormal behavior or appearance was observed. No toxicological significant changes were observed in body weight, food consumption, blood chemistry or organ weight. No alterations were observed in the gross and microscopic examination of tissues. Based on the results of the study NOAEL > 1%. No information on guideline and GLP, but the study was in compliance with OECD 407, even though only male rats were used (17).

A 90-day dietary feeding study followed by 46 days with control diet was conducted with 60 male and 60 female Sprague-Dawley rats (0, 0.01, 0.1, and 1.0% EBTPI. Six rats died during the study. No toxicological significant changes were observed in body weight, food consumption, blood chemistry or organ weight. No alterations were observed in the gross and microscopic examination of tissues. Based on the results of the study NOAEL > 1%. No information on guideline and GLP, but in compliance with OECD 408 (18).

Subchronic oral exposure showed low toxicity of EBTPI. No information on chronic toxicity.

3.3.3.6 Genotoxicity

EBTPI was found not to induce mutations, either with or without metabolic activation, in ***Salmonella typhimurium*** strains TA98, TA100, TA1535, and TA1537 (19). The test was performed in a preincubation modification of the Ames method.

EBTPI was tested in the Ames Salmonella/Microsomal assay for mutagenicity with ***Salmonella typhimurium*** (TA1535, TA1537, TA1538, TA98, TA100), and ***Escherichia coli*** (WP2 uvrA) at concentrations of 10, 50, 100, 500, 1000, and 5000 g/plate. No mutagenic activity was detected either with or without metabolic activation. The test was performed in a modification of the Ames

method in accordance with the industrial safety and health law from 1979 (20).

EBTPI was tested in the Ames Salmonella assay for mutagenicity with ***Salmonella typhimurium*** (TA1535, TA1537, TA1538, TA98, TA100), and with ***Saccharomyces cerevisiae*** (D4) at concentrations of 1, 10, 100, 500, and 1000 µg/plate. No mutagenic activity was detected. No information on guideline and GLP (21).

No mutagenic activity was observed when EBTPI was tested in Salmonella typhimurium, Saccharomyces cerevisiae, or Escherichia coli with and without metabolic activation. EBPTI does not seem to pose a mutagenic risk.

3.3.3.7 Long-term toxicity

A range finding study was performed in pregnant Sprague-Dawley rats with BT93 administered by gavage (0, 200, 500, 1000, 1500, 2000 mg/kg/day) daily from gestation day 6 to 15. Based on results from this study, a NOEL = 2000 mg/kg/day was established (22). Based on results from the range finding study 25 pregnant rats/group were dosed by gavage (0, 100, 500 and 1000 mg/kg/day) from gestation day 6 to 15 with termination on gestation day 20. No deaths were observed until termination. No absorption, resorptions or premature delivers were observed and maternal survival was 100%. No clinical signs of toxicity, no effect on mean maternal body weight gains and food intake were observed. There were no treatment–related morphopathological lesions or developmenetal malformations. Not maternally or teratogenic toxic when orally administered up to 1000 mg/kg. Based on the results a NOAEL (maternal) > 1000 mg/kg bw and a NOAEL (teratogen) > 1000 mg/kg bw was established. The studies were conducted in compliance with GLP regulations as described by FDA, EPA and SLS´s standard operating procedures, and in accordance with OECD and TSCA guidelines (23).

Twenty inseminated New Zealand white rabbits were gavaged with 1000 mg/kg bw (BT93) daily from gestation day 7 to 19. Termination was performed on gestation day 29. No absorption, resorptions or premature delivers were observed and maternal survival was 100%. No clinical signs of toxicity or effect on mean maternal body weight gains and food intake were observed. Intrauterine survival and fetal weights were not adversely affected by BT93. The incidence and type of developmental malformations and variations were not suggestive of a teratogenic effect produced by BT93. Oral administration of up to 1000 mg/kg was not maternally/fetotoxic or teratogenic toxic.

Based on these results NOAEL (maternal) > 1000 mg/kg bw and NOAEL (teratogen) > 1000 mg/kg bw. The study was conducted in compliance with GLP regulations as described by FDA, EPA and SLS´s standard operating procedures, and in accordance with OECD and TSCA guidelines (24).

Based on studies in rats and rabbits, EBTPI does not seem to be toxic to the reproduction or the development.

3.3.3.8 Toxicokinetics

EBTPI (^{14}C-labeled [unspecified labeling site]) was administered by gavage for 14 consecutive days to seven female Sprague–Dawley rats Two rats were used as controls. Two rats were sacrificed 24 hours after the last treatment,

and the other three were sacrificed 7, 14, and 30 days after the last treatment. The compound was mainly excreted in the feces (65%), urine (15%) and breath (1%). All organs contained radioactive residues. One animal exhibited abnormal behavior (locomotor activity, pilorection, tremors, and loss of righting reflex) and gross tissue abnormalities were observed at termination (inflamed, reddish, distended intestinal tract which contained gelatinous-appearing material). All other animals in the study had normal weight gain and contained no gross tissue abnormalities at necropsy. No guideline was specified, but the study was in compliance with OECD 417. No information on GLP (25).

Metabolism of radioactive EBTPI showed excretion of EBPTI in the faeces (65% of dose), urine (15% of dose), and breath (1% of dose).

3.3.3.9 Conclusion

In conclusion, the acute oral LD_{50} in rats was greater than 7.5 g/kg. No dermal irritation or reactivity was observed in rabbits, but eye irritation was observed at 100 mg. It was mildly toxic to rats when inhaled. In two subchronic exposure studies in rats, no remarkable changes were observed.

No information was found on carcinogencity or chronic toxicity. No reproductive or teratological effects were seen in rats or rabbits.

Metabolism in rats showed excretion in the feces (65% of dose), urine (15% of dose), and breath (1% of dose) 24 hours after oral dosing. No genotoxicity was observed when tested in strains of ***Salmonella typhimurium***, ***Saccharomyces cerevisiae***, or ***Escherichia coli*** with and without metabolic activation.

3.3.3.10 Data sources

The presented data for EBTPI are gathered and reviewed in the IUCLID dataset (7) and in a review report on toxicological literature (8). All the described studies are of older date and based on information from microfilm. In the majority of the studies reported no information was available on guideline and GLP conditions, but the studies were estimated to be in compliance with standardised OECD guidelines. Only a few studies were conducted in accordance with GLP conditions.

3.3.4 Critical effects

3.3.4.1 CMR

There was no information on the carcinogenicity of EBTPI. No mutagenic activity was observed when EBTPI was tested in Salmonella typhimurium, Saccharomyces cerevisiae, or Escherichia coli with and without metabolic activation. EBPTI does not seem to pose a mutagenic risk. Based on results in rats and rabbits EBPTI does not seem to be toxic to the reproduction.

3.3.4.2 Endocrine disruption

Based on results from studies in rats and rabbits regarding reproductive and teratological effects, EBTPI is not considered to have endocrine disruption potential.

3.3.4.3 Sensitisation

There was no avaible information on sensitisation of EBTPI in animals. Cases of respiratory problems in humans were reported, but no clear conclusion regarding health effect of EBTPI in humans could be stated.

3.3.4.4 Summary of critical effects

Based on available data above, EBPTI seems not to be mutagenic or toxic to the reproduction including endocrine disruption. No data on a possible carcinogenic potential were found. Data were not sufficient to conclude on the sensitisation potential of EBTPI.

3.3.5 PBT assessment

3.3.5.1 Persistence

EBTPI is not readily biodegradable based on the results of a single test. In such cases, the TGD recommends that a simulation test for environmental degradation should be performed, but no such data are available. At a screening level, EBTPI is thus considered to meet the persistent (P) and very persistent (vP) criteria until otherwise proved.

3.3.5.2 Bioaccumulation

Based on the estimated log Kow value (9.80) EBTPI meets the screening criterion for consideration as bioaccumulative (B) and very bioaccumulative (vB) (log Kow >4.5). The confirmatory criterion is a BCF > 2000 for the B criterion and BCF > 5000 for the vB criterion. Little uptake of EBTPI has been seen in fish exposed via water (BCF <3.3). Based on data from the single bioaccumulation study available, the bioaccumulation criterion is not fulfilled. In support of the results from the bioaccumulation study, the high molecular weight of EBTPI (951.5 g/mol) indicates that EBTPI is unlikely to bioaccumulate significantly regardless of the log K_{ow} value due to possible steric hindrance of passage of gill membranes or cell membranes of respiratory organs (the TGD states that certain classes of chemicals with a molecular mass >700 are not readily bioaccumulable in fish).

3.3.5.3 Toxicity

The only available study of the aquatic toxicity of EBTPI indicates that acute toxic effects occur at levels much higher than the estimated water solubility. Long-term NOEC values are not found in the literature. More ecotoxicology data are required for assessment of the toxicity (T) criterion.

3.3.5.4 Summary of PBT assessment

Based on the available data, EPBTI is considered to be very persistent (vP). EBTPI is not considered to meet the B or vB criteria. The available data suggests that EBTPI is not acutely toxic at concentrations up to the water solubility limit, but further data is required for assessment of the T criteria for EBTPI.

3.3.6 Comparison with deca-BDE

The key toxicological and environmental properties of EBTPI are compared to those of deca-BDE and summarised in Table 3.3. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.3 Summary of toxicological and environmental properties of EBTPI and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
EBTPI	32588-76-4	n.d.	-	(-)	-	n.d.	+	-	(-)
Deca-BDE	1163-19-5	(-)	-	(-)	-	(-)	+	-	-

3.4 Tetrabromobisphenol A (TBBPA)

This assessment considers the commercial flame retardant product 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (Tetrabromobisphenol-A, TBBPA) and the data given here are excerpts from the EU Risk Assessment Report (2006) on 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol and the Environmental Health Criteria on Tetrabromobisphenol A and Derivatives from WHO (environmental data) (26).

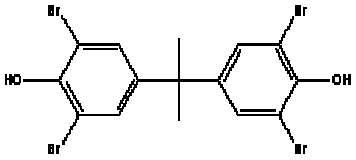
3.4.1 Substance Identification and Physical-Chemical Data

3.4.1.1 Identification

TBBPA has the following key identification data:

CAS Number: 79-94-7
EINECS Number: 201-236-9
IUPAC Name: 2,2'6,6'-Tetrabromo-4,4'-isopropylidenediphenol
Molecular Formula: $C_{15}H_{12}Br_4O_2$
Molecular weight: 543,9

Structural formula:



Several studies have investigated the levels of brominated dibenzo-*p*-dioxins and dibenzofurans present in tetrabromobisphenol-A. All studies have indicated that the levels are very low. In all cases the concentrations found appear to be below the levels specified in the USEPA test rule.

3.4.1.2 Physical chemical properties

TBBPA has a low solubility in water with reported solubility values in the range 0.063-2.34 mg/L depending on pH and temperature. TBBPA can exist in an ionised form at pH values around 7 and above (27).

The vapour pressure of tetrabromobisphenol-A at 20°C has been investigated using the spinning rotor gauge method (Wildlife International, 2001a). The method used was based on the OECD 104 Vapour Pressure Curve method and the USEPA Product Properties Test Guideline OPPTS 830.7950. The

vapour pressure for TBBPA was below the limit of quantification of the method used i.e. $<1.19 \times 10^{-5}$ Pa at 20°C. Based on the available data, the vapour pressure of TBBPA at ambient temperature will be assumed to be $<1.19 \times 10^{-5}$ Pa, and is probably considerably lower than this value. Where an actual value for the vapour pressure is needed the value of 6.24×10^{-6} Pa determined by Watanabe and Tatsukawa (1989) will be used in the environmental risk assessment, but it should be recognised that the reliability of this value is uncertain (27).

The octanol-water partition coefficient for TBBPA has recently been determined by a generator column method (Wildlife International, 2001b). The method used was based on the USEPA Product Properties Test Guideline OPPTS 830.7560. The mean log K_{ow} value determined was 5.90 ± 0.034. TBBPA is thus regarded as being a highly hydrophobic substance. A log K_{ow} value of 5.9 will be used for TBBPA in the risk assessment as it is from a well described study and the generator column method used is an appropriate method to use for substances with high log K_{ow} values; the OECD 307 shake flask method, which is similar to the method used in the Yu (1978) study, is recommended for log K_{ow} values in the range -2 to 4, whereas the generator column method can be used for substances with log K_{ow} values in the range 1 to >6 (27).

3.4.2 Environmental Assessment

Table 3.4 shows the key ecotoxicity and fate data for TBBPA.

Table 3.4 Key ecotoxicity and fate data for TBBPA

Acute toxicity	
Algae	EC50(72h) = 0.09-0.89 mg/L
Crustaceans	LC50(48h) =0.96 mg/L
Fish	LC50(96h) =0.40-0.54 mg/L
Chronic toxicity	
Algae	No data.
Crustaceans	NOEC(21d)=0.30 mg/L
Fish	NOEC (35d)=0.16 mg/L
Bioaccumulation	
BCF (Fish)	20-1200
Biodegradation	
Aerobic degradation	Not readily biodegradable
Anaerobic degradation	No data.

3.4.2.1 Acute toxicity

Several data describing the acute toxicity towards algae, invertebrates and fish are available, most of them indicating that TBBPA is highly toxic to aquatic organisms with typical L(E)C50 values < 1 mg/L.

Toxicity to algae

EC_{50} values (72-96h) have been reported for various species of algae and are in the range 0.09->5.6 mg/L. Walsh et al (1987) studied the responses of marine unicellular algae to TBBPA in six different growth media. The 72h EC_{50} values were in the range 0.09-0.89 for ***Skeletonema costatum*** (EC_{50} in natural seawater = 0.55 mg/L) and 0.13-1.0 mg/L for ***Thalassiosira pseudonana*** (EC_{50} in natural seawater = 0.83 mg/L). The growth of ***Chlorella*** sp. was not inhibited by as much as 50% by 1.5 mg/L of TBBPA (96h). For the green algae ***Selenastrum capricornutum***, the reported EC_{50}(96h) > 5.6 mg/L (based on measured concentrations) exceeds the water solubility of TBBPA (26).

Toxicity to invertebrates

For invertebrates, $L(E)C_{50}$ values <1-1.2 mg/L are reported for different species. The 48h acute LC_{50} for ***Daphnia magna*** (less than 20 h old) was 0.96 mg TBBPA/L. At the lowest concentration studied (0.32 mg/L), 5% of the organisms died. The water conditions were: temperature 17.5°C, pH 7.32, and total hardness and total alkalinity, 64 and 32 mg/L, respectively (26).

Goodman et al. (1988) exposed Mysid shrimp ***(Mysidopsis bahia),*** aged < 1, 5, and 10 days old, to TBBPA in a flow-through system for 96 h. The test conditions were: mean salinity 20.6%, pH 7.96-8.16, and mean dissolved oxygen concentration 6.9 mg/L. The TBBPA was dissolved in a mixture of triethylene glycol and acetone. The 96h LC_{50} values for the three live stages were 0.86, 1.1 and 1.2 mg/L, respectively (26).

The acute EC_{50}, defined as reduction of shell deposition, was determined in Eastern oysters ***(Crassostrea virginica)*** in a flow-through system (oysters had a mean valve height of 41 mm). The mean measured test concentrations were 0.018, 0.032, 0.051, 0.087, and 0.150 mg TBBPA/L. Salinity range was 29-32%, dissolved oxygen ranged from 86 to 95% of saturation, pH 8.0-8.1. The 96-h EC_{50} was calculated to be 0.098 mg TBBPA/L with a observed-effect concentration below 0.018 mg/L. An estimated NOEC of 0.0062 mg/L was calculated (Surprenant, 1989c) (26).

Toxicity to fish

The 96-h, acute LC_{50} of TBBPA for bluegill sunfish ***(Lepomis macrochirus;*** 6 months old, length 38 mm, weight 0.59 g) was 0.51 mg/L (nominal concentration), in a static system. The conditions of the water were: temperature 21.7°C, pH 7.47, and total hardness and total alkalinity, 44 mg/L and 33 mg/L as $CaCO_3$, respectively. With dose levels above 0.32 mg/L, the fish became irritated and exhibited abnormal sounding and skittering swimming behaviour. The no-effect concentration was 0.10 mg/L (Calmbacher, 1978a) (26).

The 96h LC_{50} of TBBPA for rainbow trout (***Salmo gairdneri***; 3 months old, length 41 mm, weight 0.51 g) was 0.40 mg/L (nominal concentration) in a static system. The conditions of the water were: temperature 12.3°C, pH 7.48, total hardness and total alkalinity, 40 and 35 mg/L as $CaCO_3$, respectively). The no-effect level was 0.18 mg/L. With higher levels, the fish became irritated and exhibited twitching, erratic swimming, dark discoloration, and laboured respiration (Calmbacher, 1978b) (26).

The LC_{50} of TBBPA for fathead minnow (***Pimephales promelas;*** mean wet weight 0.50 g and total length 36 mm) (20 fish/group) was determined under flow-through conditions. The total duration of the study was 144 h. Well-water was used with total hardness and alkalinity ranges of 22-30 and 21-24 mg/L, as $CaCO_3$, respectively. The pH was 6.7-7.1, the dissolved oxygen concentration range, 91-96% of saturation, and the temperature 21-22°C. The mean measured test concentrations were 0.19, 0.26, 0.32, 0.45, and 0.63 mg/L. The 96h LC_{50} was determined to be 0.54 mg/L with a no-observed-effect concentration of 0.26 mg/L (Surprenant, 1988) (26).

3.4.2.2 Chronic toxicity

Toxicity to invertebrates

Daphnia magna were continuously exposed (flow-through system) for 21 days to measured concentrations of 0.056, 0.10, 0.19, 0.30, and 0.98 mg TBBPA (99.15%)/L. Well water was used with a total hardness of 170 mg/L and an alkalinity of 120 mg/L (both as $CaCO_3$), pH 8.1-8.2, temperature 20°C, and dissolved oxygen of 8.0-8.7 mg/L. At the termination of the study, daphnid survival at all concentrations ranged from 95 to 100%, which was comparable with the 98% survival of control organisms. Daphnid growth, as determined by the measurement of individual body lengths at the end of the test, was also not adversely affected by any of the test concentrations. Reproduction, as determined by cumulative numbers of offspring per female at test termination, was the most sensitive indicator of toxicity of TBBPA for ***Daphnia magna*** in the concentration range tested. Reproduction in 0.98 mg/L was 21 offspring per female, which was significantly less than the reproduction of the pooled control organisms (60 offspring per female). Reproduction at the remaining test concentrations was statistically similar to that of the pooled control organisms. The Maximum Acceptable Toxicant Concentration (MATC) for ***Daphnia magna*** was > 0.30 and < 0.98 mg/L (geometric mean 0.54 mg/L) (Surprenant, 1989b) (26)**.**

A partial life-cycle test with Chironimus tentans (14 days), no effects on survival was observed in the concentration range tested, corresponding to a maximum of 0.045-0.046 mg/L in the interstitial water and 230-340 mg/kg sediment (26).

Toxicity to fish

One study describing the chronic toxicity of TBBPA in fish has been found in the literature. Fathead minnow (***Pimephales promelas***) embryos and larvae were continuously exposed for 35 days (30 days post-hatch) to mean, measured TBBPA concentrations ranging from 0.024 to 0.31 mg/L. The water quality was: mean total hardness 28-29 mg/L and alkalinity 23-24 mg/L (both as $CaCO_3$), pH 7.0-8.2, temperature 24°C, and mean dissolved oxygen 8.1-8.6 mg/L. Observations were made on the survival of organisms at hatch, and survival and growth (wet weight and total length) of larvae after 30 days post-hatch exposure. The survival at the end of the hatching period (day 5) at the highest concentration of 0.31 mg/L was 28% and was significantly less than survival in the control organisms, 84% (pooled control and solvent control data). The survival of embryos exposed to mean concentrations of 0.16, 0.084, 0.040, and 0.024 mg/L ranged from 74 to 90% and was unaffected compared with the control embryos. All larvae exposed to 0.31 mg/L died within the initial 7 days of the post-hatch exposure period. The survival of larvae exposed to the remaining concentrations of TBBPA (0.16-0.024 mg/L) ranged from 87 to 93% and was comparable to survival in the control larvae (93%). At test termination (30 days post-hatch), growth data (total length and wet weight) established that surviving fish at all treatment levels grew at rates comparable to those of the control larvae. The mean length and wet weight of larvae exposed to the mean, measured TBBPA concentration of 0.16 mg/L ranged from 24 to 25 mm and 112 to 126 mg, respectively, and were statistically comparable to those of control larvae (pooled data, 25 mm and 111 mg, respectively). On the basis of adverse effects on embryo and larval survival, the Maximum Acceptable Toxicant Concentration (MATC) of TBBPA for fathead minnow was estimated to be

> 0.16 mg/L and < 0.31 mg/L (geometric mean 0.22 mg/L) Surprenant, 1989a) (26).

3.4.2.3 Microorganisms and terrestrial toxicity

No relevant data found.

3.4.2.4 Bioaccumulation

Bioaccumulation of TBBPA has been studied in both fish and invertebrates. BCF of 20-170 are reported for bluegill sunfish (***Lepomis macrochirus***) after 28 days of exposure to ^{14}C-TBBPA study including a 14 day depuration period. A BCF of 1200 was calculated for fathead minnow (***Pimephales promelas***) after 24 days of exposure to ^{14}C-TBBPA. Following 6 days of depuration, 98% of the accumulated ^{14}C residues were eliminated from the tissues of exposed fish. The whole-body half-life was less than 1 day. An 8 week bioaccumulation study with carp showed BCF in the range 30-341 and 52-485, depending on the exposure concentration. There was no information of whether labelled or unlabelled TBBPA was used (26).

BCF values in the range 240-3200 have been found in a 14 day toxicity study with ***Chironimus tentans*** in sediments with different contents of organic carbon (no indication of whether radiolabelled or unlabelled TBBPA was used)**.** The BCF values increased with decreasing total organic carbon concentrations in the sediments (26).

The BCF was 780 in Eastern Oysters (***Crassostrea virginica***) after 20 days of exposure to ^{14}C-TBBPA. During the 14 day depuration periode, the half-life of the ^{14}C-residues was 3-5 days (26).

The BCF values obtained in studies with fish and oyster were based on studies with ^{14}C-labelled TBBPA, and distinction can thus not be made between parent compound and metabolites. As TBBPA is readily metabolised, the BCF for the parent compound may be overestimated when ^{14}C-labelled TBBPA is used.

3.4.2.5 Aerobic biodegradability

TBBPA did not biodegrade in a BOD test (activated sludge, 14 days), and is thus not considered readily biodegradable. Other degradation studies show that TBBPA is partly degraded in both water/sediment and soil. The half-lives ranged from 48-84 days in a 56 day study of the degradation in a water/sediment system. The half-lives were dependant on the TBBPA concentration and the microbial population. In a soil degradation study, 36%-82% remained after 64 days depending on the soil type. Less than 6% of the applied 14C-TBBPA was mineralised to $^{14}CO_2$ (26).

3.4.2.6 Anaerobic biodegradability

In a soil degradation study, TBBPA was partly degraded with 44%-91% TBBPA remaining in the soil after 64 days, depending on the soil type. Less than 0.5% of the applied 14C-TBBPA was mineralised to $^{14}CO_2$ (26).

3.4.2.7 Abiotic degradation

The calculated half-life of decomposition of TBBPA in water by UVR was 10.2 days in spring, 6.6 in summer, 25.9 in autumn, and 80.7 days in winter. Cloud cover lengthened the calculated half-life by a factor of 2. The water depth influenced the direct photodegradation more as the UV-absorption of the given body of water increased (26).

In photodegradation experiments, TBBPA absorbed onto silica gel was exposed to UVR (254 nm). Eight metabolites were detected. The half-life value for TBBPA obtained in this test was 0.12 days (Bayer, 1990). It is difficult to derive environmental conclusions from the results of these experiments (26).

3.4.2.8 Conclusion

TBBPA is highly toxic to aquatic organisms with typical $L(E)C_{50}$ values < 1 mg/L. The chronic NOEC was 0.16 mg/L in a 35 day embryo-larvae fish test and 0.30 mg/L in a 21 day reproduction test with ***Daphnia magna***. BCF values ranging from 20 to 3200 have been measured in fish and invertebrates. The half-life in fish is less than 1 day. During depuration, most of the accumulated TBBPA (and metabolites) will be eliminated within 3-7 days. The BCF values obtained may be overestimated as ^{14}C-labelled substance was used, which does not allow distinction between parent compound and metabolites. TBBPA is not readily biodegradable. Biodegradation studies showed that TBBPA is partly degraded under both aerobic and anaerobic conditions, in soil, and in river sediment and water. Depending on soil type, temperature, humidity and the composition of the soil, approximately 40-90% of TBBPA remained in the soils after 56-64 days under both aerobic and anaerobic conditions. Because of the high log K_{ow} and low water solubility, the mobility and availability of TBBPA in the environment is expected to be limited. TBBPA is expected to adsorb strongly to sludge during sewage treatment.

The proposed classification in the EU RAR for TBBPA is N; R50/53 based on the high acute toxicity, the lack of biodegradation in standard test for ready biodegradability and the high BCF (>100) measured in fish (27).

3.4.2.9 Predicted No Effect Concentration (PNEC)

No calculations of PNEC have been found in the literature.

3.4.2.10 Data sources

An environmental assessment of TBBPA is not yet included in the final EU RAR. The environmental assessment is primarily based on WHO Environmental Health Criteria (26). Most of the studies herein are well described, and the toxicity data for TBBPA towards aquatic organisms show a large degree of consistence.

3.4.3 Health Assessment

3.4.3.1 Observations in humans

There are no data available on acute or repeated exposure to TBBPA in humans. Data from a modified Draize multiple insult test in humans provide evidence that TBBPA does not have the potential to cause skin sensitisation. Furthermore, there are no case reports of skin or respiratory sensitisation, despite widespread occupational use of TBBPA (27). In a well-conducted chromosomal aberration study using human peripheral lymphocytes, TBBPA tested negative (27).

From these data, TBBPA is expected not to cause skin or respiratory sensitisation.

3.4.3.2 Acute toxicity

Based on LD_{50} values the acute oral and dermal toxicity of TBBPA is low. The oral LD_{50} in rats is > 50 g/kg and in mice >10 g/kg. The dermal LD_{50} is > 10 g/kg (27).

Whole body exposure of rats to aerosol concentrations of 1.3 mg/L for 1 hours or 0.5 mg/L for 8 hours produced no mortality and on necropsy no gross pathological lesions were observed. The results of these studies indicate that the acute inhalation toxicity of TBBPA is low (27).

The acute toxicity of TBBPA is low by oral, dermal and inhalatory exposure.

3.4.3.3 Irritation

In a well-conducted 3 week dermal toxicity study, TBBPA (applied as a paste in physiological saline) was administered to the backs of rabbits at dose levels of 0, 100, 500 and 2500 mg/kg/day, 6 hours/day, 5 days/week. It was unclear from the study report whether the application was occlusive or non-occlusive. Very slight erythema was elicited in some of the rabbits at all dose levels. It appeared on day 3, 2 and 1 respectively in rabbits administered at dose 100, 500 or 2500 mg/kg/day (27).

Other studies showed no signs of irritation to rabbits when applied with 0,5 g TBBPA on abraded or intact skin, with and without occlusion (27).

In a well-conducted study 100 mg TBBPA was applied to the conjunctival sac of the right eye of 6 rabbits. In four animals slight conjunctival redness was observed after 1 hour but not after 24 hours. No other signs of ocular irritation were observed at any other point of time (27).

In a similar study, 100 mg of TBBPA was inserted into the conjunctival sac of the right eye of 6 male albino rabbits. Soon after the instillation of the test material slight lacrimation and conjunctival erythema was observed. These signs had completely disappeared by 24 hours. However, at 48 hours slight conjunctival redness, conjunctival chemosis and iridial irritation was observed. At 72 hours slight conjunctival chemosis and iridial irritation was still observed. At day 7 there were no signs of irritation (27).

There is No data on irritation by inhalation. The only evidence in relation to irritation of the respiratory tract comes from a 14-day inhalation study. Rats were whole body exposed for 4 hours/day, 5 days/week for 2 weeks to an atmosphere containing TBBPA dust at concentrations of 2, 6 or 18 mg/L. Any sign of irritation in this study was interpreted as being due to mechanical irritation resulting from exposure to very high dust concentrations. Furthermore due to the lack of chemical reactivity of TBBPA it was not considered to be irritating to the respiratory tract (27).

TBBPA is not regarded as a skin or eye irritant. There is no data on irritation by inhalation but TBBPA is considered not to be a respiratory irritant.

3.4.3.4 Sensitisation

0.5 g TBBPA was applied occlusively to the shaved flanks of 10 guinea pigs. The animals received 9, 6-hour inductions (applications every other day, 3 times a week for 3 weeks). 14 days after the last induction the animals were challenged using the same concentrations of TBBPA as had been used for induction. 48 hours after the first challenge animals received a second challenge. This study has been criticised for its absence of a negative control. No irritation was elicited at either induction or challenge in the group exposed to TBBPA (27).

In another study the potential of TBBPA to cause skin sensitisation in 12 guinea pigs was evaluated. 0.1% TBBPA was injected intradermally into a shaved area on the right flank. Rather than using a separate group of animals, the negative control was injected into a shaved area on the left flank of all 12 animals. The test and control substances were injected every other day (3 times a week) until each animal had received 10 inducing doses. At 24 and 48 hours post injection, the injection sites were scored for the diameter and the intensity of any erythema and the height of any oedema. 2 Weeks following the final inducing dose, a challenge dose was administered intradermally. 3 treated animals showed a mild skin reaction at the induction site, no treated animal showed a skin reaction at the challenge site. Although the result of this study is negative, the possibility that it is a false negative cannot be excluded. The test substance failed to provoke skin reactions in all but three animals at induction; to maximize the ability of the test substance to elicit a reaction, the dose at induction should be sufficient to elicit an irritant response (27). Furthermore negative data were available from two other skin sensitisation tests, neither of which were conducted to current regulatory standards and both of which are considered to possess methodological weaknesses. Taking all of the strands of evidence into account it was however considered that the sensitisation potential of TBBPA has been adequately examined and TBBPA is considered not to be a skin sensitizer (27).

TBBPA is considered not to be a skin sensitizer. No animal studies have investigated the respiratory sensitisation potential of TBBPA but due to its unreactive nature and the lack of skin sensitisation TBBPA is suggested not to be a respiratory sensitizer.

3.4.3.5 Repeated dose toxicity

In a 90-day study conducted in accordance with GLP and OECD guidelines no toxicologically significant effects were seen following oral exposure of up to a dose of 1000 mg/kg. This is supported by the results of other studies (27).

In a well-conducted 3 week dermal toxicity study, TBBPA was administered to the backs of rabbits at dose levels of 0, 100, 500 and 2,500 mg/kg/day, 6 hours/day, 5 days/week. Each group consisted of 4 male and 4 female animals. The skin of 4 rabbits per group was abraded at the application site twice each week. It is unclear from whether the application was occlusive or non-occlusive. There were no significant signs of irritation. Changes in body weight were similar for all groups and no treatment related changes in haematological, biochemical and urinary parameters were observed. At the end of the administration period animals were sacrificed, necropsied and selected tissues from the control and 2,500 mg/kg group were prepared for histopathological examination. No toxicologically significant compound related lesions were apparent (27). TBBPA was furthermore found to be an agent not causing “bromacne” (27).

In a 14 day inhalation study rats were whole body exposed for 4 hours/day, 5 days/week for 2 weeks to an atmosphere containing TBBPA dust at concentrations of 2, 6 or 18 mg/L. There is no evidence for treatment-related systemic toxicity upon repeated dosage to the highest dose of 18mg/L. Some evidence of local irritation of the eyes and the upper respiratory tract, probably as a consequence of mechanical irritation caused by the very high dust concentration, was seen at all dose levels (27).

Subchronic toxicity of TBBPA is low. TBBPA is not causing bromacne.

3.4.3.6 Genotoxicity

TBBPA has demonstrated consistently negative results in a range of in vitro tests using bacterial strains (Ames test) and yeast both in the presence and absence of metabolic activation. These studies were conducted in a manner largely compatible with current regulatory guidelines. Similarly, in an unconventional in vitro recombination assay, TBBPA tested negative. No in vivo data are available (27).

The available genotoxicity data indicate that TBBPA is negative in standard in vitro test systems. No in vivo data were available, but in view of the negative profile in vitro and given that there are no structural indications that TBBPA would be genotoxic, there are no concerns for this endpoint.

3.4.3.7 Long-term toxicity

Carcinogenicity

There are no studies available on carcinogenicity. However, there is no evidence from the available in vitro mutagenicity data and no indications from repeated exposure studies (for example, no target organ toxicity or proliferative changes) of concerns for carcinogenicity (27).

There are no studies available on carcinogenicity. However, the available in virto mutagenicity studies indicate that TBBPA is not a genotoxic carcinogen.

Reproduction toxicity

Information available from a 2-generation reproductive toxicity study in rats indicates that TBBPA has no toxicologically significant effects on fertility or reproductive performance at doses of up to 1000 mg/kg (27).

The effects of TBBPA on development have been investigated in a pilot range finding study and two standard developmental studies, which involved traditional morphological examination of the foetuses. No evidence of developmental toxicity was seen at doses up to 10,000 mg/kg/d in these studies (27).

In addition, 2 well-conducted developmental neurotoxicity studies have been conducted in rats. The rat studies involved exposure of mothers during pregnancy and lactation periods. The first study was part of a 2-generation study and included behaviour and learning/memory tests, specialised neurohistopathology and morphometric examination of the brain. This study provided no convincing evidence of an adverse effect on neurodevelopment at dose levels up to 1000 mg/kg/d. The second study included behaviour and learning/memory tests, neurohistochemistry, but no specialised neurohistology. Pregnant rats were administered 0, 50 or 250 mg/kg/d TBBP-A by gavage in peanut oil from gestation day 7 to postnatal day 17 and a neurobehavioral assessment was carried out on weanling rats. The study showed limited evidence of changes in the habituation behaviour of female offspring and learning and memory in male offspring in the 250 mg/kg/d group. However, it is not possible to draw definitive conclusions from this study because the size of the reported changes was very small and there was not a convincingly consistent pattern of changes in investigations conducted at different time points. Also, the evidence of developmental neurotoxicity is weakened by absence of consistent changes in the two genders, the lack of histopathological investigations that could provide corroborative findings, and the lack of any similar findings in the first study at dose levels of 100 and 1000 mg/kg/d (27).

One or two Member States were of the opinion that an effect on neurobehavioural development was observed and that a NOAEL of 50 mg/kg/day could be derived. However, the majority of Member States were in agreement with the above conclusion.

In a non-standard study an effect on the kidneys of newborn rats dosed from day 4 up to day 21 after birth by gavage with 200 and 600 but not 40 mg/kg TBBPA was reported. A NOAEL of 40 mg/kg/day was identified in this study. No similar effect was observed in 5-week old rats administered by gavage 2,000 and 6,000 mg/kg TBBPA for 18 days and in a comprehensive GLP- and OECD-compliant rat 2-generation study with gavage doses of up to 1,000 mg/kg/day. It is noted that in this 2-generation study the pups might have been exposed to TBBPA indirectly via lactation. In view of this, it can be concluded that the kidney changes reported above are likely to be the consequence of the unconventional direct gavage administration of very high doses of TBBPA to such young animals, which appear to be more susceptible than adult animals to the nephrotoxic effects of TBBP-A. This is likely to be due to the immature metabolic capability and/or the immature kidneys of such young animals (27).

The proliferation of human breast cancer cells (MCF-7 cells) was used as a means of assessing the oestrogenic potential of TBBPA at concentrations between 10-9 M and 10 4 M. Overall, the weight of evidence from in vitro screening assays indicates that TBBPA has no significant oestrogenic potential (27).

In vitro studies have demonstrated that TBBPA has a high potency in competing with T4 for binding to TTR in animals, however no firm conclusions regarding the affinity of TBBPA for TTR in vivo can be drawn from the limited data available (27).

One or two Member States expressed concern regarding the significance for human health of the decreases in T4 levels observed in the rat. However, the majority of Member States agreed with the conclusion that these effects are considered being non-adverse.

In vitro study has shown that TBBPA causes inhibition of neurotransmitter uptake and affects membrane potential in rat brain synaptosome. No conclusions can be drawn about extrapolation of these findings to the in vivo situation (27).

TBBPA has no toxicologically significant effects on fertility or reproduction at doses of up to 1000 mg/kg and no developmental effects was seen at doses up to 10,000 mg/kg. Based on exposure of newborn rats a NOAEL of 40 mg/kg/day was identified. Overall, the data do not provide strong evidence of the potential for TBBPA to act as a developmental toxicant, a neurotoxicant or as an endocrine disruptor.

3.4.3.8 Toxicokinetics

The available data indicate that TBBPA is absorbed in humans given that it has been detected in serum samples of both occupational and non-occupational groups. There is also evidence that once absorbed, TBBP-A and/or its metabolites can be excreted via breast milk (27).

In experimental animals, toxicokinetic data are available in the rat only. Following oral exposure, 100% of the administered dose of TBBP-A is absorbed from the gastro-intestinal tract. Following oral administration, TBBPA and/or its metabolites are excreted predominantly in the faeces (approximately 95 % of the administered dose) within 72 h post-administration, with only a small amount (< 1 %) eliminated through the urine (27).

One or two Member States expressed concern over the oral absorption of undissolved TBBP-A particles, particularly when administered as a suspension at high dose levels. In the opinion of these Member States, there was some uncertainty as to whether 100% of the administered dose would be absorbed at these higher dose levels and consequently whether the dosing of particles in suspension will underestimate the toxicity. However, although this concept is important, the majority of Member States agreed upon that the data do not allow a quantitative estimate of oral absorption at such high dose levels to be determined. Therefore, it was agreed to assume that 100% of an orally administered dose of TBBP-A is absorbed.

Toxicokinetic studies following inhalation and dermal exposure have not been conducted. Predictions of the fate of TBBPA following exposure can however be made based on its physico-chemical properties. Following inhalation of TBBPA particles, approximately 70 % of particles will be available for absorption through the gastrointestinal tract with only a small fraction (< 4 %) being absorbed through the lungs. Regarding dermal exposure, the low water solubility, the high n-octanol/water partition coefficient (5.9), and the high molecular weight (>500) of TBBPA, suggest dermal absorption would be low. In view of this a default value of 10% will be assumed for dermal exposure, as indicated in the EU Technical Guidance Document (TGD) (3).

Following intraperitoneal administration, a similar faecal excretion profile is reported, though characterisation of the faecal radioactivity revealed that the majority appeared as unchanged, parent compound (27).

As the majority of TBBPA is excreted within 72 h after administration, no evidence suggests that it has the potential to bioaccumulate.

3.4.3.9 Conclusion

There are No data available. on acute or repeated exposure to TBBPA in humans. The available data indicate that TBBPA is absorbed in humans given that it has been detected in serum samples of both occupational and non-occupational groups. There is also evidence that once absorbed, TBBPA and/or its metabolites can be excreted via breast milk.

Based on animal data the acute oral, dermal, and respiratory toxicity of TBBPA is low. TBBPA is not regarded as a skin or eye irritant and due to the lack of chemical reactivity of TBBPA it not considered to be irritating to the respiratory tract neither. TBBPA is furthermore not considered to be a skin or respiratory sensitizer.

The available genotoxicity data indicate that TBBPA is negative in standard ***in vitro*** test systems. There are no studies available on carcinogenicity, but data indicates no concern for carcinogenic effect. Data on reproduction do not provide strong evidence of the potential for TBBPA to act as a developmental toxicant or neurotoxicant. ***In vitro*** study has shown that TBBPA causes

inhibition of neurotransmitter uptake and affects membrane potential in rat brain synaptosome. No conclusions can however be drawn about extrapolation of these findings to the in vivo situation.

Furthermore, the data indicates that TBBPA has no significant oestrogenic potential and no firm conclusions regarding the affinity of TBBPA for TTR in vivo can be drawn.

Based on adverse effects on the kidneys of newborn rats dosed with TBBPA by gavage a NOAEL of 40 mg/kg/day was identified.

3.4.3.10 Data sources

The data sources are used as quoted in EU RAR (27).

3.4.4 Critical effects

3.4.4.1 CMR

There are no studies available on carcinogenicity. However, there is no evidence from the available in vitro mutagenicity data and no indications from repeated exposure studies of concerns for carcinogenicity. TBBPA has demonstrated consistently negative results in a range of ***in vitro*** mutagenicity tests using bacterial strains and yeast both in the presence and absence of metabolic activation. No in vivo data are available. TBBPA has no toxicologically significant effects on fertility or reproduction at doses of up to 1000 mg/kg and no developmental effects was seen at doses up to 10,000 mg/kg.

3.4.4.2 Endocrine disruption

The proliferation of human breast cancer cells (MCF-7 cells) was used as a means of assessing the oestrogenic potential of TBBPA at concentrations between 10^{-9} M and 10^{-4} M. Overall, the weight of evidence from in vitro screening assays indicates that TBBPA has no significant oestrogenic potential. In vitro studies have demonstrated that TBBPA has a high potency in competing with T4 for binding to TTR in animals; however no firm conclusions regarding the affinity of TBBPA for TTR in vivo can be drawn from the limited data available.

3.4.4.3 Sensitisation

Taking all strands of evidence into account it is considered that the sensitisation potential of TBBPA has been adequately examined and TBBPA is considered not to be a skin sensitizer.

3.4.4.4 Summary of critical effects

There are no studies available on carcinogenicity. However, there is no evidence of concern for carcinogenic potential. The available genotoxicity data indicate that TBBPA is negative in standard in vitro test systems. No in vivo data are available, but in view of the negative profile in vitro and given that there are no structural indications that TBBPA would be genotoxic, there are no concerns for this endpoint. Furthermore the data do not provide strong evidence of the potential for TBBPA to act as a developmental toxicant or as an endocrine disruptor. TBBPA is considered not to be a skin sensitizer. No animal studies have investigated the respiratory sensitisation potential of TBBPA but due to its unreactive nature and the lack of skin sensitisation it is suggested not to be a respiratory sensitizer.

3.4.5 PBT assessment

3.4.5.1 Persistence

TBBPA is not readily biodegradable. Simulation type studies in water/sediment and soil show half-lifes ranging from 48-84 days and indicate only partial degradation of TBBPA. Studies in soil under aerobic and anaerobic conditions likewise indicate partial degradation of TBBPA, but no half-lives were reported for these studies (26). Based on the above studies, TBBPA is considered to fulfil the P and vP criteria (half-life > 40 days and >60 days in freshwater, respectively).

3.4.5.2 Bioaccumulation

The maximum BCF for TBBPA has been obtained in ***Chironimus tentans*** (range 650-3200 in low organic carbon sediments) whereas BCF in studies with three different fish species attained a maximum of 1200. The large BCF range stated for ***Chironimus tentans*** indicates some uncertainty in the BCF estimate, and the studies conducted with fish are considered more representative. Thus, TBBPA is not considered to fulfil the B criteria (BCF > 2000) as the validity of the results obtained for ***Chironimus tentans*** can be questioned.

3.4.5.3 Toxicity

TBBPA is toxic towards aquatic organisms (L(E)C50 < 1 mg/L). Chronic NOEC values of 0.16 mg/L and 0.30 mg/L has been obtained in embryo-larvae test with fish and in a reproduction study with ***Daphnia magna***, respectively. Based on these data, TBBPA does not meet the T criterion (long-term NOEC <0.01 mg/L in fresh-water or marine organisms).

3.4.5.4 Summary of PBT assessment

Based on the available data, TBBPA is considered to be very persistent (vP), but not the vB critierium. TBBPA is not considered to fulfil the B or the T criteria.

3.4.6 Comparison with deca-BDE

The key toxicological and environmental properties of TBBPA are compared to those of deca-BDE and summarised in Table 3.5. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.5 Summary of toxicological and environmental properties of TBBPA and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that No data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
TBBPA[1]	79-94-7	n.d.	-	-	(-)	-	+	-	-
Deca-BDE	1163-19-5	(-)	-	(-)	?	(-)	+	-	-

[1] Assessment for unreacted TBBPA

The hazardous properties assessed here relates to the TBBPA as a raw material flame retardant. It should be noted that in the actual use TBBPA in Western Europe is used mainly reactively rather than additively. This entails that TBBPA is bound covalent to the polymer and it is therefore not

bioavailable in the products. The toxicological and environmental effects will be related only to a fraction of TBBPA which may be unreacted, and the impact will be dramatically reduced in such cases.

3.5 Tetrabromobisphenol A carbonate oligomer (TBBPA carbonate oligomer)

This assessment considers phenoxy-terminated tetrabromobisphenol-A carbonate oligomer (BC-52) and tribromophenoxy-terminated tetrabromobisphenol-A carbonate oligomer (BC-58) and the data given here are excerpts from the final EU Risk Assessment Report (2006) on 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (27) and Environmental Health Criteria on Tetrabromobisphenol A and Derivatives from WHO (26).

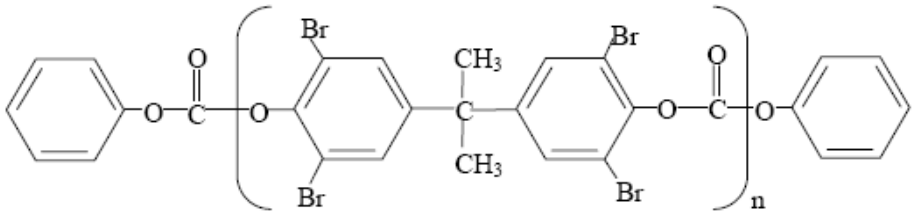
3.5.1 Substance Identification and Physical-Chemical Data

3.5.1.1 Identification

TBBPA carbonate oligomer has the following key identification data:

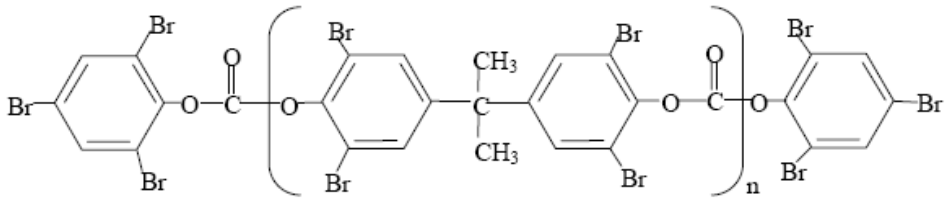
CAS Number BC-52: 94334-64-2
CAS Number BC-58: 71342-77-3
EINECS Number: -
IUPAC Name: -
Molecular Formula BC-52: $(C_7H_5O_2)$ $(C_{16}H_{10}Br_4O_3)_n$ (n= 3-5)
Molecular Formula BC-58: $(C_7H_2Br_3O_3)$ $(C_{16}H_{10}Br_4O_3)_n$ (C_6H_2Br)(n= 3-5)

Structure formula BC-52:



n = 3-5

Structure formula BC-58:



n = 3-5

The main use of these derivatives is as flame retardants, usually in niche applications.

3.5.1.2 Physical chemical properties

According to the MSDS for the commercial product BC-52, TBBPA carbonate oligomer is insoluble in water. No other relevant information regarding the physical-chemical properties have been found in the literature.

3.5.2 Environmental Assessment

3.5.2.1 Acute toxicity
No data found..

3.5.2.2 Chronic toxicity
No data found..

3.5.2.3 Microorganisms and terrestrial toxicity
No data found..

3.5.2.4 Bioaccumulation
No data found..

3.5.2.5 Aerobic biodegradability
No data found..

3.5.2.6 Anaerobic biodegradability
No data found..

3.5.2.7 Abiotic degradation
No data found.

3.5.2.8 QSAR data
No data available.

3.5.2.9 Conclusion
No data regarding the environmental properties of TBBPA carbonate oligomer have been found. The environmental assessment of TBBPA carbonate oligomer is thus based on the monomer TBBPA, as presented in chapter 3.4.4.

3.5.3 Health Assessment

3.5.3.1 Observations in humans
There are no data available on acute or repeated exposure to TBBPA oligomers in humans (26).

3.5.3.2 Acute toxicity
Based on LD_{50} values the acute oral and dermal toxicity of the TBBPA oligomers are low. The oral LD_{50} in rats is > 5 g/kg and the dermal LD_{50} is > 2 g/kg (26).

3.5.3.3 Irritation
BC-52 and BC-58 are not primary skin or eye irritants (26).

3.5.3.4 Sensitisation
No data.

3.5.3.5 Repeated dose toxicity
No data.

3.5.3.6 Genotoxicity
BC-52 and BC-58 were tested in 5 strains of Salmonella typhimurium at doses ranging from 100 to 10,000 g/plate, in the presence, and absence, of metabolic activation. Both gave negative results (26).

A few data indicate that BC-52 and BC-58 are not mutagenic.

3.5.3.7 Long-term toxicity

Carcinogenicity
No data.

Reproduction
No data.

3.5.3.8 Toxicokinetics

No data.

3.5.3.9 Conclusion

No data were available on acute or repeated exposure to BC-52 and BC-58 in humans. Based on animal data the acute oral and dermal toxicity of the two oligomers are low. They are not regarded as skin or eye irritants. There are no studies available on long term exposure to TBBPA oligomers. BC-52 and BC-58 gave negative results when tested in 5 strains of ***Salmonella typhimurium*** at doses ranging from 100 to 10,000 g/plate.
Since there is a lack of toxicologically data available on the two oligomers it is a common scientific procedure to evaluate the potential health hazards of the monomeric constituents of the oligomers. Tetrabromobisphenol-A carbonate oligomers are produced by a reaction of TBBPA with phosgene. For further toxicological information refer to the presented data on TBBPA in chapter 3.5.3.

3.5.3.10 Data sources

The data sources are used as quoted in EU RAR (27) and IPCS (28).

3.5.4 Critical effects

3.5.4.1 CMR

There are no studies available on carcinogenicity. BC-52 and BC-58 gave negative results when tested in 5 strains of ***Salmonella typhimurium*** at doses ranging from 100 to 10,000 µg/plate. There are no studies available on reproduction toxicity of TBBPA oligomers.

3.5.4.2 Endocrine disruption

There are no studies available on the ability of TBBPA oligomers as endocrine disruptors.

3.5.4.3 Sensitisation

There are no studies available on the ability of TBBPA oligomers to cause sensitisation.

3.5.4.4 Summary of critical effects

There are no studies available on carcinogenicity, reproduction toxicity, endocrine effects or sensitisation. A few data indicates that the TBBPA oligomers are not mutagenic.

3.5.5 PBT assessment

No data regarding the environmental properties of TBBPA carbonate oligomer have been found. The PBT assessment of TBBPA carbonate

oligomer is thus based on the monomer TBBPA, as presented in chapter 3.4.2.

Thus, TBBPA carbonate oligomer is considered to be very persistent (vP), but not the vB critierium. TBBPA is not considered to fulfil the B or the T criteria.

3.5.6 Comparison with deca-BDE

The key toxicological and environmental properties of TBBPA carbonate oligomer are compared to those of deca-BDE and summarised in Table 3.6. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.6 Summary of toxicological and environmental properties of TBBPA carbonate oligomer and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
TBBPA carbonate oligomer	79-94-7	n.d.	(-)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
TBBPA[1]	79-94-7	n.d.	-	-	(-)	-	+	-	-
Deca-BDE	1163-19-5	(-)	-	(-)	?	(-)	+	-	-

As seen in Table 3.5, no data regarding the environmental and toxicologivcal properties except from a genotoxicity study of TBBPA carbonate oligomer have been found. The comparison of key toxicological and environmental profiles of TBBPA carbonate oligomer and deca-BDE is therefore based on the evaluation of TBBPA, as presented in chapter 3.4.5. It should be noted that due to the oligomeric nature of TBBPA carbonate the vast majority of TBBPA is not bioavailable in the flame retardant product. The toxicological and environmental effects will be related only to a fraction of TBBPA which may be unreacted and monomeric. The impact of polymers and oligomers is dramatically reduced compared to monomers (27).

3.6 Triphenyl phosphate (TPP)

Triphenyl phosphate (TPP) is a non-flammable, non-explosive, colourless, crystalline organophosphorus substance with extensive use as a plasticiser and a flame-retardant (7).

3.6.1 Substance Identification and Physical-Chemical Data

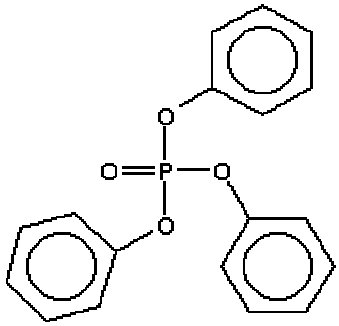
3.6.1.1 Identification

Triphenyl phosphate (TPP) has the following key identification data:

CAS Number: 115-86-6
EINECS Number: 204-112-2
EINECS Name: Triphenyl phosphate

Molecular formula: $C_{18}H_{15}O_4P$
Molecular weight: 326.3

Structural formula:



3.6.1.2 Physical chemical properties

The reported solubility data indicate that TPP is slightly soluble in water with aqueous solubility values in the range 0.75-2.1 mg/L. Both experimental and estimated log K_{ow} values are in good agreement and are within the range 4.58-4.67 (selected data reported in appendix). A vapour pressure of $6.28 \cdot 10^{-6}$ mmHg (25°C) has been extrapolated using experimentally derived parameters (29).

3.6.2 Environmental Assessment

Table 3.7 shows the key ecotoxicity and fate data for TPP.

Table 3.7 Key ecotoxicity and fate data for TPP

Acute toxicity	
Algae	EC50(96h) = 2 mg/L NOEC(72h) = 0.1-1 mg/L
Crustaceans	LC50(48h) =1-1.35 mg/L
Fish	LC50(96h) =0.36-1.2 mg/L
Chronic toxicity	
Algae	NOEC(22d) = 0.1 mg/L
Crustaceans	No data.
Fish	(NOEC (30d)=0.087 mg/L)*
Bioaccumulation	
BCF (Fish)	84-271
Biodegradation	
Aerobic degradation	Inherently biodegradable, degrades rapidly in pond and river sediment
Anaerobic degradation	Partially degradable in river sediment and soil

*Validity of study is questionable

3.6.2.1 Acute toxicity

A large number of acute studies in algae, invertebrates and fish are available, most of them indicating that TPP is moderately to highly toxic to aquatic organisms.

Toxicity to algae

For algae, typical NOEC values (72-96h) are in the range 0.1-1 mg/L for a range of species: ***Pseudokirchneriella subcapitata*** EC_{50}(96h)=2 mg/L (approximates the water solubility limit), NOEC(72h)=0.1-1 mg/L, ***Chlorella***

vulgaris NOEC(72h)=1 mg/L, ***Scenedesmus subcapitatus*** NOEC(72h)=0.1-1 mg/L (29). The above values are all based on nominal concentrations, and analytical validation of the exposure concentrations was not performed. The EC_{50}/NOEC values obtained for different algal species are rather consistent. The 72h studies were based on OECD Test Guideline No. 201.

Toxicity to invertebrates

$L(E)C_{50}$ values in the range 1-1.35 mg/L (48h) are reported in four studies with ***Daphnia magna*** (29). According to the evaluation of the studies performed in the report "Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam" (published by US EPA) (29), some reporting deficiencies (e.g. lack of identity of exposure concentrations, TPP purity, solvent concentrations, analytical confirmation of test concentrations) were observed in all studies. However, due to the conformity of the results, the data appear adequate for providing confidence in the reported effect concentrations (29). $L(E)C_{50}$ values < 1 mg/L (96h) have been reported for other invertebrates, e.g. scud (***Gammarus pseudolimnaeus***) and mysid shrimp (***Mysidopsis bahia***) (29).

Toxicity to fish

In numerous studies with fish, typical $L(E)C_{50}$ values are in the range < 1 mg/L (96h) for various species (see appendix). In the report "Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam" (published by US EPA) (29) it was stated that sufficient detail was not included in many of the study reports in order to allow for a comprehensive and independent evaluation of the data adequacy. Many of the studies were conducted prior to introduction of the OECD GLP principles. Looking at the conformity of most of the results presented (96h $L(E)C_{50}$ values ≤ 1 mg/L), the acute fish toxicity is adequately described by the studies reported. Single studies, however, report much higher $L(E)C_{50}$ values (LC_{50}(96h)=95 mg/L, ***Menida beryllina***, and LC_{50}(96h)=290 mg/L, ***Lepomis macrochirus***). These results are, however, inconsistent with the results from multiple other studies, and the reported LC_{50} values exceed the water solubility of TPP by approximately 50-150 times (29).

3.6.2.2 Chronic toxicity

Toxicity to fish

Two chronic toxicity studies with fish have been found in the literature reviewed. In a 30 day study with fathead minnow (***Pimephales promelas***) the NOEC value was 0.087 mg/L for survival of fry. In a 90 day study with rainbow trout (***Salmo gairdneri***) the NOEC value was 0.0014 mg/L for survival, growth, deposits of vertebral collagen and cataract formation. Both studies have been reviewed in the US EPA published report "Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam" (29). The study with fathead minnow was considered invalid due to large variation in the measured concentrations, and the study with rainbow trout was considered inadequate since the NOEC value obtained was equal to the highest concentration level tested (no effects seen), and since measured concentrations were not stated.

3.6.2.3 Microorganisms and terrestrial toxicity

No data found.

3.6.2.4 Bioaccumulation

Several studies of bioaccumulation in fish have been reported in the literature. Two 90 day studies report similar BCF values of 271 and 132-364, respectively, for rainbow trout (***Salmo gairdneri***). A BCF of 110-150 has been obtained in a 2-3 day study with goldfish (***Carrasius auratus***), and BCF values in the range 84-189 have been obtained in a 18-35 day study with killifish (***Oryzias latipes***). Other, short-term BCF values in fish (<24h) have been found in the literature, but the results of these studies are not considered to represent equilibrium conditions (29).

3.6.2.5 Aerobic biodegradability

No data are available on ready biodegradability. TPP is inherently biodegradable (83-94% degradation after 28 days, MITI II test) and TPP biodegrades in sludge (94% after 14 days, OECD 303A), in water/sediment systems and soil under aerobic conditions. Degradation half-lives range from 3-60 days under various conditions in water/sediment/pond systems (2-25°C). In the experiment with soil (loamy sand soil, 20°C), identified metabolites were diphenyl phosphate and CO_2 (29).

3.6.2.6 Anaerobic biodegradability

TPP has been found to degrade under anaerobic conditions in water/sediment systems and in soil. In a river sediment (sediment: water ratio 1:20), 10.3% of the initially added TPP remained after 40 days (25°C). In a loamy sand soil, 50.2% and 31.4% of the initially added TPP remained after 32 and 101 days, respectively (20°C). Identified metabolites were diphenyl phosphate, phenol and CO_2 (29).

3.6.2.7 Abiotic degradation

TPP is rapidly hydrolysed in water with half-lives between 1.3 and 19 days under different experimental conditions. TPP has been found to photodegrade 100% after 1-6 hours (7,29).

3.6.2.8 Conclusion

The environmental properties of TPP are well described in the literature reviewed. TPP is highly toxic to algae, invertebrates and fish with typical $L(E)C_{50}$ values <1 mg/L. Two studies of the chronic toxicity in fish report NOEC values in the range 0.014-0.23 mg/L, however, the validity of the studies are questionable. BCF values >100 have been reported in several long-term studies with different species of fish, and TPP is considered to be potentially bioaccumulable. This is supported by the log K_{ow} value for TPP (range 4.58-4.67). TPP is inherently biodegradable, and is furthermore found to biodegrade under both aerobic and anaerobic conditions in water/sediment and soil systems under various conditions. The log K_{ow} and log K_{oc} values indicate that the availability and the mobility of TPP in the environment is limited.

3.6.2.9 Predicted No Effect Concentrations (PNEC)

No calculations of PNEC have been found in the literature.

3.6.2.10 Data sources

The presented data for TPP are gathered and reviewed in the US EPA published report "Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam" (29). All studies are reviewed and are well described in the report. The majority of the studies reported are conducted according to

standardised guidelines (OECD, EPA). Many of the studies reported are of older date (>20 years) and are published prior to introduction of the OECD GLP principles.

3.6.3 Health Assessment

3.6.3.1 Observations in humans:

No neurological disease or signs of other clinical abnormalities were recorded in workers exposed to triphenyl phosphate vapour, mist, or dust for at medium period of 7.4 years at a time-weighted average air concentration of 3.5 mg/m^3 of respirable particle size. Six regularly exposed workers had asymptomatically reduced erythrocyte but not plasma cholinesterase levels (30).

This work is dated and not in accordance with any guideline but is of good credibility both with respect to the environmental and the clinical examinations. It is published in a peer reviewed journal.

A number of studies have tested the number of verified cases of sensitisation and contact allergy to triphenyl phosphate and found a low number of cases, whether in an occupational contact allergy survey where triphenyl phosphate was found in the patch material or among persons showing allergic reactions to plastic spectacle frames (31,32,33,34). Triphenyl phosphate is not a potent sensitizer. All the quoted studies are published in peer reviewed dermatology journals and the results seem reliable.

Triphenyl phosphate (TPP) did not cause significant suppression of an antigen–specific lymphocyte proliferation ***in vitro*** in seeded human lymphocytes treated with either phytehaemagglutinin or tetanus toxoid antigen. Triphenyl phosphate therefore did not suppress immune responses in human lymphocytes ***in vitro*** (35). The study which is not a guideline study seems well performed and the validity of the system was demonstrated as TPP caused a 60% reduction in a control experiment using untreated cells. It is also published in a peer reviewed journal.

The calculated intake of triphenyl phosphate in each of the 8 age groups, in ng/kg bw/day was:

6–11 month olds – 0.3,
2 year olds – 4.4,
14–16 year old males – 1.2,
14–16 year old females – 1.6,
25–30 year old males – 1.6,
25–30 year old females – 0.8,
60–65 year old males – 0.5 and
60–65 year old females – 0.5.

These levels were considered safe (36). This study is a US Food and Drug Administration total diet study and the results seem reliable.

No neurological or clinical effects could be demonstrated in humans exposed via occupation for an average of 7.4 years. The skin sensitising potential of TPP seems to be very low. Both exposure of the general population and occupational exposure to triphenyl phosphate are low.

3.6.3.2 Acute toxicity

The acute oral LD_{50} values of triphenyl phosphate in rats vary between 3500 and 10800 mg/kg bw in various studies. In one study performed in mice the oral LD_{50} was reported to be 1300 mg/kg bw whereas in another reported study on single oral dose toxicity in mice the LD_{50} value exceeded 3000 mg/kg bw. No lethality was recorded of single oral doses of 3000 mg/kg bw in rats or mice or of 4000 mg/kg bw in cats in other studies. In hens where the delayed neurotoxicity of organo-phosphorus compounds is normally examined single oral doses up to 20,000 mg/kg bw caused neither lethality nor delayed neurotoxicity (7).

The dermal LD_{50} was reported to exceed 10,000 mg/kg bw in rabbits and a single dermal application of 7900 mg/kg bw for 24 hours in the same species did not result in mortality (7).

No data were identified with respect to acute inhalational toxicity of triphenyl phosphate.

A number of single dose studies with triphenyl phosphate administration via the subcutaneous, intramuscular or intraperitoneal way in various mammal species have been found all indicating low toxicity by parenteral routes as well (7).

The data on the acute toxicity are all cited from IUCLID and the only attempt that has been made to verity the data further was for the fairly low oral LD_{50} value in mice (dated 1975). This reference could not be obtained.

For many years it was thought that parenteral administration of triphenyl phosphate (TPP) even in single doses to cats caused delayed neurotoxicity and axon degeneration or demyelination of axons. However, in 1979 studies were performed from which is could be concluded that triphenyl phosphate is not neurotoxic in the cat. The earlier studies were complicated by the fact that TPP prepared from coal–tar sources contains impurities which are neurotoxic (37). Although this study is not performed according to any standards or with any mention of GLP, it was published in a peer reviewed journal, and the quality of the study seems to be high and the conclusions seem reliable.

Irrespective of the route of administration and the species examined triphenyl phosphate shows low toxicity in mammals.

3.6.3.3 Irritation:

Triphenyl phosphate is reported not to be irritating to rabbit or rat skin in a series of guideline and non-guideline studies (7).

The data on skin irritation are all cited from IUCLID and no attempts have been made to verity the data further.

Only one study on eye irritation has been available and only in a IUCLID (7) summary version (Ciba-Geigy Pharmaceutical Division data):
“In rabbits: slightly irritating leading to an EU classification as “irritating to the eye” (signs of irritation were observed in all animals during the first 24 hours post-dose. Unwashed eyes returned to normal later than washed. All eyes had returned to normal by day 6)”.
However, triphenyl phosphate shall not be labelled as dangerous to the eye in according to the “Hazardous Substances List”.

Triphenyl phosphate produces no skin irritation, whereas the eye irritation cannot be evaluated.

3.6.3.4 Sensitisation

No studies have been found on the studying of triphenyl phosphate with respect to sensitising potential in animals.

The skin sensitising properties have not been examined in animals. (However, a high number of patch-testing with TPP in humans indicate that the sensitising potential of the substance is low.)

3.6.3.5 Repeated dose toxicity

In a 35-day feeding study 5 male rats/dosing group were administered triphenyl phosphate at dietary concentrations of 0, 1000 and 5000 ppm. A depression of body weight gain and an increase of liver weight were observed in the high-dose group. No haematological changes were reported (30). Due to the low number of animals, and a change in the dosing regimen in the low dose group after 3 days (from 50,000 to 1000 ppm) the study is not found reliable.

The only effects noted were a decreased rate of growth at high levels of triphenyl phosphate and increased levels of - and ß-globulins when triphenyl phosphate was fed to weanling Sprague-Dawley rats (10/sex/dose) at dietary concentrations of 0, 2500, 5000, 7500, or 10,000 ppm for 120 days. No significant effects on the response were noted for either sex at any of the dose levels tested (38).
The data from this study are regarded as reliable and of good quality and they were published in a peer reviewed journal. The study was not performed according to any standards, and there is no mention of GLP, but since the study was performed at the US Food and Drug Administration's Division of Toxicology GLP is assumed.

Male rats exposed for 4 months to dietary concentrations of 2500, 5000, 7500, or 10,000 ppm triphenyl phosphate, corresponding to mean daily intakes of triphenyl phosphate of 161, 345, 517 or 711 mg/kg bw/day showed statistically significantly decreased weight gain throughout the study for the 5000 and the 10,000 ppm dose groups, but only for the first period of the study for the 7500 ppm dose group. No treatment related effects were noted for any behavioural measures at any of the monthly test sessions. (39).
The data from this study are regarded as reliable and of good quality and they were published in a peer reviewed journal. The study was not performed according to any standard guidelines, and there is no mention of GLP, but since the study was performed at the US Food and Drug Administration's Division of Toxicology GLP is assumed.

The only sensitive parameter noted following repeated dose administration of triphenyl phosphate to rats was the weight gain especially during the early dosing periods. In the only study where a NOAEL could be identified this was 2500 ppm in the diet corresponding to 161 mg/kg bw/day in male rats.

3.6.3.6 Genotoxicity

Negative results were reported with triphenyl phosphate (TPP) in a paper disk method using streptomycin-dependent mutants of ***Escherichia coli*** (40).

Triphenyl phosphate (TPP) did not demonstrate mutagenic activity in microbial assays employing ***Salmonella typhimurium*** (TA 1535, TA 1537, TA

1538, TA 98, and TA 100 strains) and ***Saccharomyces cerevisiae*** (D4 strain) indicator organisms. All studies were carried out both with and without metabolic activation (Monsanto 1979) (40).

Negative results were also reported in Ames tests conducted in accordance with a protocol approved by the National Toxicology Program with ***Salmonella typhimurium*** strains TA 98, TA 100, TA 1535, and TA 1537, in the absence or presence of rat liver S9 (41).

The data from the four studies on mutagenicity and genotoxicity are regarded as reliable and of good quality by a WHO expert group who quoted them in an WHO/IPCS publication Environmental Health Criteria 111 on triphenyl phosphate (40).

TPP has not shown mutagenic or genotoxic effects in vitro and no in vivo examinations for this endpoint have been found.

3.6.3.7 Long term toxicity

Carcinogenicity

The occurrence of lung adenomas in strain A/St male mice was studied using doses of 80, 40, or 20 mg TPP/kg bw injected intraperitoneally 1, 3, and 18 times, respectively, into groups of 20 mice. Twenty-four weeks after the first injection, the animals were sacrificed, and the frequency of lung tumours was compared with that in the control group of 50 animals treated with tricarpylin (vehicle). The pulmonary adenoma response to TPP was not significantly greater than the response of the control mice.

This study has been considered inadequate by the WHO/IPCS expert group producing the Environmental Health Criteria 111 on triphenyl phosphate (40) due to low survival of animals in two of the three experimental groups and the short duration of the study (42).

There are no data from which one can adequately conclude with respect to the carcinogenic properties of TPP.

Reproduction toxicity

Sprague-Dawley (Spartan) rats (40/sex/dose) were fed dietary levels of 0, 2500, 5000, 7500, or 10,000 ppm (= mg triphenyl phosphate (TPP)/kg feed) from 4 weeks post weaning for 91 days, through mating and gestation. At these dietary levels, the daily intake of TPP during pregnancy was 0, 166, 341, 516, and 690 mg/kg bw, respectively. TPP exposure had no toxic effects on mothers or offspring at these dosages. It could be concluded that triphenyl phosphate was not teratogenic in Sprague-Dawley rats at the levels tested (43). The NOAEL was 690 mg/kg bw. Although no reference was given to a testing guideline or to GLP the protocol is in accordance with the OECD Guideline for the Testing of Chemicals no. 414 (Prenatal Developmental Toxicity Study). The results and conclusions are considered reliable.

TPP is not teratogenic and does not affect the fertility in rats when administered to male and female rats from shortly post weaning, through mating and gestation in dietary daily doses up to 690 mg/kg bw (NOAEL).

Neurotoxicity

Smith and coworkers found that single and multiple doses of technical grade triphenyl phosphate produced generalised delayed paralysis in cats and monkeys but not in chickens or rabbits (40).

These studies have not been available for direct evaluation (published in 1930) but are cited here from Environmental Health Criteria 111 on triphenyl phosphate.

Male rats exposed for 4 months to dietary concentrations of 2500, 5000, 7500, or 10,000 ppm triphenyl phosphate, corresponding to mean daily intakes of triphenyl phosphate of 161, 345, 517 or 711 mg/kg bw/day showed statistically significantly decreased weight gain throughout the study for the 5000 and the 10,000 ppm dose groups, but only for the first period of the study for the 7500 ppm dose group. No treatment related effects were noted for any behavioural measures at any of the monthly test sessions (39). The NOAEL with respect to neurotoxicity was 711 mg/kg bw/day, whereas an overall NOAEL for the reported part of the study was as low as 161 mg/kg bw/day due to reduced weight development at higher dietary concentrations. The data from this study are regarded as reliable and of good quality and were published in a peer reviewed journal. The study was not performed according to any standard guideline, and there is no mention of GLP, but since the study was performed at the US Food and Drug Administration's Division of Toxicology GLP is assumed.

Triphenyl phosphate (TPP)(99.99%-pure) did not produce any evidence of axonal degeneration, demyelination, or any other pathological changes at 11 levels of the nervous system (from the cerebral cortex to peripheral nerves) when subcutaneously injected into cats at single doses of 400, 700, or 1000 mg/kg. Prostration occurred at the higher doses. The authors therefore concluded that TPP is not neurotoxic in the cat and that earlier studies were complicated by the fact that TPP prepared from coal–tar sources may have contained impurities that were capable of producing axonal degeneration and demyelination (37).
Although not performed in accordance with any guideline and before GLP was introduced the results and the conclusions drawn by the researchers in this study seem reliable due to the targeted protocol and performance.

Dosing 9 adult hens with cumulative doses of 60 g triphenyl phosphate/kg bw (5 g/kg bw twice daily for 2 times 3 consecutive days(study days 1-3 and 21-23) failed to produce either ataxia or histologic neurotoxic response suggestive of organophosphate-induced delayed neuropathy (44).
Although not performed in complete accordance with the OECD guideline for organophosphate-induced delayed neuropathy testing the study results and conclusions drawn are reliable.

Despite early reports on the contrary, TPP is not considered neurotoxic in animals up to and including 711 mg/kg bw/day. Also it does not produce organophosphorus-induced delayed neurotoxicity in hens.

"Special ***in vitro*** studies"
Three different ***in vitro*** studies on triphenyl phosphate are all considered reliable but the data produced seem difficult to use in relation to concluding the toxicity to man:

Significant direct inhibition of monocyte antigen presentation at non-cytotoxic concentrations was recorded as low as 1 µmol/L (35).

Triphenyl phosphate demonstrated a dose dependent inhibition of growth in a cell culture assay on ***in vitro*** cytotoxicity to human (KB and HEL-R66),

monkey (Vero) and dog (MDCK) cell lines. The dose to inhibit growth 50% varied between 0.4 and 0.6 mM (45).

Triphenyl phosphate reduced the GABA-induced $^{36}Cl^-$ influx in rat brain below control values with a 50% inhibitory concentration (IC_{50}) of 18.2 M but there seems to be poor correlation between inhibition capacity in relation to the chloride channel proteins and delayed neurotoxicity (46).

3.6.3.8 Toxicokinetics

No information has been found about the toxicokinetic behaviour of triphenyl phosphate in humans or in mammals.

The experts of the WHO/IPCS group who prepared the Environmental Health Criteria Report No. 111 on triphenyl phosphate conclude that the available data indicate no hazard to humans.

3.6.3.9 Conclusion

No data have been found with respect to acute or repeated human exposure to triphenyl phosphate (TPP). In animal studies the acute oral and dermal toxicity is low, and the inhalational toxicity has not been investigated. Triphenyl phosphate has not been reported to cause respiratory tract irritation in human beings exposed to the vapour, mist or dust during occupation. TPP is not considered to be a skin irritant, and only old and contradictory information has been available with respect to a single eye irritation study. The only parameter affected in subacute and subchronic dietary studies in rats seems to be retardation in weight gain. In a subchronic neurotoxicity study this effect was recorded from 0.5% TPP in the feed. The NOAEL was 161 mg/kg bw/day.

The ***in vitro*** genotoxicity data available for evaluation all show negative results with or without metabolic activation and no ***in vivo*** tests for genotoxicity have been available. There are no data from which one can adequately conclude with respect to the carcinogenic properties of TPP. The only available study was inadequate with respect to survival and duration of the study. However, a carcinogenic potential for TPP is not expected since no mutagenicity has been discovered. TPP is not teratogenic and does not affect the fertility in rats when administered to male and female rats from shortly after weaning, through mating and gestation in dietary daily doses up to 690 mg/kg bw. Despite early reports on the contrary, TPP is not neurotoxic in animals, with a subchronic dietary study in rats showing a NOAEL of 711 mg/kg bw/day with respect to neurotoxicity and it is not considered to be neurotoxic in human beings, either. Also it does not produce organophosphorus-induced delayed neurotoxicity in hens. Neither ***in vitro*** nor ***in vivo*** studies indicate that the immune system is affected by administration of TPP. There is no data with respect to toxicokinetic behaviour of triphenyl phosphate.

3.6.3.10 Data sources

Major parts of the data used are based on original literature published in peer reviewed journals, but for some of the information the original works have not been available. In these cases quotations are made primarily from the Environmental Health Criteria 111 – Triphenyl phosphate. Data with respect to acute toxicity are quoted almost entirely from the IUCLID dataset on triphenyl phosphate. Only very little information has been found on toxicological examination of triphenyl phosphate which has been performed in accordance with any standard guideline or even under GLP rules also

because much of the experimental work was performed before testing guidelines and GLP were implemented.

3.6.4 Critical effects

3.6.4.1 CMR

There are no studies available from which a conclusion on the carcinogenic potential of triphenyl phosphate can be drawn. However, no mutagenic effect was found in any of the ***in vitro*** genotoxicity studies available although the studies included tests with and without metabolic activation. ***In vivo*** genotoxicity is not tested. In a well performed and reported study no effects on reproduction and no teratogenic potential was found of daily doses up to and including 690 mg/kg bw administered before and during mating and throughout gestation.

3.6.4.2 Endocrine disruption

No studies have been found from which data can be used for any kind of conclusion with respect to endocrine disruption.

3.6.4.3 Sensitisation

No animal studies have been found testing triphenyl phosphate for sensitisation properties. However, due to the inclusion of TPP in many patch-testing series used for occupational screening and in dermatological clinics a large number of reports including a vast number of test persons indicate a very low skin sensitising potential of triphenyl phosphate in human beings. No animal studies have been available with respect to the respiratory sensitisation potential.

3.6.4.4 Summary of critical effects

The only study available on carcinogenic potential of triphenyl phosphate is inadequate due to low survival and short duration. However, there is no evidence for concern with respect to carcinogenicity of TPP since no mutagenicity was discovered in standard mutagenicity tests performed ***in vitro*** with and without metabolic activation system. TPP did not affect fertility or show teratogenic properties in rats. Triphenyl phosphate has not shown skin sensitising potential to a marked degree in a number of patch-testing in humans, but this endpoint has never been examined in animal studies.

3.6.5 PBT assessment

3.6.5.1 Persistence

TPP is inherently biodegradable and has been found to biodegrade extensively under both aerobic and anaerobic conditions in various test systems. Half-lives in water/sediment simulation tests range from 3-12 days in river water/sediment and pond sediment, whereas half-lives ranging from 50-60 days are obtained in pond hydrosoil. No data have been found on ready biodegradability. Based on the available data, TPP is not considered to meet the P or vP criteria (half-life > 40 days and >60 days in freshwater, respectively and half-life > 120 days and >180 days in freshwater sediment, respectively)

3.6.5.2 Bioaccumulation

TPP does not meet the B criterion as the experimentally determined BCF values (range 84-364) are <2000.

3.6.5.3 Toxicity

It is questionable whether TPP meets the T criterion, as the validity of the chronic NOEC values reported (range 0.087-0.23 mg/L) are uncertain. The acute $L(E)C_{50}$ values are typically <1 mg/L but higher than 0.1 mg/L, which is the screening level assignment of potentially toxic substances.

3.6.5.4 Summary of PBT assessment

TPP is not considered persistent or bioaccumulable according to the PBT criteria.

3.6.6 Comparison with deca-BDE

The key toxicological and environmental properties of TPP are compared to those of deca-BDE and summarised in Table 3.8. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.8 Summary of toxicological and environmental properties of TPP and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
TPP	115-86-6	n.d.	-	-	n.d.	-	-	-	(+/-)
Deca-BDE	1163-19-5	(-)	-	(-)	?	(-)	+	-	-

When used as a candidate for substituting brominated flame retardants in thermosets TPP are typically incorporated into the polymer structure. It is not expected to migrate from the polymer.

3.7 Red phosphorus

Three allotropic forms exist of phosphorus red, black and a form termed yellow or white. Red phosphorus may be polymeric, crystalline or amorphous and may in this form contain trace amounts of white/yellow phosphorus at up to 50 mg/kg in commercial grades.

While white/yellow phosphorus is toxic to man and environment, red phosphorus is less harmful. Red and yellow/white phosphorus share the same EINECS-number and care has to be taken when data are extracted from sources based on the EINECS-number.

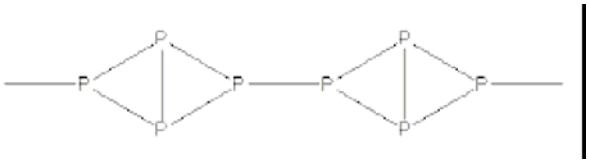
When properly applied as a flame retardant, red phosphorus is usually completely embedded into a polymer matrix so that it cannot react with air or water. Due to its own polymeric nature it will not migrate or evaporate from the final product. Although the substance is classified as highly flammable and may explode when exposed to heat or by chemical reaction with oxidisers, it does not react until >260 °C.

3.7.1 Substance Identification and Physical-Chemical Data

3.7.1.1 Identification

Red phosphorus has the following key identification data:

CAS number: 3258-76-4
EINECS number: 251-118-6
IUPAC name: Phosphorus
Molecular formula: P_n
Molecular weight: 123.90 (P_4 with atomic weight of P=30.97376)
Structural formular:



3.7.1.2 Physical chemical properties

Red phosphorus is reported to be insoluble (47) or slightly soluble in cold water and insoluble in hot water (48). No data for the log K_{ow} value has been identified for red phosphorus. A vapour pressure of 0.026 mmHg (20°C) is stated for phosphorus (no distinction between allotropic forms)(48).

3.7.2 Environmental Assessment

Only limited data describing the environmental properties of red phosphorus are available. Table 3.9 shows the key ecotoxicity and fate data for red phosphorus.

Table 3.9 Key ecotoxicity and fate data for red phosphorus

Acute toxicity	
Algae	EC50(72h) = 18.3 mg/L (nominal conc.), 1.3 mg/L (measured conc. of total P in solution)
Crustaceans	EC50(48h) = 10.5 mg/L (nominal conc.), 0.63 mg/L (measured conc. of total P in solution)
Fish	LC50(96h) = 33.2 mg/L (nominal conc.), 0.95 mg/L (measured conc. of total P in solution)
Chronic toxicity	
Algae	No data.
Crustaceans	No data.
Fish	No data.
Bioaccumulation	
BCF (Fish)	No data.
Biodegradation	
Aerobic degradation	Not applicable
Anaerobic degradation	Not applicable

3.7.2.1 Acute toxicity

Red phosphorus is toxic to alge, crustaceans and fish. The reported key L(E)C_{50} values are in the range 10.5-33.2 mg/L (nominal concentrations) and 0.63-1.3 mg/L (measured concentrations of total phosphorus in solution)(OECD/EEC Test Guidelines)(49,50,51). Red phosphorus is practically insoluble in water, but slowly decomposes to phosphorus acids in aqueous solution. The measured concentrations are based on total dissolved P in the test solutions, and not the amorphous polymer red phosphorus. The data implies that the aquatic toxicity of red phosphorus occurs at levels exceeding the water solubility, and that the toxicity may be related to the decompositions products of red phosphorus.

3.7.2.2 Chronic toxicity
No data found.

3.7.2.3 Microorganisms and terrestrial toxicity
No data found.

3.7.2.4 Bioaccumulation
No data found.

3.7.2.5 Aerobic biodegradability
Not applicable

3.7.2.6 Anaerobic biodegradability
Not applicable

3.7.2.7 Abiotic degradation
Red phosphorus is an inorganic substance, and biodegradability is thus not a relevant parameter. In the presence of water and oxygen, red phosphorus will slowly react to phosphoric acid via intermediates such as hypophosphorus acid, phosphorus acid and phosphine (52). In an oxidising environment, the toxic phospine is readily transformed to phosphates (53).

3.7.2.8 Conclusion
The available data material regarding the environmental properties of red phosphorus is limited. The few available studies indicate that red phosphorus has a relatively high aquatic toxicity with $L(E)C_{50}$ values in the range 10.5-33.2 mg/L (nominal concentrations) and 0.63-1.3 1 mg/L (measured concentrations of total phosphorus in solution). No BCF data are available. As red phosphorus is an inorganic substance, biodegradability is not a relevant parameter. In the aquatic environment, red phosphorus will react slowly, producing phosphoric acid via different intermediates, i.e. phosphine, which is a higly toxic gas. Phosphine is, however, readily transformed to phosphates under oxidising conditions (53).

3.7.2.9 Predicted No Effect Concentration (PNEC)
No calculations of the PNEC have been found in the literature.

3.7.2.10 Data sources
The ecotoxicological data are based on GLP test reports for the acute toxicity of the substance Red Phosphorus SF towards algae, daphnia and fish. The studies are conducted according to OECD/EEC Test Guidelines and are considered quality data Data regarding the environmental fate is described consistently in different technical reports prepared by manufacturers of red phosphorus, and seem reliable.

3.7.3 Health Assessment

3.7.3.1 Observations in humans
Red phosphorus is non-volatile, insoluble, unabsorbable and thus non-toxic when ingested, unless it is contaminated with traces of yellow phosphorus. Repeated doses of red phosphorus, however, may induce systemic phosphorus poisoning.

In contrast to acute poisoning, chronic phosphorus intoxication, once common in some industries because of inhalation of phosphorus fumes, is virtually unknown in modern times. It was characterized as cachexia, anemia,

bronchitis and necrosis of the mandible, the socalled “phossy” or “Lucifers jaw” (brittle bones) (54).

This reference is a secondary reference of good credibility. It does not elaborate on the quantities needed to induce the mentioned poisoning symptoms.

Red phosphorus is unabsorbable, but traces of yellow phosphorus may induce systemic phosphorus poisoning upon repeated exposure.

3.7.3.2 Acute toxicity

Acute toxicity was given for rats by oral exposure: LD_{50}>15000 mg/kg bw (7). The data on oral acute toxicity is from IUCLID and is referenced as unpublished data from Hoechst with no further information.

Acute toxicity by inhalation has not been determined for red phosphorus per se. However, several studies have been made on the toxicity of red phosphorus smoke. When ignited, red phosphorus burns to phosphorus pentoxide, and in conditions of normal humidity this gives rise to a strongly hygroscopic aerosol consisting largely of orthophosphoric acid. The smoke can also contain cyclotetraphosphoric and other polyphosphoric acids, as well as small amounts of phosphine, produced from phosphorus trioxide (55).

	1 hour-LC_{50}-values	
	expressed as P	ortho-phosphoric acid equiv.
Male rabbits	1689 mg/m^3	5337 mg/m^3
Male rats	1217 mg/m^3	3846 mg/m^3
Male mice	271 mg/m^3	856 mg/m^3
Male guinea pigs	61 mg/m^3	193 mg/m^3
	Non-lethal 1 hour concentrations	
Male rats	450 mg/m^3	1422 mg/m^3
Male mice	111 mg/m^3	351 mg/m^3
Male guinea pigs	36 mg/m^3	114 mg/m^3

Cause of death in rabbits, rats and mice was respiratory tract injury from the corrosive effects. Guinea pigs died from alveolar capillary congestion, and showed no lesions in the larynx and trachea. These findings are compatible with lethal toxicity in the guinea pig as a consequence mainly of asphyxia secondary to laryngospasm (56).

Although this study is not performed according to any standards or with any mention of GLP, it was published in a peer reviewed journal, and the quality of the study seems to be high.

1 hour LC_{50}, rats for smoke was found at 4.3 mg/L (red phoshorus/butyl rubber aerosol) equal to 4.03mg/L of H_3PO_4 equal to 4033 mg/m^3 (57).

It should be noted that the exposure in this study was not only from the smoke of red phosphorus, but also from the smoke of butyl rubber. However, when expressed as orthophoshoric acid it fits nicely with the value found for rats in the study above. The study was not performed according to any standards or GLP, but it was published in a peer reviewed journal, and the quality of the study seems high.

No other studies pertaining to results of acute exposure by any other routes could be found.

Acute toxicity in orally exposed rats is very low. Acute toxicity by inhalation has not been determined for red phosphorus per se. Smoke from ignited red phosphorus exerts corrosive effects in the respiratory tract. 1 hour LC_{50}, rats for smoke was found at 4.3 mg/L (red phoshorus/butyl rubber aerosol) equal to 4.03mg/L of H_3PO_4 equal to 4033 mg/m^3.

3.7.3.3 Skin irritation

I a 24 hour patch test on rabbits gave no irritation (7). Dose not given. This information is from IUCLID where the companies Hoechst and Clariant are mentioned as sources.

Red phosphorous showed no skin irritation.

3.7.3.4 Eye irritation

100 mg in the eyes of rabbits was not found irritating (7). This is information from IUCLID where Hoechst and Clariant are mentioned as sources. Further information on this particular study may be obtained on microfiche if need be.

Pieces of red phosphorus lodged in the eyes of a 15 year old boy after an explosion due to mixture with potassium chlorate had a benign course and outcome, without any late complications (58).

The case was reported in a peer reviewed journal, and the data must be regarded as high quality.

Another similarly benign case has been described. However, an entirely different course of sequelae has been described from Czechoslovakia, in a boy who was reported to have burns of both eyes with red phosphorus, and to have suffered for more than two years from inflamed conjunctiva and photophobia.

The difference in severity of reactions of the three patients may be explainable by a difference in the amount of red phosphorus that entered the eyes. A rabbit experiment showed that when enough of this substance is present it can produce considerable inflammation in the eye, even while appearing inert in the cornea. Apparently the amount which can be tolerated without inflammation is very small, as in the first patient, in whom the particles were so fine that they could be seen only with a slit-lamp biomicroscope (59).

The latter data and the evaluation is from "Toxicology of the eye", a renowned and very reliable handbook.

Small amounts in the surface of the eyes did not causse irritation. Larger amounts penetrating the cornea may give persistent inflamed conjunctiva and photophobia.

3.7.3.5 Subchronic and chronic toxicity

No data was found on subchronic and chronic exposure to red phosphorus by the oral and dermal route.

<u>Inhalation</u>

The toxicity of red phosphorus smoke was tested on mice, rats and guinea pigs at dose levels: 0, 15; and 130 mg/m^3 (expressed as P) 1 h/day, 5 d/week for up to 40 weeks.

The lethality during the study was:

Mice: 59, 63, and 78%, respectively.
Rats: 26, 24, and 20%, respectively.
Guinea pigs: 15, 38, and 100%, respectively.

Growth of the test groups of mice and rats were depressed during the exposure period. Organ specific toxicity appeared not to be present in rats and was generally confined to the respiratory tract of the mice and guinea pigs. Severe congestion was observed in practically all the lungs from the high dose guinea pigs, all of whom died during or just after the first exposure.

For survivors, specific damage of the respiratory tract was only rarely seen in the present study. If, at the end of exposure, damage was present, it had been reversed by the end of the observation period. However, the very marked species differences in lethality, observed in the present study, indicates that caution must be taken in quantitative extrapolation to humans of the study data (55).

The data from this study are regarded as reliable and of good quality, and they were published in a peer reviewed journal. The study was not performed according to any standards, and there is no mention of GLP.

Blacktailed prairie dogs showed no mortality to either 2000, 4000 or 6000 mg/m^3 concentrations of smoke within 30 days after 1-4 successive daily 1-hour exposure sessions. 70.5-76% of the aerosols consisted of phosphoric acid.

Rock doves exposed to either 3000 or 6000 mg/m^3 over 1-4 sessions, however, showed 26% mortality within 8 days postexposure. Male rock doves were much more vulnerable, with 42% mortality, in contrast to 6% in females. Lost or affected vocalisation capability in both species, abnormal body postures in rock doves, and increased respiratory congestion in prairie dogs was found postexposure (60).

Whole-body exposure of the same two species to 0; 1000; and 4000 mg/m^3 in 80 minutes/day for 4 consecutive days for the prairie dogs and 2 consecutive days for the rock doves produced no deaths among the 24 prairie dogs and 1 death out of 8 doves exposed to the largest conc. Enhanced postexposure water replenishment was the main finding (61).

No data was found on subchronic and chronic exposure to red phosphorus by the oral and dermal route. Death during long- term exposure up to 40 weeks is usually caused by congestion of the lungs. Critical effect is growth depression. Note marked species differences in lethality.

3.7.3.6 Long-term toxicity

Mutagenicity
No data found.

Genotoxicity
No data found.

Carcinogenicity
No data found.

Reproductive Toxicity, Embryotoxicity and Teratogenicity
No data found.

3.7.3.7 Toxicokinetics
No data found.

3.7.3.8 Data sources
Some of the presented data are gathered and reviewed in the IUCLID dataset. Most of the described studies are of older date and based on peer reviewed scientific articles. In the majority of the studies reported no information was available on guideline and GLP conditions.

3.7.3.9 Conclusion
Red phosphorus is non-volatile, insoluble, unabsorbable and thus non-toxic when ingested, unless it is contaminated with traces of yellow (white) phosphorus.

Toxicity data on red phosphorus ***per se*** are scarce.

Smoke generated from the ignition of red phosphorus has been tested on different animals. When ignited, red phosphorus burns to phosphorus pentoxide, and in conditions of normal humidity this gives rise to a strongly hygroscopic aerosol consisting largely of orthophosphoric acid. The smoke can also contain cyclotetraphosphoric and other polyphosphoric acids, as well as small amounts of phospine, produced from phosphorus trioxide.

One hour LC_{50} values for rats vary between 3846 and 4033 mg/m^3 when expressed as orthophosphoric acid, which is the main reaction product formed from red phosphorus smoke.

When comparing the toxicity of the smoke on rats, mice and guinea pigs, guinea pigs appear to be the more sensitive and rats the least. Lethality is mostly due to damage to the respiratory tract. In surviving animals, damage appear to be reversible. The very marked species differences in lethality must indicate caution in quantitative extrapolation to humans of the study data.

Results of exposure of the eye to red phosphorus can vary from the benign with no late complications at small amounts with small particle size to extended (for years) inflamed conjunctiva and photophobia at larger amounts and bigger pieces.

3.7.4 Critical effects

3.7.4.1 CMR
There are no studies available on carcinogenicity, mutagenicity or reproduction toxicity.

3.7.4.2 Endocrine disruption
There are no studies available on the endocrine disruption of red phosphorus.

3.7.4.3 Sensitisation
There are no studies available on the ability of red phosphorus to cause sensitisation.

3.7.4.4 Summary of critical effects

There are no studies available on carcinogenicity, mutagenicity, reproduction toxicity, endocrine effects or sensitisation.

3.7.5 PBT assessment

The OECD Technical Guidance Document (TGD) for risk assessment (3) does not clarify how inorganic substances should be evaluated in relation to the PBT criteria. In the following, red phosphorus is thus evaluated according to the general PBT criteria.

3.7.5.1 Persistence

Red phosphorus is an inorganic compound, and biodegradation is thus not a relevant parameter. In the aquatic environment, red phosphorus will slowly undergo abiotic transformation to phosphoric acid via intermediates such as hypophosphorus acid, phosphorus acid and phosphine (52). Phosphine is transformed to phosphates under oxidising conditions (53). Reaction rates have not been reported, but experimental determination of hydrolysis products of red phosphorus have shown that soluble reaction products accounted for up to 2.7% of the nominal concentration of solid red phosphorus after 4 months, indicating that the reactivity of red phosphorus is low in water (52). Red phosphorus is thus considered to meet the persistent (P) and very persistent (vP) criteria.

3.7.5.2 Bioaccumulation

No data describing bioaccumulation of red phosphorus are available.

3.7.5.3 Toxicity

Red phosphorus has a relatively high aquatic toxicity with $L(E)C_{50}$ values of < 1-1.3 mg/L, based on measured concentrations of total P in the solutions. As red phosphorus is insoluble in water, the aquatic toxicity exceeds the solubility limit of red phosphorus. The toxicity may be related to decomposition products of red phosphorus in aquatic solutions. Chronic NOEC values are not available. As a screening assignment of the T criterion, a substance is considered potentially toxic if the acute $L(E)C_{50}$ to aquatic organisms is less than 0.1 mg/L. Based on the available data, red phosphorus does not meet the T criteria at a screening level, as the lowest $L(E)C_{50}$ value reported is 0.63 mg/L (***Daphnia magna***, measured concentrations of total P), but further data are required for assessment of the T criterion.

3.7.5.4 Summary of PBT assessment

Based on the available data, red phosphorus is considered to meet the P and vP criteria due to the inorganic nature of the substance. The data are insufficient for evaluation of the B and T criteria. At a screening level, red phosphorus does not meet the T criteria.

3.7.6 Comparison with deca-BDE

The key toxicological and environmental properties of red phosphorus are compared to those of deca-BDE and summarised in Table 3.10. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.10 Summary of toxicological and environmental properties of red phosphorus and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that No data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
Red phosphorus	7723-14-0	n.d.	n.d.	n.d.	n.d.	n.d.	+	n.d.	(-)
Deca-BDE	1163-19-5	(-)	-	(-)	?	(-)	+	-	-

When properly applied as a flame retardant, red phosphorus is usually completely embedded into a polymer matrix so that it cannot react with air or water. Due to its own polymeric nature it will not migrate or evaporate from the final product.

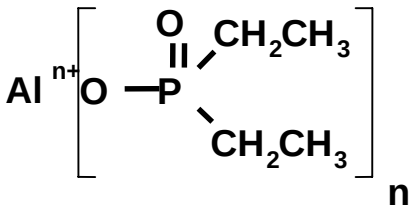
3.8 Diethylphosphinic acid, aluminum salt

Commercially, diethylphosphinic acid, aluminium salt is marketed as the flame retardant Exolit OP 1230 (Clariant). Only limited data describing the environmental and toxicological data exists. The environmental and toxicological properties identified refer to either Exolit OP 1230 or "DEPAL" (Diethylphosphinic acid, aluminium salt). The specific chemical composition of Exolit OP 1230 is known to the authors of this report, but is classified as confidential information. According to information from the producer of Exolit OP 1230 (Clariant) the active and main component of Exolit OP 1230 is diethylphosphinic acid, aluminium salt. The data given here are based on information from the producer.

3.8.1 Substance Identification and Physical-Chemical Data

3.8.1.1 Identification

Diethylphosphinic acid, aluminium salt has the following key identification data:
CAS number: 225789-38-8
EINECS Number: No data.
IUPAC Name: No data.
Molecular formula: $Al^{n+}[PO_2(CH_2CH_3)_2]_n$
Molecular weight: No data.
Structural formula:



3.8.1.2 Physical-chemical data

The commercial product Exolit OP 1230 has a low water solubility with reported values of 2.5 g/L and <1 g/L (62,63). The estimated log K_{ow} value is -0.44 for Exolit OP 1230 (62).

3.8.2 Environmental Assessment

Table 3.11 shows the key ecotoxicity and fate data for diethylphosphinic acid, aluminium salt.

Table 3.11 Key ecotoxicity and fate data for diethylphosphinic acid, aluminium salt

Acute toxicity	
Algae	NOEC(72h) >180 mg/L (nominal conc.)
Crustaceans	EC50(48h) >100 mg/L (nominal conc.), 33.7 mg/L (measured conc.)
Fish	LC50(96h) = >100 mg/L (nominal conc.), 11 mg/L (measured conc.)
Chronic toxicity	
Algae	No data.
Crustaceans	NOEC(21d) 1-10 mg/L (nominal conc.)
Fish	No data.
Bioaccumulation	
BCF (Fish)	No data.
Biodegradation	
Aerobic degradation	Not readily biodegradable
Anaerobic degradation	Not anaerobically biodegradable

3.8.2.1 Acute toxicity

The available data for Exolit OP 1230/DEPAL indicates that this flame retardant has a relatively low aquatic toxicity, with $L(E)C_{50}$ >100 mg/L for algae, daphnia and fish (nominal concentrations). Based on measured concentrations, the $L(E)C_{50}$ correspond to 11 mg/L for fish (96h) and 33.7 mg/L (48h) for daphnia (64). The reported effect concentrations exceed the reported water solubility, and it is not clear from the data material how the exposure concentrations have been verified.

3.8.2.2 Chronic toxicity

No data available.

3.8.2.3 Microorganisms and terrestrial toxicity

In an activated sludge respiration inhibition test (OECD 209), the EC_{50} was 1968 mg/L for Exolit OP 1230 (64). The EC values obtained in the study exceeds the water solubility reported for diethylphosphinic acid, aluminium salt.

3.8.2.4 Bioaccumulation

No data available.

3.8.2.5 Aerobic biodegradability

Exolit OP 1230 did not biodegrade in standardised tests for ready and inherent biodegradability (OECD 301 C and OECD 302 B) (64), (63).

3.8.2.6 Anaerobic biodegradability

Exolit OP 1230 did not biodegrade in a standardised test for anaerobic degradation (ISO/DIS 14853)(64).

3.8.2.7 Abiotic degradation

Exolit was stable to hydrolysis in a standardised test for hydrolysis (OECD 111, tier 1)(63).

3.8.2.8 Conclusion

The available data material is related to the commercial product Exolit OP 1230. The few studies reported indicate that Exolit OP 1230 is not readily or inherently biodegradable, and has a relatively low aquatic toxicity with ($L(E)C_{50}$ values > 100 mg/L (nominal conc) and approximately 11-33.7 mg/L (measured conc.). Data for bioaccumulation and mobility in soil of Exolit OP 1230 are not available. In the aquatic environment, equilibrium will establish between the acid (phosphinic acid) and its anion (62). Phosphinic acid is a relatively strong acid with a pKa of 3.3. The estimated log K_{ow} is negative, indicating that Exolit OP 1230 is not hydrophobic. The data material is insufficient for an adequate environmental assessment of diethylphosphinic acid, aluminium salt, as the full test reports are not available. However, the reported test results are rather consistent and indicate that the environmental hazard of diethylphosphinic acid, aluminium salt is low.

3.8.2.9 Predicted No Effect Concentrations (PNEC)

No calculations of the PNEC have been found in the literature.

3.8.2.10 Data sources

The above data are obtained from summaries of test reports and other product information for Exolit OP 1230 supplied by Clariant. The full test reports are not available, and the quality of the data can thus not be assessed. The tests were performed according to standardised test guidelines (OECD, EEC). The full test reports are required for evaluation of the adequacy of the data The specific composition of the commercial product Exolit OP 1230 is confidential, but is known by the authors of this report.

3.8.3 Health Assessment

3.8.3.1 Observations in humans

No data.

3.8.3.2 Acute toxicity

Acute oral toxicity was determined in male and female rats, in accordance with OECD guideline 401. No death observed and no effect on body weight or. No macroscopically changes observed. It was concluded that LD_{50} > 2000 mg/kg (64).

In an acute dermal toxicity test in male and female rats, no death observed and no effect on body weight were observed. No sign of irritation of the skin and no macroscopically changes were observed. It was concluded that LD_{50} > 2000 mg/kg. The test was performed in accordance with OECD guideline 402 (64).

The acute toxicity of diethylphosphinic acid, aluminium salt is low by oral and dermal exposure.

3.8.3.3 Irritation

A skin irritation test was performed on rabbits in a 4 h test period. The test was performed in accordance with OECD guideline 404. It was concluded that the test substance was non-irritant (64).

Eye irritation was tested in rabbits in accordance with OECD guideline 405. It was concluded that there was a slightly irritant effect (64).

Diethylphosphinic acid, aluminium salt does not seem to be of concern with regard to skin irritation, but slight eye irritation was observed. No information on respiratory irritation.

3.8.3.4 Sensitisation

Skin sensitisation was investigated in female guinea pigs in accordance with OECD guideline 406. The Guinea Pig Maximisation Test (GPMT) was conducted with 5% induction (first) and 25% induction (second) and challenge. It was concluded that the test substance was non-sensitizing (64).

Diethylphosphinic acid, aluminium salt does not seem to be of concern with regard to skin sensitisation.

3.8.3.5 Repeated dose toxicity (e.g. 4w and 13w studies)

A subchronic oral toxicity study was performed in groups of 5 male and female rats by gavage dosing (0, 62.5, 250 or 1000 mg/kg bw/day) for 28 days. No treatment-related abnormal behavior or appearance was observed, including neurotoxicological measurement. No toxicological significant changes were observed in body weight, food consumption, blood chemistry or organ weight. No alterations were observed in the gross and microscopic examination of tissues. The study was performed in accordance with OECD guideline 407. Based on the results a NOAEL > 1000 mg/kg/day was established (64).

Subchronic oral exposure showed low toxicity of diethylphosphinic acid, aluminium salt. No information on chronic toxicity.

3.8.3.6 Genotoxicity

Mutagenicity was tested in the Bacterial Reverse Mutation Test (Ames-test) with ***Salmonella typhimurium*** (TA1535, TA1537, TA1538, TA98, and TA100) at 6 concentrations (from 4 to 5000 g/plate). The study was performed in accordance with OECD guideline 471. No mutagenic activity was detected either with or without metabolic activation (64).

Chromosome aberrations were tested in the cytogenetic Chromosome Aberration Test with V79 Chinese Hamster Cells at 5 concentrations (from 7.8 to 780 g/ml). Because of precipitation of the test substance, the highest test level was 78 g/ml. The study was performed in accordance with OECD guideline 473. No chromosome mutations were induced with or without metabolic activation at the levels tested (64).

No mutagenic activity was observed when diethylphosphinic acid, aluminium salt was tested in the Ames test and in the cytogenetic Chromosome Aberration Test with and without metabolic activation.

3.8.3.7 Long-term toxicity

No data was identified for carcinogenicity, reproduction toxicity or long-term toxicity e.g. neurotoxicity.

3.8.3.8 Toxicokinetics

Diethyl phosphinic acid was excreted almost quantitatively via the urine within 12 hours after oral application.

Metabolism of diethyl phosphinic acid showed excretion in the urine.

3.8.3.9 Conclusion

In conclusion, the acute oral and dermal LD_{50} in rats was greater than 2000 mg/kg bw. No dermal irritation or sensitisation was observed, but slightly eye irritation was observed. In a subchronic study in rats, no changes were observed and NOAEL > 1000 mg/kg/day was established. No genotoxicity was observed when tested in strains of ***Salmonella*** typhimurium or in a cytogenetic assay in vitro with and without metabolic activation. No information was found on reproduction or teratogenicity as well as carcinogencity or chronic toxicity.

3.8.3.10 Data sources

The data used in this evaluation is based on information from a report provided by the producer of Exolit OP 1230 (Clariant). All the cited studies are of recent date and in accordance with OECD and EU-guidelines, and carried out according to the principles of GLP.

3.8.4 Critical effects

3.8.4.1 CMR

There was no information on the carcinogenicity of diethylphosphinic acid, aluminium salt. No mutagenic activity was observed when tested in Salmonella typhimurium or in a cytogenetic assay in vitro with and without metabolic activation. Diethylphosphinic acid does not seem to pose a mutagenic risk. There was no information on the effects of diethylphosphinic acid, aluminium salt on reproduction.

3.8.4.2 Endocrine disruption

No information on endocrine disruption potential of diethylphosphinic acid, aluminium salt.

3.8.4.3 Sensitisation

Diethylphosphinic acid, aluminium salt was found to be not sensitizing.

3.8.4.4 Summary of critical effects

Based on available data in this report there are no indication of mutagenic or sensitizing potential of diethylphosphinic acid, aluminium salt. Data are not sufficient to conclude on carcinogenic, reproductive or endocrine disruption potential.

3.8.5 PBT assessment

3.8.5.1 Persistence

The commercial product Exolit OP 1230 is not biodegradable based on the results of a single test for inherent biodegradability. In such cases, the TGD recommends that a simulation test for environmental degradation should be performed, but no such data are available. Exolit OP 1230 is thus considered to meet the persistent (P) and very persistent (vP) criteria until otherwise proved.

3.8.5.2 Bioaccumulation

Based on the estimated log Kow value (-0.44) Exolit OP 1230 does not meet the screening criterion for consideration as bioaccumulative (B) and very bioaccumulative (vB). No experimental BCF values have been found in the literature.

3.8.5.3 Toxicity

The results of the aquatic toxicity tests with Exolit OP 1230 indicate that toxic effects occur at levels much higher than the estimated water solubility with $L(E)C_{50}$ values > 100 mg/L, corresponding to measured concentrations between 11-33.7 mg/L. Based on these data, Exolit OP 1230 does not meet the toxicity (T) criterion.

3.8.5.4 Summary of PBT assessment

Based on the available data, Exolit OP 1230 is considered to be very persistent (vP). Exolit OP 1230 is not considered to meet the criteria for bioaccumulation. The available data indicate that Exolit OP 1230 is not acutely toxic at concentrations up to the water solubility limit, and has a low acute toxicity towards aquatic organisms.

3.8.6 Comparison with deca-BDE

The key toxicological and environmental properties of diethylphosphinic acid, aluminium salt are compared to those of deca-BDE and summarised in Table 3.12. The toxicological and environmental profile of the substances is expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (Endo), sensibilisation (Sens), persistence (P), bioaccumulation (B) and aquatic toxicity (T).

Table 3.12 Summary of toxicological and environmental properties of diethylphosphinic acid, aluminium salt and deca-BDE. Values in parentheses indicate that high quality data or sufficient data are not available for the assessment. The assessment in parentheses is thus only indicative (may e.g. be based on a limited data set, data from non-standardised tests or QSAR estimates). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

		Human toxicology					Environment		
Substance	CAS No.	C	M	R	Endo	Sens	P	B	T
Diethylphosphinic acid, aluminium salt	225789-38-8	n.d.	-	n.d.	n.d.	-	+	-	-
Deca-BDE	1163-19-5	(-)	-	(-)	?	(-)	+	-	-

4 Assessment of key data used for environmental and health assessment

This section assessed the quality of the key data that are decisive of the evaluation of each compound.

In general, the assessment is based on standard and quality assured tests, preferably performed under GLP conditions. However, some compounds have only recently been developed and the information available is still limited limited. Other compounds have been many years on the market and are existing chemicals according to European law. The data availability concerning test performed after contemporary standards may also be limited for this type of compound.

The data availability of the compounds may be summarised as follows

Substance	Available literature
Decabromodiphenyl ether (deca-BDE)	EU Risk Assessment Report, Updata and Addendum
Ethylene bis(tetrabromophthalimide) (EBTPI)	IUCLID, Open literature
Tetrabromobisphenol A (TBBPA)	Draft EU Risk Assessment Report, WHO/IPCS
Tetrabromobisphenol A carbonate oligomer	Manufacturer's data
Triphenyl phosphates (TPP)	WHO/IPCS, IUCLID, US EPA, Open literature
Red phosphorus (RP)	IUCLID
Diethylphosphinic acid, aluminum salt	Manufacturer's data

This assessment considers the commercial flame retardant product decabromobiphenyl ether, deca-BDE, and the data given here are excerpts from the final EU Risk Assessment Report (2002) on Bis(pentabromophenyl) ether (4). The references are given as found in the EU-RAR. A few data are from the "Update of the Risk Assessment of Bis(pentabromophenyl) ether (Decabromodiphenyl ether)" (2004) (5), the "Addendum to the May 2004 Environmental Risk Assessment of Decabromodiphenyl ether (CAS no. 1163-19-5) (2005) (6), and the human health draft of the "Update of the Risk Assessment Addendum of Bis(pentabromophenyl) ether (Decabromodiphenyl ether) of May 2005 (2).

The health assessment data are excerpts from the final EU RAR on deca-BDE from 2002 (4). A few data are from the draft for the update of the risk assessment (2). These documents have formed the basis on the assessment of deca-BDE, and the selection, evaluation, and recommendation of the EU review regarding the quality and significance of studies are reflected in the overview provided here. Thus, only studies acceptable to the Member States technical experts and the Scientific Committee on Toxicity, Ecotoxicity, and the Environment (CSTEE) are included.

Environmental data for EBTPI are based on standardised test guidelines (MITI, OECD) and QSAR predictions (EPIwin V. 3.04). The experiments were performed according to GLP and are all > 20 years old. The toxicological data presented for EBTPI are gathered and reviewed in the IUCLID dataset (7) and in a review report on toxicological literature (8). These studies are of older date and based on information from microfilm. The studies were estimated to be in compliance with standardised OECD guidelines, and most were published prior to introduction of the OECD GLP principles.

The health assessment data on TBBPA are excerpts from the draft EU RAR on 2006 (27). Although, still a draft this document is very close to completion. An environmental assessment of TBBPA is not yet included in the final EU RAR. The environmental assessment is primarily based on WHO Environmental Health Criteria (26). Most of the studies herein are well described, and the toxicity data for TBBPA towards aquatic organisms show a large degree of consistence. The data sources are used as quoted in EU RA (27) and the IPCS report (28).

Environmental data presented for TPP were included in the US EPA published report “Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam”(29). All studies are reviewed and are well described in the report. The majority of the studies reported are conducted according to standardised guidelines (OECD, EPA). Many of the studies reported are of older date (>20 years) and are published prior to introduction of the OECD GLP principles. Major parts of the toxicological data used are based on original literature published in peer reviewed journals, but for some of the information the original works have not been available. In these cases quotations are made primarily from the Environmental Health Criteria 111 – Triphenyl phosphate. Data with respect to acute toxicity are quoted almost entirely from the IUCLID dataset on TPP. Limited information was found from toxicological studies of TPP performed in accordance with guideline or GLP rules, primarily because much of the experimental work was performed before testing guidelines and GLP were implemented.

The ecotoxicological data are based on GLP test reports for the acute toxicity of the substance Red Phosphorus SF towards algae, daphnia and fish. The studies are conducted according to OECD/EEC Test Guidelines and are considered quality data. Data regarding the environmental fate is described consistently in different technical reports prepared by manufacturers of red phosphorus, and seem reliable. Most health data on red phosphorous are quoted from the IUCLID dataset on phosphorous. Much information is on red phosphorous smoke, which in fact does not consist of elemental phosphorous but phosphorous oxides. Thus data on red phosphorous are limited.

No information was identified on diethylphosphinic acid, aluminium salt, in the open literature. The environmental and toxicological data were obtained from summaries of test reports and other product information for Exolit OP 1230 supplied by Clariant GmBH. The full test reports are not available, and the quality of the data can not be assessed. All the cited studies are of recent date and in accordance with OECD and EU-guidelines, and carried out according to the principles of GLP. The full test reports are required for evaluation of the adequacy of the data. The specific composition of the commercial product Exolit OP 1230 is confidential, but is known to the authors of this report.

5 Risk assessment note

This section describes a preliminary assessment of risk, i.e. combining the detailed study of inherent properties with a preliminary exposure assessment developed for key exposures.

5.1 Exposure implications of substituting deca-BDE with alternatives

Flame retardants are a crucial part of the fire safety protection in homes and industry. The Bromine Science and Environment Forum is formed by the largest producers of bromine flame retardants and the following statements are quoted on their webpage:

- In terms of fire hazard, the plastics which are contained in a typical TV set are equivalent to 6 litres of petrol in your living room.

- In the United Kingdom alone, government scientists have estimated that over 3,000 lives were saved in the period from 1988 – 2000 as a result of flame retardants.

It is obvious that flame retardants and in this case brominated FRs save lives every year. When alternatives are sought the alternatives must provide a similar protection of the electronics' consumer. It is shown in the report of COWI (1) that all of the alternatives treated in the present report may be used in plastics to obtain the UL 94 vertical flame test V-0 grade. It may therefore be concluded that a life saving capacity of the alternatives similar to that of BFRs is possible, although no statistics can yet be presented for saved lives as a specific result of the use of alternatives to BFRs.

Expensive formulations have little practical impact, but cost is not a matter of the present report. The material prices of V-0 grade PA6 GF for four different flame retardants (deca-BDE, brominated polystyrene, magnesium hydroxide and organic phosphinates) showed a cost for the alternatives of 84, 114 and 127% compared to the cost of using dec-BDE. The use of the cheap magnesium hydroxide may, however, not be technically feasible.

However, if the V-0 grade is achieved by using excessive amounts of the alternatives the practical application may be limited. The concentration of deca-BDE in plastics range from 12-13% in HIPS and 13-15% in ABS to 20-30% in polyolefins. In the case of V-0 grade ABS the use of the alternative TBBPA requires a concentration of 22%. The comparison of health and environmental properties between deca-BDE and TBBPA does not suggest prohibitive risk increase from using TBBPA as judged from the inherent properties. In another case the substitution of deca-BDE in PA requires 10-13 % red phosphorus compared to 16-18 % deca-BDE.

Deca-BDE is used in combination with antimony trioxide (ATO) which acts as a synergist in a 5% concentration, and it is used in a broad range of plastics. ATO is generally used with other BFRs in concentrations from 4-6% (up to 10%), but also in some non-BFRs where no range data for ATO are available.

There is, however, no indication that ATO must be used in dramatically larger concentrations with alternatives to deca-BDE.

There is no data on migratory properties such as volatility of the alternatives. The chemical structures and molecular weights of the alternatives do not suggest a greater loss from plastics of BFR or non-BFR alternatives compared to deca-BDE.

A key issue regarding deca-BDE has been the rate of degradation of the highly brominated substance and the possible formation of lower brominated congeners, which may already be subject to a ban in the EU. There is scientific agreement that a biotic degradation route exists and environmental conditions may exist in anaerobic (freshwater) sediments or in landfills. The formation rates appear to be slow. The abiotic route proceeds via photolysis and is also estimated to be slow due to strong adsorption properties of deca-BDE. An unequivocal conclusion regarding the environmental significance has not been reached on this issue (quote):

'In summary, the new data provide clear evidence that debromination of decabromodiphenyl ether to form lower brominated congeners can occur under certain conditions in laboratory tests, but the results are difficult to extrapolate to the environment.' (EU RAR Environmental Addendum 2005) (6).

5.2 Assessment of the risk profile using alternatives compared to deca-BDE

5.2.1 Ethylene bis(tetrabromophthalimide)

EBPTI has a broad application range comparable to that of deca-BDE and it has been marketed as general purpose alternative to deca-BDE. For most applications EBPTI has superior technical properties (except for colour), but it is more expensive than deca-BDE. Indications are that EBTPI is not biodegradable, does not bioaccumulate and that the aquatic toxicity is very low. EBPTI is not considered to have critical effects concerning MR on human health. On carcinogenicity no data is available for EBPTI, and a classification for deca-BDE is not possible, although results suggest a cautious approach.

Based on the available data on there appear to be no health and environmental properties of EBPTI prohibitive to the substitution of deca-BDE in the assessed applications.

5.2.2 Tetrabromobisphenol A

TBBPA has a narrow but important application range for HIPS and ABS in enclosures. It is used in higher concentrations (14-22%) than deca-BDE (12-15%). TBBPA is more toxic to aquatic organisms than deca-BDE, but none of the compounds meet the T criteria of PBT. There are few data on critical effects, but based on chemical structure there is no indications that TBBPA display CMR characteristics.

Based on the available data on there appear to be no health and environmental properties of TBBPA prohibitive to the substitution of deca-BDE in the assessed applications.

5.2.3 Tetrabromobisphenol A carbonate oligomer

TBBPA carbonate oligomer again has a narrow but important application range for co-polymers like PC/ABS and PPE/HIPS for enclosures. Few data for the TBBPA carbonate oligomer are available and they suggest less effect than TBBPA. As a worst case the assessment is based on the TBBPA monomer (se above).

Based on the available data there appear to be no health and environmental properties of TBBPA carbonate oligomer prohibitive to the substitution of deca-BDE in the assessed applications.

5.2.4 Triphenyl phosphates

The non-halogenated FR triphenylphosphate is used primarily in enclosures (PC/ABS and PPE/HIPS) in concentrations of e.g. 8-12% in PC/ABS. There is insufficient data for a firm conclusion on TPP, but there is no evidence for concern with respect to CMR of TPP. TPP is not considered persistent or bioaccumulative according to the PBT criteria. Many data are available on toxicity, and one test result possibly violates the T criteria. The validity of this dataset is uncertain. When used as a candidate for substituting brominated flame retardants in thermosets TPP are typically incorporated into the polymer structure.

The use of triphenylphosphate (TPP) as FR in the assessed applications does not appear to infer significant additional hazard to the environment or human health when compared to deca-BDE.

5.2.5 Red phosphorus

Red Phosphorus is normally used in flame-retardant-modified polymer compounds in a concentration range between 5 and 15% (w/w). Red phosphorus has actually been used for many years in polyamide at 7% (comparable deca-BDE percentage 16-18%), but in glass-fiber-reinforced polyamide 10-13% is used. These figures suggest that FR amounts of RP are not expected to grossly exceed the percentage of deca-BDE although differences will exist between plastics. Red phosphorus with its own inherent polymeric nature is usually completely embedded into a polymer matrix when applied as a flame retardant. It does not react with air or water, migrate or evaporate from the final product.

There are no studies available on carcinogenicity, mutagenicity, reproduction toxicity, endocrine effects or sensitisation. Based on the available data, red phosphorus is considered to meet the P and vP criteria due to the inorganic nature of the substance. The data are insufficient for evaluation of the B and T criteria. At a screening level, red phosphorus does not meet the T criteria.

Red phosphorus has been used as FR for a number of years. The available studies are limited, but do not suggest that red phosphorus should be more hazardous to man or environment than deca-BDE.

5.2.6 Diethylphosphinic acid, aluminum salt

Organic phosphinate can be used as FR in PA at 15-20% compared to 16-18% of deca-BDE. There are no indications of mutagenic or sensitising

potential of diethylphosphinic acid (aluminium salt). Data are not sufficient to conclude on carcinogenic, reproductive or endocrine disruption potential. Based on the available data, the tested FR product containing is considered to be very persistent (vP), but not to meet the criteria for bioaccumulation. The available data indicate that diethylphosphinic acid, aluminium salt, is not acutely toxic at concentrations up to the water solubility limit, and has a low acute toxicity towards aquatic organisms.

For diethylphosphinic acid, aluminium salt, few data are available from the manufacturer. The available studies do not suggest that the compound should be more hazardous to man or environment than deca-BDE.

6 Conclusions

A market analysis presented 26 potential substitute chemicals for decabromodiphenyl ether in electric and electronic equipment. Six brominated and non-brominate alternatives to deca-BDE were selected in order to cover the same range of applications as deca-BDE: enclosures, connectors and wires/cables. The six FRs were assessed with respect to their health and environmental properties and compared to deca-BDE.

In evaluating the environmental parameter ***persistence*** it should be realised that FRs by their nature are meant to resist oxidation. The same chemical composition of organic compounds that allows fire retardation will in general also resist biodegradation. Thus, all the FRs for which data exist display persistence characteristics.

Ethylene bis(tetrabromophthalimide)

EBPTI has a broad application range comparable to that of deca-BDE and it has been marketed as general purpose alternative to deca-BDE. Indications are that EBTPI is not biodegradable, does not bioaccumulate and that the aquatic toxicity is very low. EBPTI is not considered to have critical effects concerning mutagenic, reprotoxic or endocrine effects on human health.

Based on the available data on there appear to be no health and environmental properties of EBPTI prohibitive to the substitution of deca-BDE in the assessed applications.

Tetrabromobisphenol A

TBBPA has a narrow but important application range for HIPS and ABS in enclosures. It is used in higher concentrations than deca-BDE. TBBPA is more toxic to aquatic organisms than deca-BDE, but neither of the compounds meet the T criteria of PBT. There are few data on critical human effects, but based on chemical structure there is no firm indications that TBBPA display CMR or ES characteristics. It appear to be qualitatively similar to deca-BDE concerning effect profile.

Based on the available data on there appear to be no health and environmental properties of TBBPA prohibitive to the substitution of deca-BDE in the assessed applications.

Tetrabromobisphenol A Carbonate Oligomer

The TBBPA carbonate oligomer is produced to meet the requirements of a narrow but important application range in PC/ABS and PPE/HIPS for enclosures and PBT/PET in connectors. Few data for the TBBPA carbonate oligomer are available and they suggest less effect than TBBPA. As a worst case the assessment can be qualitatively based on the TBBPA monomer (see above), but the risk will be quantitative lesser than TBBPA. It is considered less persistent than deca-BDE.

Based on the available data there appear to be no health and environmental properties of TBBPA carbonate oligomer prohibitive to the substitution of deca-BDE in the assessed applications.

Triphenyl phosphate

The non-halogenated FR triphenylphosphate is used primarily in enclosures (PC/ABS and PPE/HIPS) in concentrations of e.g. 8-12% in PC/ABS. There is insufficient data for firm conclusions on TPP, but there is no evidence for concern with respect to MR or S of TPP. TPP is not considered persistent or bioaccumulative according to the PBT criteria. Many data are available on toxicity, and one test result possibly violates the T criteria. The validity of this dataset is uncertain due to fluctuations in test concentrations.

The use of triphenylphosphate (TPP) as FR in the assessed applications does not appear to infer significant additional hazard to the environment or human health when compared to deca-BDE.

Red Phosphorus

Red Phosphorus is normally used in flame-retardant-modified polymer compounds in a concentration range between 5 and 15% (w/w). Red phosphorus has been used for many years in polyamide. Red phosphorus is usually embedded into the polymer matrix so that it cannot react with air or water. Due to its own polymeric nature it will not migrate or evaporate from the final productThe percentage of RP are not expected to grossly exceed the percentage of deca-BDE although differences will exist between plastics. There are no studies available on carcinogenicity, mutagenicity, reproduction toxicity, endocrine effects or sensitisation. Based on the available data, red phosphorus is considered to meet the P criteria due to the inorganic nature of the substance. The data are insufficient for evaluation of the B and T criteria. At a screening level, red phosphorus does not meet the T criteria.

Red phosphorus has been used as FR for a number of years. The available studies are limited, but do not suggest that red phosphorus should be more hazardous to man or environment than deca-BDE.

Diethyphosphinic acid, aluminium salt

Diethyphosphinic acid can be used as FR in PA at 15-20% compared to 16-18% of deca-BDE. There are no indications of mutagenic or sensitizing potential of diethylphosphinic acid (aluminium salt). Data are not sufficient to conclude on carcinogenic, reproductive or endocrine disruption potential. Based on the available data, the tested FR product containing is considered to be persistent, but not to meet the criteria for bioaccumulation. The available data indicate that diethylphosphinic acid, aluminium salt, is not acutely toxic at concentrations up to the water solubility limit, and has a low acute toxicity towards aquatic organisms.

For diethylphosphinic acid, aluminium salt, few data are available from the manufacturer. The available studies do not suggest that the compound should be more hazardous to man or environment than deca-BDE.

Table 6.1 The key toxicological and environmental properties of decabfromodiphenyl ether (deca-BDE) and its halogenated and non-halogenated alternatives are expressed by the following key parameters: carcinogenicity (C), mutagenicity (M), reproductive toxicity (R), endocrine disrupting effects (E), sensibilisation (S), persistence (P), bioaccumulation (B) and aquatic toxicity (T). The symbols + indicate a potential hazard, - indicates no potential hazard identified and n.d. indicates that no data are available.

Halogenated alternatives	CAS No.	Data availability environment/health		CMR; ES	PBT
Decabromodiphenyl ether	1163-19-5		+++	C0/M-/R- ; E0/S-	P+/B-/T-
Ethylene bistetrabromo-phthalimide (EBTPI)	32588-76-4	+	++	C0/M-/R- ; E-/S0	P+/B-/T-
Tetrabromobisphenol A (TBBPA)	79-94-7	++	+++	C0/M-/R- ; E-/S-	P+/B-/T-
Tetrabromobisphenol A carbonate oligomer [A]	94334-64-2 71342-77-3	-	+	C0/M-/R0 ; E0/S0	N.d.
Non halogenated alternatives	CAS No.:	Data availability environment/health		CMR	PBT
Triphenyl phosphate (TPP)	115-86-6	++	++	C0/M-/R- ; E0/S-	P-/B-/T-
Red phosphorus	7723-14-0	++	++	C0/M0/R0 ; Eo/S0	P+/B0/T-
Diethylphosphinic acid, aluminium salt[B]	225789-38-8	+	+	C0/M-/R0 ; Eo/S-	P-/B-/T-

[A] As a worst case polymers are assessed by their monomer, in this case TBBPA.
[B] Only data for test with the product Exolit OP 1230

In conclusion, it does seem likely that the substitution of deca-BDE by one of the alternatives available today is possible in compliance with the requirement of the RoHS Directive article 5(1)(b): here an exemption to continue using polybrominated diphenyl ethers, including deca-BDE, is granted only if "***the negative environmental, health and/or consumer safety impacts caused by substitution are likely to outweigh the environmental, health and/or consumer safety benefits thereof;***

Thus, a number of readily available altenatives exists that allows for the substitution of deca-BDE in a range of flame retardant applications

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Appendix A Long list

Long list of alternative flame retardents

Flame retardant	CAS No	Product name (examples)	Relevant resins to be used with the flame retardant *
Halogen-containing alternatives:			
Bis(pentabromophenyl) ethane (DBDE)	84852-53-9	SAYTEX 8010 (Albemarle) Firemaster 2100 (Great Lakes)	HIPS, ABS, PC/ABS, HIPS/PPO , PBT. Polyolefins (PE, PP...)
Ethylene bistetrabromophthalimide (EBTPI)	32588-76-4	Saytex BT 93 (Albemarle)	HIPS, ABS, PC/ABS and HIPS/PPO
Tetrabromobisphenol A epichlorohydrinpolymer	40039-93-8	Starex (Hexion Specialty Chemicals, Korea)	
Bis(tribromophenoxy)ethane	37853-59-1	FF-680 (Great Lakes).	HIPS, ABS, PC
Hexabromocyclododecane (HBCD)	3194-55-6 25637-99-4	SAYTEX HP-900 9006L (Albemarle) SP-75 and CD-75P (Great Lakes Chemical Corp.)	HIPS
Tetrabromobisphenol A (TBBPA)	79-94-7	SAYTEX CP-2000 (Albemarle) BA-59P (Great Lakes)	ABS, PC
Tetrabromobisphenol A bis (2,3-dibromopropyl ether)	21850-44-2	SAYTEX HP-800A, HP-800AG, and HP-800AGC (Albemarle) PE-68 (Great Lakes) 403AF (LG Chem - actually polymer with the substance) FR 750 (ICL Industrial)	PP,PE,HIPS
Tetrabromobisphenol A carbonate oligomer	94334-64-2 71342-77-3	Great Lakes BC-52 Great Lakes BC-58HP	PBT, PC, ABS, PC/ABS
Brominated polystyrene	88497-56-7	SAYTEX® HP-7010G (Albemarle) SAYTEX® HP-3010 (Albemarle) PYRO-CHEK® 68PB (Albemarle) Part of SAYTEX® PBT-620 (blend with polyester resin) Firemaster PBS 64 (Great Lakes) FR-803P (ICL Industrial)	PA, PBT
Poly(dibromostyrene)	148993-99-1	PDBS-80	PBT
Poly (pentabromobenzyl acrylate) fr 1025	59447-57-3	FR 1025 (ICL Industrial)	PA, PBT/PET
2,4,6-Tris(2,4,6-tribromophenoxy)-1,3,5 triazine	25713-60-4	FR 245 (ICL Industrial)	ABS, HIPS
Brominated epoxy oligomer	68928-70-1	FR 2300 (ICL Industrial)	PBT, HIPS, ABS, PC/ABS
Chloroparaffins	63449-39-8 85535-85-9	No manufacturers identified yet	PP, PE

Flame retardant	CAS No	Product name (examples)	Relevant resins to be used with the flame retardant *
Dodecachlorododecahydro-dimethanodibenzocyclooctene (Dechlorane Plus)	13560-89-9	Dechlorane Plus® (Occidental Petroleum Corporation)	PA, ABS, PP, PE, Epoxy
Halogen-free alternatives:			
Resorcinol bis(diphenylphosphate) (RDP)	57583-54-7 125997-21-9	Fyrolflex RDP (Akzo Nobel/Supresta) Reofos RDP (Great Lakes)	PC/ABS PPE/HIPS
Bisphenol A bis(diphenylphosphate) (BDP, BAPP)	181028-79-5	Reofos BAPP (Great Lakes) NcendX P-30 (Albemarle Corp.)	PC/ABS PPE/HIPS
	5945-33-5	Fyrolflex BDP (Akzo Nobel/Supresta)	ABS, HIPS
Cresyl diphenyl phosphate (CDP)	26444-49-5	Disflamoll® DPK (Lanxess)	PC/ABS
Triphenyl phosphates (TPP) Triaryl phosphates butylated	115-86-6 68937-40-6	Reofos TPP (Great Lakes) Reofos 507 (Great Lakes) Fyrolflex TPP (Akzo Nobel/Supresta)	PC/ABS PPO/PC
Red phosphorus	7723-14-0	Exolit RP 690 and other in the RP series (Clariant)	PA, PE
Melamine polyphosphate	218768-84-4	MELAPUR® 200/70 (Ciba)	PA
Melamine cyanurate	37640-57-6	MELAPUR® MC XL (Ciba)	PA
Ammonium polyphosphate	14728-39-9 68333-79-9	Exolit AP 750 (TP) and other in the AP series (Clariant)	PE, PP
Phosphinates Diethylphosphinic acid, aluminiumsalt	225789-38-8	Exolit OP 1230 and other in the OP series (Clariant) Marketed by Clariant as "Test product, can be supplied in commercial quantities on short notice"	PA, PBT/ PC/ABS, PPO/HIPS
Aluminium trihydroxide	21645-51-2		PE, PP
Magnesium dihydroxide	1309-42-8	MAGNIFIN H-5 IV (Albemarle)	PA

Appendix B Data compilation

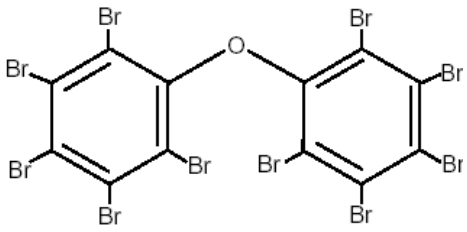
Preface

Appendix B contains the physical-chemical, environmental and health data identified in the evaluation of the environmental and toxicological properties of selected alternatives to deca-BDE. The contents of Appendix B represent the complete results of the literature review for these substances. The data presented are based primarily on risk assessments, test reports, electronic databases, review literature and original papers, when available.

The information marked by * represents the key data for the assessment. The key data are selected based on the data quality. For substances with few data, the selected data are based on data quality and/or availability.

Table of contents

Decabromobisdiphenyl ether (deca-BDE)

Identification of the substance	This summary is solely based on the EU Risk Assessment Report	
CAS No.	1163-19-5	(1)
EINECS No.	214-604-9	(1)
EINECS Name	Bis(pentabromophenyl) ether	(1)
Synonyms	Decabromodiphenyl ether	(1)
Molecular Formula	$C_{12}Br_{10}O$	(1)
Molecular Structure		(1)
SMILES Notation	O(c(c(c(c(c1Br)Br)Br)Br)c1Br)c(c(c(c(c2Br)Br)Br)Br)c2Br	
Major Uses	Flame retardant	
EU Classification	Not classified	

Physico-Chemical Properties (3.2.1.2)

Physical form	Solid, white to off-white powder	(1)
Molecular weight	959.2	(1)
Melting point (ºC)	300-310	(1)
Boiling point (ºC)	Not applicable (decomposes at >320ºC)	(1)
Decomposition temperature (ºC)	>320	(1)
Flash point (ºC)	Not applicable	(1)
Vapour pressure (Pa at 21 ºC)	$4.63 \cdot 10^{-6}$	(1)
Density (g/cm^3 at ºC)	Relative density 3.0	(1)
Solubility (mg/L at ºC)	<0.1 µg/L	(1)

Decabromobisdiphenyl ether (deca-BDE)

Partition coefficient (log P_{ow})	6.27	(1)
pKa	No data found	
Henry's Law constant ($atm/m^3/mol$ at ºC)	$1.19 \cdot 10^{-8}$ (estimated, bond method)	(1)
	$4.45 \cdot 10^{-8}$ (estimated, group method)	(1)

Ecotoxicity

Algae	*Skeletonema costatum*	
(3.2.2.1)	EC_{50}(72h)>1 mg/L (exceeds the water solubility)	(1)
	Thalassiosira pseudomona	
	EC_{50}(72h)>1 mg/L (exceeds the water solubility)	(1)
	Chlorella sp.	
	EC_{50}(96h)>1 mg/L (exceeds the water solubility)	(1)
	Algae	
	EC_{50}(72-96h)=30.3 µg/L (estimated) (exceeds the water solubility)	(1)
Crustaceans (3.2.2.1)	No data (NOEC was above the solubility limit (2 µg/L) in a 21 d reproduction test with *Daphnia magna* for octa-BDE)	(1)
	Daphnia sp	
	EC_{50}(48h)=50.7 µg/L (estimated) (exceeds the water solubility)	(1)
(3.2.2.2)	NOEC(16d)=3.5 µg/L (estimated) (exceeds the water solubility)	(1)
Fish	*Oryzias latipes*	
(3.2.2.1)	LC_{50}(48h)>500 mg/L (exceeds the water solubility)	(1)
	Fish	
	LC_{50}(96h)=183 µg/L (estimated) (exceeds the water solubility)	(1)
(3.2.2.2)	NOEC(28d)=10.9 µg/L (estimated) (exceeds the water solubility)	(1)
Other aquatic organisms	*Lumbriculus variegatus*	
(3.2.2.4)	NOEC(28d)=4.5 mg/kg dry weight (2.4% organic carbon sediment)	(1)
	NOEC(28d)=3.8 mg/kg dry weight (5.9% organic carbon sediment)	(1)
Bacteria (3.2.2.3)	NOEC(3h) ≥15 mg/L (OECD 209)	(1)
Terrestrial organisms	Terrestrial plants (6 species: *Zea mays, Allium cepa, Lolium perenne, Cucumis sativa, Glycine max, Lycopersicon esculentum)*	
(3.2.2.3)	NOEC(21d)≥5349 mg/kg dry weight (OECD 208)	(1)
	Eisenia fetida	
	NOEC(56d)≥4910 mg/kg (OECD 207)	(1)
Other information	*Secondary poisoning*	

Decabromobisdiphenyl ether (deca-BDE)

	Deca-BDE has been found to be present at low concentrations in some types of marine mammals and possible also other aquatic organisms. Deca-BDE has also been found in the content of predatory birds' eggs at relatively low concentrations	(1,2)

Environmental fate

BCF (Fish) (3.2.2.7)	Little or no uptake occurs in aquatic organisms exposed via the water phase. Limited uptake in fish exposed via food has been seen, but with tissue concentrations lower than food concentrations	(1,2)
Aerobic degradation (3.2.2.8)	Not readily biodegradable (test method comparable to MITI 1 test)	(1)
Anaerobic degradation (3.2.2.9)	Not biodegradable under anaerobic conditions	(1)
	Debromination of at least 5% deca-BDE to lower brominated congeners was observed in sewage sludge after 238 d under favourable conditions (37°C, high inoculum conc.)	(3)
Hydrolysis	Stable to hydrolysis	(1)
Photodegradation (3.2.2.10)	Deca-BDE photodegrades under a wide range of conditions. Reductive debromination of deca-BDE into lower brominated diphenyl ethers occurs, but these are generally not the major degradation products formed	(1,2,3)
Metabolic pathway	No data found	
Mobility in soil (K_{oc})	22,100-149·10^6 (estimated)	(1)

Toxicological data

Observations in humans	50 volunteers were exposed to 5% deca-BDE (purity unknown) in petrolatum on the skin. Induction was 3 times a week for 3 weeks and challenge 2 weeks later. No skin sensitisation was seen. 9/50 subjects had skin irritation. 200 volunteers (80 males and 120 females) were induced with deca-BDE with 9 patches applied to the skin, one every second day. Two batches of unknown purity was used, one as received and one diluted to 2% (w/v) in water. 15/200 showed slight irritation reactions. The subjects were challenged 12 days after the induction period. Neither of two test materials showed sensitisation.	(1)

Decabromobisdiphenyl ether (deca-BDE)

	Health assessment of workers exposed at least 6 weeks to polybromobiphenyls and polybromobiphenyl oxides, incl. deca-BDE. 4/35 showed higher prevalence of primary hypothyroidism, low serum T4 and free thyroxine (0/80 control subjects). Also a significant reduction in sensory and fibula motor velocities was observed. No deca-BDE was detected in serum. It is unclear whether polybromobiphenyls or deca-BDE is the etiological agent.	(1)
Studies in animals	No data found	

Acute toxicity

Oral (3.2.3.2)	Groups of 5 male albino Spartan rats were administered single doses of 50, 500 or 5,000 mg/kg of deca-BDE in corn oil (Great Lakes DE-83). All rats survived for 14 days and normal weight gain during were observed. Female Sprague-Dawley rats received a single dose of 126, 252, 500, 1,000 or 2,000 mg/kg as a 10% corn oil suspension of deca-BDE dosed by intubation (Dow FR-300-BA: 77.4% deca-BDE, 21.8% nona-BDE and 0.8% octa-BDE). No indications of toxicity after intubation or during the 14-day period were observed. No gross pathological changes were observed at necropsy carried out on one rat/dose level.	(1)
Dermal (3.2.3.2)	Groups of 2 male and 2 female New Zealand White rabbits were administered single doses of 200 or 2,000 mg/kg of deca-BDE (Great Lakes DE-83) under occlusive wraps for 24 hours. All the animals survived. Animals were observed for 14 days. At the 2,000 mg/kg dosage level all rabbits exhibited normal body weight gains. Local and general signs of toxicity were not reported and necropsies not performed.	(1)
Inhalation (3.2.3.2)	Groups of 5 male and 5 female Spartan rats were exposed for one hour to 2 or 48.2 mg/l deca-BDE (Great Lakes DE-83) in air and subsequently observed for 14 days. All rats survived. Dyspnoea and ocular discharge was noted one animal in the 2 mg/l group. In the 48.2 mg/l group, eye squint and increasing motor activity were observed. All rats were normal at the end of 14-day-observation period. Necropsy was not performed. The usefulness of this assay is dubious since no data on particle size distribution are given.	(1)
Other routes	No data found	
Skin irritation	Commercial deca-BDE (74.4% deca-BDE,	(1)

Decabromobisdiphenyl ether (deca-BDE)

(3.2.3.3)	21.8% nona-BDE, 0.8% octa-BDE) applied to shaved skin under occlusion as dry solid (500 mg) in 2 groups of 3 New Zealand White rabbits did not cause irritation on intact or abraded skin. No erythematous and oedematous response was observed after a single exposure for 24h or the following observation period of 72h. In another study, deca-BDE (purity unknown) applied as dry solid on shaved skin of New Zealand albino rabbits caused no response on intact skin and a slight erythematous and oedematous response on abraded skin after a single confined exposure of 24 hours. The skin responses after repeated exposures to intact skin for five days/week for two weeks and to abraded skin for three days did not differ from responses following a single administration. No more information is available.	
Eye irritation (3.2.3.3)	deca-BDE (93 - 98.5% purity) as dry solid (100 mg) caused transient (reversible in 48h) mild irritation of the conjunctival membranes (grade 1) in New Zealand White rabbits (3 females and 3 males). The cornea, iris and lens were unaffected. A single installation of 100 mg deca-BDE (purity unknown) caused mild irritation of the conjunctival membrane in New Zealand White rabbits (3 females and 3 males): very slight erythema in 3/6 animals and slight erythema in 1/6 animal at 24 hours, and very slight erythema in 1/6 animals at 48 hour. Erythema was reversible in 72 hours. Very slight chemosis in 2/6 animals at 24 and 48 hours, and in 1/6 animals at 72 hours and at day 7. Slight discharge in 1/6 animals at 24 hours and 72 hours, and moderate discharge in 1/6 animals at 48 hours.	(1)
Irritation of respiratory tract (3.2.3.3)	Spartan rats inhaled aerosols of deca-BDE (Great Lakes DE-83), 2 mg/l and 48.2 mg/l, showed marked dyspnoea in 1/5 and 3/5 animals, respectively.	(1)
Skin sensitization (3.2.3.4)	No animal data on deca-BDE were available. Skin irritation was observed in 9/50 persons subjected to repeated application of a suspension of 5% deca-BDE in petrolatum 3 times a week for 3 weeks and challenged two weeks subsequent to the last induction application. None showed skin sensitisation.	(1)

Decabromobisdiphenyl ether (deca-BDE)

Repeated Dose Toxicity

Oral (3.2.3.5)	In a 14-day study (NTP), groups of 5 female and 5 male B6C3F1 mice were fed diet containing to up to 100,000 ppm deca-BDE (99% pure). No effects on health, survival or body weights were observed and no compound-related clinical signs or gross pathological effects on major tissues or organs were reported at the highest dose level, corresponding to approximately 25,000 mg/kg/day for females and 15,000 mg/kg/day for males. In a 13-week study (NTP), groups of 10 female and 10 male B6C3F1 mice were fed diet containing up to 50,000 ppm deca-BDE (99% or 97% pure). Survival, food consumption or final mean body weights were not adversely affected, and no compound related clinical signs or gross or microscopic pathology were observed at the highest dose level, corresponding to approximately 11,000 mg/kg/day for females and 7,000 mg/kg/day for males. In a 14-day study (NTP), groups of 5 female and 5 male F344/N rats were fed diet containing up to 100,000 ppm deca-BDE (99% pure). No effects on health, survival or body weight were observed, and no compound-related clinical signs or gross pathological effects on major tissues and organs were seen at the highest dose level, corresponding to approximately 7,500 mg/kg/day. In a 28-day study, groups of 10 female and 10 male rats were fed diet containing up to 1,000 ppm deca-BDE (purity unknown). No compound-related changes were seen in behaviour, appearance, body weights or food consumption. No gross pathologic lesions or variations in organ weights, nor microscopical lesions in the examined tissues (liver, kidneys and thyroid) were observed at the highest dose level, corresponding to80 mg/kg/day for males and 70 mg/kg/day for females. Dose-depending increase in bromine content were seen in liver and fat samples was observed. In a 30-day study, male Sprague Dawley rats (number unspecified) were fed diet containing up to 10,000 ppm deca-BDE (77.4% deca-BDE, 21.8% nona-BDE and 0.8% octa-BDE. No clinical signs of toxicity, no changes in feed consumption, body weight gain, organ weights (heart, testes and kidneys), hematological and urinary values were observed. Enlarged livers were found at the two highest dose levels.	(1)

Decabromobisdiphenyl ether (deca-BDE)

	Hepatic centrilobular cytoplasmic enlargement and vacuolisation and renal hyaline degenerative cytoplasmic changes were found at the highest dose level. Thyroid hyperplasia was reported at the two highest dose levels. In this study, NOAEL is 8 mg/kg/day and LOAEL is 80 mg/kg/day. In a 13-week study (NTP), groups of 10 female and 10 male F344/N rats were fed diet containing up to 50,000 ppm deca-BDE (97 - 99% pure). were administered in the diet to. No effects on survival, health, body weight or feed consumption were observed, and no gross or microscopical effects were reported the highest dose level, corresponding to approximately 3,800 mg/kg/day for females and 2,800 mg/kg/day for males.	
Dermal	No data found	
Inhalation (3.2.3.5)	Male Sprague Dawley rats (50) were dosed with deca-BDE dust (20 mg; mean diameter 3.17 µm; 77.4% pure) by intratracheal installation. No untoward effects were observed, except on days 10 and 556 (but not on days 30 and 416). The lungs contained scattered focal aggregates of alveolar macrophages showing clear, angulated, cytoplasmic vacuoles or spaces, which probably represented the location of the dust particles. A very slight focal thickening of the interalveolar septae was noted in 2 rats. Particles were not present in the regional lymph nodes. No evidence of fibrosis or other proliferative response was detected in the lungs or regional lymph nodes. The half-life of deca-BDE in lungs was determined to be150 days.	(1)
Mutagenicity (3.2.3.6)	Deca-BDE (97% pure). S. typhimurium TA98, TA100, TA1535 and TA1537 in the presence and absence of S9-mix. Negative in TA1535 and TA1537. Equivocal in TA98 and TA100 in the presence of S9-mix. Two commercial deca-BDE products (unknown purity). S. typhimurium TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of S9-mix. Positive in TA98, TA100 and TA 1535 in the presence and absence of S9-mix. Negative in TA1537 and TA1538. Positive results may be due to impurities. Deca-BDE (98% pure). S. typhimurium TA98, TA100, TA1535 and TA1537, and E. coli WP2uvrA in the presence and absence of S9-mix. Negative response was found in all strains.	(1)

Decabromobisdiphenyl ether (deca-BDE)

Genotoxicity (3.2.3.6)	Deca-BDE (unknown purity). Mouse lymphoma cells (L 5178 Y/TK$^{+/-}$) in the presence and absence of S9-mix. Not mutagenic. Deca-BDE (unknown purity). CHO cells in the presence and absence of S9-mix. No sister chromatid exchange nor chromosomal aberrations were seen. In vivo cytogenetic study on bone marrow cells from rat femur (parental and neonate animals in a reproduction study) showed no chromosomal aberrations.	(1)
Carcinogenicity (3.2.3.7)	In a two-year study (NTP), groups of 50 female and 50 male B6C3F1 mice were fed diet containing 0, 25,000 or 50,000 ppm deca-BDE (97% pure). Body weights and food consumption were comparable controls. No compound-related clinical signs of toxicity were reported. No significant differences in survival were observed. Increased incidences of non-neoplastic lesions were observed in several tissues (liver, thyroid gland, stomach. In this study a NOAEL was not established, a LOAEL is 25,000 ppm, corresponding to approximately 3,700 mg/kg/day for females and 3,200 mg/kg/day for males. In a two year study (NTP), groups of 50 female and 50 male Fisher 344/N rats were fed diet containing 0, 25,000 or 50,000 ppm deca-BDE (94 - 97% pure). No clinical signs of toxicity or differences in survival rates were reported. Several non-neoplastic lesions were observed: high dose males exhibited increased incidence of thrombosis and degeneration in the liver without foci of necrosis associated, fibrosis of the spleen and lymphoid hyperplasia of the mandibular lymph nodes. Haematopoïesis in spleens of females and acanthosis of the forestomach in dosed males were slightly increased. Dose dependent decreased incidence of C-cell hyperplasia of the thyroid gland in males was also seen. In this study, a NOAEL for systemic toxicity was 25,000 ppm (1,120 mg/kg/day for males. For local effects, a LOAEL of 25,000 ppm (forestomach acanthosis). In a two-year study, groups of 25 female and 25 male Sprague-Dawley rats were diet containing deca-BDE (purity: 77.4% deca-BDE; 21.8% deca-BDE; 0.8%deca-BDE) corresponding to 0, 0.01, 0.1 or 1 mg/kg bw/day. No effects were seen on survival rates, appearance, mean body weights, feed consumption, hematology, urinalysis, clinical chemistry and organ	(1)

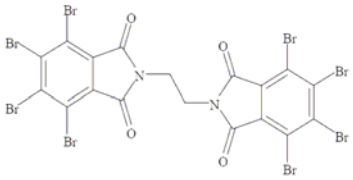
	weights, and no gross and microscopic findings were seen. The maximum dose tested was very low.	
Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity (3.2.3.7)	Sprague-Dawley rats exposed to commercial deca-BDE (77.4% deca-BDE, 21.8% nona-BDE, 0.8% octa-BDE) in the feed corresponding to 3, 30 (10 males and 20 females) or 100 mg/kg bw/day (15 males and 30 females). 60 days prior to mating, 15 days during mating, through gestation and lactation. No macroscopic signs of toxicity in adults or in neonates. Minor developmental variations in soft tissues and skeleton, incidence comparable to controls, no dose-response relationship. Rats and mice treated with deca-BDE (purity >94%) in the feed. 13 weeks or 2 years with up to 50,000 ppm. No macroscopic or microscopic effects seen on testes, prostate, ovaries or uterus. A recent study on developmental neurotoxicity studied spontaneous behaviour and habituation capability. Purity of deca-BDE >98%. Neonate NMRI mice exposed on PD 3 or PD 19 (2.22 or 20.1 mg/kg bw), or PD 10 (1.34, 13.4 or 20.1 mg/kg bw). The animals were tested 2, 4 and 6 months after exposure. Effects were seen in animals exposed on PD 3. The effect was marginal at 2.22 mg/kg but significant at 20.1 mg/kg. No treatment related effects were seen at the other exposure days.	(1)
Embryotoxicity	No data found	
Teratogenicity (3.2.3.7)	20 pregnant Sprague-Dawley rats exposed to commercial deca-BDE (77.4% deca-BDE, 21.8% nona-BDE, 0.8% octa-BDE) by gavage, 10, 100 or 1000 mg/kg bw/day on GD 6-15. No effects seen on the dams except higher liver bromine content at 1000 mg/kg. Increased, but not dose-dependent incidence of resorptions from 10 mg/kg and delayed ossification of the skull and subcutaneous oedema at 1000 mg/kg in the foetuses. Pregnant rats (Crl:CD(SD)IGS BR) exposed on GD 0-19 to deca-BDE (purity 97.34%) by gavage, 100, 300 or 1000 mg/kg bw/day. No macroscopic or microscopic effects in the	(1)

	dams. In the foetuses low incidences of vascular and heart defects. Early resorptions were statistically significant but within the upper limit of the historic control.	
Toxicokinetics		
(3.2.3.8)	Male F344/N rats were exposed by feeding to up to 50.000 ppm deca-BDE (purity 97.9-99.2%) for 11 days, corresponding to 3,718 mg/kg bw/day. On the 8, deca-BDE was radiolabelled (^{14}C-deca-BDE). 91.3-101% of the radioactivity was recovered in the faeces within 72 hours. Recovery was not dose-related. Small amounts were found in the liver (0.008-0.064%) and in fatty tissue (0.09-0.157%), highest amounts at the lowest dose level (238 ppm). Rats exposed by feeding to 227 ppm (22-25 mg/kg bw/day) or 48.000 ppm (4.5-5 g/kg bw/day) deca-BDE for 9-11 days. On the 8, deca-BDE was radiolabelled (^{14}C-deca-BDE). 82.5-86.4% of the radioactivity was recovered in the faeces independent of time of sacrifice (24, 48 or 72 hours). Recovery was not dose-related. Small amounts were found in the liver: 0.45, 0.21 and 0.11% at 24, 48 and 72 hours after the radioactive dose, respectively. After 10 days only deca-BDE was found in the liver. Approximately 0.01% was excreted in the urine. 3 main metabolites (not mentioned) were found in faeces in increasing amounts with increasing dose. 72 hours after intravenous injection of ^{14}C-deca-BDE 74% in rats (F344/N) was found in the faeces, indicating biliary excretion. The remainder radioactivity was found mainly in muscles, skin, liver and fat. Only traces were found in urine, spleen and brain. Three metabolites were also detected in the faeces, but not identified. Biliary excretion was studied after intravenous injection of ^{14}C-deca-BDE to F344/N rats. Bile was collected over 4 hours showing an excretion rate of 2.2%/hour of the dose. One metabolite detected, but not identified. Neonate NMRI mice were dosed with 2.22 mg/kg bw ^{14}C-labelled deca-BDE (purity <98%) on PD 3, 10 or 19. Radioactivity was measured 1 and 7 days after dosing in brain, heart and liver. Minor concentrations were found in brain and heart. The concentration in the brain doubled from day 1 to day 7. The concentration in the heart remained at the same level from day 1 to	(1)

day 7. The concentration in the liver was considerably higher at day 1 and approximately the half at day 7.

Ethylenebistetrabromophthalimide (EBTPI)

Identification of the substance

CAS No.	32588-76-4	(4)
EINECS No.	251-118-6	(4)
EINECS Name	N,N'–ethylenebis(3,4,5,6–tetrabromophthalimide)	(4)
Synonyms	2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione); BT 93; BT 93W; BT-93D; Citex BT 93; Ethylene bis(tetrabromophthalimide); Phthalimide, N,N'-ethylenebis(tetrabromo- (8CI); Saytex BT 93; Saytex BT 93W.	(5)
Molecular Formula	$C_{18}H_4Br_8N_2O_4$	(4)
Molecular Structure		(6)
SMILES Notation	O=C(N(C(=O)c1c(c(c(c2Br)Br)Br)Br)CCN(C(=O)c(c3c(c(c4Br)Br)Br)c4Br)C3=O)c12	
Major Uses	Flame retardant in polyolefins, high-impact polystyrene (HIPS), thermoplastic polyesters (PBT, PET), polycarbonate and elastomers; brominated additive flame retardant; flame retardant in electrical and electronics components, wire and cable insulation, switches, and conductors.	(7)
EU Classification	Not classified in the Annex 1 of Directive 67/548/EEC or listed in a priority list (European Priority lists and Risk Assessment information – EEC No 793/93).	(8)

Physico-Chemical Properties

Physical form	Solid	(4)
	Light yellow powder	(9)
Molecular weight	951.5	(4)
Melting point (°C)	>445	(4)
	456	(9)

Ethylenebistetrabromophthalimide (EBTPI)

	350 (estimated)	(10)
Boiling point (ºC)	886.97 (estimated)	(10)
Decomposition temperature (ºC)	No data found	
Flash point (ºC)	No data found	
Vapour pressure (mmHg at 25 ºC)	*$2.54 \cdot 10^{-22}$ (estimated)	(10,11)
Density (g/cm^3 at ºC)	Relative density 2.77	
Solubility (mg/L at 25 ºC)	*<1.63 mg/L	(4)
	<0.01%	(9)
	*$3.029 \cdot 10^{-9}$ (estimated)	(10,11)
Partition coefficient (log P_{ow})	*9.80 (estimated)	(10,11)
pKa	No data found	
Henry's Law constant (atm/m^3/mol at 25ºC)	*$3.64 \cdot 10^{-21}$ (estimated)	(10,11)

Ecotoxicity

Algae	No data found	
Crustaceans	No data found	
Fish (3.3.2.1)	*Oryzias latipes* LC_{50}(48h) >500 mg/L (exceeds the estimated water solubility)	(4,10,11)
	Fish LC_{50}(96h) 0.000612 mg/L (estimated, not expected to be soluble at this level)	(11)
Bacteria	No data found	
Environmental fate		
BCF (Fish) (3.3.2.4)	*Cyprinus carpio* *<0.3-1.3 (MITI Guideline, exp. conc. 2 mg/L)	(4,10,11)
	Cyrpinus carpio *<3.3 (MITI Guideline, exp. Conc. 0.2 mg/L)	(4,10,11)
	Fish 9.5 (estimated)	(11){1780
Aerobic degradation (3.3.2.5)	*Ready biodegradability*	
	*0% after 14/28 days (OECD 301C)	(10) (4,11)
Anaerobic degradation	No data found	

Ethylenebistetrabromophthalimide (EBTPI)

Hydrolysis	No data found	
Photodegradation	No data found	
Metabolic pathway	No data found	
Mobility in soil (K_{oc})	800.000 (estimated)	(10,11)
Toxicological data		
Observations in humans (3.3.3.1)	Two cases of possible human exposure to ethylene bis(tetrabromophthalimide) resulting in adverse health effects have been reported (respiratory problems).	(12)
Studies in animals		
Acute toxicity		
Oral (3.3.3.2)	Rat: Test dose was 7500 mg/kg. LD_{50} > 7500 mg/kg bw	(13)
Dermal (3.3.3.2)	Rabbit: Test dose was 2000 mg/kg. LD_{50} > 2000 mg/kg bw	(14)
Inhalation (3.3.3.2)	Rat: Test dose was 4.5 ± 3.0 g/l (1 hr) LD_{50} > 4.5 ± 3.0 g/l.*	(15)
Other routes	No data found.	
Skin irritation (3.3.3.3)	Rabbit: Test dose was 0.5 g. Scores for erythema, eschar and edema formation were negative (0) at 72 hrs post-application (Draize test). Not irritating.*	(16)
Eye irritation (3.3.3.3)	Rabbit: Test dose was 0.1 g. The eyes were examined at 1, 24, 48 and 72 hours, 5 and 7 days post–administration. Conjunctival redness in 6 animals (1 h), 2 animals (24 hours), none (48 hours) and none (end of study). Chemosis, corneal lesions and iris effects were negative (Draize test). Mild irritating.*	(17)
Irritation of respiratory tract	No data found	
Skin sensitization	No data found	

Ethylenebistetrabromophthalimide (EBTPI)

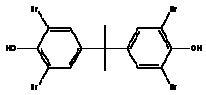
Repeated Dose Toxicity		
Oral (3.3.3.5)	Rat: 0.01, 0.1 or 1% BT93 in the diet for 28 days to weanling Sprague-Dawley rats. No compound related changes were observed in the study. Based on test results a NOAEL >1% was established.	(18)
	0.01, 0.1 or 1% BT93 in the diet for 90 days followed by 46 days with control diet to Sprague-Dawley rats. No compound related changes were observed in the study. Based on test results a NOAEL >1% was established.*	(19)
Dermal	No data found	
Inhalation	No data found	
Mutagenicity (3.3.3.6)	Ethylenebis(tetrabromophthalimide) was found not to induce mutations, either with or without metabolic activation, in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537.*	(20)
	10, 50, 100, 500, 1000, and 5000 µg/plate of Ethylene bis(tetrabromophthalimide) was tested in the Ames Salmonella/Microsomal Assay for mutagenicity with *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98, TA100), and *Escherichia coli* (WP2 uvrA). No mutagenic activity was detected in any of the strains, either with or without metabolic activation.*	(21)
	1, 10, 100, 500, and 1000 µg/plate of Ethylenebis (tetrabromophthalimide) was determined to be nonmutagenic, both with and without metabolic activation in *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98, and TA100) and *Saccharomyces cerevisiae* (D4).	(22)
Genotoxicity	No data found	
Carcinogenicity	No data found	

Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity	No data found	
Embryotoxicity	No data found	
Teratogenicity	Rat:	(23)

(3.3.3.7)	A range finding study was performed in pregnant Sprague-Dawley rats with BT93 administered by gavage (0, 200, 500, 1000, 1500, 2000 mg/kg/day) mg/kg/day) daily from gestation day 6 to 15. NOEL = 2000 mg/kg/day.*	
	A teratogenicity study was performed in pregnant Sprague-Dawley rats with BT93 administered by gavage (0, 100, 500, 1000, mg/kg/day) mg/kg/day) daily from gestation day 6 to 15. Not maternally or teratogenic toxic when orally administered up to 1000 mg/kg. NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogen) > 1000 mg/kg bw*	(24)
	Rabbit: A teratogenicity study was performed in twenty inseminated New Zealand white rabbits gavaged with 1000 mg/kg bw (BT93) daily from gestation day 7 to 19. Not maternally or teratogenic toxic when orally administered to 1000 mg/kg. NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogen) > 1000 mg/kg bw*	(25)
Toxicokinetics		
Metabolism (3.3.3.8)	Rat: ^{14}C–labelled BT93 was administered orally by gavage to 5 female Sprague–Dawley rats for 14 days. The compound was excreted mainly in the faeces (app. 65%), urine (15%) and breath (1%). All organs contained radioactive residues.	(26)

Tetrabromobisphenol A (TBBPA)

Identification of the substance

CAS No.	79-94-7	(27)
EINECS No.	201-236-9	(27)
EINECS Name	2,2'6,6'-Tetrabromo-4,4'-isopropylidenediphenol	(27)
Synonyms	Tetrabromobisphenol-A, TBBPA	(27)
Molecular Formula	$C_{15}H_{12}Br_4O_2$	(27)
Molecular Structure		(27)
SMILES Notation	Oc1c(cc(cc1Br)C(c1cc(c(O)c(c1)Br)Br)(C)C)Br	(28)
Major Uses	As a Reactive flame retardant the primary use of tetrabromobisphenol-A, accounting for approximately 90 % of tetrabromobisphenol-A used, is as an intermediate in the manufacture of epoxy and polycarbonate resins. It is also used as a reactive flame retardant in unsaturated polyester resins. When used as an intermediate it becomes covalently bound in the polymer. The only potential for exposure is from unreacted tetrabromobisphenol-A, which may exist where excess, has been added during the production. Polycarbonates are used in communication and electronics equipment, electronic appliances, transportation devices, sports and recreation equipment, lighting fixtures and signs. Unsaturated polyesters are used for making simulated marble floor tiles, bowling balls, glass-reinforced panels, furniture parts, sewer pipes coupling compound, automotive patching compounds, buttons, and for encapsulating electrical devices. The main use of epoxy resins is in the manufacturing of rigid epoxy laminated printed circuit boards. As an additive flame retardant tetrabromobisphenol-A, is added to polymers to impact flame retardant properties. It does not react chemically with the other components of the polymer and, therefore may leach out of the polymer matrix. Additive use accounts for approximately 10% of tetrabromobisphenol-A used. Its main uses as an additive flame retardant are in acrylonitrile-butadiene-styrene (ABS) resins, high impact	(27)

	polystyrene and phenolic resins. ABS resins are used in automotive parts, pipes and fittings, refrigerators, other appliances, business machines, and telephones. Polystyrene is used in packaging, consumer products, disposables, electrical end electronic equipment, furniture and in building and construction materials.	
EU Classification	Not classified	(27)
List of unwanted substances	Bromated flame retardants are on the Danish EPAs list of unwanted substances.	(29)

Physico-Chemical Properties

Physical form	White crystalline powder	(27)
Molecular weight	543.9 g/mol	(27)
Melting point (ºC)	178	(27)
	181-182	(27)
Boiling point (ºC)	~316	(27)
Decomposition temperature (ºC)	200-300	(27)
Flash point (ºC)	Decomposes at 200-300 ºC	(27)
Vapour pressure (Pa at ºC)	*<$1.19 \cdot 10^{-5}$ (20°C)	(27)
	$6.24 \cdot 10^{-6}$ (25°C)	(27)
Density (g/cm^3 at ºC)	Relative density 2.12 (20°C)	(4,27)
	Relative density 2.18	(27,30)
Solubility (mg/L at ºC)	*0.148 (pH 5, 25° C, buffered solution)	(27)
	*1.26 (pH 7, 25° C, buffered solution)	(27)
	*2.34 (pH 9, 25° C, buffered solution)	(27)
	*0.063 (pure water, 21° C)	(27)
	*0.24 (pure water, 25° C)	(27)
Partition coefficient (log P_{ow})	*5.90 (generator column method)	(27)
pKa	*pKa_1=7.5 *pKa_2=8.5	(27)
Henry's Law constant (atm/m^3/mol at 20-25ºC)	*<$1.0 \cdot 10^{-6}$	(27)

Ecotoxicity

Algae (3.4.2.1)	*Skeletonema costatum*

Tetrabromobisphenol A (TBBPA)

	*EC_{50}(72h)=0.09-0.89 mg/L	(30,31)
	Thalassiosira pseudonana	
	EC_{50}(72h)=0.13-1.0 mg/L	(30,31)
	Chlorella sp	
	EC_{50}(96h)>1.5 mg/L	(30)
	Selenastrum capricornutum	
	EC_{50}(96h)>5.6 mg/L (measured concentration)	(30)
Crustaceans	*Daphnia magna*	
(3.4.2.1)	*LC_{50}(48h)=0.96 mg/L	(4,30)
(3.4.2.2)	*NOEC(21d)=0.30 mg/L, MATC=0.54 mg/L (reproduction)	(4,30)
	Mysidopsis bahia	
(3.4.2.1)	LC_{50}(96h)=0.86 mg/L (<1 days old)	(4,30)
	LC_{50}(96h)=1.1 mg/L (5 days old)	(4,30)
	LC_{50}(96h)=1.2 mg/L (10 days old)	(4,30)
Other invertebrates	*Crassostrea virginica*	
(3.4.2.1)	EC_{50}(96h)=0.098 mg/L	(4,30)
	Chironimus tentans	
(3.4.2.2)	NOEC(14d)= 0.045-0.046 mg/L interstitial water and 230-340 mg/kg sediment (measured concentrations) in low, medium and high organic carbon sediments	(4,30)
Fish	*Lepomis macrochirus*	
(3.4.2.1)	*LC_{50}(96h)=0.51 mg/L	(4,30)
	Salmo gairdneri	
	*LC_{50}(96h)=0.40 mg/L	(4,30)
	Pimephales promelas	
	*LC_{50}(96h)=0.54 mg/L	(4,30)
(3.4.2.2)	*NOEC (35d)=0.16 mg/L (hatching and larval mortality)	(4,30)
	MATC=0.22 mg/L (embryo and larvae survival	(30)
Bacteria	No data found	
Terrestrial organisms	No data found	
Other information	TBBPA had no estrogenic effects in quails after distribution to eggs at 15 µg/g egg. TBBPA caused embryo mortality at 45 µg/g egg, but no estrogen like effects	(32) (33)
	TBBPA increased the activity of gluthathione reductase in juvenile rainbow trout at 100 mg/kg after 4, 14 and 28 days, indicating oxidative stress-inducing activity of TBBPA	(34)

Environmental fate

BCF (Fish) (3.4.2.4)	*Lepomis macrochirus*	
	*20-170 (28/14d, 0.01 µg/L, ^{14}C-labelled TBBPA)	(4,30)
	Pimephales promelas	
	*1200 (24/6d, 4.7 µg/L, ^{14}C-labelled TBBPA)	(4,30)
	Carp	
	30-341 (8 weeks, 80µg/L)	(4,30)
	52-485 (8 weeks, 8 µg/L)	(30)

Tetrabromobisphenol A (TBBPA)

BCF (Invertebrates) (3.4.2.4)	*Chironimus tentans*	
	240-510 (14d, high organic carbon sediment	(30)
	490-1100 (14d, medium organic carbon sediment	(30)
	650-3200 (14d, low organic carbon sediment	(30)
	Crassostrea virginica	
	780 (20/14d, 1.0 µg/L, ^{14}C-labelled TBBPA)	(30)
Aerobic degradation (3.4.2.5)	*Ready biodegradability*	
	*0% after 14 d (BOD test)	(4,30)
	Degradability in water/sediment	
	*t½=48d in natural river water/sediment (24-26°C, 10 µg/L). <8% mineralisation of ^{14}C-TBBPA to $^{14}CO_2$	(4,30)
	*t½=84d in natural river water/sediment (24-26°C, 1000 µg/L). <8% mineralisation of ^{14}C-TBBPA to $^{14}CO_2$	(4,30)
	Degradability in soil	
	*≤6% mineralisation of ^{14}C-TBBPA to $^{14}CO_2$ in three soil types. 36-82% TBBPA remained in the soils after 64 d	(4,30)
Anaerobic degradation (3.4.2.6)	*Degradability in soil*	
	*<0.5% mineralisation of ^{14}C-TBBPA to $^{14}CO_2$ in three soil types. 44-91% TBBPA remained in the soil after 56 d	(4,30)
Hydrolysis	No data found	
Photodegradation (3.4.2.7)	t½=0.12 d	(30)
	*t½=6.6 d (summer), 10.2 d (spring), 25.9 d (autumn), 80.2 d (winter) in water by UVR	(30)
	*t½ = 16-350 min (in water by UVR, pH range 10-5.5)	(35)
Metabolic pathway	TBBPA was metabolised to bisphenol A (BPA) in an anaerobic sediment slurry. BPA was further metabolised to 4-hydroxybenzoic acid (HBZ) and 4-hydroxyacetophenone (HAP) under aerobic conditions.	(36)
	TBBPA is dehalogenated to bisphenol A (BPA) under methaonogenic and sulphate reducing conditions with no further degradation of BPA in estuarine sediment	(37)
Mobility in soil (K_{oc})	$5.6 \cdot 10^6$ (estimated)	(7)

Toxicological data

Observations in humans (3.4.3.1)	Data from a modified Draize multiple insult test in humans provide evidence that TBBPA does not have the potential to cause skin sensitisation. Despite widespread occupational use of TBBPA, there are no case reports of skin or respiratory sensitisation. The available human data do not provide any evidence that TBBPA is a skin or respiratory sensitizer.	(27)
	In a well-conducted chromosomal aberration	(27)

	study using human peripheral lymphocytes, TBBPA tested negative*. No *in vivo* data are available on human genotoxicity, carcinogenicity or reproduction.	
(3.4.3.8)	The available data indicate that TBBPA is absorbed in humans given that it has been detected in serum samples of both occupational and non-occupational groups. There is also evidence that once absorbed, TBBP-A and/or its metabolites can be excreted via breast milk.	(27)
Studies in animals	No data found	
Acute toxicity		
Oral (3.4.3.2)	Rat: LD_{50} > 50 g/kg Mice: LD_{50} >10 g/kg.	(27)
Dermal (3.4.3.2)	Rabbit: LD_{50} > 10 g/kg.	(27)
Inhalation (3.4.3.2)	Rat: Whole body exposure to aerosol concentrations of 1.3 mg/l for 1 hours or 0.5 mg/l for 8 hours. No mortality or gross pathological lesions.	(27)
Skin irritation (3.4.3.3)	Rabbit: Test doses: 0, 100, 500 and 2500 mg/kg/day, 6 hours/day, 5 days/week. Duration: 3 weeks. Very slight erythema in some of the rabbits at all dose levels. It appeared on day 3, 2 and 1 respectively in rabbits administered at dose 100, 500 or 2500 mg/kg/day*. Rabbit: Test dose: 0,5 g TBBPA. No irritation when applied to abraded or intact skin, with and without occlusion.	(27)
Eye irritation (3.4.3.3)	Rabbit: Test dose: 100 mg TBBPA, applied to the conjunctival sac of the right eye of 6 rabbits. In four animals slight conjunctival redness after 1 hour but not after 24 hours. No ocular irritation at any other point of time*. Rabbit: Test dose: 100 mg of TBBPA to the conjunctival sac of the right eye of 6 animals. Soon after the instillation slight lacrimation and conjunctival erythema. These signs had completely disappeared by 24 hours. After 48 hours slight conjunctival redness, conjunctival chemosis and iridial irritation. At 72 hours slight conjunctival chemosis and iridial irritation. At day 7 no signs of irritation.	(27)

Irritation of respiratory tract (3.4.3.3)	Rat: Test dose: Whole body exposure for 4 hours/day, 5 days/week for 2 weeks to an atmosphere containing TBBPA dust at concentrations of 2, 6 or 18 mg/l. Signs of irritation explained by mechanical irritation resulting from exposure to very high dust concentrations. TBBPA was not considered to be irritating to the respiratory tract.	(27)
Skin sensitization (3.4.3.4)	Guinea pig: Test dose: 0.5 g applied occlusively. The animals received 9, 6-hour inductions (applications every other day, 3 times a week for 3 weeks). Challenge on day 14 and 16. No irritation was elicited at either induction or challenge in the group exposed to TBBPA. Guinea pig: Test dose: 0.1% injected intradermally. Injection every other day (3 times a week) until each animal had received 10 inducing doses. 2 Weeks following the final inducing dose, a challenge dose was administered intradermally. 3 treated animals showed a mild skin reaction at the induction site, no treated animal showed a skin reaction at the challenge site. Could be a false negative since the test substance failed to provoke skin reactions in all but three animals at induction. Further negative data were available from two other skin sensitisation tests, not conducted to current regulatory standards. However considering all strands of evidence TBBPA is considered not to be a skin sensitizer.	(27)
Respiratory sensitisation (3.4.3.4)	No animal studies have investigated the respiratory sensitisation potential of TBBPA. The absence of significant skin sensitisation potential and the generally unreactive nature of TBBPA suggest that it would not be a respiratory sensitizer.	(27)

Repeated Dose Toxicity

Oral (3.4.3.5)	Rat: Test dose: 1000 mg/kg for 90-days. No toxicologically significant effects*. Supported by results of other studies.	(27)
Dermal (3.4.3.5)	Rabbit: Test dose: TBBPA was administered to the backs of rabbits at dose levels of 0, 100, 500 and 2,500 mg/kg/day, 6 hours/day, 5 days/week. Each group consisted of 4 male and 4 female animals. There were no significant signs of irritation or toxicologically significant	(27)

	compound related lesions*. TBBPA is not an agent that causes "bromacne".	
Inhalation (3.4.3.5)	Rat: Test dose: TBBPA dust at concentrations of 2, 6 or 18 mg/l in a 14 day inhalation study rats. Whole body exposure for 4 hours/day, 5 days/week for 2 weeks. No evidence for treatment-related systemic toxicity upon repeated dosage to the highest dose of 18mg/l. Some evidence of local irritation of the eyes and the upper respiratory tract, probably as a consequence of mechanical irritation caused by the very high dust concentration, was seen at all dose levels.	(27)
Mutagenicity (3.4.3.6)	TBBPA has demonstrated consistently negative results in a range of *in vitro* tests using bacterial strains (Ames test) and yeast both in the presence and absence of metabolic activation. These studies were conducted in a manner largely compatible with current regulatory guidelines. Similarly, in an unconventional *in vitro* recombination assay, TBBPA tested negative. No *in vivo* data are available.	(27)
Genotoxicity (3.4.3.6)	Genotoxicity data indicate that TBBPA is negative in standard *in vitro* test systems. No *in vivo* data are available, but in view of the negative profile *in vitro* and given that there are no structural indications that TBBPA would be genotoxic, there are no concerns for this endpoint.	(27)
Carcinogenicity (3.4.3.7)	No studies available on carcinogenicity. However, there is no evidence from the available *in vitro* mutagenicity data and no indications from repeated exposure studies (for example, no target organ toxicity or proliferative changes) of concerns for carcinogenicity.	(27)
Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity (3.4.3.7)	Rat: Test dose: 1000 mg/kg/d. 2-generation reproductive toxicity study indicates that TBBPA has no toxicologically significant effects on fertility or reproductive. Test dose: 10000 mg/kg/d. No evidence of developmental toxicity was seen. Test dose: 1000 mg/kg/d. Exposure of mothers during pregnancy and lactation periods. Part of a 2-generation study and included behaviour	(27)

	and learning/memory tests, specialised neurohistopathology and morphometric examination of the brain. No convincing evidence of an adverse effect on neurodevelopment **.* Test dose: 0, 50 or 250 mg/kg/d by gavage in peanut oil to pregnant rats from gestation day 7 to postnatal day 17. Limited evidence of changes in the habituation behavior of female offspring and learning and memory in male offspring in the 250 mg/kg/d group. Not possible to draw definitive conclusions from this study. Test dose: 40, 200 or 600 mg/kg TBBPA dosed from day 4 up to day 21 after birth by gavage. Effects on the kidneys were seen at doses of 200 and 600 but not 40 mg/kg. *This is a non standard study.* A NOAEL of 40 mg/kg/day was *never the less* identified *and used* in *the EU RAR for risk characterisation of infants exposed to TBBPA via the environment** Test dose: 2,000 or 6,000 mg/kg TBBPA for 18 days in 5-week old rats by gavage and a 2-generation study with gavage doses of up to 1,000 mg/kg/day. No similar effect on the kidneys was observed **.* Overall, the data do not provide strong evidence of the potential for TBBPA to act as a developmental toxicant or neurotoxicant.	
Embryotoxicity	No data found	(27)
Teratogenicity	No data found	(27)
Oestrogenicity (3.4.3.7)	The proliferation of human breast cancer cells (MCF-7 cells) was used as a means of assessing the oestrogenic potential of TBBPA at concentrations between 10^{-9} M and 10^{-4} M. Overall, the weight of evidence from *in vitro* screening assays indicates that TBBPA has no significant oestrogenic potential. *In vitro* studies have demonstrated that TBBPA has a high potency in competing with T4 for binding to TTR in animals, however no firm conclusions regarding the affinity of TBBPA for TTR *in vivo* can be drawn from the limited data available.	(27)
Neurotoxicity (3.4.3.7)	*In vitro* study has shown that TBBPA causes inhibition of neurotransmitter uptake and affects membrane potential in rat brain synaptosome. No conclusions can be drawn about extrapolation of these findings to the *in vivo* situation.	(27)

Tetrabromobisphenol A (TBBPA)

Toxicokinetics		
(3.4.3.8)	Rat: Oral exposure, 100% of the administered dose of TBBP-A is absorbed from the gastro-intestinal tract. TBBPA and/or its metabolites are excreted in the faeces (approximately 95 %) within 72 h post-administration and urine (< 1 %). By inhalation of particles, approximately 70 % will be available for absorption through the gastrointestinal tract and < 4 % through the lungs. Dermal exposure. Due to the low water solubility, the high n-octanol/water partition coefficient (5.9), and the high molecular weight of TBBPA the dermal absorption is expected to be low. A default value of 10% is assumed. No evidence to suggest that it has the potential to bioaccumulate.	(27)

Tetrabromobisphenol A carbonate oligomer

Identification of the substance

CAS No.	BC-52: 94334-64-2 BC-58: 71342-77-3	(27)
EINECS No.	-	
EINECS Name	-	
Synonyms	Phenoxy-terminated tetrabromobisphenol-A carbonate oligomers (BC-52)/ Tribromophenoxy-terminated tetrabromobisphenol-A carbonate oligomers (BC-58)	(27)
Molecular Formula	BC-52: $(C_7H_5O_3)$ $(C_{16}H_{10}Br_4O_3)_n$ (C_6H_5) (n 3-5) BC-58: $(C_7H_2Br_3O_3)$ $(C_{16}H_{10}Br_4O_3)_n$ $(C_6H_2Br_3)$ (n = 3-5)	(38)
Molecular Structure	BC-52 BC-58	
SMILES Notation	SMILES notationer for n=1 BC-52: c1ccccc1OC(=O)[Oc(c(Br)c2)c(Br)cc2C(C)(C)c(cc3(Br))cc(Br)c3OC(=O)]$_n$Oc4ccccc4 BC-58: c1(Br)cc(Br)cc(Br)c1OC(=O)[Oc(c(Br)c2)c(Br)cc2C(C)(C)c(cc3(Br))cc(Br)c3OC(=O)]$_n$Oc4c(Br)cc(Br)cc4(Br)	

Major Uses	Tetrabromobisphenol-A carbonate oligomers (both phenoxy-terminated tetrabromobisphenol-A carbonate oligomers (CAS Number 94334-64-2) and tribromophenoxy-terminated tetrabromobisphenol-A carbonate oligomers (CAS Number 71342-77-3)) are produced by reaction of tetrabromobisphenol-A with phosgene. In this respect they can be considered similar to the reactive use of tetrabromobisphenol-A in polycarbonate. These oligomers are used as an additive flame retardant in ABS and engineering thermoplastics such as polybutylene terephthalate, polycarbonate, polyethylene terephthalate and phenol-formaldehyde resins. The main use of these derivatives is as flame retardants, usually in niche applications.	(27)
EU Classification	Not classified	

Physico-Chemical Properties

Physical form	White solid (powder or granules)	(39,40)
Molecular weight	BC-52: 624	(39)
Melting point (ºC)	BC-58: 3.500 BC-52: 180-210 210-230 BC-58: 200-230	(40) (39) (30) (40)
Boiling point (ºC)	No data found	
Decomposition temperature (ºC)	No data found	
Flash point (ºC)	No data found	
Vapour pressure (mmHg at ºC)	No data found	
Density (g/cm^3 at ºC)	BC-52/BC-58: Relative density 2.2	(39,40)
Solubility (mg/L at ºC)	BC-52: Insoluble in water BC-58: <0.1% at 25 °C	(39) (30,40)
Partition coefficient (log P_{ow})	No data found	
pKa	No data found	
Henry's Law constant (atm/m^3/mol at ºC)	No data found	

Ecotoxicity

Algae	No data found
Crustaceans	No data found
Fish	No data found

Bacteria	No data found
Terrestrial organisms	No data found
Other information	No data found

Environmental fate

BCF (Fish)	No data found
Aerobic degradation	No data found
Anaerobic degradation	No data found
Hydrolysis	No data found
Photodegradation	No data found
Metabolic pathway	No data found
Mobility in soil (K_{oc})	No data found

Toxicological data

Observations in humans	No data found
Studies in animals	No data found

Acute toxicity

Oral (3.5.3.2)	Rat: BC-52: LD_{50} > 5 g/kg BC-58: LD_{50} > 5 g/kg	(38)
Dermal (3.5.3.2)	Rabbit: BC-52: LD_{50} >2 g/kg BC-58: LD_{50} >2 g/kg	(38)
Inhalation	No data found	
Other routes	No data found	
Skin irritation (3.5.3.3)	BC-52 and BC-58 are not primary skin irritants	(38)
Eye irritation (3.5.3.3)	BC-52 and BC-58 are not primary eye irritants	(38)
Irritation of respiratory tract	No data found	
Skin sensitization	No data found	

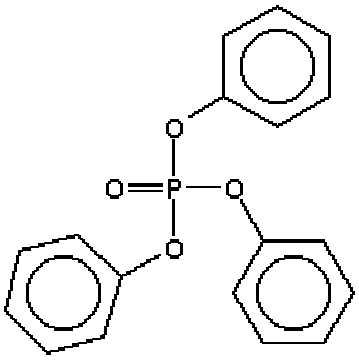
Repeated Dose Toxicity

Oral	No data found
Dermal	No data found
Inhalation	No data found

Mutagenicity (3.5.3.6)	BC-52 and BC-58 were tested in 5 strains of *Salmonella typhimurium* at doses ranging from 100 to 10000 µg/plate, in the presence, and absence, of metabolic activation. Both gave negative results.	(38)
Genotoxicity	No data found	
Carcinogenicity	No data found	
Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity	No data found	
Embryotoxicity	No data found	
Teratogenicity	No data found	
Toxicokinetics		
	No data found	

Triphenyl phosphate (TPP)

Identification of the substance

CAS No.	115-86-6	(4)
EINECS No.	204-112-2	(4)
EINECS Name	Triphenyl phosphate	(4)
Synonyms	Phosphoric acid, Triphenyl ester, TPP, Triphenylphosphate, Triphenyl phosphoric acid ester, Triphenoxyphosphine oxide, Phenyl phosphate($(PhO)_3PO$),	{1779}
Molecular Formula	$C_{18}H_{15}O_4P$	(4)
Molecular Structure		(8)
SMILES Notation	O=P(Oc(cccc1)c1)(Oc(cccc2)c2)Oc(cccc3)c3	
Major Uses	Non-combustible substitute for camphor in celluloid; rendering acetylcellulose, nitrocellulose, airplane ”dope”, etc., stable and fireproof, impregnating roofing paper; plasticisers in lacquers and varnishes.	(41)
	Plasticiser for hot-melt adhaesives	(7)
	Triphenyl phosphate has been used as a plasticiser in automobile upholstery, as a fireproofing agent, as a noncombustible substitute for camphor in celluloid, and for impregnating roofing paper. It has also been found as one component of lubricating oil and hydraulic fluids.	(42)
	Used in the polymer industry as a plasticiser	(4)
EU Classification	This chemical substance is a HPV (High Production Volume) chemical, but is not classified in the Annex I of Directive 67/548/EEC.	(8)

Triphenyl phosphate (TPP)

Physico-Chemical Properties

Physical form	Solid	(43)
	White flakes	(44)
Molecular weight	326.3	
Melting point (ºC)	50	(45)
	*49-50	(45)
	50.5	(45)
	49.5-50	(45)
Boiling point (ºC)	*245	(45)
	244	(45)
	414 (extrapolated)	(45)
Decomposition temperature (ºC)	*>250	(43)
	>410	(45)
Flash point (ºC)	>220	(43)
Vapour pressure (mmHg at 25ºC)	*$6.28 \cdot 10^{-6}$ (extrapolated)	(45)
Density (g/cm^3 at 50 ºC)	1-21	(4)
Solubility (mg/L at ºC)	0.75 (OECD 105)	(4)
	*1.9 (Shake flask method)	(45)
	*2.1 (25ºC) (OECD 105)	(45)
Partition coefficient (log P_{ow})	*4.59	(46)
	*4.61	(45)
	*4.63 (Shake flask method)	(45)
pKa	Not applicable	(45)
Henry's Law constant ($atm/m^3/mol$ at ºC)	*$1.2 \cdot 10^{-5}$	(45)
	$3.31 \cdot 10^{-6}$ (estimated)	(45)

Ecotoxicity

Algae (3.6.2.1)	*Pseudokirchneriella subcapitata (Selanastrum capricornutum)*	
	*EC_{50}(96h)=2 mg/L	(45,47)
	*NOEC(72h)=0.1-1 mg/L (OECD 201) (range stated for different test media)	(45)
	Chlorella vulgaris	
	*NOEC(72h)= 1 mg/L (OECD 201)	(45)
	Scenedesmus subspicatus	
	*NOEC(72h)=0.1-1 mg/L (OECD 201) (range stated for different test media)	(45)

Triphenyl phosphate (TPP)

(3.6.2.2)	*Ankistrodesmus falcatus*	
	NOEC(22d)=0.1 mg/L	(45)
Crustaceans	*Daphnia magna*	
(3.6.2.1)	*EC_{50}(48h)=1 mg/L (EPA 660/3-75-009)	(4,45)
	*EC_{50}(48h)=1 mg/L	(4,45)
	*EC_{50}(48h)=1.28 mg/L	(45)
	*EC_{50}(48h)=1.35 mg/L (EPA 660/3-75-009)	(4,45)
	Mysidopsis bahia	
	EC_{50}(96h)>0.18, <0.32 mg/L (EPA 660/3-75-009)	(4,45)
	Gammarus pseudolimnaeus	
	EC_{50}(96h)=0.25 mg/L	(4,45)
	Chironimus riparius	
	EC_{50}(48h)=0.36 mg/L	(4,45)
Fish	*Pimephales promelas*	
(3.6.2.1)		
	*LC_{50}(96h)=0.66 mg/L (EPA 660/3-75-009	(4,45)
	LC_{50}(96h)=3.8 mg/L (exceeds the water solubility)	(45)
	LC_{50}(96h)=1.00 mg/L	(45)
	*LC_{50}(96h)=0.87 mg/L	(45)
(3.6.2.2)	NOEC(30d)=0.087-mg/L	(4,45)
(3.6.2.1)	*Salmo gairdneri*	
	*LC_{50}(96h)= 0.4 mg/L (EPA 660/3-75-009)	(4,45)
	*LC_{50}(96h)= 0.76 mg/L (EPA 660/3-75-009)	(45)
(3.6.2.2)	NOEC(90d)=0.0014 mg/L (EPA 660/3-75-009)	(4)
(3.6.2.1)	*Cyprinodon variegatus*	
	*LC_{50}(96h)>0.32, <0.56 mg/L (EPA 660/3-75-009	(4,45)
	Lepomis macrochirus	
	*LC_{50}(96h)=0.78 mg/L	(4,45)
	LC_{50}(96h)=290 mg/L (exceeds the water solubility)	(4,45)
	Oryzias latipes	
	*LC_{50}(96h)=1.2 mg/L	(4,45)
	Oncorhynchus mykiss	
	*LC_{50}(96h)=0.85 mg/L (OECD 203)	(4,45)
	LC_{50}(96h)=0.4 mg/L	(45)
	LC_{50}(96h)=0.37 mg/L	(45)
	*LC_{50}(96h)= 0.36 mg/L (EPA 660/3-75-009)	(45)
	Channel catfish	
	LC_{50}(96h)=0.42 mg/L	(45)
	Goldfish (*Carassius auratus*)	
	LC_{50}(96h)=0.7 mg/L	(45)
Bacteria	No data found	
Terrestrial organisms	No data found	
Other information	No data found	

Environmental fate

BCF (Fish)	*Oryzias latipes*	
(3.6.2.4)	*84(18d)	(4)

	*193 (32d)	(45)
	*189 (35d)	
	Pimephales promelas	
	68-160 (105d, radiolabelled substance)	(4)
	Salmo gairdneri	
	*271 (90d)	(4) (45)
	Carrasius auratus	
	*110-150 (2-3d)	(45,47)
Aerobic degradation (3.6.2.5)	*Ready biodegradability*	
	No data found	
	Inherent biodegradability	
	*83-94% after 28 d (MITI II test)	(45) (48)
	Other biodegradability tests	
	*93.8% after 20 d (OECD 303 A)	(4) (45)
	81.8% (28d) (CO_2 evolution)	(4) (45)
	82% after 27d (CO_2 evolution)	(45)
	Degradation in water/sediment	
	t½=50-60 days in pond hydrosoil at 25°C	(45)
	t½=2.8-11.9 days in pond sediment at 2-25°C	(45)
	t½=7 days in river sediment at 25°C	(45)
	13.1% TPP remaining after 40 days in pond sediment at 25°C, no t½ reported	(45)
	Degradation in soil	
	30.4% TPP remaining after 60 days in loamy sand at 20°C, t½ < 32d	(45,49)
Anaerobic degradation (3.6.2.6)	*Anaerobic degradation in water/sediment*	
	10.3 % TPP remaining after 40 days in river sediment at 25°C, no t½ reported	(45)
	Anaerobic degradation in soil	
	35.4% TPP remaining after 60 days in loamy sand at 20°C, t½ ~ 32d	(45,49)
Hydrolysis (3.6.2.7)	*t½=19 d at 25°C, pH 7	(4)
	*t½=3 d at 25°C, pH 9	(45)
	*t½=7.5 d at 21°C in river/lake water, pH 8.2	(4)
	*t½=1.3 d at 21°C in river/lake water, pH 9.5	(45)
Photodegradation (3.6.2.7)	*100% after 1 hour	(4)
	*100% after 6 hours (pH 3.4 and pH 12)	(45)
Metabolic pathway (3.6.2.6)	Identified metabolites of TPP degradation are diphenylphoshate and CO_2 under aerobic conditions and diphenylphosphate, phenol and CO_2 under anaerobic conditions in soil	(45)
Mobility in soil (K_{oc})	2514, loamy sand at 20°C	(4,49)
	3561, silty clay at 20°C	(49)
	2756, silt loam at 20°C	(49)

Toxicological data

Observations in humans (3.6.3.1)	Thirty two workers exposed to triphenyl phosphate vapour mist, or dust over a period of	(50)

10 years showed no neurological disease or other clinical abnormalities. The particle size of the dusts was: 100% less than 7 µm, 97.6% less than 2.5 µm, and 90% less than 1 µm. The time-weighted air concentration was determined as 3.5 mg/m^3. The examination of the environmental conditions for the workers seems to have been thorough. Besides medical reports following periods of illness among the workers, regular health checks were performed of the most exposed persons and clinical chemistry and haematological examinations of blood. The results seem to be reliable.

A report indicated a case of allergic contact dermatitis associated with exposure to triphenyl phosphate (TPP) that was contained in plastic eyeglass frames. In relation to the observed dermatitis associated with wearing the plastic eyeglass frames, the investigators reported positive dermal patch test results for TPP. (51)

A number of patch testing of humans for sensitisation were reported in IUCLID: 23192 persons had been patch-tested between 1950 and 1962 using plastic disc patches. Of these persons 4 tested positive to the plastic discs (0.065%) and of these all 4 tested positive to triphenyl phosphate. (4)

A single person who responded positively to celluloid acetate film patch tested positive to triphenyl phosphate.

One case report on allergy from spectacle frames was presented. At patch-testing the patient reacted to triphenyl phosphate down to 0.05%. (52)

In a review of literature from 1937 to 1983 with respect to contact dermatitis caused by spectacle frames two cases of positive patch testing to triphenyl phosphate was identified. (53)

Patch-test reactions to plastic and glue allergens during a six-year period were reported. Among 358 persons with occupational dermatoses that were allergic patch-tested one tested positive and three tested positive to irritant patch tests. (54)

Patch-testing to plastic and glue allergens 3 years earlier by the same group of researchers using the same “plastic and glue series” gave zero allergic reactions and one irritant reaction among 174 persons with occupational dermatoses. (55)

Triphenyl phosphate caused a delayed peripheral neuritis involving motor neurons, resulting in a flaccid paralysis, particularly of the distal muscles. No sensory disturbances (56)

were reported.

Moderately toxic by ingestion. Absorbed slowly, particularly by skin contact. (57)

Large quantities of triphenyl phosphate inhibit human cholinesterase *in vitro* and *in vivo*; however, it is not considered a potent anticholinesterase agent. (51)

Human lymphocytes were seeded *in vitro* onto plates and treated with either phytohaemagglutinin (PHA) or tetanus toxoid (TET) antigen. Both antigens were pulsed with tritiated thymidine and read with at beta counter. Triphenyl phosphate (TPP) did not cause significant suppression of the antigen–specific lymphocyte proliferation.
The validity of the test system was demonstrated by TPP significantly inhibiting TET antigen presentation up to 60% as compared to control values. (58)

In vitro studies indicated that cholinesterase inhibition by triphenyl phosphate was greater in human blood than in rodent blood. (42)

A group of workers exposed to triaryl phosphates in a manufacturing plant were evaluated for possible inhibition of monocyte non–specific esterase (MNSE). Blood samples from these workers, a group of in–plant non–exposed workers, and a group of non–exposed people living in a neighbourhood 50 miles away were collected and the monocyte non-specific esterase measured using four different methods. Monocyte counts were done using four different techniques – two automated counting machines, and two manual methods, one using an esterase stain and one a Wright stain. The average monocyte percentage for the triaryl phosphate exposure group was just over 4.0% compared to a value of 5.43% for the plant controls; they were significantly different. One counting machine reported decreased MNSE positivity as compared to the other methods. (4)

A total diet study (Gunderson RD, Chemical Contaminants Monitoring, J. Assoc. Off. Anal. Chem., 71 (6), 1200-1209 (1988)) evaluated chemical contaminants in foods/diets eaten by 8 different age groups of people in the US. More than 200 foods were analysed and an average diet was determined for 8 age ranges and separated according to sex.
About 105 chemical contaminants were identified including triphenyl phosphate. (42)

The calculated intake of triphenyl phosphate in each of the 8 age groups, in mg/kg bw/day was:

	6–11 month olds – 0.3, 2 year olds – 4.4, 14–16 year old males – 1.2, 14–16 year old females – 1.6, 25–30 year old males – 1.6, 25–30 year old females – 0.8, 60–65 year old males – 0.5 and 60–65 year old females – 0.5. These levels were considered safe.	
	In 39 workers exposed to an organophosphate ester mixture with about 30% TPP and 70% different isopropyl TPPs, a significantly lower level of serum IgM and a lower activity (of borderline significance; p = 0.05) of erythrocyte cholinesterase, compared to controls, were reported. However, plasma cholinesterase activity and the other observed parameters were not significantly affected (Emmett et al., 1984).	(59)
Studies in animals	No data found	
Acute toxicity		
Oral (3.6.3.2)	Oral LD_{50} values (mg/kg bw) reported in IUCLID were: Rat: 3800 (dosing range 500-5000 mg/kg bw) (1975) 3500 (25 % in olive oil, no dose range given) (1957) 10800 (top dose administered 15800 mg/kg bw) (1977) Mouse 1300 (dosing range 500-5000 mg/kg bw) (1975)	(4)
	Oral LD_{Lo} values (mg/kg bw) reported in IUCLID were: Rat 3000 mg/kg bw (1960) Rabbit 3000 mg/kg bw (1932) Mouse > 3000 (no mouse died following single oral administration of 3000 mg/kg bw) (1960) Cat > 2000 (no cat died following single oral administration of 2000 mg/kg bw) (1957) Guinea pig > 4000 (no guinea pig died following single oral administration of 4000 mg/kg bw) (50) Hen > 5000 (dosing range 500-5000 mg/kg bw)	(4)

	(1977) > 10000 (no hen died following single oral administration of 10000 mg/kg bw) (1958) > 12500 (dosing range 2000-12500 mg/kg bw) - no signs of delayed neurotoxicity (1980) > 20000 (doses administered were 12000 or 20000 mg/kg bw) - no signs of delayed neurotoxicity (1981) > 500 (60% decrease in blood cholinesterase activity 24 hours later) - no signs of delayed neurotoxicity (1961) Leghorn cockerel > 1000 (no signs of delayed neurotoxicity) (1956) > 1000 (severe depression of plasma cholinesterase activity, but no significant change in activity in cord or brain) (1956) Chicken > 2000 (no effects observed) (1932)	
Dermal (3.6.3.2)	Dermal LD_{50} values reported in IUCLID were: Rabbit: > 10000 mg/kg bw (1975) Dermal LD_{Lo} values reported in IUCLID were: Rabbit: > 7900 mg/kg bw (no rabbit died following single dermal application for 24 hours of 79000 mg/kg bw) (1977)	(4) (4)
Inhalation	No data found	
Other routes (3.6.3.2)	LDLo values from other administration routes reported in IUCLID were: Rat > 3000 mg/kg bw after s.c. injection (no rat died during 30 days observation period) (50) Guinea pig > 3000 mg/kg bw after s.c. injection (no guinea pig died during 30 days observation period) (50) Cat ≥ 400 mg/kg bw after s.c. injection of doses ranging from 200-800 mg/kg bw. All had peripheral nerve degeneration at necropsy (50). Five cats were given a single s.c. dose of triphenyl phosphate (TPP) (99.9% pure) and observed for signs of neurotoxicity for up to 3 months. One cat received 1000 mg/kg TPP, and 2 received doses of 700 mg/kg TPP, and 2 received doses of 400 mg/kg TPP. Control cats (2) received injections of corn oil. All dosed cats except one receiving 400 mg/kg lost weight. The cat that lost weight after receiving 400 mg/kg (about 31% of its original body weight) showed no signs of unusual	(4)

weakness or ataxia during the 5 weeks after dosing.
It returned to about its original weight within 3 months and seemed to be normal in behaviour and appearance. The other cat receiving 400 mg/kg never showed any signs of toxicity.
The cat receiving 1000 mg/kg became anorexic 1 week after injection and by 3 weeks was prostrate having lost 48% of its body weight. Sections of the brain and spinal cord did not reveal evidence of axon degeneration or demyelination of axons in any tract. The 2 cats given 700 mg/kg TPP became anorexic shortly after dosing and prostrate in 3–7 days after injection. One was found to have a perforated ulcer in
the stomach, and both had hyperaemic intestines. Microscopic examination showed no evidence of neuropathology, but did show generalised vascular damage with oedema in many tissues, especially the colon. Blood samples showed that cholinesterase levels were similar to the controls.
It was concluded that triphenyl phosphate is not neurotoxic in the cat. Earlier studies were complicated by the fact that TPP prepared from coal–tar sources contains impurities which are neurotoxic (1979) (60).

Monkey
Between 500 and 1000 mg/kg bw after s.c. injection of single dose (1932)

LD_{Lo} after single i.m. injection in rabbit was reported to be 1000 mg/kg bw (no details available) (1932) (4)

Single s,c, admininistration of 200 mg triphenyl phosphate/kg bw caused paralysis in cats and fatal doses ranged between 300-1000 mg/kg bw. (42)

Single i.p. administration of 100-200 mg/kg bw to rabbits caused no perceptible effects (1943) (4)

Six cats were administered triphenyl phosphate (TPP) (70% w/v solution of TPP in 95% v/v aqueous ethanol) at dosages ranging from 100–400 mg/kg, and observed for signs of neurotoxicity for up to 1 month. (4)
The cat receiving 100 mg/kg, and one of the cats receiving 300 mg/kg showed no signs of any kind for 30 days postdose. The other cat receiving 300 mg/kg was found dead
on day 3, due probably to a perforated ulcer unrelated to TPP administration. The cat receiving 400 mg/kg developed paralysis on day 16 followed by depression, anorexia and weight loss (force feeding was necessary) and was killed. One of the two cats receiving 200 mg/kg developed paralysis
on day 18 followed by anorexia and weight loss

	(force feeding was necessary), depression; it died on day 50 from a recurrent respiratory infection. The other cat receiving 200 mg/kg showed no symptoms and was killed on day 28. The small number of animals used, i.p. route of exposure and questions of sample purity make these results difficult to interpret (1960)	
Skin irritation (3.6.3.3)	Not irritating to rabbit or rat skin in a series of guideline and non-guideline studies.	(4)
Eye irritation (3.6.3.3)	Only one study has been available and only in a IUCLID summary version: "In rabbits: slightly irritating leading to an EU classification as "irritating to the eye" (signs of irritation were observed in all animals during the first 24 hours post-dose. Unwashed eyes returned to normal later than washed. All eyes had returned to normal by day 6)". However, triphenyl phosphate shall not be labelled as dangerous to the eye in according to the "Hazardous Substances List".	(4)
Irritation of respiratory tract	No data found	
Skin sensitization	No data found	

Repeated Dose Toxicity

Oral (3.6.3.5)	In a 35-day feeding study in male rats with triphenyl phosphate at dietary concentrations of 1000 and 5000 ppm a depression of body weight gain and an increase of liver weight were observed in the high-dose group. No haematological changes were reported.	(50)
	Triphenyl phosphate (TPP) was fed to weanling Sprague-Dawley rats (10/sex/dose) at dietary concentrations of 0, 2500, 5000, 7500, or 10000 ppm for 120 days. The immuno-toxicity evaluation included total protein analysis, electrophoretic analysis of serum proteins, lymphoid organ weights in relation to growth, and histopathology, together with expanded immuno-histo-chemical evaluation of B- and T-lymphocyte regions in the spleen, thymus, and lymph nodes using immuno-peroxidase staining. Assessment was made of the humeral response to a T-lymphocyte-dependent antigen, sheep red blood cells; it began at mid-term of the feeding period for the primary response and was followed by secondary and tertiary booster immunisations at intervals of 3 weeks. The kinetics of the response were measured by haemolysin assay of relative antibody titres at days 3, 4, 5, and 6 post injection. No significant	(61)

	effects on the response were noted for either sex at any of the dose levels tested. The only effects noted were a decreased rate of growth at high levels of TPP and increased levels of α- and ß-globulins	
	Another 4-month feeding study in rats was aimed at examining the neorotoxic reactions in relation to feeding with triphenyl phosphate and is therefore placed under Neurotoxicity.	(62)
Dermal	No data found	
Inhalation	No data found	
Mutagenicity (3.6.3.6)	Negative results were reported with TPP in a paper disk method using streptomycin-dependent mutants of *E.coli. (1958)*	(59)
	TPP did not demonstrate mutagenic activity in microbial assays employing *Salmonella typhimurium* (TA 1535, TA 1537, TA 1538, TA 98, and TA 100 strains) and *Saccharomyces cerevisiae* (D4 strain) indicator organisms. All studies were carried out both with and without metabolic activation (Monsanto 1979).	
	Negative results were also reported in Ames tests conducted with *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537, in the absence or presence of rat liver S9 (Zeiger et al., 1987).	
	TPP was tested for its ability to induce mutations at the thymidine kinase (TK) locus in cultured L5178Y mouse lymphoma cells. When tested with or without metabolic activation, TPP did not induce significant mutations at the TK locus (Monsanto 1979).	
Genotoxicity	No data found	
Carcinogenicity (3.6.3.7)	The occurrence of lung adenomas in strain A/St male mice, 6 to 8 weeks old, was studied using doses of 80, 40, or 20 mg triphenyl phosphate (TPP)/kg bw injected intraperitoneally 1, 3, and 18 times, respectively, into groups of 20 mice. Twenty-four weeks after the first injection, the animals were sacrificed, and the frequency of lung tumours was compared with that in the control group of 50 animals treated with tricarpylin (vehicle). The pulmonary adenoma response to TPP was not significantly greater than the response of the control mice. This study was considered inadequate due to the low survival of animals in two of the three experimental groups and the short duration of the study.	(63)

Triphenyl phosphate (TPP)

Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity (3.6.3.7)	Male and female Sprague-Dawley (Spartan) rats (40/sex/dose) were fed dietary levels of 0, 2500, 5000, 7500, or 10000 ppm (= mg triphenyl phosphate (TPP)/kg feed) from 4 weeks post weaning for 91 days, through mating and gestation. At these dietary levels, the daily intake of TPP during pregnancy was 0, 166, 341, 516, and 690 mg/kg bw, respectively. TPP exposure had no toxic effects on mothers or offspring at these dosages. The types of developmental anomalies were similar in both treated and control animals, and no significant increase in the incidence of anomalies was seen in the treated groups as compared to control values. TPP was not teratogenic in Sprague-Dawley rats at the levels tested.	(64)
Embryotoxicity	No data found	
Teratogenicity	No data found	

Neurotoxicity

(3.6.3.7)

Smith and his associates found that single and multiple doses of technical grade triphenyl phosphate produced generalised delayed paralysis in cats and monkeys but not in chickens or rabbits (Smith et al., 1930).	(59)
Groups of 10 male rats/dose were exposed for 4 months to dietary concentrations of 2500, 5000, 7500, or 10000 ppm triphenyl phosphate, corresponding to mean daily intakes of the test substance of 161, 345, 517 or 711 mg/kg bw/day. Statistically significantly decreased weight gain was recorded throughout the study for the 5000 and the 10000 ppm dose groups, but only for the first period of the study for the 7500 ppm dose group. No treatment related effects were noted for any behavioural measures at any of the monthly test sessions.	(62)
99.9%-pure triphenyl phosphate (TPP) did not produce any evidence of axonal degeneration, demyelination, or any other pathological changes at 11 levels of the nervous system (from the cerebral cortex to peripheral nerves) when subcutaneously injected into cats at doses of 400, 700, or 1000 mg/kg. Prostration occurred at the higher doses.	(60)

	Study details: Five cats were given a single s.c. dose of triphenyl phosphate (TPP) (99.9% pure) dissolved in corn oil or propylene glycol and observed for signs of neurotoxicity for up to 3 months. One cat received 1000 mg/kg TPP in corn oil, and 2 received doses of 700 mg/kg TPP in corn oil, and 2 received doses of 400 mg/kg TPP in propylene glycol. Control cats (2) received injections of corn oil. All cats dosed except one receiving 400 mg/kg lost weight. The cat that lost weight after receiving 400 mg/kg (about 31% of its original body weight) showed no signs of unusual weakness or ataxia during the 5 weeks after dosing. It returned to about its original weight within 3 months and seemed to be normal in behaviour and appearance. The other cat receiving 400 mg/kg never showed any signs of toxicity. The cat receiving 1000 mg/kg became anorexic 1 week after injection and by 3 weeks was prostrate having lost 48% of its body weight. Sections of the brain and spinal cord did not reveal evidence of axon degeneration or demyelination of axons in any tract. The 2 cats given 700 mg/kg TPP became anorexic shortly after dosing and prostrate in 3–7 days after injection. One was found to have a perforated ulcer in the stomach, and both had hyperaemic intestines. Microscopic examination showed no evidence of neuropathology, but did show generalised vascular damage with oedema in many tissues, especially the colon. Blood samples showed that cholinesterase levels were similar to the controls. The authors concluded that TPP is not neurotoxic in the cat. Earlier studies were complicated by the fact that TPP prepared from coal–tar sources may have contained impurities that were capable of producing axonal degeneration and demyelination..	
	Dosing 9 adult hens with cumulative doses of 60 g triphenyl phosphate/kg bw (5 g/kg bw twice daily for 2 times 3 consecutive days(1-3 and 21-23) failed to produce either ataxia or histologic neurotoxic response suggestive of organophosphate-induced delayed neuropathy.	(65)
"Special in vitro studies"		
(3.6.3.7)	*In vitro* triphenyl phosphate was found to cause significant direct inhibition of monocyte antigen presentation at non-cytotoxic concentrations as low as 1 µmol/litre.	(58)
	When studied in a cell culture assay on *in vitro* cytotoxicity to human (KB and HEL-R66),	(66)

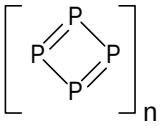
	monkey (Vero) and dog (MDCK) cell lines, triphenyl phosphate demonstrated a dose dependent inhibition of growth.	
	Triphenyl phosphate reduced the GABA-induced $^{36}Cl^-$ influx in rat brain below control values with an inhibitory concentration $_{50}$ (IC_{50}) of 18.2 µM. Triphenyl phosphate was also inhibiting the [^{35}S]TBPS ([^{35}S]butylbicyclophospho-thionate) binding to the $GABA_A$ receptor (IC_{50} = 12.9 µM) and to the voltage- dependent Cl^- channel (IC_{50} = 10.3 µM). There seems to be poor correlation between inhibition capacity in relation to the two chloride channel proteins and delayed neurotoxicity.	(67)

Toxicokinetics

No data found

Red phosphorus

Identification of the substance

CAS No.	7723-14-0 (CAS No. covering all allotrophic forms of elementary phosphorus)	(4)
EINECS No.	231-768-7	(4)
EINECS Name	Phosphorus	(4)
Synonyms	Phosphorus, red amorphous, Red-P	Ref!
Molecular Formula	$(P_4)_n$	Ref!
Molecular Structure		Ref!
SMILES Notation	P1=PP=P1 (n=1)	
Major Uses	Striking surfaces for matches, fireworks, flame retardants in polymers, semiconductors, incendiary shells, smoke bombs, tracer bullets and manufacture of phosphoric acid, phospine, phosphoric anhydride, phosphorus pentachloride, phosphorus trichloride, fertilizers and pesticides.	(7)
EU Classification	Not classified	Ref!

Physico-Chemical Properties

Physical form	Red to violet powder	(7)
	Exolit RP 690: Brownish red droplets	(68)
Molecular weight	Amorphous polymer (P_n)	(69)
Melting point (ºC)	>590	(4)
Boiling point (ºC)	>400	(4)
Decomposition temperature (ºC)	No data found	
Flash point (ºC)	Flammable. Auto-ignition temperature: 260 ºC. May be ignited by an inginition source, heat, friction, static electrical spark, oxidizing agents or physical impact	(70) (7)
Vapour pressure (mmHg at 20ºC)	*0.026	(7)
	<0.001	(4)
Density (g/cm^3 at 20 ºC)	2.2	(4)

Red phosphorus

Solubility (mg/L at ºC)	Sligthly soluble in cold water, insoluble in hot water	(7)
	None	(71)
Partition coefficient (log P_{ow})	No data found	
pKa	No data found	
Henry's Law constant (atm/m^3/mol at ºC)	No data found	

Ecotoxicity

Algae (3.7.2.1)	*Scenedesmus subspicatus (Desmodesmus subspicatus)*	
	*EC_{50}(72h)=18.3 mg/L (nominal conc.), 1.3 mg/L (measured conc. of total phosphorus in solution)(OECD 201)	(72)
	EC_{50}(72h)=246 mg/L (nominal conc.), 3.13 mg/L (measured conc. of total phosphorus in solution) (extrapolated values) (	(73)
Crustaceans (3.7.2.1)	*Daphnia magna*	
	*EC_{50}(48h)=10.5 (nominal conc.), 0.63 mg/L (measured conc. of total phosphorus in solution) (OECD 202)	(74)
Fish (3.7.2.1)	*Danio rerio*	
	*LC_{50}(96h)=33.2 (nominal conc.), 0.95 mg/L (measured conc. of total phosphorus in solution) (OECD 203)	(75)
	LC_{50}(96h)=>100 (nominal conc.), >0.73 mg/L (measured conc. of total phosphorus in solution) (OECD 203)	(73)
Bacteria	No data found	
Terrestrial organisms	No data found	
Other information (3.7.3.5)	Exposure of prairie dogs to red phosphorus smoke up to 6.0 mg/L affected the vocalization capability and increased respiratory congestion postexposure. Exposure of rock doves to red phosphorus smoke up to 6.0 mg/L showed effects on the vocalization capability, body postures and caused mortality	(76)

Environmental fate

BCF (Fish)	No data found	
Aerobic degradation	Not applicable	
Anaerobic degradation	Not applicable	
Hydrolysis	*Red phosphate slowly hydrolyses to	(70)

Red phosphorus

(3.7.2.7)	phosphine and phosphorus acids in the environment	(69,77)
Photodegradation	No data found	
Metabolic pathway (3.7.2.7)	*In the presence of water and oxygen, red phosphorous will slowly react to phosphoric acid via intermediates such as hypophosphorus acid, phosphorus acid and phosphine	(69)
	*Reacts slowly with water vapour and oxygen at normal temperature and humidity in the air to form phosphine gas	(70)
Mobility in soil (K_{oc})	No data found	

Toxicological data

Observations in humans (3.7.3.1)	Red phosphorus is non-volatile, insoluble, unabsorbable and thus non-toxic when ingested, unless it is contaminated with traces of yellow phosphorus. Repeated doses of red phosphorus, however, may induce systemic phosphorus poisoning. In contrast to acute poisoning, chronic phosphorus intoxication, once common in some industries because of inhalation of phosphorus fumes, is virtually unknown in modern times. It was characterized as cachexia, anemia, bronchitis and necrosis of the mandible, the socalled "phossy" or "Lucifers jaw" (brittle bones).	(1)
Studies in animals	No data found	

Acute toxicity

Oral (3.7.3.2)	LD_{50}, rat: >15000 mg/kg bw	(2)
Dermal	No data found	
Inhalation (3.7.3.2)	Red phosphorus smoke Several studies have been made on the toxicity of red phosphorus smoke. When ignited, red phosphorus burns to phosphorus pentoxide, and in conditions of normal humidity this gives rise to a strongly hygroscopic aerosol consisting largely of orthophosphoric acid. The smoke can also contain cyclotetraphosphoric and other polyphosphoric acids, as well as small amounts of phosphine, produced from phosphorus trioxide.	(3)

1 hour-LC_{50}-values expressed as P: as OPA*

Male rabbits	1689 mg/m^3	5337 mg/m^3
Male rats	1217 mg/m^3	3846

Red phosphorus

	mg/m^3	
	Male mice 271 mg/m^3	856 mg/m^3
	Male guinea pigs 61 mg/m^3	193 mg/m^3
	*ortho-phosphoric acid equivalents	
	Non-lethal 1 hour concentrations were (expressed as P)	as OPA
	Male rats 450 mg/m^3	1422 mg/m^3
	Male mice 111 mg/m^3	351mg/m^3
	Male guinea pigs 36 mg/m^3	114 mg/m^3
	Cause of death in rabbits, rats and mice was respiratory tract injury from the corrosive effects. Guinea pigs died from alveolar capillary congestion, and showed no lesions in the larynx and trachea. These findings are compatible with lethal toxicity in the guinea pig as a consequence mainly of asphyxia secondary to laryngospasm.	(4)
	1 hour LC_{50}, rats for smoke was found at 4.3 mg/L (red phoshorus/butyl rubber aerosol) equal to 4.03mg/L of H_3PO_4 equal to 4033 mg/m^3.	(5)
Other routes	No data found	
Skin irritation (3.7.3.3)	24 hour patch test on rabbits gave no irritation. Dose not given.	(2)
Eye irritation (3.7.3.4)	100 mg in the eyes of rabbits was not found irritating.	(2)
	Pieces of red phosphorus lodged in the eyes of a 15 year old boy after an explosion due to mixture with potassium chlorate had a benign course and outcome, without any late complications.	(6)
	Another similarly benign case has been described. However, an entirely different course of sequelae has been described from Czechoslovakia, in a boy who was reported to have burns of both eyes with red phosphorus, and to have suffered for more than two years from inflamed conjunctiva and photophobia.	(7)
	The difference in severity of reactions of the three patients may be explainable by a difference in the amount of red phosphorus that entered the eyes. A rabbit experiment showed that when enough of this substance is present it can produce considerable inflammation in the eye, even while appearing inert in the cornea. Apparently the amount	

	which can be tolerated without inflammation is very small, as in the first patient, in whom the particles were so fine that they could be seen only with a slit-lamp biomicroscope.	
Irritation of respiratory tract	No data were found on inhalation of red phosphorus as is. However, smoke from red phosphorus produces phosphoric acid when combining with the humidity in the air or in mucous membranes. And this is, of course, irritating to the respiratory tract. Epiglottal and laryngeal lesions resulted from 1 hour exposure of rats to red phosphorus smoke in concentrations of 3150 -8460 mg/m^3 or 4 hours in 1530 mg/m^3.	(5)
Skin sensitization	Test on guinea pigs showed no sensitization.	(2)

Repeated Dose Toxicity

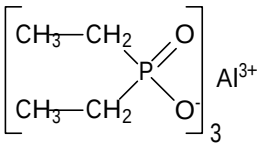
Oral	No data found	
Dermal	No data found	
Inhalation (3.7.3.5)	Red phosphorus smoke Exposure to smoke 1 h/day, 5 d/week for up to 40 weeks, two dose levels, one control. Mice, rats and guinea pigs dose levels: 0, 15; and 130 mg/m^3 (expressed as P). Lethality during study: Mice: 59, 63, and 78%, respectively. Rats: 26, 24, and 20%, respectively. Guinea pigs: 15, 38, and 100%, respectively. Growth of the test groups of mice and rats were depressed during the exposure period. Organ specific toxicity appeared not to be present in rats and was generally confined to the respiratory tract of the mice and guinea pigs. Severe congestion was observed in practically all the lungs from the high dose guinea pigs, all of whom died during or just after the first exposure. For survivors, specific damage of the respiratory tract was only rarely seen in the present study. If, at the end of exposure, damage was present, it had been reversed by the end of the observation period. However, the very marked species differences in lethality, observed in the present study, must indicate caution in quantitative extrapolation to humans of the study data.	(78)

Red phosphorus

	Blacktailed prairie dogs showed no mortality to either 2000, 4000 or 6000 mg/m^3 concentrations of smoke within 30 days after 1-4 successive daily 1-hour exposure sessions. 70.5-76% of the aerosols consisted of phosphoric acid.	
	Rock doves exposed to either 3000 or 6000 mg/m^3 over 1-4 sessions, however, showed 26% mortality within 8 days postexposure. Male rock doves were much more vulnerable, with 42% mortality, in contrast to 6% in females. Lost or affected vocalization capability in both species, abnormal body postures in rock doves, and increased respiratory congestion in prairie dogs was found postexposure.	(79)
	Whole-body exposure of the same two species to 0; 1000; and 4000 mg/m^3 in 80 minutes/day for 4 consecutive days for the prairie dogs and 2 consecutive days for the rock doves produced no deaths among the 24 prairie dogs and 1 death out of 8 doves exposed to the largest conc. Enhanced postexposure water replenishment was the main finding.	(80)
Mutagenicity	No data found	
Genotoxicity	No data found	
Carcinogenicity	No data found	
Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity	No data found	
Embryotoxicity	No data found	
Teratogenicity	No data found	
Toxicokinetics		
	No data found	

Diethylphosphinic acid, aluminium salt

Identification of the substance

CAS No.	225789-38-8	
EINECS No.	No data found	
EINECS Name	No data found	
Synonyms	No data found	
Molecular Formula	$(C_4H_{10}O_2P)_3$, Al $M^{n+}[PO_2(CH_2CH_3)_2]_n$	
Molecular Structure		(81)
SMILES Notation	Not valid for salts	
Major Uses	EXOLIT OP 1230 In the plastic processing industry as flame proofing agent	(82)
EU Classification	No data found	

Physico-Chemical Properties

Physical form	Exolit OP 1230: Solid, white powder	(82)
Molecular weight	393	
Melting point (ºC)	No data found	
Boiling point (ºC)	No data found	
Decomposition temperature (ºC)	Exolit OP 1230: >300	(82)
Flash point (ºC)	Exolit OP 1230: Not applicable	(82)
Vapour pressure (mmHg at ºC)	Exolit OP 1230: Not applicable	(82)
Density (g/cm^3 at 23ºC)	Exolit OP 1230: 1.2 (EEC A.3)	(82)
Solubility (mg/L at ºC)	Exolit OP 1230: <1 g/L (EEC A.6)	(82)
Partition coefficient (log P_{ow})	Exolit OP 1230: 2.5 g/L Not applicable according to the Guideline 921691EEC, appendix A.8. due to the low solubility of the test substance (DEPAL) in	(81) (83)

Diethylphosphinic acid, aluminium salt

	water and organic solvents	
	Exolit OP 1230: -0.44	(81)
pKa	Phosphinic acid: 3.3	(81)
Henry's Law constant ($atm/m^3/mol$ at ºC)	No data found	

Ecotoxicity

Algae (3.8.2.1)	*Scenedesmus subspitatus*	
	*DEPAL: NOEC(72h) > 180 mg/L (nominal conc., exceeds the water solubility)(EEC C.3)	(83)
Crustaceans (3.8.2.1)	*Daphnia magna*	
	*DEPAL: EC_{50}(48h)>100 mg/L (nominal conc.), 33.7 (measured conc., exceeds the water solubility) (OECD 202)	(83)
(3.8.2.2)	*DEPAL: NOEC(21d): 1-10 mg/L (nominal conc., exceeds the water solubility) (OECD 211)	(83)
Fish (3.8.2.1)	*Danio rerio*	
	*DEPAL (83.3% diethylphosphinic acid, aluminium salt): LC_{50}(96h)>100 mg/L (nominal conc.), 11.0 (measured conc., exceeds the water solubility) (OECD 203)	(83)
Bacteria (3.8.2.3)	*DEPAL: EC_{50}(3h)=1968 mg/L (nominal conc., exceeds the water solubility) (OECD 209)	(83)
Terrestrial organisms	No data found	
Other information	No data found	

Environmental fate

BCF (Fish)	No data found	
Aerobic degradation (3.8.2.5)	Exolit OP 1230: Not degradable (OECD 302B, data refer to organic component)	(82)
	*Not readily biodegradable (the test item was hydrolysed to aluminium and diethylphosphinic acid, neither components were biodegraded) (OECD 301 C)	(83)
Anaerobic degradation (3.8.2.6)	*Not biodegradable under anaerobic conditions (ISO/DIS 14853)	(83)
Hydrolysis (3.8.2.7)	Exolit OP 1230: Stable (OECD 111, tier 1)	(81)
Photodegradation	Exolit OP 1230: Photolytically stable (No uv-vis absorption)	(81)
Metabolic pathway	No data found	

Diethylphosphinic acid, aluminium salt

Mobility in soil (K_{oc})	No data found	
Toxicological data		
Observations in humans	No data found	
Studies in animals	No data found	
Acute toxicity		
Oral (3.8.3.2)	EXOLIT OP 1230 Rat: LD50 >2000 mg/kg*	(82)
Dermal (3.8.3.2)	EXOLIT OP 1230 Rat: LD50 >2000 mg/kg*	(82)
Inhalation	No data found	
Other routes	No data found	
Skin irritation (3.8.3.3)	EXOLIT OP 1230 Rabbit: Non-irritant (4 h)*	(82)
Eye irritation (3.8.3.3)	EXOLIT OP 1230 Rabbit: Slight irritant effect – does not require labelling.*	(82)
Irritation of respiratory tract	No data found	
Skin sensitization (3.8.3.4)	EXOLIT OP 1230 Guinea pig: Non-sensitizing*	(82)
Repeated Dose Toxicity		
Oral (3.8.3.5)	EXOLIT OP 1230 Rat: NOAEL > 1000 mg/kg*	(82)
Dermal	No data found	
Inhalation	No data found	
Mutagenicity (3.8.3.6)	EXOLIT OP 1230 Not mutagenic in the Ames test.*	(82)
Genotoxicity (3.8.3.6)	EXOLIT OP 1230 No experimental indications on genotoxicity in	(82)

Diethylphosphinic acid, aluminium salt

	vivo found.*	
Carcinogenicity	No data found	
Reproductive Toxicity, Embryotoxicity and Teratogenicity		
Reproductive Toxicity	No data found	
Embryotoxicity	No data found	
Teratogenicity	No data found	
Toxicokinetics		
(3.8.3.8)	Rat: Diethyl phosphinic acid was excreted almost quantitatively via the urine within 12 hours after oral application.	(82)

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