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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

Butylbenzylphthalate

Canada

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Canadian Environmental Protection Act

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Environment Canada
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LIST OF ACRONYMS AND ABBREVIATIONS

BBP	butylbenzylphthalate
BCF	bioconcentration factor
BMD	benchmark dose
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
CFC	chlorofluorocarbon
CTV	Critical Toxicity Value
DEHP	bis(2-ethylhexyl) phthalate; di(2-ethylhexyl) phthalate
EC_{50}	median effective concentration
ED_{50}	median effective dose
EEV	Estimated Exposure Value
ENEV	Estimated No-Effects Value
GWP	Global Warming Potential
K_{oc}	organic carbon/water partition coefficient
K_{ow}	octanol/water partition coefficient
kg-bw	kilogram body weight
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	Lowest-Observed-Adverse-Effect Level
LOEC	Lowest-Observed-Effect Concentration
LOEL	Lowest-Observed-Effect Level
MATC	Maximum Acceptable Toxicant Concentration
NOAEL	No-Observed-Adverse-Effect Level
NOEC	No-Observed-Effect Concentration
NOEL	No-Observed-Effect Level
NTP	National Toxicology Program
ODP	Ozone Depletion Potential
POCP	Photochemical Ozone Creation Potential
PSL	Priority Substances List
PVC	polyvinyl chloride
SCE	sister chromatid exchange
TD_{05}	tumorigenic dose
TI	Tolerable Intake

Synopsis

Butylbenzylphthalate, also known as BBP, is used mainly as a plasticizer for polyvinyl chloride flooring and other materials. It is not manufactured in Canada, but about 4 kilotonnes are imported into the country per year. BBP is released into the environment from facilities that blend the substance with resins. Most releases of BBP appear to be to the atmosphere, but the substance has also been detected in industrial and municipal liquid effluents.

BBP is removed from the atmosphere by photooxidation and by rainwater, with a half-life of a few hours to a few days. It is not persistent in water, sediments or soil under aerobic conditions, with a half-life of a few days. Under anaerobic conditions, BBP is more persistent, with a half-life of a few months. BBP is readily metabolized by vertebrates and invertebrates. Reported bioconcentration factors are less than 1000, based on total residues, and well under 100, based on intact residues.

Monitoring data are available for BBP in Canadian air, water, sediments, soil, biota and food.

Data on acute and chronic toxicity were identified for aquatic algae, invertebrates and fish, but no information is available on the toxicity of BBP to benthic or soil organisms, terrestrial plants or wildlife. The Equilibrium Partitioning approach and data on toxicity of dibutyl phthalate were used as surrogates in this assessment when information on BBP was lacking.

Concentrations of BBP in all compartments of the Canadian environment are lower than the adverse effects thresholds estimated for sensitive organisms.

BBP is not likely to contribute significantly to depletion of stratospheric ozone, ground-level ozone formation or climate change.

Food and, to a lesser extent, indoor air appear to be the major sources of human exposure to BBP in Canada. Based upon results of a wide range of well-conducted studies in experimental animals, effects that occur at lowest concentrations in rats are increases in organ to body weight ratios, primarily for the liver and kidney, and histopathological effects on the pancreas and kidney. In studies with protocols specific for investigating reproductive toxicity, adverse effects on testes have been reported, although at dose levels higher than those that had effects on other organs, such as liver and kidney. Although results of available studies do not support the conclusion that BBP is estrogenic, the potential for other endocrine-mediated effects cannot be precluded at this time. On the basis of currently available data, the pancreas appears to be the most sensitive target for BBP-induced toxicity in laboratory animals. The estimated average daily and reasonable worst-case intakes of BBP by the general population in Canada from environmental sources are less than a Tolerable Intake derived on the basis of a benchmark dose for non-neoplastic pancreatic effects. A Tolerable Intake is the level of intake to which it is believed a person may be exposed daily over a lifetime without deleterious effect.

Based on information available, it is concluded that butylbenzylphthalate is not entering the environment in a quantity or concentration or under conditions having or that may have an immediate or long-term harmful effect on the environment; constituting or that may constitute a danger to the environment on which human life depends; or constituting or that may constitute a danger

in Canada to human life or health. Therefore, butylbenzylphthalate is not considered to be "toxic" as defined in Section 11 of the *Canadian Environmental Protection Act* **(CEPA).**

The evaluation of options under CEPA to reduce exposure to BBP is not considered to be a priority at this time. However, this is based upon current use patterns; thus, future releases of this compound should continue to be monitored to ensure that exposure does not increase to any significant extent. Phthalates, including butylbenzylphthalate, are also likely early candidates for testing for potential endocrine-disrupting effects when test protocols are finalized.

BBP may be emitted from building materials and is present in some consumer products. Better characterization of the significance of emissions from these sources is desirable.

1.0 INTRODUCTION

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of Environment and of Health to prepare and publish a Priority Substances List (PSL) that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act, which states:

> …a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions
> (a) having or that may have an immediate or long-term harmful effect on the environment;
> (b) constituting or that may constitute a danger to the environment on which human life depends; or
> (c) constituting or that may constitute a danger in Canada to human life or health.

Substances that are assessed as "toxic" as defined in Section 11 may be placed on Schedule I of the Act and considered for possible risk management measures, such as regulations, guidelines or codes of practice to control any aspect of their life cycle, from the research and development stage through manufacture, use, storage, transport and ultimate disposal.

Based on initial screening of readily accessible information, the rationale for assessing butylbenzylphthalate (BBP) provided by the Ministers' Expert Advisory Panel on the Second Priority Substances List (Ministers' Expert Advisory Panel, 1995) was as follows:

> There is considerable potential for human exposure to BBP. It is used in a wide range of consumer products including floor coverings, hairsprays, pesticides, colourants, insect repellents and perfumes. BBP has been detected in Canadian aquatic systems and biota, soils, foods, tap water and indoor air. BBP is bioaccumulative, and toxicological studies show

that it may cause adverse effects in humans and other organisms. There are also concerns that this substance may interfere with endocrine function. An assessment is needed to determine the extent of exposure and associated risks.

Descriptions of the approaches to assessment of the effects of Priority Substances on the environment and human health are available in published companion documents. A document entitled "Environmental Assessments of Priority Substances under the *Canadian Environmental Protection Act*. Guidance Manual Version 1.0 — March 1997" (Environment Canada, 1997a) provides guidance for conducting environmental assessments of Priority Substances in Canada. This document may be purchased from:

> Environmental Protection Publications
> Environmental Technology Advancement
>   Directorate
> Environment Canada
> Ottawa, Ontario
> K1A 0H3

It is also available on the Internet at www.ec.gc.ca/cceb1/eng/psap.htm under the heading "Technical Guidance Manual."

The approach to the assessment of effects on human health is outlined in the following publication of the Environmental Health Directorate of Health Canada: "*Canadian Environmental Protection Act* — Human Health Risk Assessment for Priority Substances" (Health Canada, 1994), copies of which are available from:

> Environmental Health Centre
> Room 104
> Health Canada
> Tunney's Pasture
> Ottawa, Ontario
> K1A 0L2

or on the Environmental Health Directorate publications web site (www.hc-sc.gc.ca/ehp/ehd/catalogue/bch.htm). The approach is also described in an article published in the *Journal of Environmental Science and Health — Environmental Carcinogenesis & Ecotoxicology Reviews* (Meek *et al.*, 1994). It should be noted that the approach outlined therein has evolved to incorporate recent developments in risk assessment methodology, which are described on the Environmental Substances Division web site (www.hc-sc.gc.ca/ehp/ehd/bch/env_contaminants/psap/psap.htm) and which will be addressed in future releases of the approach paper for the assessment of effects on human health.

The search strategies employed in the identification of data relevant to the assessment of potential effects on the environment (prior to May 1998) and human health (prior to April 1998) are presented in Appendix A. Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether BBP is "toxic" under CEPA have been critically evaluated by staff of Environment Canada (entry and environmental exposure and effects) and Health Canada (human exposure and effects on human health).

The environmental sections of this Assessment Report and the supporting documentation (Environment Canada, 1998) were produced by K. Taylor, Environment Canada, and reviewed by members of the Environmental Resource Group, established by Environment Canada to support the environmental assessment of BBP:

> E. Brien, Environment Canada
> B.K. Burnison, National Water Research Institute, Environment Canada
> G. Coyle, Solutia Inc.
> J. Headley, National Water Research Institute, Environment Canada
> T. Parkerton, Exxon Biomedical Sciences Inc.

> J. Prinsen, Environment Canada
> A. Sardella, Solutia Inc.
> N. Tremblay, Environment Canada

The health-related sections of this Assessment Report and the supporting documentation were prepared by the following staff of Health Canada:

> G. Long
> M.E. Meek

Sections of the Assessment Report and the supporting documentation on genotoxicity and reproductive and developmental toxicity were reviewed by D. Blakey and W. Foster, respectively, of the Environmental and Occupational Toxicology Division of Health Canada.

Sections of the supporting documentation pertaining to human health were reviewed externally by R. Nair, Solutia Inc., primarily to address adequacy of coverage. Accuracy of reporting, adequacy of coverage and defensibility of conclusions with respect to hazard characterization and dose–response analyses were considered in a written review by staff of the Information Department of BIBRA International and at a panel meeting of the following members, convened by Toxicology Excellence for Risk Assessment (TERA) on April 27, 1998, in Cincinnati, Ohio:

> M. Abdel-Rahman, University of Medicine & Dentistry of New Jersey
> J. Christopher, California Environmental Protection Agency
> G. Datson, The Procter & Gamble Company
> J. Donohue, U.S. Environmental Protection Agency
> M. Dourson, TERA
> D. Proctor, ChemRisk
> R. Rudel, Silent Spring Institute (submitted written comments; not able to attend panel meeting)

A. Stern, New Jersey Department of Environmental Protection

A Concise International Chemical Assessment Document (CICAD), which was prepared on the basis of the content of this Assessment Report, was also externally reviewed by:

R.A. Andersen, Norwegian University of Science and Technology, Norway

T. Berzins, National Chemicals Inspectorate, Sweden

R. Cary, Health and Safety Executive, United Kingdom

R. Chapin, National Institute of Environmental Health Sciences, USA

R.S. Chhabra, National Institute of Environmental Health Sciences, USA

J. DeFouw, RIVM, The Netherlands

R.J. Fielder, Department of Health, United Kingdom

P. Foster, Chemical Industry Institute of Toxicology, USA

S. Jordan, Food Directorate, Health Canada

P. Lundberg, National Institute for Working Life, Sweden

C. Nilsson, Institute of Environmental Medicine, Sweden

P. Ridgeway, Health and Safety Executive, United Kingdom

E. Soderlund, National Institute of Public Health, Norway

F.M. Sullivan, consultant toxicologist, United Kingdom

K. Svensson, National Food Administration, Sweden

S. Tarkowski, Nofer Institute of Occupational Medicine, Poland

J. Taylor, Agency for Toxic Substances and Disease Registry, USA

G. Ungvary, Jozsef Fodor National Centre of Public Health, Hungary

A. Wibbertmann, Fraunhofer Institute for Toxicology and Aerosol Research, Germany

Subsequently, a revised version of the CICAD was approved at a meeting in Tokyo, Japan, on June 30 – July 2, 1998, by a Final Review Board composed of:

R. Benson, Environmental Protection Agency, USA

T. Berzins, National Chemicals Inspectorate, Sweden

R. Cary, Health and Safety Executive, United Kingdom

C. DeRosa, Agency for Toxic Substances and Disease Registry, USA

S. Dobson, Institute of Terrestrial Ecology, United Kingdom

H. Gibb, Environmental Protection Agency, USA

R.F. Hertel, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Germany

I. Mangelsdorf, Fraunhofer Institute for Toxicology and Aerosol Research, Germany

M.E. Meek, Health Canada, Canada

J. Sekizawa, National Institute of Health Sciences, Japan

S.A. Soliman, Alexandria University, Egypt

D. Willcocks, Worksafe Australia, Australia

P. Yao, Chinese Academy of Preventative Medicine, People's Republic of China

The health-related sections of the Assessment Report were reviewed and approved by the Health Protection Branch Risk Management meeting of Health Canada.

The entire Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

A draft of the Assessment Report was made available for a 60-day public comment period (May 1 to June 29, 1999) (Environment Canada and Health Canada, 1999). Following consideration of comments received, the

Assessment Report was revised as appropriate. A summary of the comments and their responses is available on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

The text of the Assessment Report has been structured to address environmental effects initially (relevant to determination of "toxic" under Paragraphs 11(a) and (b)), followed by effects on human health (relevant to determination of "toxic" under Paragraph 11(c)).

Copies of this Assessment Report are available upon request from:

Inquiry Centre
Environment Canada
Main Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or on the Internet at:

www.ec.gc.ca/cceb1/eng/final/index_e.html

Unpublished supporting documentation, which presents additional information, is available upon request from:

Commercial Chemicals Evaluation
    Branch
Environment Canada
14th Floor, Place Vincent Massey
351 St. Joseph Blvd.
Hull, Quebec
K1A 0H3

or

Environmental Health Centre
Room 104
Health Canada
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

2.0 SUMMARY OF INFORMATION CRITICAL TO ASSESSMENT OF "TOXIC" UNDER CEPA

2.1 Identity and physical/chemical properties

Butylbenzylphthalate, referred to hereafter as BBP, has the empirical molecular formula $C_{19}H_{20}O_4$, the structural formula $C_4H_9OOCC_6H_4COOC_7H_7$ and a molecular weight of 312.4 g/mol. The chemical structure is presented in Figure 1. Its Chemical Abstracts Service (CAS) registry number is 85-68-7. BBP is a clear, oily liquid with a water solubility of 2.69 mg/L at 25°C (Howard *et al.*, 1985), an octanol/water partition coefficient (log K_{ow}) of 4.9 (Leyder and Boulanger, 1983), an organic carbon/water partition coefficient (log K_{oc}) of 3.3 (Williams *et al.*, 1995), a vapour pressure of 1.15 mPa at 20°C (Gledhill *et al.*, 1980) and a Henry's law constant of 0.133 Pa·m³/mol (Lyman *et al.*, 1982). A more complete listing of physical and chemical properties reported in the literature and criteria for selecting preferred values are presented in the supporting document (Environment Canada, 1998).

FIGURE 1 Structure of BBP
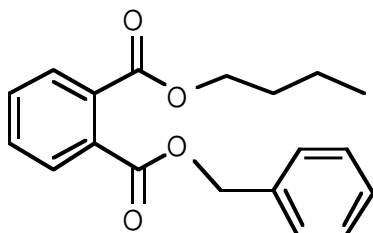
Synonyms for BBP include 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester; benzyl n-butyl phthalate; and phthalic acid, benzyl butyl ester.

2.2 Entry characterization

2.2.1 Production, importation and uses

According to data submitted to Environment Canada in a survey conducted under the authority of Section 16 of CEPA, BBP is not manufactured in Canada. About 4 kilotonnes of BBP were imported into Canada in 1996 (Environment Canada, 1997b).

According to the survey, BBP is used in Canada as a plasticizer in polyvinyl chloride (PVC) flooring and other materials, in paints and coatings, in adhesive formulations and in printing inks. BBP had been used as a component of certain pest control products, but the registration of all such products in Canada expired as of December 31, 1996 (Ballantine, 1997).

In Canada, BBP is not used to any significant extent in applications involving direct contact with food (Pelletier, 1998).

2.2.2 Sources and releases

2.2.2.1 Natural sources

There are no natural sources of BBP in the environment.

2.2.2.2 Anthropogenic sources

BBP is released from facilities that manufacture the substance or blend it with resins (Howard, 1989).

Information on releases of BBP from a number of industrial plants and municipal water pollution control plants from across Canada is presented in Table 1. BBP has been detected in

TABLE 1 Sources and releases of BBP

Source	Concentration	Reference
Canadian organic chemical plants	<1–22 µg/L (total effluents, 5 plants)	Sigma, 1985
B.C. paint and coatings plant	9 µg/L, latex effluent 0.1 µg/g, spent solvent sludge effluent 0.06 µg/g, latex sludge leachate 0.04 µg/g, spent solvent sludge leachate 0.39 µg/g, paint skins sludge leachate	Sigma, 1985
B.C. paint manufacturer	4 µg/L, combined effluent 22 µg/L, tank washing effluent <0.05 µg/g, baghouse dust <0.02 µg/g, baghouse dust leachate	Sigma, 1985
Petrochemical plants, St. Clair River	Detected in 1 of 7, within range of 1–10 µg/L (final effluent)	Munro *et al.*, 1985
Ontario organic chemical manufacturing sector effluents	0.002–1.0 µg/L 0.114 kg/day (average daily loading)	OMOE, 1991a, 1992
Ontario iron and steel sector	0.360 kg/day (average daily loading)	OMOE, 1991b
Ontario petroleum refining sector	ND–12 µg/L (average = 0.871 µg/L) (process effluent streams)	OMOE, 1990
Industrial plants on St. Lawrence River	0.516 kg/day (average daily loading, n = 48)	MENVIQ and Environment Canada, 1993
Waste disposal site, Trenton, Ontario	<1 µg/L	Water and Earth Science Associates Ltd., 1989
Canadian coal mine wastewater sediments	Detected at 1 of 2 mines at concentrations between 1000 and 5000 ng/g, and at 2 of 3 coal storage transfer terminals at <1 ng/g	Atwater *et al.*, 1990
Canadian municipal sludges	Trace–25 000 ng/g dry weight	Webber and Lesage, 1989
Canadian municipal sludges	<3200–35 100 ng/g dry weight	Webber and Bedford, 1996
Canadian municipal sludges and sludge compost	<5000–16 800 ng/g dry weight	Webber and Nichols, 1995

TABLE 1   (continued)

Source	Concentration	Reference
Iona Sewage Treatment Plant, Vancouver, B.C.	<1.0 µg/L	Rogers *et al*., 1986; Analytical Service Laboratories, 1992
Alberta wastewater	1.0–3.0 µg/L (n = 12)	ENVIRODAT, 1993
Calgary, Alberta, storm sewer effluent	up to 50 µg/L	Hargesheimer and Lewis, 1987
Ontario sewage treatment plant effluent	2 µg/L	Beak Consultants, 1991
Ontario municipal water pollution control plants	raw sewage: <10–82.9 µg/L; 5.85 µg/L (geometric mean) primary effluent: <2–9.2 µg/L; 1.42 µg/L (geometric mean) secondary effluent: <2–25.0 µg/L; 1.09 µg/L (geometric mean) tertiary effluent: <2–3.3 µg/L; 1.13 µg/L (geometric mean) raw sludge: ND–48 701.8 ng/g dry weight; 3445.6 ng/g dry weight (geometric mean) treated sludge: ND–914 498 ng/g dry weight; 1916.9 ng/g dry weight (geometric mean)	OMOE, 1988

ND = not detected

Canadian storm sewer effluents at concentrations up to 50 µg/L (Hargesheimer and Lewis, 1987) and in effluents from municipal sewage treatment plants and industrial plants at concentrations up to 22 µg/L (Munro *et al*., 1985; Sigma, 1985; OMOE, 1988, 1990, 1991a,b; ENVIRODAT, 1993). BBP has been detected at concentrations up to 914 µg/g dry weight (geometric mean 1.9 µg/g dry weight) in 6 of 34 sludges sampled from Ontario sewage treatment plants in 1987 (OMOE, 1988).

Total on-site environmental releases of BBP reported to the National Pollutant Release Inventory in 1994 were 3.7 tonnes (NPRI, 1996). Most of this, 3.55 tonnes, was released into the atmosphere from one facility in Quebec. By industrial sector, reported releases were 0.13 tonnes from "chemical and chemical products industries," 0.02 tonnes from "paper and allied products industries" and 3.55 tonnes from "other manufacturing industries." All of these reported releases were to the atmosphere. Total transfers of BBP for off-site disposal were much higher, amounting to 33.3 tonnes in 1994, with 25.1 tonnes going to incinerators and the remainder, 8.2 tonnes, to landfill. A reported total of 3.68 tonnes of BBP was sent for recovery in 1994 — 2.29 tonnes for energy recovery and 1.39 tonnes for recovery, reuse or recycling (NPRI, 1996).

In 1995, total on-site environmental releases of BBP reported to the National Pollutant Release Inventory were 6.54 tonnes (NPRI, 1997). All of these reported releases were to the atmosphere, with most, 4.32 tonnes, coming from the same facility in Quebec. Total transfers of BBP for off-site disposal were again considerably higher, amounting to 18.87 tonnes. A reported

total of 3.82 tonnes of BBP was sent for recovery in 1995 (NPRI, 1997).

According to data reported under a survey carried out under the authority of Section 16 of CEPA, releases of BBP to the Canadian environment were about 6 tonnes in 1996 (all to the atmosphere), whereas releases to landfills were about 1 tonne the same year (Environment Canada, 1997b).

There have been no spills of BBP reported on the Statistics Database produced by the Canadian Transport Emergency Centre for the years 1992 to 1997, inclusive (CANUTEC, 1997).

BBP has been detected in stack emissions from hazardous waste combustion and from coal-fired power plants in the United States (Oppelt, 1987). Reasonable worst-case emissions of BBP from incinerators, boilers and industrial furnaces burning wastes were predicted to be 3 $\mu g/m^3$ waste gas (Dempsey and Oppelt, 1993). In a study of four U.S. coal-fired utility boiler plants, the emission rates for BBP in flue gases ranged from 210 to 3400 mg/hour (Haile *et al*., 1984). BBP was identified, but not quantified, in extracts of municipal incinerator fly ash from the Netherlands, but it was not detected in extracts from Ontario (detection limits not stated) (Eiceman *et al*., 1979).

BBP has been detected in emissions from carpets (Bayer and Papanicolopoulos, 1990), PVC flooring (Bremer *et al*., 1993) and vinyl wall coverings (Etkin, 1995). It is also a component of some consumer products and could be used as a component of certain cosmetics, such as nail polish (Martin, 1996).

2.3   Exposure characterization

2.3.1   Environmental fate

2.3.1.1   Air

Photooxidation is the most important process for the breakdown of BBP in the atmosphere (Atkinson, 1987). BBP is also readily removed from air by rain (Ligocki *et al*., 1985a). Howard *et al*. (1991) estimated a half-life in air of 6–60 hours for BBP, based on photooxidation rates.

2.3.1.2   Water

BBP is readily biodegraded in aerobic surface water, with a half-life of ≤2 days (Saeger and Tucker, 1976; Gledhill *et al*., 1980; Adams and Saeger, 1993). Biodegradation is considerably slower in cold water, as BBP was almost completely biodegraded after 7 days in Rhine River water at 20°C but was not biodegraded in the same water after 10 days at 4°C (Ritsema *et al*., 1989).

Photolysis and hydrolysis of BBP in water are not significant (Gledhill *et al*., 1980; Howard *et al*., 1991).

2.3.1.3   Sediments

Biodegradation is the most important degradation pathway for BBP in sediments (Gledhill *et al*., 1980; Adams and Saeger, 1993). In a freshwater/sediment microcosm, the aerobic degradation pathway appeared to be BBP $\rightarrow$ monobutyl/monobenzyl phthalate $\rightarrow$ phthalic acid $\rightarrow$ 4,5-dihydroxyphthalic acid $\rightarrow$ oxalic acid $\rightarrow$ formic acid $\rightarrow$ carbon dioxide (Adams *et al*., 1986, 1989; Adams and Saeger, 1993). The half-life for complete mineralization of BBP in this study was 13 days (Adams and Saeger, 1993). BBP can also be biodegraded under anaerobic conditions (Shelton and Tiedje, 1984; Painter and Jones, 1990; Ejlertsson *et al*., 1996), with an estimated half-life of about 1–6 months (Howard *et al*., 1991). The end products of anaerobic degradation were monobutyl phthalate,

monobenzyl phthalate, methane and carbon dioxide (Ejlertsson *et al.*, 1996).

2.3.1.4　Soils

BBP is readily biodegraded in aerobic soils, with an estimated half-life of about 1–7 days (Howard *et al.*, 1991). It is also biodegraded in anaerobic soils. Painter and Jones (1990) reported 78% anaerobic biodegradation in soil after 22 days and 100% after 100 days. BBP sorbs to organic matter in soil, so soil leaching should not be significant (Zurmühl *et al.*, 1991).

2.3.1.5　Biota

With a log K_{ow} of 4.9 (Leyder and Boulanger, 1983), BBP would appear to have a high potential for bioaccumulation. However, reported bioconcentration factors (BCFs) are less than 1000, because BBP is readily metabolized, with a depuration half-life of less than two days (Barrows *et al.*, 1980; Veith *et al.*, 1980). The highest reported BCF was 772 for bluegill (*Lepomis macrochirus*), based on total ^{14}C-labelled residues (Veith *et al.*, 1980). Several other authors have reported BCFs for fish in the same general range. The measured BCF in bluegills based on whole-body residues of intact ^{14}C-labelled BBP, rather than total residues, was 12.4 (Carr *et al.*, 1997). In this study, intact BBP comprised approximately 3% of the total radioactive residue, and there was insufficient tissue to further characterize the remainder.

Eastern oysters (*Crassostrea virginica*) exposed to a measured concentration of 0.012 mg ^{14}C-BBP/L for 11 days reached an apparent steady-state whole-body tissue concentration within three days, with a BCF of 135. The calculated steady-state BCF, based on uptake and depuration rate constants, was 380, whereas

the projected half-life of the steady-state tissue residues was calculated to be 7.4 days. Experimentally, 50% of the ^{14}C-residue was eliminated between days 1 and 2 of the 42-day depuration period; by day 14 of depuration, 85% of the ^{14}C-residue had been eliminated (Springborn Bionomics, 1986a).

Based on physical/chemical properties of BBP, Wild and Jones (1992) predicted that retention of the substance by root surfaces of plants would be high, but that subsequent uptake of BBP by plants would be low. This prediction was confirmed by Mueller and Koerdel (1993), who reported that plants grown on phthalate-enriched soil did not take up BBP from the soil through the roots. However, plants exposed to phthalate-treated dust did take up BBP in leaf cuticles.

2.3.1.6　Environmental partitioning

EQC Fugacity Level III modelling was used to estimate the environmental partitioning of BBP when it is released into air, water or soil (DMER and Angus Environmental Limited, 1996). Values for input parameters were as follows: molecular weight, 312.4 g/mol; vapour pressure, 0.001 15 Pa (Gledhill *et al.*, 1980); water solubility, 2.69 mg/L (shake flask method; Howard *et al.*, 1985); log K_{ow}, 4.9 (shake flask method; Leyder and Boulanger, 1983); Henry's law constant, 0.133 Pa·m^3/mol (Lyman *et al.*, 1982); half-life[1] in air, 55 hours; half-life in water, 170 hours; half-life in soil, 550 hours; and half-life in sediment, 1700 hours. Modelling was based upon an assumed emission rate of 1000 kg BBP/hour, although the emission rate used would not affect the estimated percent distribution. If BBP is emitted into air, the EQC Fugacity Level III model predicts that about 72% will partition to soil, about 22% to air, about 4% to water and about 2% to sediment. If BBP

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[1] For each environmental compartment, DMER and Angus Environmental Limited (1996) use a series of ranges of half-lives (<10 hours, 10–30 hours, 30–100 hours, etc.), and the half-life of the particular substance is assigned to the appropriate range, based on a consideration of available persistence data. The geometric mean of this range is then used as an input parameter for the fugacity model. For example, the atmospheric half-life of BBP in air is judged to be between 30 and 100 hours. The geometric mean of this range, 55 hours, is used as an input parameter in the model. Conservative values for persistence were selected (i.e., longer rather than shorter half-lives) to ensure that persistence is not underestimated.

is emitted into water, about 65% is predicted to partition to water, about 35% to sediment and a very small fraction to soil. If BBP is released to soil, more than 99% will be found in soil.

2.3.2 Environmental concentrations

Phthalates have been routinely detected in laboratory air and equipment, and care must be taken to prevent the contamination of environmental samples during collection and analysis. BBP may be less problematic in this regard than some other phthalates, particularly bis(2-ethylhexyl) phthalate (DEHP), but contamination is a possibility. BBP was detected in a laboratory absorbent at a concentration of 7950 ng/g, in plastic pipette tips at a concentration of 500 ng/g and in so-called "plasticizer-free" hose at 100 ng/g (Furtmann, 1996).

2.3.2.1 Ambient air

There is limited available information on concentrations of BBP in the atmosphere, and there are no data from the immediate vicinity of known sources. The only Canadian data identified are for Greater Vancouver, British Columbia, where concentrations of BBP in ambient air ranged from 0.38 to 1.78 ng/m^3 (n = 5) (Belzer, 1997).

Outside Canada, BBP was not detected in the vapour phase at Portland, Oregon (n = 7) (Ligocki et al., 1985a), but it was measured in the aerosol phase at concentrations up to 9.6 ng/m^3 (Ligocki et al., 1985b). Lower atmospheric concentrations have been reported for a few other locations in the United States and Spain (Environment Canada, 1998).

BBP was detected at concentrations ranging from <0.04 to 2.14 μg/L in rainwater samples (n = 105) collected in Germany in 1991 and 1992 (Furtmann, 1996) and from 0.020 to 0.074 μg/L in samples (n = 7) collected at Portland, Oregon, in 1984 (Ligocki et al., 1985a).

2.3.2.2 Surface water

Data on concentrations of BBP in Canadian surface water have been identified for British Columbia, Alberta, the Great Lakes region and Quebec. BBP has been detected in these surface waters at concentrations up to 1 μg/L (ENVIRODAT, 1993). Generally, concentrations of BBP in Canadian surface waters are considerably less than 1 μg/L (Munro et al., 1985; Germain and Langlois, 1988; OMOE, 1992; ENVIRODAT, 1993, 1996; Environment Canada et al., 1995, 1996).

The highest reported concentration of BBP in non-Canadian surface waters in North America is 2.4 μg/L in the Mississippi River south of St. Louis, Missouri (Gledhill et al., 1980). Concentrations of BBP ranged from <0.04 to 13.9 μg/L in water from the Rhine River, Germany, and its tributaries (Furtmann, 1996) and from <0.01 to 6.6 μg/L in water from the Rieti District of Italy (Vitali et al., 1997).

2.3.2.3 Sediments

Data on concentrations of BBP in Canadian sediments are available only from British Columbia and the Detroit River. Concentrations of BBP up to 370 ng/g dry weight were reported for marine sediments from British Columbia (n = 34) (Axys Analytical Services Ltd., 1992; Goyette, 1993). Generally, concentrations of BBP in freshwater and marine sediments from British Columbia are considerably less than 100 ng/g dry weight (Rogers and Hall, 1987; Swain and Walton, 1990a,b; Axys Analytical Services Ltd., 1992; SEAM, 1996). BBP was detected in Detroit River sediments at 3 of 31 sites, at concentrations ranging from 120 to 220 ng/g dry weight (Fallon and Horvath, 1985).

Outside Canada, the highest reported concentration of BBP in sediments is 3800 ng/g dry weight, from the Lower Passaic River, Newark, New Jersey, adjacent to combined sewer overflow outfalls (n = 40) (Iannuzzi et al., 1997).

2.3.2.4   Soils

BBP has been detected in soil samples in a lime disposal area at Regina, Saskatchewan, at concentrations of 150 and 550 ng/g dry weight (Saskatchewan Department of Environment and Public Safety, 1989) and in 3 of 30 soil samples from the Port Credit, Oakville and Burlington area of Ontario at concentrations up to 290 ng/g dry weight (Golder Associates, 1987). Concentrations of BBP in 30 samples of agricultural soils from across Canada were all below the detection limit of 200 ng/g dry weight (Webber, 1994; Webber and Wang, 1995).

Outside Canada, BBP was detected in soil in the neighbourhood of phthalate-emitting plants in Germany at concentrations ranging from <5 to 100 ng/g dry weight (Mueller and Koerdel, 1993). In this study, the median concentration of BBP in the 24 soil samples was <5 ng/g dry weight.

2.3.2.5   Biota

Data on concentrations of BBP in Canadian biota are available mainly for marine and estuarine organisms from British Columbia, where values are generally <100 ng/g wet weight (Swain and Walton, 1990a; Axys Analytical Services Ltd., 1992; Goyette, 1993; SEAM, 1996), although higher values have occasionally been reported. BBP has been detected in Canadian biota ($n \approx 110$) at concentrations up to 1470 ng/g wet weight (in a sample of butter sole [*Isopsetta* (*Pleuronectes*) *isolepis*] from Boundary Bay, B.C.) (Swain and Walton, 1990a; SEAM, 1996). The mean concentration of BBP in five samples of butter sole from this study was 500 ng/g wet weight. The highest concentration of BBP reported for other species in this study was 830 ng/g wet weight (in a liver sample from starry flounder [*Platichthys stellatus*]) Swain and Walton, 1990a; SEAM, 1996). Data on concentrations of BBP in biota from other areas in Canada are limited to one study in which levels in white suckers (*Catostomus commersoni*) from the Sackville River, Nova Scotia, were below the detection limit of 200 ng/g wet weight (Barringer Laboratories, 1997).

Concentrations of BBP in bottom-dwelling organisms, including fish and invertebrates, from Commencement Bay, Tacoma, Washington, ranged up to 695 ng/g wet weight (Nicola *et al*., 1987).

2.3.2.6   Food

Health Canada carried out a survey in 1987–1989, analysing composites of foodstuffs that were packaged in plastic (Page and Lacroix, 1995). The Department also monitored for the presence of BBP in composites of a variety of foodstuffs purchased in Ontario in 1985 and 1988, as part of the Total Diet Program (Page and Lacroix, 1995). Of approximately 100 foodstuffs sampled in these surveys, BBP was detected only in yoghurt (0.6 μg/g), cheddar cheese (1.6 μg/g), butter (0.64 μg/g), pork (0.8 μg/g), mixed vegetable juice (0.11 μg/g) and crackers (0.48 μg/g). The Total Diet Program included representative samples of meat, poultry, fish, cereal products, vegetables, fruits and miscellaneous foodstuffs, including soups and desserts.

No data were identified on concentrations of BBP in either breast milk or infant formula in Canada.

The results of a survey of retail infant formula have been published by the British Ministry of Agriculture, Fisheries and Food (MAFF, 1996). Fifty-nine individual samples of 15 different brands of infant formula were purchased from retail outlets in five towns across the United Kingdom. The range of concentrations was <0.004–0.25 mg/kg (limit of detection 0.001 mg/kg).

2.3.2.7   Drinking water

BBP was not detected in 329 samples of water from 28 municipalities (18 surface water, 10 groundwater) in Alberta in 1985–1986 (Spink,

1986). Sampling of treated water from 278 sites (1550 samples) in Alberta from 1987 to 1993 did not result in the detection of BBP (limit of detection 1 µg/L) (Halina, 1994); similar results were obtained from analyses of approximately 400 samples during 1994–1995 (Halina, 1996).

The Quebec Ministry of the Environment analysed water for the presence of BBP between 1990 and 1993 (Riopel, 1994, 1996). Concentrations of BBP in tap water were either <1 or <2 µg/L in 27 of 28 communities. BBP was detected (2.8 µg/L) in only one sample in 1991.

Although BBP has been identified at several water treatment plants or well supplies in Ontario, analyses were carried out by mass spectrometry, and hence the data are considered semi-quantitative only (McGrachan, 1996).

In three samples of tap water in Toronto, concentrations of BBP ranged from "not detected" (limit of detection 0.02 ng/L) to 0.8 ng/L. Concurrently, concentrations of BBP in seven brands of bottled spring water ranged from <1 ng/L (detection limit) to 120 ng/L (City of Toronto, 1990).

BBP was not detected (limit of detection 3 µg/L) in a limited number of samples at three raw water sources in Greater Victoria in 1991 and 1994 (Greater Victoria Water District, 1996).

2.3.2.8   Indoor air

The California Environmental Protection Agency (1992) has reported concentrations of BBP in 125 homes and in ambient air near 65 of those homes. In the autumn of 1990, a field monitoring study was carried out at 125 homes in Riverside, California. In each home, two 12-hour indoor air samples were collected during daytime and overnight periods. In a subset of 65 homes, outdoor air samples were also collected. The protocol stated that "combined particulate and vapor-phase PAHs and phthalates were collected."

In indoor air, median daytime and nighttime concentrations were 34 and 35 ng/m^3, respectively. The 90th percentiles for daytime and nighttime concentrations were 140 and 120 ng/m^3, respectively.

In corresponding samples of outdoor air, the median (for both daytime and nighttime sampling) concentration of BBP was below the method quantifiable limit of 5.1 ng/m^3; the 90th percentiles were 5.3 and 6.7 ng/m^3 for daytime and nighttime sampling, respectively (California Environmental Protection Agency, 1992).

Otson *et al*. (1994) sampled indoor air in 757 single-family dwellings in Canada. BBP was detected, but not quantified, in composite samples.

Oie *et al*. (1997) sampled particulate matter in 38 residences in Norway. Mean BBP concentrations in sedimented dust were 11 µg/100 mg (total dust) and 14 µg/100 mg (organic fraction). The mean concentration of BBP in suspended particulate matter in six homes was 14 µg/100 mg. The protocol did not include concurrent measurement of the concentration of BBP in the vapour phase.

2.3.2.9   Consumer products

Quantitative data on concentrations of BBP in consumer products were not identified.[2]

2.4   Effects characterization

2.4.1   *Ecotoxicology*

2.4.1.1   Pelagic organisms

Data on acute toxicity are available for approximately two dozen species, including microorganisms, algae, invertebrates and fish. The lowest reported acute toxicity value was a 96-hour LC_{50} of 510 µg/L for the shiner perch

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[2]   Analyses of phthalate esters in soft vinyl plastic children's products are currently being conducted by Health Canada (Tom, 1998).

(*Cymatogaster aggregata*) in a flow-through study using measured concentrations (Ozretich *et al*., 1983). LC_{50} values for most other fish species exceeded 1000 µg/L. The most sensitive invertebrate species in acute toxicity tests was the mysid shrimp (*Mysidopsis bahia*), with a 96-hour LC_{50} of 900 µg/L in a static bioassay using nominal concentrations (Gledhill *et al*., 1980). Reported LC_{50} values for other invertebrates exceeded 1000 µg/L.

Data on chronic toxicity are available for about a dozen species, including algae, invertebrates and fish. The lowest reported chronic toxicity value was a 96-hour EC_{50} of 110 µg/L, reported for the green alga (*Selenastrum capricornutum*), based on chlorophyll-a measurements and cell number reductions using nominal concentrations (Sugatt and Foote, 1981). The most sensitive invertebrate species in chronic toxicity tests was *Mysidopsis bahia*, with a 28-day Lowest-Observed-Effect Concentration (LOEC) of 170 µg/L, based on reproduction and growth in a flow-through study using measured concentrations (Springborn Bionomics, 1986b). The most sensitive fish species in chronic toxicity tests was the fathead minnow (*Pimephales promelas*), with a 30-day LOEC of 360 µg/L, based on hatching of eggs and survival and growth of larvae using measured concentrations (LeBlanc, 1984).

2.4.1.2   Benthic organisms

No toxicity studies using spiked sediment were identified for BBP.

A toxicity value for benthic organisms can be estimated from a toxicity value for a pelagic organism using the Equilibrium Partitioning approach. This approach is based on the assumption that the partitioning of non-ionic organic compounds between the organic carbon fraction of sediments and pore water is at equilibrium (Di Toro *et al*., 1991). The most sensitive pelagic invertebrate species in chronic toxicity tests was *Mysidopsis bahia*, with a 28-day LOEC of 170 µg/L (Springborn Bionomics, 1986b).

Using this value, a chronic toxicity value for benthic organisms may be calculated using the equation:

$$LOEC_{benthic} = f_{oc} \times K_{oc} \times LOEC_{pelagic}$$

where:
- f_{oc} is the organic carbon fraction in sediment (average dry-weight organic carbon fraction in St. Clair River sediments is 0.02, according to Kauss, 1997),
- K_{oc} is the organic carbon/water partition coefficient (lowest reported K_{oc} is 2000 L/kg), and
- $LOEC_{pelagic}$ is the LOEC for pelagic aquatic organisms, or 170 µg/L.

Therefore:

$$LOEC_{benthic} = 0.02 \times 2000 \text{ L/kg} \times 170 \text{ µg/L}$$

$$= 6800 \text{ µg/kg dry weight}$$

$$= 6800 \text{ ng/g dry weight}$$

Tetra Tech Inc. (1986) used the Equilibrium Partitioning approach to calculate a sediment quality value for Puget Sound of 55 000 ng BBP/g dry weight for sediment containing 1% organic carbon, based on 1980 U.S. Environmental Protection Agency water quality criteria.

The estimated LOEC calculated above is supported by the findings of Clark *et al*. (1987), who reported a 10-day LC_0 of 10 000 ng dibutyl phthalate/g dry weight for the grass shrimp (*Palaemonetes pugio*). More recently, Call *et al*. (1997) reported a Maximum Acceptable Toxicant Concentration (MATC)[3] of 127 000 ng dibutyl phthalate/g dry weight for the midge (*Chironomus tentans*) exposed for 10 days in sediment with a total organic carbon content of 2.45%. The toxicity of dibutyl phthalate is generally similar to that of BBP for aquatic organisms (Staples *et al*., 1997).

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[3] Geometric mean of the No-Observed-Effect Concentration (NOEC) and the Lowest-Observed-Effect Concentration (LOEC).

2.4.1.3   Soil organisms

No information was identified concerning the toxicity of BBP to soil organisms.

A toxicity value for soil organisms can be estimated from a toxicity value for a pelagic organism using the Equilibrium Partitioning approach described above. The most sensitive invertebrate species in chronic toxicity tests was *Mysidopsis bahia*, with a 28-day LOEC of 170 µg/L (Springborn Bionomics, 1986b). Using this value, a chronic toxicity value for soil organisms may be calculated as follows:

$$LOEC_{soil} \; = \; f_{oc} \times K_{oc} \times LOEC_{pelagic}$$

where:
- f_{oc} is the organic carbon fraction in soil (the average dry-weight organic carbon fraction of 30 soil samples taken from across Canada by Webber, 1994, or 0.02),
- K_{oc} is the organic carbon/water partition coefficient (lowest reported K_{oc} is 2000 L/kg), and
- $LOEC_{pelagic}$ is the LOEC for pelagic aquatic organisms, or 170 µg/L.

Therefore,

$$LOEC_{soil} \; = \; 0.02 \times 2000 \; L/kg \times 170 \; µg/L$$

$$= \; 6800 \; µg/kg \; dry \; weight$$

$$= \; 6800 \; ng/g \; dry \; weight$$

2.4.1.4   Terrestrial plants

No data have been identified on the effects of BBP on terrestrial plants exposed via the atmosphere or soil. There are some data, however, for dibutyl phthalate. The lowest reported atmospheric concentration of dibutyl phthalate having adverse effects on plants is 360 ng/m^3, a concentration that caused growth restriction, chlorosis and cotyledon death in cabbage

(*Brassica oleracea*) plants after a four-week exposure (Hardwick *et al.*, 1984).

Concentrations of dibutyl phthalate in soil of 200 000 ng/g dry weight and above reduced the germination of soybeans (*Glycine max*) by >33% and decreased the growth of corn and soybeans by 29–80% after three weeks (Overcash *et al.*, 1982).

2.4.1.5   Wildlife

No data were available on the effects of BBP on wildlife, but there are data on the effects of BBP on experimental animals. These data are presented in Section 2.4.3. Data on the toxicity of BBP based on inhalation exposure are limited. Two short-term studies and one subchronic study, all using rats, were identified.

There are few data on the effects of BBP on birds. BBP injected into three-day chicken eggs resulted in the death or malformation of 13 of 30 treated embryos at 25 µmol (~7.8 mg) per egg, whereas only 1 of 20 embryos was affected at 13 µmol (~4.1 mg) per egg. Malformations included small eye cups (7 embryos) and deformations in eyelids and cornea (2 embryos), beak (5 embryos) and back and neck (1 embryo). The estimated ED_{50} for BBP was 27 µmol (~8.4 mg) per egg. Similar results were obtained with dibutyl phthalate, with death or malformation of 11 of 30 treated embryos at 26 µmol per egg, and 2 of 30 embryos at 13 µmol per egg. The estimated ED_{50} for dibutyl phthalate was 33 µmol per egg. By contrast, the ED_{50} for the most potent chemical in the study, cyclohexylthiophthalimide, was 0.04 µmol per egg (Korhonen *et al.*, 1983).

Ring doves [ringed turtle-doves] (*Streptopelia risoria*) were fed a diet containing 10 000 ng dibutyl phthalate/g wet weight for three weeks prior to mating through completion of a clutch of two eggs (Peakall, 1974). Eggshell thickness was reduced by 10% (a 15% decrease is considered to be significant for reproductive success).

2.4.1.6 Endocrine modulation

There was weak estrogen receptor-mediated activity for BBP in several *in vitro* bioassays (Jobling *et al.*, 1995; Meek *et al.*, 1996). For example, BBP at a concentration of approximately 10 µg/L reduced the *in vitro* binding of the tritiated natural estrogen, 17ß-estradiol, to the rainbow trout (*Oncorhynchus mykiss*) estrogen receptor by about 40%; approximately 10 000 µg BBP/L reduced the binding by about 60% (Jobling *et al.*, 1995). BBP tested at concentrations of about 300–30 000 µg/L increased the transcriptional activity of the estrogen receptor in the presence of 10^{-11} M 17ß-estradiol, indicating that BBP does not act as an anti-estrogen, but would enhance the effects of endogenous estrogens if they are present (Jobling *et al.*, 1995). In an *in vitro* study, BBP displaced ^{3}H-estradiol from the rainbow trout hepatic estradiol receptor, but was about 10^5 times less potent than estradiol (Knudsen and Pottinger, 1999). BBP did not displace ^{3}H-testosterone from the high affinity testosterone binding site in rainbow trout brain cytosol, or ^{3}H-cortisol from the high affinity cortisol binding site in rainbow trout liver cytosol (Knudsen and Pottinger, 1999). In a study using *in vivo* vitellogenin synthesis in immature rainbow trout as a biomarker, BBP was only weakly estrogenic, increasing the concentration of vitellogenin about three times (Christiansen *et al.*, 1998).

The implications of this endocrine modulation activity for populations of organisms in the environment are not known.

In another study, BBP did not show estrogenic activity. BBP, when injected intraperitoneally at doses of 5 and 50 mg/kg-bw, had no effect on the *in vivo* binding capacity of the hepatic estradiol receptor of rainbow trout, and plasma zona radiata protein levels were significantly reduced (Knudsen *et al.*, 1998). An induction of zona radiata protein would have been an indication of estrogenic activity, and the reduction in levels may indicate an inhibitory

or antagonistic effect of BBP at the level of the receptor (Knudsen *et al.*, 1998).

2.4.2 Abiotic atmospheric effects

Worst-case calculations were made to determine if BBP has the potential to contribute to depletion of stratospheric ozone, ground-level ozone formation or climate change (Bunce, 1996).

The Ozone Depletion Potential (ODP) is 0, since BBP is not a halogenated compound.

The Photochemical Ozone Creation Potential (POCP) was estimated to be 26 (relative to the value of an equal mass of the reference compound ethene, which has a POCP of 100), based on the following formula:

$$POCP = (k_{BBP}/k_{ethene}) \times (M_{ethene}/M_{BBP}) \times 100$$

where:
- k_{BBP} is the rate constant for the reaction of BBP with OH radicals (2.5×10^{-11} cm^3/mol per second),
- k_{ethene} is the rate constant for the reaction of ethene with OH radicals (8.5×10^{-12} cm^3/mol per second),
- M_{ethene} is the molecular weight of ethene (28.1 g/mol), and
- M_{BBP} is the molecular weight of BBP (312.4 g/mol).

The Global Warming Potential (GWP) was calculated to be 1.2×10^{-5} (relative to the reference compound CFC–11, which has a GWP of 1), based on the following formula:

$$GWP = (t_{BBP}/t_{CFC-11}) \times (M_{CFC-11}/M_{BBP}) \times (S_{BBP}/S_{CFC-11})$$

where:
- t_{BBP} is the lifetime of BBP (0.0016 years),
- t_{CFC-11} is the lifetime of CFC-11 (60 years),
- M_{CFC-11} is the molecular weight of CFC-11 (137.5 g/mol),
- M_{BBP} is the molecular weight of BBP (312.4 g/mol),
- S_{BBP} is the infrared absorption strength of BBP (2389/cm^2 per atmosphere, default), and

- S_{CFC-11} is the infrared absorption strength of CFC-11 ($2389/cm^2$ per atmosphere).

These figures imply that BBP is not likely to contribute significantly to depletion of stratospheric ozone, ground-level ozone formation or climate change.

2.4.3   Experimental animals and in vitro

2.4.3.1   Acute toxicity

The acute toxicity of BBP is relatively low. Reported oral LD_{50} values for rats range from 2 to 20 g/kg-bw (NTP, 1982; Hammond *et al*., 1987); a dermal LD_{50} of 6.7 g/kg-bw in both rats and mice has been reported (Statsek, 1974). Clinical signs following oral exposure of rats included weight loss, apathy and leukocytosis. Histological examination revealed toxic splenitis and degenerative lesions of the central nervous system with congestive encephalopathy, myelin degeneration and glial proliferation.

2.4.3.2   Short-term toxicity

In short-term investigations by the oral route (excluding those addressing specifically reproductive effects or peroxisomal proliferation, which are discussed in Sections 2.4.3.6 and 2.4.3.8, respectively), for which the range of endpoints examined was often limited, consistent effects on body weight gain in rats were observed at doses of approximately 1000 mg/kg-bw per day and above, sometimes accompanied by a decrease in food consumption (NTP, 1982; Hammond *et al*., 1987). Although some effects on body weight gain were observed at lower doses, the pattern was inconsistent. In one study, minimal testicular changes were observed in one of six male rats at 480 mg/kg-bw per day (BIBRA, 1985; Hammond *et al*., 1987[4]). In general, though, testicular effects were observed only at much higher doses (i.e., atrophy at 1500 mg/kg-bw per day; Hammond *et al*., 1987). In a six-week investigation, there were no adverse histopathological effects on the nervous system

of rats exposed to 3000 mg/kg-bw per day, although reversible clinical signs were observed (Robinson, 1991).

In an inhalation study in rats, there were no effects upon hematology, urinalysis, blood chemistry or histopathology following exposure for four weeks to 144 mg/m^3 (Hammond *et al*., 1987). At 526 mg/m^3, effects included reduced body weight gain and reduced serum glucose. In a similar study, exposure to 2100 mg/m^3 resulted in death of some animals; effects after four weeks included reduced body weight gain and atrophy of the spleen and testes (Hammond *et al*., 1987).

2.4.3.3   Subchronic toxicity

The protocol of an early study in Charles River rats included examination of body weight, clinical signs, organ weight and limited histopathology of liver, spleen, kidney, adrenal, stomach and small and large intestines (Hazleton Laboratories, 1958). The only effect observed was a decrease in body weight gain in males at the highest dose (1253 mg/kg-bw per day).

In a range-finding National Toxicology Program (NTP) subchronic (13-week) dietary bioassay in F344 rats, the only adverse effects observed upon examination of body weight, clinical signs and histopathological examination, the latter for control and high-dose animals only, were depressed weight gain and testicular degeneration (nature of degeneration not specified) at the highest dose (1250 mg/kg-bw per day) (NTP, 1982).

Sprague-Dawley rats were administered BBP in the diet for three months at dose levels of 0, 188, 375, 750, 1125 or 1500 mg/kg-bw per day in males and females (Hammond *et al*., 1987). Endpoints examined included body weight gain, hematology, urinalysis and histopathology (control and high-dose groups only). No compound-related lesions were observed at necropsy or upon histopathological examination. In females, the increase in liver to body weight

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[4]   Full study reports for several of the investigations described therein were available to the authors.

ratio was significant at 750 mg/kg-bw per day and higher; in males, the increase was significant at 1125 mg/kg-bw per day and higher. No change occurred in kidney to body weight ratio in females, but there was a significant increase in males at 750 mg/kg-bw per day and higher.

A subchronic dietary study was also conducted in Wistar rats (Monsanto, 1980; Hammond *et al*., 1987) at dose levels of 0, 151, 381 or 960 mg/kg-bw per day in males and 0, 171, 422 or 1069 mg/kg-bw per day in females for three months. Intake of BBP, based on body weight and food consumption, was calculated at four-day intervals throughout the study. Observations included slight anemia in the males at the highest dose and decreased urinary pH in males at the mid and high doses. At the highest dose, no reduction in food consumption was apparent, suggesting that the reduced body weight gain in this group may have been compound related. The liver to body weight ratio was significantly increased at all dose levels in females and at the highest dose in males. A significant increase in kidney to body weight ratio occurred in a dose-related manner in both sexes at the mid and high doses. The cecum to body weight ratio was unaffected in males but was increased at all dose levels in females in a dose-related manner. Gross pathological lesions were limited to increased incidence of red spots on the liver of mid- and high-dose males. Histopathological lesions of the pancreas were observed in males at the mid and high doses and included islet enlargement with cell vacuolization and peri-islet congestion. The liver of high-dose males had small areas of cellular necrosis. No histopathological lesions were described for females. The Lowest-Observed-Adverse-Effect Level (LOAEL) is 381 mg/kg-bw per day, based upon histopathological effects in the pancreas in males. The Lowest-Observed-Effect Level (LOEL) is 171 mg/kg-bw per day, based upon increases in organ to body weight ratio at all doses for the liver and cecum in females (No-Observed-Effect Level, or NOEL, in males is 151 mg/kg-bw per day).

In a six-month dietary study in F344 rats (NTP, 1997a), effects on hematological parameters were reported at 550 mg/kg-bw per day. Only transitory changes in hematological parameters were reported at 180 mg/kg-bw per day.

In a three-month dietary study in dogs (Hammond *et al*., 1987), decreases in body weight gain were associated with decreases in food consumption at the highest dose (1852 and 1973 mg/kg-bw per day for males and females, respectively).

In a 90-day study in mice, there were decreases in body weight gain at 208 mg/kg-bw per day and greater, although no histopathological effects were observed and food consumption was not reported (NTP, 1982). Endpoints included clinical observations, body weight and histopathology (control and high-dose groups only).

One subchronic inhalation bioassay was identified, in which groups of 25 male or 25 female Sprague-Dawley rats were exposed to concentrations of 0, 51, 218 or 789 mg/m³, six hours per day, five days per week, for a total of 59 exposures. Endpoints examined were limited to organ weight changes and histopathological examination of control and high-dose groups (Monsanto, 1982; Hammond *et al*., 1987). A LOEL of 218 mg/m³ was reported, based upon increases in kidney weight, measured at interim sacrifice only, although histopathological changes were not observed at the highest concentrations. The NOEL was 51 mg/m³.

2.4.3.4   Chronic toxicity and carcinogenicity

A carcinogenicity bioassay was conducted by the NTP (1982) in F344 rats. Fifty rats per sex per group were administered BBP via the diet, at levels of 0, 6000 or 12 000 ppm (0, 300 and 600 mg/kg-bw per day, respectively).[5] Females were exposed for 103 weeks. Because of poor survival, all males were sacrificed at weeks 29–30; this part of the study was later repeated (NTP, 1997a).

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[5]   Conversion factor: 1 ppm in food = 0.05 mg/kg-bw per day (Health Canada, 1994).

Only females were examined histopathologically. The incidence of mononuclear cell leukemias was increased in the high-dose group (p = 0.011); the trend was significant (p = 0.006). (Incidences for the control, low- and high-dose groups were 7/49, 7/49 and 18/50, respectively.) The incidence in the high-dose group and the overall trend remained significant (p = 0.008 and p = 0.019, respectively) when compared with historical control data. The NTP concluded that BBP was "probably carcinogenic for female F344/N rats, causing an increased incidence of mononuclear cell leukemias" (NTP, 1982).

However, these results were not repeated in the two-year dietary study in F344/N rats recently completed by NTP (1997a). The average daily doses (reported by the authors) were 0, 120, 240 or 500 mg/kg-bw per day for males and 0, 300, 600 or 1200 mg/kg-bw per day for females. The protocol included periodic hematological evaluation and hormonal assays and a 15-month interim sacrifice.

There were no differences in survival between exposed groups and their controls (NTP, 1997a). A mild decrease in triiodothyronine concentration in the high-dose females at 6 and 15 months and at termination was considered to be related to a non-thyroidal disorder. Changes in hematological parameters were sporadic and minor. In this bioassay, there was no increase in the incidence of mononuclear cell leukemias in female rats, as was reported in the earlier bioassay (NTP, 1982), although the level of exposure (600 mg/kg-bw per day) at which the incidence was observed in the early bioassay was common to both studies.

At the 15-month interim sacrifice, the absolute weight of the right kidney in the females at 600 mg/kg-bw per day and the relative kidney weight in all exposed males were significantly greater than in controls. The severity of renal tubular pigmentation in high-dose males and females was greater than in controls, at both 15 months and two years. The incidence of mineralization in kidney in low- and high-dose

females at two years was significantly less than in controls; severity decreased in all groups of exposed females. The incidence of nephropathy was significantly increased in all groups of exposed females (34/50, 47/50, 43/50 and 45/50 in control, 300, 600 and 1200 mg/kg-bw per day groups, respectively) (see Table 2). The incidence of transitional cell hyperplasia (0/50, 3/50, 7/50 and 4/50 in control, 300, 600 and 1200 mg/kg-bw per day groups, respectively) was significantly increased at 600 mg/kg-bw per day (NTP, 1997a).

At final necropsy, the incidences of pancreatic acinar cell adenoma (3/50, 2/49, 3/50 and 10/50 in control, 120, 240 and 500 mg/kg-bw per day groups, respectively) and pancreatic acinar cell adenoma or carcinoma (combined) (3/50, 2/49, 3/50 and 11/50 in control, 120, 240 and 500 mg/kg-bw per day groups, respectively) in the high-dose males were significantly greater than in the controls and exceeded those in the ranges of historical controls from NTP two-year feeding studies. One carcinoma was observed in a high-dose male; this neoplasm had never been observed in the historical controls. The incidence of focal hyperplasia of the pancreatic acinar cell in the high-dose males was also significantly greater than in the controls (4/50, 0/49, 9/50 and 12/50 in control, 120, 240 and 500 mg/kg-bw per day groups, respectively). Two pancreatic acinar cell adenomas were observed in the high-dose females (NTP, 1997a).

The incidences of transitional epithelial papilloma of the urinary bladder in female rats at two years were 1/50, 0/50, 0/50 and 2/50 in the control, 300, 600 and 1200 mg/kg-bw per day groups, respectively (NTP, 1997a).

The authors concluded that there was "some evidence of carcinogenic activity" in male rats, based upon the increased incidences of pancreatic acinar cell adenoma and of acinar cell adenoma or carcinoma (combined). There was "equivocal evidence of carcinogenic activity" in female rats, based upon the marginally increased incidences of pancreatic acinar cell adenoma and of transitional cell papilloma of the urinary bladder (NTP, 1997a).

TABLE 2 Benchmark doses for non-neoplastic effects of BBP

Study (reference)	Effect levels	Data for calculating benchmark dose		Parameter estimates	
		Dose	**Response**	**Benchmark dose**	**Goodness of fit**
Subchronic dietary study Wistar rats, 27–45 per group 3-month duration (Monsanto, 1980; Hammond *et al.*, 1987)	LOAEL = 381 mg/kg-bw per day (based on histopathological lesions in males in pancreas at two highest doses) (*males*) LOEL = 171 mg/kg-bw per day (based on increases in organ to body weight ratios at all doses for the liver and cecum) (*females*)	Males: control 151 mg/kg-bw per day 381 mg/kg-bw per day 960 mg/kg-bw per day	Lesions in pancreas: 0/27 (0%) 0/14 (0%) 8/15 (53%) 13/14 (93%)	5% dose: 167 mg/kg-bw per day 95% lower confidence limit: 132 mg/kg-bw per day	Chi-square goodness of fit: 9.3×10^{-4} Degrees of freedom: 1 p-value: 0.98
Reproductive study Male F344 rats, 10 per group 14-day dietary administration (Kluwe *et al.*, 1984; Agarwal *et al.*, 1985)	LOAEL = 312.5 mg/kg-bw per day (based on significant increase in the relative weight of liver and both the absolute and relative weights of kidney and proximal tubular regeneration at all levels of exposure)	Males: control 312.5 mg/kg-bw per day 625 mg/kg-bw per day 1250 mg/kg-bw per day 2500 mg/kg-bw per day	Kidney, proximal tubular regeneration: 0/10 2/10 2/10 4/10 3/10	5% dose: 228 mg/kg-bw per day 95% lower confidence limit: 117 mg/kg-bw per day	Chi-square goodness of fit: 3.01 Degrees of freedom: 3 p-value: 0.39
Carcinogenicity bioassay F344/N rats, 60 males and 60 females per group Dietary administration for 2 years NTP (1997a)	LOEL = 120 mg/kg-bw per day (based on increased relative kidney weight in males at interim sacrifice) (not determined at terminal sacrifice) Increase in renal nephropathy in females at all doses (300 mg/kg-bw per day and above); however, unacceptable goodness of fit for benchmark dose	Females: control 300 mg/kg-bw per day 600 mg/kg-bw per day 1200 mg/kg-bw per day	2-year sacrifice; kidney nephropathy: 34/50 47/50 (p < 0.01) 43/50 (p < 0.05) 45/50 (p < 0.01)	5% dose: 50 mg/kg-bw per day 95% lower confidence limit: 28 mg/kg-bw per day	Chi-square goodness of fit: 7.09 Degrees of freedom: 2 p-value: 0.029
F344/N rats, 5 females per group Dietary administration for 1 or 12 months NTP (1997a)	LOEL = 300 mg/kg-bw per day (based on increase in peroxisomal proliferation)				
F344 males, 15 males per group Modified mating protocol NTP (1997a)	LOAEL = 200 mg/kg-bw per day (based on decrease in epididymal spermatozoal concentration without histopathological evidence of hypospermia or decrease in fertility)				

The NTP (1997b) has released a technical report of a study that compared outcomes when chemicals were evaluated under typical NTP bioassay conditions as well as under protocols employing dietary restriction. The experiments were designed to evaluate the effect of dietary restriction on the sensitivity of bioassays towards chemical-induced chronic toxicity and carcinogenicity and to evaluate the effect of weight-matched control groups on the sensitivity of the bioassays. BBP was included in the protocol; the results were summarized as follows:

> Butyl benzyl phthalate caused an increased incidence of pancreatic acinar cell neoplasms in ad libitum-fed male rats relative to ad libitum-fed and weight-matched controls. This change did not occur in rats in the restricted feed protocol after 2 years… Butyl benzyl phthalate also caused an increased incidence of urinary bladder neoplasms in female rats in the 32-month restricted feed protocol. The incidences of urinary bladder neoplasms were not significantly increased in female rats in any of the 2-year protocols, suggesting that the length of the study, and not body weight, was the primary factor in the detection of this carcinogenic response.

Fifty B6C3F$_1$ mice per sex per group were exposed to 0, 6000 or 12 000 ppm BBP (0, 780 and 1560 mg/kg-bw per day, respectively[6]) via the diet for 103 weeks (NTP, 1982). Approximately 35 tissues were examined histopathologically. The only compound-related sign of exposure was a dose-related decrease (statistical significance not specified) in body weight in both sexes. Survival was not affected, and there was no increased incidence of any neoplasm that was compound related. As well, non-neoplastic changes were all within the normal limits of incidence for B6C3F$_1$ mice. The NTP concluded that, under the conditions of the bioassay, BBP "was not carcinogenic for B6C3F$_1$ mice of either sex."

2.4.3.5 Genotoxicity

In the (few) published reports of Ames assays with BBP, results have been negative (Litton Bionetics Inc., 1976; Rubin *et al*., 1979; Kozumbo *et al*., 1982; Zeiger *et al*., 1982, 1985). Negative results have also been reported for mouse lymphoma assays (Litton Bionetics Inc., 1977; Hazleton Biotechnologies Company, 1986), although equivocal findings have also been published (Myhr *et al*., 1986; Myhr and Caspary, 1991). In an assay for *in vitro* transformation of Balb/c-3T3 cells (Litton Bionetics Inc., 1985), results were negative. In an assay for chromosomal aberrations and sister chromatid exchanges (SCEs) in Chinese hamster ovary cells (Galloway *et al*., 1987), there was slight evidence for a trend in one SCE test without activation, but no convincing evidence for positive results for SCEs or chromosomal aberrations.

The results from the mouse lymphoma (Myhr *et al*., 1986; Myhr and Caspary, 1991) and chromosomal aberration (Galloway *et al*., 1987) assays are equivocal. For the mouse lymphoma assay, NTP concluded that "Increases in mutant colonies were observed in the absence of S9 in cultures treated with concentrations that produced precipitation, but such responses were not considered valid by experimental quality control parameters." However, it is difficult to dismiss the observed dose–response across several trials as spurious, although the repeat tests were negative, particularly in view of inconsistencies of results of the latter. In repeat studies (n = 5) in the absence of S9, there was limited evidence of activity in only one case; however, although BBP was positive at 80 nL/mL in the second trial, it was toxic at concentrations above 30 nL/mL in the third. The inconsistently observed increase in small colony mutants and percent damaged Chinese hamster ovary cells may be indicative of weak clastogenic activity that warrants proper confirmation in well-conducted assays.

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[6] Conversion factor: 1 ppm in food = 0.13 mg/kg-bw per day (Health Canada, 1994).

A negative response was reported for an assay for the induction of sex-linked recessive lethals in *Drosophila melanogaster* (Valencia *et al*., 1985). The NTP (1997a) has recently published summary results of mouse bone marrow tests for SCEs and induction of chromosomal aberrations; responses were weak, and the SCE test was not repeated. Both of these responses, although statistically significant, were small and indicative of only weak clastogenic activity. Ashby *et al*. (1997a) reported negative results in a micronucleus assay in rats.

Although the weight of evidence of genotoxicity is clearly negative, available data are inadequate to conclude unequivocally that BBP is not clastogenic, although in available studies it has induced, at most, weak activity.

2.4.3.6 Reproductive and developmental toxicity

With respect to reproductive effects, in repeated-dose toxicity studies by the oral route, decreases in the weight of and histopathological effects in the testes have been observed, although only at doses greater than those that induce other effects, such as variations in organ to body weight ratios for the kidney and liver or histopathological effects in the pancreas or kidney. With the exception of a short-term gavage study in which minimal histopathological effects in the testes of one of six rats were observed at 480 mg/kg-bw per day (control data not presented, and no statistical analysis) (Hammond *et al*., 1987), testicular atrophy or degeneration has been observed in rats only at doses exceeding 1250 mg/kg-bw per day (NTP, 1982, 1997a; Hammond *et al*., 1987).

In a combined reproductive/developmental screening protocol, there was a decrease in body weight gain, fluctuation in food consumption, reduction in the weight of testis and epididymis and increase in testicular degeneration in male rats at 1000 mg/kg-bw per day. In females at this dose,

there was a decrease in body weight gain, effects on food consumption and adverse effects on reproductive indices. With the exception of a transient decrease in pup weight, there were no effects on the parental generation or offspring at 500 mg/kg-bw per day (Piersma *et al*., 1995).

Reproductive effects of BBP in male Fischer 344 rats have been investigated by the NTP (Kluwe *et al*., 1984; Agarwal *et al*., 1985). Groups of 10 males were administered 0, 0.625, 1.25, 2.5 or 5.0% (0, 312.5, 625, 1250 or 2500 mg/kg-bw per day[7]) in the diet for 14 days. The protocol included measurement of endocrine hormones and histopathological examination of brain, liver, kidney, spleen, thyroid, thymus, pituitary, testes, epididymis, prostate, seminal vesicles and mesenteric lymph nodes. Bone marrow was also examined.

No deaths occurred during the study. Body weight was reduced in the two highest dose groups. Food consumption was consistently reduced in the highest dose group throughout the experiment. Absolute weights of testis, epididymis, prostate and seminal vesicles were significantly reduced at the two highest dose levels in a dose-related manner and were accompanied by "generalized histological atrophy." Statistical analyses were presented for histopathological changes in testis (aspermatogenesis/seminiferous tubular atrophy), seminal vesicles (atrophy) and prostate (atrophy); significant changes were consistently observed at the two highest doses. The authors noted a "clear relationship" between dose and severity of morphological changes in testis, seminal vesicles and prostate; the changes occurred only at the two highest dose levels. Similarly, effects on the epididymis were observed in only the two highest dose groups (Kluwe *et al*., 1984; Agarwal *et al*., 1985).

Absolute weight of liver was increased at the two lowest doses and decreased at the highest dose. The relative liver weight was increased at

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[7] Conversion: 1 ppm in food = 0.05 mg/kg-bw per day (Health Canada, 1994).

all levels of exposure, in a dose-related manner. Histopathological changes (mild multifocal chronic hepatitis) were described only for the highest dose. Absolute weight of kidney was also increased at the two lowest doses and was decreased at the two highest. The relative kidney weight was increased at all levels of exposure, in a dose-related manner. Proximal tubular regeneration was observed at all dose levels. Thymic weight was reduced at the two highest dose groups in a dose-related manner. Although histopathological changes were described for all dose groups, atrophy was observed only in the highest dose group. There were no effects upon absolute or relative pituitary weight, nor were morphological changes observed in thyroid, pituitary, spleen or lymph nodes. Statistical analyses were not presented for histopathological observation of these organs (Kluwe *et al.*, 1984; Agarwal *et al.*, 1985).

Plasma testosterone was decreased at the highest dose. Follicle stimulating hormone was increased at the two highest doses in a dose-related manner. Luteinizing hormone was increased at the lowest dose and at the two highest doses; there was no clear dose–response, and there was a limited number of samples at the high dose.[8] No effects were observed upon such hematological parameters as red blood cell count, packed cell volume, hemoglobin, mean corpuscular volume or white blood cell count. There was no significant effect upon blood clotting ability, as measured by prothrombin time. Bone marrow cellularity was reduced at the two highest doses (Kluwe *et al.*, 1984; Agarwal *et al.*, 1985).

At the lowest dose (312.5 mg/kg-bw per day), there was a significant increase in both the absolute and relative weights of both liver and kidney. There was proximal tubular regeneration at all levels of exposure. Focal thymic medullary hemorrhage (minimal severity) was observed in a small number of animals in all BBP-exposed groups, but the incidences were not dose related.

(Luteinizing hormone was increased at the lowest dose and at the two highest doses, but there was no clear dose–response, and there was a limited number of samples at the high dose.) Based upon these observations, the LOAEL is 312.5 mg/kg-bw per day (Kluwe *et al.*, 1984; Agarwal *et al.*, 1985).

Male F344/N rats (15 per group) were administered BBP via the diet for 10 weeks, then each mated to two unexposed females (NTP, 1997a). Dietary concentrations were relatively widely spaced at 0, 300, 2800 or 25 000 ppm, which were reported by the authors to be equivalent to 0, 20, 200 and 2200 mg/kg-bw per day. The final body weight and body weight gain of the high-dose group were significantly lower than those of the controls. Minimal changes in hematological parameters were observed in the high-dose group. Both the absolute and relative weights of prostate and testis were significantly decreased in the high-dose group. (Other lower organ weights in this group were attributed to the lower mean body weight.) Other effects observed at the high dose included degeneration of the seminiferous tubular germinal epithelium and significantly reduced weight of right cauda, right epididymis and right testis. Epididymal spermatozoal concentrations were significantly reduced in a dose-related manner at the two highest doses. However, histopathological evidence of hypospermia and a decrease in fertility index were observed only at the highest dose. Ten of 30 females mated to high-dose males were found to be sperm positive, but none was pregnant at necropsy. Fertility indices were significantly lower at the high dose. At the lower two doses, no exposure-related effects on maternal body weight, maternal clinical observations or litter data were observed. A NOEL of 20 mg/kg-bw per day can be designated, based upon a significant and dose-related decrease in epididymal spermatozoal concentration at the two highest doses and associated effects on fertility at the high dose

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[8] Available data are inadequate to support the contention that a U-shaped dose–response curve may be characteristic of endocrine-disrupting chemicals.

(LOAEL = 200 mg/kg-bw per day). (It should be noted that the dose levels in this protocol increase by a factor of 10.)

Concentrations of BBP of 0.2, 0.4 or 0.8% were administered in the diet to male rats for 10 weeks and to females for 2 weeks pre-mating. Two litters were produced, and no adverse effects on fertility, pregnancy or offspring development were observed (TNO, 1993).

Sharpe *et al*. (1995) administered a single dose level of BBP via drinking water to pregnant Wistar rats, to determine the effects of gestational and lactational exposure upon male offspring. Dams were exposed for two weeks prior to mating and throughout gestation until weaning. This procedure was then repeated on the same dams, and observations were also carried out on the second litters. Based upon measurement of drinking water consumption in six animals, intake of BBP was estimated to range from 126 to 366 µg/kg-bw per day, from postnatal days 1–2 to postnatal days 20–21, respectively. There was a significant reduction in daily sperm production in the BBP-exposed animals examined at 90–95 days. Sperm production in the positive control group, which received 100 µg diethylstilbestrol/L in drinking water, was also reduced (p < 0.01); this endpoint was not assessed in the negative control group exposed to octylphenol polyethoxylate. The authors questioned the relevance of the effects to humans on the basis that this would require detailed dose–response data and measurement of the actual levels of the administered chemical in the male rats.

Ashby *et al*. (1997a) have recently reported the results of a bioassay also designed to investigate effects in offspring of pregnant rats exposed to BBP during gestation and lactation, although the exposure period was more limited. They exposed Alpk:AP$_f$SD rats during gestation

and lactation to 1000 µg BBP/L drinking water or 50 µg diethylstilbestrol/L drinking water (positive control). Negative controls received 100 µL ethanol/L drinking water. Glass drinking water bottles were used in the experiment, as the authors had determined that 60% of BBP was absorbed into plastic drinking water bottles within 24 hours (Ashby *et al*., 1997b). The authors reported that the overall exposures were 183 µg BBP/kg-bw per day and 8.6 µg diethylstilbestrol/kg-bw per day. There were no effects on weight of right testis after decapsulation, total sperm count (right testis), sperm count per gram of right testis or total sperm count in right cauda on postnatal days 90 and 137. There was, however, an increase in absolute and relative liver weights at postnatal day 90. The authors noted the contrast between these results and those reported by Sharpe *et al*. (1995).[9]

It should be noted that there were significant differences between these studies with respect to exposure of the dams. In the Sharpe *et al*. (1995) study, the dams were exposed for two weeks prior to mating and throughout gestation and weaning and were subsequently exposed for another two weeks prior to mating and during gestation and lactation. In the study by Ashby *et al*. (1997a), dams were exposed only during gestation and lactation.

Although BBP has been found to be estrogenic in human breast cancer cells *in vitro* (Jobling *et al*., 1995; Soto *et al*., 1995; Meek *et al*., 1996), results in yeast have been both positive (Coldham *et al*., 1997; Harris *et al*., 1997) and negative; the negative results have been found for both BBP and its principal metabolites (Gaido *et al*., 1997), although administered concentrations were unclear in two of the studies (Coldham *et al*., 1997; Harris *et al*., 1997). However, neither BBP (rats; Monsanto, 1995a, 1996a) nor its metabolites monobutyl phthalate

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[9] It is noted that TNO Nutrition and Food Research Institute (TNO, 1997) is conducting a study for which the protocol was designed "to investigate the reproducibility of, and expand on, the findings of Sharpe *et al*. ... related to the development of the reproductive system in Wistar rats exposed *in utero* and during lactation to butyl benzyl phthalate in drinking water." Although data from this study have not yet been published, Sharpe *et al*. (1998) reported that no adverse effects of BBP were observed.

and monobenzyl phthalate (rats and mice; Monsanto, 1995b, 1996b) have been found to be uterotrophic *in vivo*. There was no estrogenic effect in an acute *in vivo* assay (Milligan *et al*., 1998) in mice (stimulation of increased uterine vascular permeability), whereas Ema *et al*. (1998) observed a significant decrease in uterine decidual growth at 750 mg/kg-bw and higher following administration on days 0–8 to pseudopregnant rats.

The developmental toxicity of BBP following dietary administration has been well investigated by the NTP in studies in both rats and mice (NTP, 1989, 1990; Price *et al*., 1990) and in a series of investigations in rats by Ema *et al*. (1990, 1991a,b,c, 1993, 1994, 1995) following both dietary and gavage administration. In general, developmental effects of BBP have been observed only at dose levels that induced significant maternal toxicity, although malformations observed at high doses in pair feeding studies were not fully attributable to maternal toxicity (Ema *et al*., 1992). In a well-conducted NTP (1989) study in rats at 1100 mg/kg-bw per day, there were significant effects in the mothers but minimal effects in the offspring. At the highest dose (1640 mg/kg-bw per day), there was an increased incidence of rudimentary extra lumbar ribs. Results of studies by Ema *et al*. in which BBP was administered in the diet to rats for various periods, including the full 21 days of gestation, were similar. Although the No-Observed-Adverse-Effect Levels (NOAELs) for both maternal and developmental toxicity were less in the NTP (1990) study in mice (182 mg/kg-bw per day), this was primarily a function of wide dose spacing, with maternal (decreased weight gain) and developmental effects being observed at 910 mg/kg-bw per day. At both 910 and 2330 mg/kg-bw per day, there was a significant increase in the percentage of malformed fetuses per litter. Functional effects have not been investigated in available studies.

Metabolites of BBP have induced effects on the testes similar to those of BBP, with the monobutyl ester being more potent in this regard (Mikuriya *et al*., 1988). Similarly, profiles of effects (e.g., fusion of sternebrae, cleft palate) in the offspring observed at maternally toxic doses of the metabolites of BBP are similar to those induced by BBP itself, with effects being observed at lower doses of monobenzyl than of monobutyl phthalate (see, for example, Ema *et al*., 1996a,b,c).

In a recent multigeneration study by continuous breeding in rats exposed to dibutyl phthalate for which the sole metabolite is monobutyl phthalate, testicular effects observed in the F_1 generation were attributed to impairment of normal androgen signalling in the fetus, although available data were considered insufficient to allow the conclusion that the monoester was responsible (Foster, 1997). Multigeneration studies for BBP have not been identified.

2.4.3.7 Irritation and sensitization

Although BBP did not cause immediate or delayed hypersensitivity in mice in a series of studies (Little and Little, 1983), there have been no investigations conducted by conventional validated design. Data on the irritancy of BBP from early studies, the results of which were inconsistent, are inadequate for evaluation (Calley *et al*., 1966; Dueva and Aldyreva, 1969; Hammond *et al*., 1987).

2.4.3.8 Peroxisomal proliferation

BIBRA (1985) investigated peroxisomal proliferation of BBP and reported an increase in relative liver and relative kidney weights, an increase in cyanide-insensitive palmitoyl-CoA oxidation and an increase in lauric acid 11- and 12-hydroxylase activity in male F344 rats at 639 mg/kg-bw per day. In female rats, an increase in relative liver and relative kidney weights was reported at 679 mg/kg-bw per day. These were the lowest levels of exposure. The NTP (1997a) reported an increase in peroxisomal proliferation in female F344/N rats after exposure to 300 mg/kg-bw per day for either 1 or 12 months. In a comparative study, whereas DEHP induced a "very marked" increase in peroxisomal

proliferation, that for BBP was considered "moderate" (Barber *et al.*, 1987).

2.4.3.9 Neurological and immunological effects

Data additional to those presented in previous sections relevant to assessment of the potential neurotoxicity and immunotoxicity of BBP were not identified.

2.4.3.10 Toxicokinetics and mechanism of action

No data were identified concerning the absorption, metabolism or elimination of BBP in humans.

Based upon a limited number of studies (Erickson, 1965; Kluwe, 1984; Eigenberg *et al.*, 1986; Mikuriya *et al.*, 1988; Elsisi *et al.*, 1989) conducted principally in rats following oral administration, BBP is readily hydrolysed in the gastrointestinal tract and the liver to the corresponding monobutyl or monobenzyl ester. These phthalate monoesters are then rapidly eliminated (90% in 24 hours) in the excreta in proportions of approximately 80% in urine and 20% in feces, although the results of one study indicate that the latter increases at higher doses (approximately 2 g/kg-bw) (Eigenberg *et al.*, 1986). The monobutyl ester is generally present in highest amounts; for example, the ratio of monobutyl to monobenzyl phthalate in rats in one study was 5:3 (Mikuriya *et al.*, 1988).

2.4.4 Humans

Although in an early study (Mallette and von Haam, 1952) BBP was reported to have a moderately irritating effect upon 15–30 volunteers, Hammond *et al.* (1987) observed neither primary irritation nor sensitization reactions in a patch test with 200 volunteers. Other identified data in humans relevant to the assessment of the potential adverse effects of BBP are restricted to limited studies of respiratory/neurological effects or cancer in populations of workers generally exposed to mixtures of plasticizers, of which BBP was a minor component (Nielsen *et al.*, 1985; Hagmar *et al.*, 1990).

3.0 ASSESSMENT OF "TOXIC" UNDER CEPA

3.1 CEPA 11(a): Environment

The environmental risk assessment of a PSL substance is based on the procedures outlined in Environment Canada (1997a). Analysis of exposure pathways and subsequent identification of sensitive receptors are used to select environmental assessment endpoints (e.g., adverse reproductive effects on sensitive fish species in a community). For each endpoint, a conservative Estimated Exposure Value (EEV) is selected and an Estimated No-Effects Value (ENEV) is determined by dividing a Critical Toxicity Value (CTV) by an application factor. A conservative (or hyperconservative) quotient (EEV/ENEV) is calculated for each of the assessment endpoints in order to determine whether there is potential ecological risk in Canada. If these quotients are less than one, it can be concluded that the substance poses no significant risk to the environment, and the risk assessment is completed. If, however, the quotient is greater than one for a particular assessment endpoint, then the risk assessment for that endpoint proceeds to an analysis where more realistic assumptions are used and the probability and magnitude of effects are considered. This latter approach involves a more thorough consideration of sources of variability and uncertainty in the risk analysis.

3.1.1 Assessment endpoints

In Canada, BBP occurs in industrial releases to the atmosphere and in liquid effluent releases to water. Based on its environmental partitioning and detection in air, surface water, sediments, soil and biota in Canada, assessment endpoints for BBP relate to soil organisms (e.g., microorganisms, plants, arthropods, earthworms), pelagic aquatic organisms (e.g., algae, invertebrates, fish), benthic organisms (e.g., microorganisms, invertebrates)

and terrestrial biota, including plants (exposure through soil and air) and terrestrial wildlife, both mammalian and avian (exposure through inhalation and ingestion).

3.1.2 Environmental risk characterization

3.1.2.1 Pelagic organisms

For a hyperconservative risk characterization for pelagic organisms, the EEV is 2.4 µg/L, the highest reported concentration for BBP in surface water in North America. This value is believed to be conservative, because reported concentrations of BBP in Canadian surface waters have not exceeded 1 µg/L. Concentrations of BBP exceeding 2.4 µg/L have been reported for one site on the Rhine River, Germany, and for one of its tributaries and for one site in the Rieti District of Italy.

The CTV is 510 µg/L, the 96-hour LC_{50} for the shiner perch. This CTV was selected from an extensive data set composed of acute studies conducted on approximately two dozen species, including microorganisms, algae, invertebrates and fish. This CTV is conservative, because reported results from acute toxicity tests with freshwater vertebrates and invertebrates show these species to be less sensitive. Dividing this CTV by an application factor of 100 (to account for the conversion of an LC_{50} to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 5.1 µg/L.

The hyperconservative quotient (EEV/ENEV) is 2.4/5.1 = 0.47. Therefore, BBP concentrations in surface water in Canada appear to be unlikely to cause adverse effects on populations of aquatic organisms.

3.1.2.2 Benthic organisms

For a conservative risk characterization for benthic organisms, the EEV is 370 ng/g dry weight, the highest reported concentration of BBP in Canadian sediments.

The CTV is 6800 ng/g dry weight, the LOEC estimated for benthic organisms using the Equilibrium Partitioning approach, as presented in Section 2.4.1.2. Dividing this CTV by an application factor of 10 (to account for the conversion of a LOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 680 ng/g dry weight.

The conservative quotient is 370/680 = 0.54. Therefore, BBP concentrations in sediment in Canada appear to be unlikely to cause adverse effects on populations of benthic organisms.

3.1.2.3 Soil organisms

The concentration of BBP in Canadian soils is generally below 200 ng/g dry weight, a concentration that has been exceeded in only 2 out of 62 soil samples. For a conservative risk characterization for soil organisms, a value of 200 ng/g dry weight is used as the EEV.

The CTV is 6800 ng/g dry weight, the LOEC estimated for soil organisms using the Equilibrium Partitioning approach, as presented in Section 2.4.1.3. Dividing this CTV by an application factor of 10 (to account for the conversion of a LOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 680 ng/g dry weight.

The conservative quotient is thus 200/680 = 0.29. Therefore, concentrations of BBP in soils in Canada appear to be unlikely to cause adverse effects on populations of soil organisms.

3.1.2.4 Terrestrial plants

The hyperconservative EEVs for terrestrial plants are 9.6 ng/m^3, the highest reported concentration of BBP in the atmosphere, Canadian or not, and 550 ng/g dry weight, the highest concentration of BBP reported for Canadian soils.

No toxicity test results have been identified to serve as a CTV for BBP. Dibutyl phthalate at an atmospheric concentration of 360 ng/m^3 caused adverse effects on plants (see Section 2.4.1.4). Accepting this value as a CTV for BBP (as the toxicity of dibutyl phthalate and BBP are generally similar) and using an application factor of 10 (to account for the conversion of a LOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 36 ng/m^3. The resulting quotient is 9.6/36 = 0.27. Therefore, concentrations of BBP in the atmosphere in Canada appear to be unlikely to cause adverse effects on populations of terrestrial plants.

Dibutyl phthalate at soil concentrations of 200 000 ng/g dry weight and above caused adverse effects on plants (see Section 2.4.1.4). Accepting this value as a CTV for BBP and using an application factor of 10 (to account for the conversion of a LOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 20 000 ng/g dry weight. The resulting quotient is 550/20 000 = 0.028. Therefore, concentrations of BBP in soil in Canada appear to be unlikely to cause adverse effects on populations of terrestrial plants.

3.1.2.5 Terrestrial wildlife

For terrestrial wildlife exposed to BBP via inhalation, the hyperconservative EEV for BBP is 9.6 ng/m^3, the highest reported concentration of BBP in the atmosphere, Canadian or not. The CTV is 1.44×10^8 ng/m^3, the No-Observed-Effect Concentration (NOEC) for BBP for rats via inhalation. Dividing this CTV by an application

TABLE 3   Risk characterization summary for environmental effects of BBP

Parameter	Pelagic	Benthic organisms	Soil organisms	Terrestrial plants — atmospheric	Terrestrial plants — soil	Terrestrial wildlife — inhalation	Terrestrial wildlife — ingestion
EEV	2.4 µg/L	370 ng/g dry weight	200 ng/g dry weight	9.6 ng/m^3	550 ng/g dry weight	9.6 ng/m^3	830 ng/g wet weight
CTV	510 µg/L	6800 ng/g dry weight	6800 ng/g dry weight	360 ng/m^3	2×10^5 ng/g dry weight	1.44×10^8 ng/m^3	10 000 ng/g wet weight
Application factor	100	10	10	10	10	10	10
ENEV	5.1 µg/L	680 ng/g dry weight	680 ng/g dry weight	36 ng/m^3	20 000 ng/g dry weight	1.44×10^7 ng/m^3	1000 ng/g wet weight
Quotient (EEV/ENEV)	0.47	0.54	0.29	0.27	0.028	7×10^{-7}	0.83

factor of 10 (to account for the conversion of a NOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives an ENEV of 1.44×10^7 ng/m^3. The resulting quotient is $9.6/1.44 \times 10^7 = 7 \times 10^{-7}$. Therefore, concentrations of BBP in the atmosphere in Canada appear to be unlikely to cause adverse effects on populations of terrestrial wildlife.

The highest concentration of BBP reported for Canadian biota is 1470 ng/g wet weight, in a sample of butter sole from Boundary Bay, B.C. (average concentration = 500 ng/g wet weight, n = 5). The species with the second highest concentration of BBP was the starry flounder, also from Boundary Bay, with a liver concentration of 830 ng/g wet weight. This value, 830 ng/g wet weight, is used as the conservative EEV for terrestrial wildlife exposed to BBP through food. The CTV is 10 000 ng BBP/g wet weight, based on the dietary concentration of dibutyl phthalate causing reduced eggshell thickness in ring doves (see Section 2.4.1.5). Dividing this CTV by an application factor of 10 (to account for the conversion of a LOEC to a long-term no-effects value, extrapolation from laboratory to field conditions, and interspecies and intraspecies variations in sensitivity) gives

an ENEV of 1000 ng/g wet weight. The resulting quotient is 830/1000 = 0.83. Therefore, concentrations of BBP in food organisms in Canada appear to be unlikely to cause adverse effects on populations of terrestrial wildlife.

The environmental risk characterization for BBP is summarized in Table 3.

3.1.2.6   Sources of uncertainty

There are several sources of uncertainty associated with the environmental assessment of BBP. Most of the monitoring data for BBP in Canadian biota come from marine and estuarine areas of southern British Columbia. It is not known if these values are representative of other areas of Canada. However, the highest reported BCFs for BBP in aquatic organisms are in the range of 700–800, based on total residues. Given that concentrations of BBP in Canadian surface water are below 1 µg/L, BBP residues in aquatic organisms would not be expected to exceed about 800 ng/g wet weight. This concentration is very close to the EEV of 830 ng/g derived above for terrestrial wildlife exposed to BBP in food. There were no data available concerning the toxicity of BBP to benthic organisms, soil organisms, terrestrial plants or wildlife. ENEVs for benthic

and soil organisms were derived using the Equilibrium Partitioning approach, which is based on the assumption that the partitioning of non-ionic organic compounds between the organic carbon fraction of sediments or soil and pore water is at equilibrium and that toxicity resulting from exposure to such chemicals in the organic carbon fraction can be estimated based on toxicity resulting from exposure in water. ENEVs for terrestrial plants (atmospheric and soil exposure) and terrestrial wildlife (exposure by ingestion) were based on toxicity studies using dibutyl phthalate. The use of dibutyl phthalate toxicity data to derive ENEVs for BBP is based on the observation that the toxicities of dibutyl phthalate and BBP to aquatic organisms and to birds are similar. The ENEV for terrestrial wildlife (exposure by inhalation) was based on a four-week study with rats. This study was one of only three inhalation toxicity studies identified.

3.2 CEPA 11(b): Environment upon which human life depends

Worst-case calculations were made to determine if BBP has the potential to contribute to depletion of stratospheric ozone, ground-level ozone formation or climate change (Bunce, 1996). The Ozone Depletion Potential is 0, the Photochemical Ozone Creation Potential was estimated to be 26 and the Global Warming Potential was calculated to be 1.2×10^{-5} (Bunce, 1996). These figures imply that BBP is not likely to contribute significantly to depletion of stratospheric ozone, ground-level ozone formation or climate change.

3.3 CEPA 11(c): Human health

3.3.1 Estimated population exposure

Data on levels of BBP in environmental media in Canada to serve as a basis for development of estimates of population exposure are limited. Point estimates of average daily intake (per

kilogram body weight), based on the data on concentrations of BBP in ambient and indoor air, drinking water, food and soil summarized in Section 2.3.2 and reference values for body weight, inhalation volume and amounts of food and drinking water consumed daily, are presented for six age groups in Table 4. On this basis, intake is estimated to range from 0.01 to 5.0 µg/kg-bw per day.

However, it should be noted that these estimates are based on detection in only 6% of 98 single composite samples in a total diet survey in Canada; foodstuffs examined in this survey constituted approximately 70% of the total of 181 specific food items on which estimates of intake in food are based (Page and Lacroix, 1992, 1995). Estimates are also based on an almost complete lack of detection of BBP in available surveys of Canadian drinking water supplies (Halina, 1994; Riopel, 1994, 1996). Other data on levels of BBP incorporated in these estimates were restricted to those determined in a small number of soil samples in Canada (Golder Associates, 1987) and indoor and ambient air in California (California Environmental Protection Agency, 1992).

Reasonable worst-case estimates of daily intake of BBP, based on the maximum reported concentrations of BBP in food, outdoor air, indoor air, drinking water and soil in studies mentioned above and reference values for body weight, inhalation volume and amounts of food and drinking water consumed daily, are presented for six age groups in Table 5; on this basis, intake is estimated to range from 0.27 to 145 µg/kg-bw per day.

Based on the values derived by either approach, food is overwhelmingly the principal source of exposure to BBP, contributing approximately 98% of total intake for most age groups. This is consistent with apportionment predicted on the basis of physical/chemical properties and fugacity modelling.

Limitations of the data available on concentrations of BBP in the principal medium

TABLE 4   Estimated average daily intake of BBP by the population of Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of BBP by various age groups						
	0–6 months [1]		0.5–4 years [3]	5–11 years [4]	12–19 years [5]	20–59 years [6]	60+ years [7]
	Formula fed [2]	Not formula fed					
Ambient air [8]	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Indoor air [9]	0.01–0.03	0.01–0.03	0.02–0.07	0.01–0.06	0.01–0.03	0.01–0.03	0.01–0.02
Drinking water [10]	0–0.11	0–0.03	0–0.01	0–0.01	0–0.01	0–0.01	0–0.01
Food [11]	0	0.28–3.15	1.27–4.88	0.97–3.70	0.72–2.29	0.63–2.01	0.40–1.55
Soil [12]	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001
Total intake [13]	0.01–0.14	0.29–3.21	1.29–4.96	0.98–3.77	0.74–2.33	0.64–2.05	0.42–1.58

[1] Assumed to weigh 7.6 kg, to breathe 2.1 m³ per day, to drink 0.8 L of water per day (formula fed) or 0.2 L of water per day (not formula fed), to spend 21 of 24 hours indoors and to ingest 30 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[2] For formula-fed infants, intake from water is synonymous with intake from food. No data on concentrations of BBP in formula were identified for Canada.

[3] Assumed to weigh 15.6 kg, to breathe 9.3 m³ per day, to drink 0.2 L of water per day, to spend 21 of 24 hours indoors and to ingest 100 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[4] Assumed to weigh 31.2 kg, to breathe 14.5 m³ per day, to drink 0.4 L of water per day, to spend 21 of 24 hours indoors and to ingest 65 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[5] Assumed to weigh 59.7 kg, to breathe 15.8 m³ per day, to drink 0.4 L of water per day, to spend 21 of 24 hours indoors and to ingest 30 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[6] Assumed to weigh 70.7 kg, to breathe 16.2 m³ per day, to drink 0.4 L of water per day, to spend 21 of 24 hours indoors and to ingest 30 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[7] Assumed to weigh 70.6 kg, to breathe 14.3 m³ per day, to drink 0.4 L of water per day, to spend 21 of 24 hours indoors and to ingest 30 mg of soil per day. Consumption of individual food items reported in EHD (1997).

[8] The California Environmental Protection Agency (1992) monitored ambient air near 65 homes in Riverside, California. Concentrations of BBP in outdoor air used to calculate the range of average daily intakes are 5.1 ng/m³ (the quantifiable limit) and 6.7 ng/m³ (the 90th-percentile concentration for nighttime sampling). The median daytime and nighttime concentrations of BBP were less than the quantifiable limit.

[9] The California Environmental Protection Agency (1992) monitored indoor air in 125 homes in Riverside, California. Concentrations of BBP in indoor air used to calculate the range of average daily intakes are 35 ng/m³ (the median concentration for nighttime sampling) and 140 ng/m³ (the 90th-percentile concentration for daytime sampling).

[10] The upper limit of the range of average daily intakes was calculated from the limit of detection of 1 µg/L reported by Halina (1994). A concentration of BBP in drinking water of zero was assumed for the lower limits of the intake ranges. Consumption estimates are for "tap water as drinking water" (EHD, 1997). For formula-fed infants, the concentration of BBP in the water used to reconstitute formula accounts for the intake of BBP from food.

[11] Health Canada has detected BBP in composite samples of yoghurt (0.6 µg/g), cheddar cheese (1.6 µg/g), butter (0.64 µg/g), pork (0.8 µg/g), mixed vegetable juice (0.11 µg/g) and crackers (0.48 µg/g) (Page and Lacroix, 1995). These concentrations were assumed to be representative of the concentrations of BBP in 8 of the 181 specific food items in EHD (1997). A concentration of zero was assumed for the remaining 173 specific food items for calculation of the lower limits of the intake ranges, whereas concentrations equivalent to appropriate detection limits (Page and Lacroix, 1995) were assumed for 75 of the 181 specific food items for the calculation of the upper limits of the ranges of average daily intake.

[12] Of 30 soil samples collected from typical urban residential and parkland locations in Port Credit, Oakville and Burlington, BBP was detected in 3 samples ("trace", 0.14 and 0.29 µg/g dry weight) (Golder Associates, 1987). The value used for these calculations (i.e., 0.18 µg/g) is the mean of the 3 samples ("trace" was considered to be 0.1 µg/g, the limit of detection). This value is similar to the concentration of BBP in Canadian agricultural soils reported by Webber and Wang (1995).

[13] Medium-specific and total intakes were calculated on a Microsoft Excel spreadsheet. Only significant numbers have been presented, which accounts for seemingly imprecise totals.

TABLE 5   Reasonable worst-case estimates of daily intake of BBP

Route of exposure	Estimated intake (µg/kg-bw per day) of BBP by various age groups						
	0–6 months [1]		0.5–4 years [3]	5–11 years [4]	12–19 years [5]	20–59 years [6]	60+ years [7]
	Formula fed [2]	Not formula fed					
Ambient air [8]	<0.001–0.002	<0.001–0.002	<0.001–0.004	<0.001–0.003	<0.001–0.002	<0.001–0.001	<0.001–0.001
Indoor air [9]	0.06–0.09	0.06–0.09	0.13–0.20	0.10–0.16	0.06–0.09	0.05–0.08	0.04–0.07
Drinking water [10]	0.21–0.29	0.005–0.007	0.09–0.12	0.07–0.10	0.04–0.06	0.04–0.06	0.04–0.06
Food [11]	0	129–145	71–82	40–47	21–25	11–14	9–12
Soil [12]	0.001	0.001	0.002	0.001	<0.001	<0.001	<0.001
Total intake [13]	0.27–0.38	129–145	71–82	40–47	21–25	11–14	9–12

[1] Assumed to weigh 7.6 kg, to breathe 2.1 m³ per day and to drink 0.8 L of water per day (formula fed) or 0.2 L of water per day (not formula fed). Consumption of food groups reported in EHD (1997).

[2] For formula-fed infants, intake from water is synonymous with intake from food. No data on concentrations of BBP in formula were identified for Canada.

[3] Assumed to weigh 15.6 kg, to breathe 9.3 m³ per day and to drink 0.7 L of water per day. Consumption of food groups reported in EHD (1997).

[4] Assumed to weigh 31.2 kg, to breathe 14.5 m³ per day and to drink 1.1 L of water per day. Consumption of food groups reported in EHD (1997).

[5] Assumed to weigh 59.7 kg, to breathe 15.8 m³ per day and to drink 1.2 L of water per day. Consumption of food groups reported in EHD (1997).

[6] Assumed to weigh 70.7 kg, to breathe 16.2 m³ per day and to drink 1.5 L of water per day. Consumption of food groups reported in EHD (1997).

[7] Assumed to weigh 70.6 kg, to breathe 14.3 m³ per day and to drink 1.6 L of water per day. Consumption of food groups reported in EHD (1997).

[8] The California Environmental Protection Agency (1992) monitored ambient air near 65 homes in Riverside, California. Concentrations of BBP in outdoor air used to calculate the range of reasonable worst-case estimates are 11 ng/m³ (the maximum daytime outdoor concentration) and 47 ng/m³ (the maximum nighttime outdoor concentration).

[9] The California Environmental Protection Agency (1992) monitored indoor air in 125 homes in Riverside, California. Concentrations of BBP in indoor air used to calculate the range of reasonable worst-case estimates are 250 ng/m³ (the maximum nighttime indoor concentration) and 390 ng/m³ (the maximum daytime indoor concentration).

[10] The lower limits of the ranges of reasonable worst-case estimates were calculated from the highest limit of detection (i.e., 2 µg/L) reported by Riopel (1994, 1996). A concentration of BBP in drinking water of 2.8 µg/L (in Quebec) (Riopel, 1994, 1996) was assumed for calculation of the upper limits of this range. Consumption estimates are for "total tap water" (EHD, 1997). For formula-fed infants, the concentration of BBP in the water used to reconstitute formula accounts for the intake of BBP from food.

[11] The concentrations of BBP reported for four specific food items from Health Canada's Total Diet Program (Page and Lacroix, 1995) were assumed to represent the average concentration of BBP in each of four food groups that include these food items. A concentration of BBP of zero was assumed for the remaining eight food groups for calculation of the lower values of the ranges of estimates, whereas values based on reported limits of detection were assumed for the remaining eight food groups for calculation of the upper limits of the ranges of reasonable worst-case estimates. A limit of detection of 0.2 µg/g (i.e., the limit of detection for fruits and vegetables, in Page and Lacroix, 1995) was assumed for seven of the food groups, whereas a limit of detection of 0.05 (i.e., the limit of detection for beverages, in Page and Lacroix, 1995) was assumed for the remaining food group (i.e., soft drinks and alcohol, in EHD, 1997).

[12] The highest concentration (i.e., 0.29 µg/g) of BBP detected among 30 soil samples collected from typical urban residential and parkland locations in Port Credit, Oakville and Burlington (Golder Associates, 1987) was used in these calculations.

[13] Medium-specific and total intakes were calculated on a Microsoft Excel spreadsheet. Only significant numbers have been presented, which accounts for seemingly inaccurate totals.

of exposure of Canadians (i.e., levels in single composite samples of foodstuffs) preclude development of very meaningful probabilistic estimates of intake. In a survey conducted earlier than the total diet survey referred to above, the presence of BBP was determined in multiple samples of butter (n = 12) and margarine (n = 8) in Canada (Page and Lacroix, 1992). Based on limited probabilistic analyses of the data for these foodstuffs, which account for less than 1% of the estimated total daily intake of any age group, 95th percentiles were generally within the same order of magnitude as the reasonable worst-case estimates presented above.

3.3.2   Hazard characterization

Following oral administration to rats, BBP is readily hydrolysed in the gastrointestinal tract and the liver to phthalate monoesters (monobutyl and monobenzyl phthalate), which are rapidly eliminated, predominantly in urine.

Available data are inadequate to serve as a basis for assessment of the effects of long-term exposure to BBP in human populations. The remainder of this section, therefore, addresses effects in experimental animals.

The acute toxicity of BBP is relatively low, with oral LD_{50} values in rats being greater than 2 g/kg-bw. Target organs following acute exposure include the hematological and central nervous systems.

Available data are inadequate to allow the assessment of the irritant and sensitizing effects of BBP in animal species.

The repeated-dose toxicity of BBP has been well investigated in recent studies, primarily in the rat, in which dose–response was well characterized. Effects observed consistently have been decreases in body weight gain (often accompanied by decreases in food consumption) and increases in organ to body weight ratios, particularly for the kidney and liver. In addition,

histopathological effects on the pancreas and kidney and hematological effects have also been observed. At higher doses, degenerative effects on the testes and, occasionally, histopathological effects on the liver have been reported. In specialized investigations, peroxisomal proliferation in the liver has been observed, although potency in this regard was less than that for other phthalates, such as DEHP.

The chronic toxicity and carcinogenicity of BBP have been investigated in NTP bioassays in rats (including standard and feed-restricted protocols) and mice. An increase in mononuclear cell leukemias observed in female F344 rats was not confirmed in a repeat study. However, it was concluded, on the basis of this latter study, that there was "some evidence" of carcinogenicity in male rats, based on an increased incidence of pancreatic tumours, and equivocal evidence in female rats, based on marginal increases in pancreatic and bladder tumours. Dietary restriction prevented full expression of the pancreatic tumours and delayed appearance of the bladder tumours. There was no evidence of carcinogenicity in mice.

The weight of evidence of the genotoxicity of BBP is clearly negative. However, available data are inadequate to conclude unequivocally that BBP is not clastogenic, although in identified studies it has induced, at most, weak activity of a magnitude consistent with secondary effects on DNA.

Therefore, BBP has induced an increase in pancreatic tumours primarily in one sex of one species, the full expression of which was prevented in a dietary restriction protocol, and a marginal increase in bladder tumours in the other sex, which was delayed upon dietary restriction. Moreover, the weight of evidence of genotoxicity is negative, and, although weak clastogenic potential cannot be ruled out, available data are consistent with the compound not interacting directly with DNA. On this basis, BBP can be considered, at most, possibly carcinogenic to humans, likely inducing tumours through a non-genotoxic (although unknown) mechanism.

In a range of studies, including those designed to investigate the reproductive effects of BBP on the testes and endocrine hormones of male rats, a modified mating protocol conducted by the NTP and a one-generation study, adverse effects on the testes and, consequently, fertility have generally been observed only at doses higher than those that induce effects on other organs (such as the kidney and liver), although decreases in sperm counts have been observed at doses similar to those that induce effects on the latter. This is consistent with the results of repeated-dose toxicity studies.

Reductions in testes weight and daily sperm production in offspring were reported at a relatively low level in rats exposed *in utero* and during lactation in a study in which dose–response was not investigated. However, such effects were not observed in a recent study in another strain of rats in which only an increase in absolute and relative liver weights was observed at postnatal day 90. Additional investigation of potential effects on the reproductive systems of male and female animals exposed *in utero* and during lactation in studies designed to address dose–response is desirable and under way.

Although BBP has been found to be estrogenic in human breast cancer cell lines *in vitro*, results in yeast cells have been mixed. In most studies, neither BBP nor its principal metabolites have been found to be uterotrophic *in vivo* in rats or mice. Although available data do not support the conclusion that BBP is estrogenic, the potential for other endocrine-mediated effects, such as anti-androgenic activity associated with dibutyl phthalate, cannot be precluded at this time. There is currently considerable emphasis on the development of more sensitive frameworks for the testing and assessment of endocrine-disrupting substances; compounds such as phthalates are likely early candidates for additional testing.

In several well-conducted studies in rats and mice, BBP has induced marked developmental effects, but only at dose levels that induce significant maternal toxicity.

Although the potential neurotoxicity of BBP has not been well investigated, histopathological effects on the central or peripheral nervous system have not been observed following short-term exposure to relatively high dietary concentrations. Available data with which to assess the potential immunotoxicity of BBP are inadequate.

3.3.3   Dose–response analyses

Based on consideration of the complete database on repeated-dose toxicity by the oral route (including subchronic, chronic and reproductive/developmental studies), effects that occur at lowest concentrations in rats are increases in organ to body weight ratios, primarily for the liver and kidney, and histopathological effects on the pancreas and kidney at dose levels in the range of 120 to just greater than 300 mg/kg-bw per day. Specifically, these include increases in the ratio of liver to body weight and pancreatic lesions in the Wistar rat observed in a 90-day study (Hammond *et al.*, 1987), increases in (absolute and relative) kidney weight and relative liver weight and proximal tubular regeneration in a two-week reproductive study (Agarwal *et al.*, 1985) and increased relative kidney weight at interim (15 month; not determined at termination) sacrifice in male F344 rats in the two-year NTP bioassay (NTP, 1997a). Although nephropathy was also increased at all doses (300 mg/kg-bw per day and higher) in the kidney of female F344 rats in the two-year NTP bioassay (NTP, 1997a), incidence was high in all groups, with no evidence of dose–response (incidence or severity) and no increase in severity between the interim and final sacrifices.

Increases in hepatic peroxisomal proliferation in F344 rats also occur at doses similar to those at which the effects mentioned above have been observed following exposure for 1 or 12 months (NTP, 1997a). Decreases in body weight in mice (of unspecified statistical significance) have also been observed in this dose range in a 90-day study, although food consumption was not reported (NTP, 1982). Decreases in epididymal spermatozoal

concentrations have also been reported at these levels, although without accompanying histopathological effects on the testes or adverse impact on fertility (NTP, 1997a).

Benchmark doses for 5% increased incidences have been developed for histopathological lesions in the pancreas of male Wistar rats in the 90-day study (Hammond *et al.*, 1987) and renal lesions in male F344 rats in the two-week reproductive bioassay conducted by the NTP (Agarwal *et al.*, 1985; NTP, 1997a). Information on the incidence of these lesions, resulting benchmark doses calculated using the THRESH program and associated parameter estimates and statistics of fit are presented in Table 2 and illustrated graphically in Figures 2–4.

Histopathological effects have not been associated with increases in organ to body weight ratios in the same sex except at much higher doses, nor have decreases in epididymal spermatozoal concentrations at lowest doses been accompanied by histopathological effects and adverse impact on fertility. Owing principally to these considerations and less to the inadequacy of current statistical techniques to adequately model continuous data for these endpoints and for peroxisomal proliferation, benchmark doses for these endpoints have not been developed; however, for completeness, relevant effect levels are included in Table 2 for comparison.

FIGURE 2   Benchmark dose (BMD) for incidence of pancreatic lesions in male Wistar rats exposed to BBP via the diet for three months (Monsanto, 1980; Hammond *et al.*; 1987)
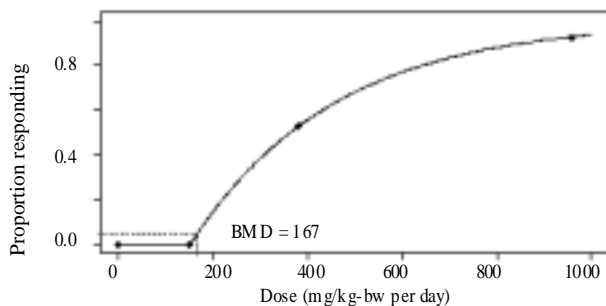
FIGURE 3   Benchmark dose (BMD) for incidence of renal proximal tubular regeneration in male F344 rats exposed to BBP via the diet for two weeks (Kluwe *et al.*, 1984; Agarwal *et al.*, 1985)
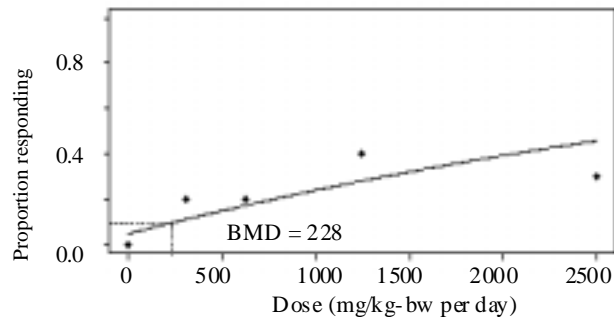
FIGURE 4   Benchmark dose (BMD) for incidence of renal nephropathy in female F344/N rats exposed to BBP via the diet for two years (NTP, 1997a)
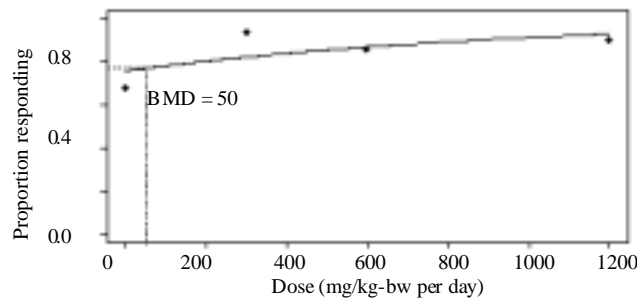
The fit of the model was best for pancreatic lesions in male Wistar rats in the subchronic study by Hammond *et al.* (1987) (p = 0.98), adequate for proximal tubular regeneration in the kidney of male rats in the two-week reproductive protocol (Agarwal *et al.*, 1985) (p = 0.39) and inadequate for nephropathy in female rats in the two-year bioassay (NTP, 1997a) (p = 0.03). Inadequate fit for the latter is attributable to high incidence in all dose groups and little evidence of dose–response. On this basis and consideration of the fact that pancreatic lesions and tumours were also observed in the NTP two-year bioassay in males of another strain of rats, the pancreatic lesions in the Hammond *et al.* (1987) study have been selected as the point of departure for development of a Tolerable Intake (TI).

TABLE 6 Benchmark doses for pancreatic hyperplasia and tumorigenic dose — NTP two-year bioassay

Study (reference)	Effect levels	Data for calculating benchmark dose		Parameter estimates	
		Dose	**Response**	**Benchmark dose**	**Goodness of fit**
Carcinogenicity bioassay F344/N rats Dietary administration for 2 years NTP, 1997a	Pancreas, acinus, focal hyperplasia	Males: control 120 mg/kg-bw per day 240 mg/kg-bw per day 500 mg/kg-bw per day	Incidence: 4/50 7/49 9/50 12/50 (p < 0.05)	5% dose: 130 mg/kg-bw per day 95% lower confidence limit: 73 mg/kg-bw per day	p-value for lack of fit: 0.916
Carcinogenicity bioassay F344/N rats Dietary administration for 2 years NTP, 1997a	Pancreas, acinus, adenoma or carcinoma	Males: control 120 mg/kg-bw per day 240 mg/kg-bw per day 500 mg/kg-bw per day	Incidence: 3/50 2/49 3/50 11/50 (p = 0.014) p = 0.003 for trend	TD_{05}: 320 mg/kg-bw per day 95% lower confidence limit: 160 mg/kg-bw per day	p-value for lack of fit: 0.854

For comparison, a benchmark dose calculated using the THRESH program and associated parameter estimates and statistics of fit for pancreatic focal hyperplasia (acinus) in male F344 rats in the two-year NTP bioassay are presented in Table 6. Although the benchmark dose and associated lower 95% confidence interval are slightly less than those calculated on the basis of the Hammond *et al*. (1987) study in Wistar rats, it should be noted that the distinction between hyperplasia and adenomas in the carcinogenesis bioassay was not readily apparent. A tumorigenic dose (TD_{05}) calculated on the basis of multistage modelling (Global 82) of the incidence of pancreatic adenomas or carcinomas (acinus) in male rats in the NTP bioassay is also presented in Table 6 and (as would be expected) is greater than the benchmark dose for hyperplasia. Data presented in the published account were insufficient to allow

a benchmark dose to be developed on the basis of hyperplasia and adenomas combined.

The TI is developed, therefore, as follows:

$$TI = \frac{132 \text{ mg/kg-bw per day}}{100}$$

$$= 1.3 \text{ mg/kg-bw per day}$$

$$= 1300 \text{ µg/kg-bw per day}$$

where:

• 132 mg/kg-bw per day is the lower 95% confidence interval for the benchmark dose (167 mg/kg-bw per day) associated with a 5% increase in the incidence of pancreatic lesions in male Wistar rats in the subchronic study of Hammond *et al*. (1987). It is noted that

increased excretion in feces at higher doses observed in one study might impact on the dose–response curve and resulting benchmark dose, although it was not possible to address this quantitatively, and

- 100 is the uncertainty factor (×10 for intraspecies variation; ×10 for interspecies variation).

An additional factor for extrapolation from subchronic to chronic has not been incorporated as, on the basis of a fairly robust database, there is no indication that effect levels are lower in chronic studies than in investigations of shorter duration; moreover, the compound is rapidly eliminated. Also, the incidence of pancreatic lesions in the Wistar rat in the subchronic study on which the benchmark dose is based is higher than that observed in the F344 rat in the two-year carcinogenesis bioassay. Available data were considered insufficient to allow default values for toxicokinetic and toxicodynamic components of interspecies and intraspecies variation to be replaced with data-derived values.

This TI is similar to values that might have been developed based on the LOELs for the continuous endpoints, such as peroxisomal proliferation and increases in organ to body weight ratios.

Data on the toxicity of BBP following repeated exposure by inhalation are limited, with information relevant to characterization of exposure–response being confined to results of two short-term and one subchronic study in rats. In the subchronic study, the range of endpoints examined was more limited (Hammond *et al*., 1987). In the short-term study with lowest concentrations, effects on body weight gain and serum glucose were observed at 526 mg/m^3; there were no effects on hematology, blood chemistry, urinalysis, organ weights or histopathology at 144 mg/m^3. Increases in organ weights were observed at 218 mg/m^3 in the subchronic study, although there were no histopathological effects at the highest dose (789 mg/m^3); the NOEL was 51 mg/m^3. Although the

database for inhalation is somewhat limited, it is of interest to note that the NOAELs for effects by this route are similar to those for ingestion. For example, the NOEL in the investigation in which the range of endpoints examined was more extensive (144 mg/m^3) is equivalent to a dose approximately three-fold less than the point of departure for the TI presented above.[10]

3.3.4 Human health risk characterization

The deterministic estimates of average intake for six age groups within the Canadian population range from 0.01 μg/kg-bw per day in infants to 5.0 μg/kg-bw per day for children between the age of six months and four years, with food representing by far the greatest single source of exposure. It should be noted that in the total diet survey on which these estimates are based, BBP was "not detected" in 75 (or 41%) of the 181 specific food items, and maximum estimates of intake were based, therefore, on corresponding limits of detection (Page and Lacroix, 1992, 1995). This is offset to some extent by the fact that limits of detection were not available for 43 (or 24%) of the 181 specific food items on which estimates of exposure can be based; as a result, assumed intake in these foodstuffs was considered to be zero.

While it is important to bear these limitations in mind, it is reassuring that the maximum values for estimated average daily intake and reasonable worst-case estimates of daily intake of 5.0 and 145 μg/kg-bw per day, respectively, although both uncertain, are one to two orders of magnitude less than the TI of 1300 μg/kg-bw per day.

Therefore, on the basis of comparison of estimates of exposure and the TI (i.e., the intake to which it is believed that a person may be exposed daily over a lifetime without deleterious effects), it has been concluded that BBP is not present in the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

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[10] Conversion factor: 1 mg/m^3 in air = 0.31 mg/kg-bw per day ingested in rats (Health Canada, 1994).

3.3.5 Uncertainties and degree of confidence in human health risk characterization

There is some uncertainty regarding the estimates of intake of BBP from food, which appears to be the single greatest source of exposure. Although there are data available from a total diet survey in Canada that constitute considerably more reliable and representative information than is available for many Priority Substances, a degree of uncertainty is introduced by the assumption of zero to detection limits or zero in a large portion of foodstuffs in the Canadian diet in which BBP was not detected or for which analyses were not conducted. Moreover, data were reported only for single composite samples for most foodstuffs.

All of the data on intake in food in Canada are based on samples collected between 1985 and 1989. It is possible that intake may be overestimated, therefore, based on the likely reduction in the use of BBP in applications involving direct contact with food.

An important source of additional uncertainty in the estimates of exposure is the lack of identified data on concentrations of BBP in breast milk in Canada or elsewhere. In view of BBP's relatively high octanol/water partition coefficient, it seems likely that breast milk would be an important source of exposure for infants, although only for a short period of the lifespan.

The possibility that toys made of plastic might contain BBP is currently being investigated, although quantitative data are not yet available. However, it is possible to provide at least an upper bound estimate of exposure from this source, based on data on DEHP, which is likely to be present in higher proportions. Although estimates of exposure from this source are considered to be uncertain as a consequence of such factors as variations in DEHP levels and mouthing behaviour and lack of reliable data on leaching rates, the maximum intake of DEHP for infants and toddlers based on a preliminary survey of children's products in Canada was estimated to be 12 µg/kg-bw per day (Government of Canada, 1994). It is unlikely, therefore, that additional information on exposure from this source would alter the conclusions concerning "toxic" drawn here.

The data on concentrations of BBP in drinking water are relatively extensive and consistent. However, in view of the likely limited contribution of this medium to total exposure, this contributes only minimally to increasing the degree of confidence in the estimates of exposure.

An additional element of uncertainty is introduced by reliance on concentrations of BBP in indoor/ambient air in a survey of 125 homes in California for estimation of intake in air. Although it is possible that the levels reported in this study might be less than those characteristic of concentrations in Canadian homes because of the lesser exchange with outdoor air in a colder climate, in view of the likely limited contribution of this medium to total exposure, this detracts only minimally from the degree of confidence in the estimates of exposure.

The overall degree of confidence in the population exposure estimates is, therefore, moderate, owing primarily to some limitations of the monitoring data for the likely principal medium of exposure of the general population in Canada (food).

The degree of confidence in the database on toxicity that serves as the basis for development of the TI is moderate to high. Although few data were identified on the effects of BBP on humans, there is a wide range of recent repeated-exposure studies on experimental animals, including short-term, subchronic and chronic studies with good characterization of exposure–response. Although additional study of potential sensitization may be warranted, there is a large number of recent studies in which reproductive and developmental endpoints have been investigated. However, the phthalates, including BBP, are likely early candidates for additional testing for potential endocrine-disrupting effects when test protocols currently under development are agreed upon.

3.4   Conclusions

CEPA 11(a): Based on available data, it has been concluded that BBP is not entering the environment in a quantity or concentration or under conditions having or that may have an immediate or long-term harmful effect on the environment. Therefore, BBP is not considered to be "toxic" as defined in Paragraph 11(a) of CEPA.

CEPA 11(b): Based on available data, it has been concluded that BBP is not entering the environment in a quantity or concentration or under conditions constituting or that may constitute a danger to the environment on which human life depends. Therefore, BBP is not considered to be "toxic" as defined in Paragraph 11(b) of CEPA.

CEPA 11(c): Based on available data, it has been concluded that BBP is not entering the environment in a quantity or concentration or under conditions constituting a danger in Canada to human life or health. Therefore, BBP is not considered to be "toxic" as defined in Paragraph 11(c) of CEPA.

Overall conclusion: Based on critical assessment of relevant information, BBP is not considered to be "toxic" as defined in Section 11 of CEPA.

3.5   Considerations for follow-up (further action)

Since BBP is not considered to be "toxic" as defined in Section 11 of CEPA, evaluation of options under CEPA to reduce exposure is not considered a priority at this time. However, this is based on current use patterns; thus, future releases of this compound should continue to be monitored to ensure that exposure does not increase to any significant extent.

Based on recent submissions, BBP no longer appears to be used to any significant extent in applications involving direct contact with food, the principal medium of exposure. However, it may be emitted from building materials and is present in some consumer products. Better characterization of the significance of emissions from these sources is desirable, although data available currently indicate that intake from indoor air for the general population is still a fraction of that from food.

There is currently considerable emphasis on the development of more sensitive frameworks for the testing and assessment of endocrine-disrupting substances; compounds such as phthalates are likely early candidates for additional testing when test protocols are agreed upon.

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APPENDIX A   SEARCH STRATEGIES EMPLOYED FOR IDENTIFICATION OF RELEVANT DATA

Environmental assessment

Data relevant to the assessment of whether BBP is "toxic" to the environment under CEPA were identified from existing review documents, published reference texts and on-line searches, conducted between January and April 1996, of the following databases: ASFA (Aquatic Sciences and Fisheries Abstracts, Cambridge Scientific Abstracts; 1990–1996), BIOSIS (Biosciences Information Services; 1990–1996), CAB (Commonwealth Agriculture Bureaux; 1990–1996), CESARS (Chemical Evaluation Search and Retrieval System, Ontario Ministry of the Environment and Michigan Department of Natural Resources; 1996), CHRIS (Chemical Hazard Release Information System; 1964–1985), Current Contents (Institute for Scientific Information; 1993, 1994, 1995, up to January 15, 1996), ELIAS (Environmental Library Integrated Automated System, Environment Canada library; January 1996), Enviroline (R.R. Bowker Publishing Co.; November 1995 – June 1996), Environmental Abstracts (1975 – February 1996), Environmental Bibliography (Environmental Studies Institute, International Academy at Santa Barbara; 1990–1996), GEOREF (Geo Reference Information System, American Geological Institute; 1990–1996), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine; 1996), Life Sciences (Cambridge Scientific Abstracts; 1990–1996), NTIS (National Technical Information Service, U.S. Department of Commerce; 1990–1996), Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1996), POLTOX (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1995), RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health; 1996), Toxline (U.S. National Library of Medicine;

1990–1996), TRI93 (Toxic Chemical Release Inventory, U.S. Environmental Protection Agency, Office of Toxic Substances; 1993), USEPA-ASTER (Assessment Tools for the Evaluation of Risk, U.S. Environmental Protection Agency; up to December 21, 1994), WASTEINFO (Waste Management Information Bureau of the American Energy Agency; 1973 – September 1995), Water Resources Abstracts (U.S. Geological Survey, U.S. Department of the Interior; 1990–1996). A survey of Canadian industry was carried out under authority of Section 16 of CEPA (Environment Canada, 1997c). Companies were required to provide information on uses, releases, environmental concentrations, effects or other data that were available to them for BBP if they met the trigger quantity of 500 kg of BBP per year. Reveal Alert was used to maintain an ongoing record of the current scientific literature pertaining to the potential environmental effects of BBP. Data obtained after May 31, 1998, were not considered in this assessment unless they were critical data received during the 60-day public review of the report (May 1 to June 29, 1999).

Health assessment

Data relevant to the assessment of whether BBP is "toxic" to human health obtained after April 1998 have not been included.

To identify data relevant to the estimation of exposure of the general human population to BBP, on-line literature searches were conducted (in February 1994) on the following databases: AQUAREF (Inland Waters Directorate, Environment Canada; 1970–1994), EMBASE (on-line version of Excerpta Medica; 1974–1994) and Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1970–1994).

Numerous provincial officials and representatives of various industrial sectors were contacted between February and August of 1996 for monitoring data relevant to exposure and effects.

To identify data relevant to the assessment of effects on human health, on-line literature searches were conducted (in February 1994) on the following databases: CESARS (Chemical Evaluation Search and Retrieval System, Ontario Ministry of the Environment and Michigan Department of Natural Resources), DART (Developmental and Reproductive Toxicology, U.S. National Library of Medicine; 1989–1994), EMIC (Environmental Mutagen Information Center database, Oak Ridge National Laboratory; 1989–1994) and EMICBACK (backfile of EMIC; 1950–1988), ETICBACK (backfile of Environmental Teratology Information Center database, U.S. Environmental Protection Agency and U.S. National Institute of Environmental Health Sciences), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine), IRIS (Integrated Risk Information System, U.S. Environmental Protection Agency), NTIS (National Technical Information Service, U.S. Department of Commerce; 1980–1994), RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health) and Toxline (U.S. National Library of Medicine; 1989–1994). Relevant data were also identified through reviews by Skinner (1992), the U.S. EPA (1987, 1991) and BIBRA (1992).