Canadian Environmental Protection Act

Priority Substances List
Assessment Report

Dibutyl Phthalate

Government of Canada / Gouvernement du Canada
Environment Canada / Environnement Canada
Health Canada / Santé Canada

Canada

CANADA'S GREEN PLAN

Canadian Environmental Protection Act

PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

DIBUTYL PHTHALATE

Government of Canada
Environment Canada
Health Canada

Also available in French under the title:
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Synopsis

Dibutyl phthalate is not currently produced in Canada. About 540 tonnes/year are imported, however, for use mainly as a plasticizer in polyvinyl emulsions. Additional dibutyl phthalate may be imported into Canada in plastic products. Dibutyl phthalate is not expected to be persistent in air and water, but may be more persistent in sediments and soil.

Dibutyl phthalate has been detected in surface waters in Canada at concentrations approximately five times less than estimated effects thresholds for aquatic organisms. The highest mean concentration of dibutyl phthalate in Canadian air is 80 times less than the adverse effects thresholds estimated for sensitive plants.

Dibutyl phthalate has a short half-life in the atmosphere. As such, it is, not expected to contribute significantly to the formation of ground-level ozone, global warming, or depletion of stratospheric ozone.

Based on the very limited data on concentrations of dibutyl phthalate in various environmental media (ambient air, indoor air, drinking water, food, and soil), the average daily intakes of dibutyl phthalate for different age groups in the general population have been estimated. Although based on limited data, these estimated total average daily intakes of dibutyl phthalate are 13 to 33 times less than the tolerable daily intake derived from bioassays in animal species. The tolerable daily intake is the intake to which it is believed a person can be exposed daily over a lifetime without adverse effects.

Based on these considerations, it has been concluded that dibutyl phthalate is not entering the environment in a quantity or concentration or under conditions that may have a harmful effect on the environment or that may constitute a danger to the environment upon which human life depends, or to human life or health.

1.0 Introduction

The *Canadian Environmental Protection Act (CEPA)* requires the Minister of the Environment and the Minister of Health to prepare and publish a Priority Substances List 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 under 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 under Section 11 may be placed on Schedule I of CEPA. Consideration can then be given to developing regulations, guidelines, or codes of practice to control any aspect of these substances' life cycle, from the research and development stage through manufacture, use, storage, transport, and ultimate disposal.

The assessment of whether dibutyl phthalate is "toxic", as defined under CEPA, was based on the determination of whether it **enters** or is likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota at levels that could cause adverse **effects**.

Data relevant to the assessment of whether dibutyl phthalate is "toxic" to the environment under CEPA were identified from existing review documents, published reference texts and on-line searches conducted between September 1991 and March 1993, of the following commercial data bases: CAB Abstracts (1984 to 1993), CHEMICAL ABSTRACTS (1985 to 1991), Chemical Evaluation Search and Retrieval System (CESARS), Hazardous Substances Data bank (HSDB), IRPTC-LEGAL and POLLUTION ABSTRACTS (1985 to 1991). Data relevant to the assessment of whether dibutyl phthalate is "toxic" to the environment obtained after April, 1993, have not been included.

For assessment of data other than those considered to be critical for determination of "toxic" to human health under the Act, existing evaluations such as those of the U.S. Environmental Protection Agency (U.S. EPA, 1980; 1981; 1987), the U.K. Health and Safety Executive (HSE, 1986), the Agency for Toxic Substances and Disease Registry (ATSDR, 1990), Woodward (1988), and a background review prepared under

contract by SENES Consultants Ltd. (June, 1989 to February, 1990) have been consulted where considered to be appropriate. On-line databases such as MEDLINE, TOXLINE, CA SEARCH, National Technical Information System (NTIS), EMBASE, ENVIROLINE, and HSDB were searched in 1990 (1981 to 1990) to identify current literature that would not have been included in any of the previous review articles. Another literature search on data bases, which included HSDB (1992), Integrated Risk Information System (IRIS), Registry of Toxic Effects of Chemical Substances (RTECS) (1992), Chemical Carcinogenesis Research Information System (CCRIS) (1992), Chemid (1992), and TOXLINE (1987 to 1992), and a manual search of the most recent three months of Current Contents were conducted in June 1992.

To identify data relevant to the estimation of exposure of the general population to dibutyl phthalate, the following data bases were searched: Environment Canada Departmental Library Catalogue (ELIAS) (1992), AQUAREF (1970 to 1992), Canadian Research Index (MICROLOG) (1979 to 1992), and Co-operative Documents Project (CODOC/GDOC) (1992). The Chemical Manufacturers' Association was also invited to provide relevant information for consideration in the preparation of the supporting documentation. Data relevant to assessment of whether dibutyl phthalate is "toxic" to human health obtained after the completion of these sections of this report (i.e., November, 1992) were not considered for inclusion.

Review articles were consulted where appropriate. However, all original studies that form the basis for determining whether dibutyl phthalate is "toxic" under CEPA have been critically evaluated by the following Environment Canada staff (entry, and environmental exposure and effects) and Health Canada staff (human exposure and effects on human health):

Environment Canada	Health Canada
L. Brownlee	P.K.L. Chan
C. Fortin	M.E. Meek
K. Lloyd	F. Wandelmaier
P. Paine	
K. Taylor	

In this report, a synopsis that will appear in the *Canada Gazette* is presented. Section 2.0 is an extended summary of the technical information that is critical to the assessment. The assessment of whether dibutyl phthalate is "toxic" is presented in Section 3.0. Supporting documentation that presents the technical information in greater detail has also been prepared.

As part of the review and approvals process established by Environment Canada for its contributions to Priority Substances List (PSL) assessments, the environmental sections of this report were reviewed by: Dr. Foster Mayer (U.S. EPA, Gulf Breeze, FL), Dr. W.J. Adams (ABC Laboratories, Columbia, MO), and Dr. V. Zitko (Fisheries and Oceans Canada, St. Andrews, NB). Following peer review by staff of the British Industrial Biological Research Association Toxicology International (U. K.), sections

related to the effects on human health were approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health Canada. The entire Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

Copies of this Assessment Report and of the unpublished supporting documentation are available upon request from:

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2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production, and Uses

Dibutyl phthalate, a phthalic acid ester, has the CAS (Chemical Abstracts Service) Registry Number 84-74-2, the molecular formula $C_{16}H_{22}0_4$, and a molecular weight of 278.4. Synonyms include: 1,2-benzenedicarboxylic acid, dibutyl ester; phthalic acid, dibutyl ester; and di-*n*-butyl phthalate. The structure of dibutyl phthalate is shown in Figure 1. Dibutyl phthalate is a colourless, oily liquid (Montgomery and Welkom, 1990), with a vapour pressure of about 0.01 Pa @ 25°C (CMA, 1984), Henry's Law Constant of 6.4 Pa·m^3/mol or lower (Howard, 1989; McKone and Layton, 1986; Montgomery and Welkom, 1990; U.S. EPA, 1982a), octanol-water partition coefficient (log K_{ow}) between 4.31 and 4.79 (Montgomery and Welkom, 1990), and solubility in water of about 10 mg/L (McKone and Layton, 1986), although values as high as 4500 mg/L have been reported (Leyder and Boulanger, 1983). Determination of the water solubility of phthalic acid esters is complicated since these compounds easily form colloidal dispersions in water (Klöpfer *et al.*, 1982) and are subject to "molecular folding" (Callahan *et al.*, 1979).

The most sensitive and selective analytical determinations of phthalic acid esters, including dibutyl phthalate, in environmental media are achieved by gas chromatography with electron capture detection (Kohli *et al.*, 1989). Phthalates frequently occur as contaminants in laboratory air and solvents, and as plasticizers in analytical equipment. This may cause contamination of environmental samples and result in overestimation of the concentration of phthalates in these samples. For example, Ishida *et al.* (1980) reported the presence of dibutyl phthalate in laboratory solvents at concentrations up to 0.17 mg/kg (in benzene) and in solid reagents at concentrations up to 9.89 mg/kg (in carboxymethylcellulose), while polyvinyl tubing contained 23.3% dibutyl phthalate.

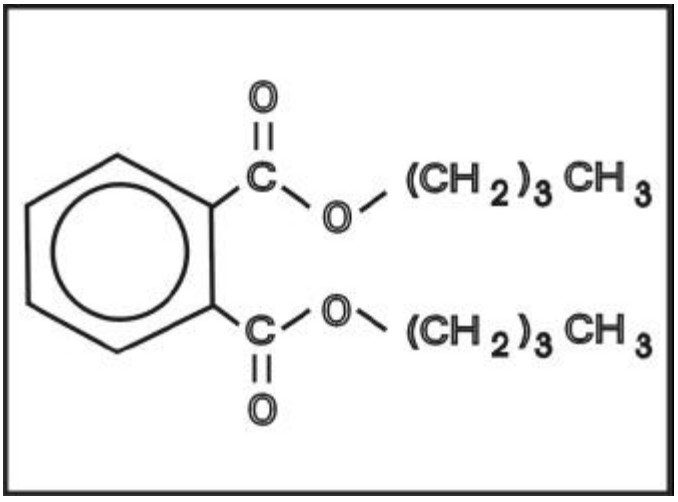

Figure 1 Structure of Dibutyl Phthalate

Therefore, great care must be taken to prevent contamination during collection, storage, and analysis of samples (Hites and Budde, 1991; Kohli *et al.,* 1989; Mathur, 1974; U.S. EPA, 1982b). In many studies reporting environmental concentrations of phthalates conducted before 1980, potential contamination was not adequately accounted for (Pierce *et al.*, 1980) and, therefore, the accuracy of such studies is doubtful.

There are no Canadian producers of dibutyl phthalate (CIS, Inc., 1992). One company had been producing dibutyl phthalate in quantities less than 1000 tonnes per year, but stopped production in early 1988. About 540 tonnes of dibutyl phthalate were imported into Canada in 1991, down from the 860 tonnes in 1988. About 83% of the imported dibutyl phthalate came from the United States in 1991 (CIS, Inc., 1992). Available information does not permit an estimation of the amount of dibutyl phthalate imported in finished plastic products.

Dibutyl phthalate is used mainly as a plasticizer in polyvinyl emulsions. In 1991, approximately 54% of the total Canadian supply of dibutyl phthalate was used in adhesives, about 15% was used in coatings (including lacquers), and 31% in miscellaneous applications, including paper coating (CIS, Inc., 1992). Dibutyl phthalate is used in cosmetics as a perfume solvent and fixative, a suspension agent for solids in aerosols, a lubricant for aerosol valves, an antifoamer, a skin emollient, and as a plasticizer in nail polish, fingernail elongators, and hair spray (CIR, 1985).

2.2 Entry into the Environment

The occurrence of phthalates from natural sources in biological and geochemical samples has been suggested, but has not been confirmed, at least in part because of possible contamination during sampling or analysis (Mathur, 1974). However, it is unlikely that the amounts of phthalates present naturally would be significant compared with those from anthropogenic sources (IPCS, 1992).

Worldwide, the release of phthalates directly to the atmosphere is believed to be the most important mode of entry to the environment. The sources of such releases include emissions during the manufacture and use of dibutyl phthalate and through the incomplete combustion of plastic material (IPCS, 1992). Recent data on releases of phthalates in Canada have not been identified. Leah (1977) estimated that 2 to 4.5% of the total Canadian supply of phthalates was lost to the environment during production and processing, with about 95% of this loss resulting from processing. Peakall (1975) estimated that articles containing phthalate-plasticized material may lose about 1%/yr of their phthalate content when in contact with liquids and 0.1%/yr when in contact with air. In Canada, Eisenreich *et al.* (1981) predicted that atmospheric deposition is a significant source of dibutyl phthalate in the Great Lakes, with a calculated total deposition of 48 tonnes/year (t/yr) to the five Great Lakes, with values for each ranging from 3.7 t/yr in Lake Ontario to 16 t/yr in Lake Superior.

In a 1985/86 survey on effluents from Canadian textile mills, dibutyl phthalate was detected at concentrations up to 158 µg/L (detection frequency = 17/19; detection limit = 1 µg/L) (Environment Canada, 1989). Dibutyl phthalate has also been detected in

Canadian chemical plant effluents at concentrations within the range of 1 to 100 µg/L (Munro *et al.,* 1985*;* OME, 1992a;b). Loadings in liquid effluents from Ontario's organic chemical industry totalled about 1.7 kg dibutyl phthalate/day (12-month average) (OME, 1992a), while those from the inorganic chemical industry totalled about 0.06 kg dibutyl phthalate/day (12-month average) (OME, 1992b).

Concentrations of dibutyl phthalate have ranged up to 3.0 µg/L in sewage effluents from Ontario municipalities (Beak Consultants, 1991). Dibutyl phthalate was detected in 12 of 15 Canadian municipal sludges sampled between 1980 and 1985, with concentrations ranging from 0.2 to 430 mg/kg dry weight (d.w.) and a median concentration of 10 mg/kg (Webber and Lesage, 1989).

Dibutyl phthalate was detected at concentrations often exceeding 10 µg/L (actual concentrations not reported) in samples of wastewater collected from 1982 to 1984 at Canadian coal mines, coal preparation plants, and coal storage transfer terminals. Concentrations in sediments from these facilities were within the range of 5 to 30 mg/kg (d.w.) (actual concentrations not reported) (Atwater *et al.,* 1990).

The presence of dibutyl phthalate in leachates from municipal waste landfill sites was documented by Lesage (1991), who reported a concentration of approximately 1 mg/L for a single sample from a landfill site in Guelph, Ontario.

Dibutyl phthalate has been detected, but not quantified, in extracts of municipal incinerator fly ash from Ontario (Eiceman *et al.,* 1979).

2.3 Exposure-related Information

2.3.1 *Fate*

The most important processes affecting the distribution and transformation of dibutyl phthalate in the environment include photo-oxidation, atmospheric deposition, and aerobic biodegradation (Eisenreich *et al.,* 1981; Howard, 1989; Howard *et al.,* 1991; Schouten *et al.,* 1979).

In the atmosphere, dibutyl phthalate has been measured in both the vapour and the particulate phases. Cautreels and Van Cauwenberghe (1978) and Giam *et al.* (1980) demonstrated that most of the dibutyl phthalate in the atmosphere (>66%) occurred in the vapour phase, while Hoff and Chan (1987) reported that in the Niagara River region, more than 57% of atmospheric dibutyl phthalate occurred in the suspended particulate phase. Howard *et al.* (1991) reported an estimate of the photo-oxidation half-life of dibutyl phthalate in air of 7.4 hours to 3.1 days. Washout by precipitation and dry deposition are believed to play a significant role in the removal of dibutyl phthalate from the atmosphere.

Most of the dibutyl phthalate in surface water (>75%) occurs in the water fraction rather than in the suspended solids (NRDIG, 1990). Dibutyl phthalate is biodegradable

in natural surface waters, with an estimated half-life in the range of 1 to 14 days (Johnson *et al.,* 1984; Schouten *et al.,* 1979).

No information was identified concerning the half-life of dibutyl phthalate in freshwater sediments, however, by analogy with other phthalates such as di(2-ethylhexyl) phthalate, it is expected to be more persistent under anaerobic conditions. Dibutyl phthalate came into solution when air-dried coal mine sediments were added to distilled water (Atwater *et al.,* 1990), demonstrating that some of the dibutyl phthalate adsorbed onto sediments may subsequently be desorbed back into the water column.

In anaerobic sludge, degradation of dibutyl phthalate proceeded through monobutyl phthalate and phthalic acid, followed by ring cleavage and mineralization (Shelton *et al.,* 1984). The half-life for dibutyl phthalate in undiluted sludge was about three days.

Howard *et al.* (1991) (using scientific judgement based on review of data on concentrations in unacclimated aerobic soil grab samples), predicted a half-life for dibutyl phthalate in soil of 2 to 23 days. Overcash *et al.* (1982), however, reported half-lives of longer than 26 weeks in loam and sand at application rates of 800 mg dibutyl phthalate/kg and above. At a lower application rate (200 mg/kg), the half-life of dibutyl phthalate in loam and sand was about 12 weeks (Overcash *et al.,* 1982). Dibutyl phthalate is moderately adsorbed to soil (Zurmühl *et al.,* 1991), but it forms a complex with water-soluble fulvic acid, and this may increase its mobilization and reactivity in soil to some degree (Kohli *et al.,* 1989). Volatilization of dibutyl phthalate from soil is not expected to be significant because of its low vapour pressure and moderate adsorption to soil (Howard, 1989).

Since dibutyl phthalate is readily metabolized in fish (Johnson *et al.,* 1977; Stalling *et al.,* 1973; Wofford *et al.,* 1981), bioaccumulation is likely to be limited in fish species. The limited data that are available fail to confirm this, however, as the reported bioconcentration factors for dibutyl phthalate for various aquatic organisms range from 2.9 for the brown shrimp, *Penaeus aztecus* (Wofford *et al.,* 1981) to 2125 for the fathead minnow, *Pimephales promelas* (Call *et al.,* 1983).

No information is available on the bioaccumulation of dibutyl phthalate in wild mammals.

2.3.2 *Concentrations*

Data on concentrations of dibutyl phthalate in the Canadian environment have been identified for the atmosphere, surface water, groundwater, sediment, soil, and biota. As noted in Section 2.1, laboratory contamination is a problem with the analysis of phthalic acid esters in environmental samples. It is difficult, however, on the basis of available data, to assess the extent of this problem.

Dibutyl phthalate has been detected in samples of air taken in 1982 (n = 5, detection limit not stated) along the Niagara River, with mean concentrations of

1.9 ±1.3 ng/m3 in the gas phase and 4.0 ± 2.2 ng/m3 in the particulate phase (Hoff and Chan, 1987). In 1983, mean levels were 4.5 ± 3.5 ng/m3 in 15 samples of the gas phase, and 6.2 ± 2.6 ng/m3 in 19 samples of the particulate phase. Based on atmospheric concentrations of dibutyl phthalate from a number of oceanic and inland areas as reported by Giam et al. (1978; 1980), Eisenreich *et al*. (1981) estimated that atmospheric concentrations of dibutyl phthalate in the Great Lakes area ranged from 0.5 to 5 ng/m3, and that concentrations of dibutyl phthalate in rain water in the same area ranged from 4 to 10 ng/L. Weschler (1981) reported dibutyl phthalate in the Arctic aerosol at Barrow, Alaska, at a concentration of approximately 1 ng/m3 (detection limit not stated).

Data identified on concentrations of dibutyl phthalate in indoor air in Canada are restricted to a maximum level of 2.85 µg/m3 in a limited and probably unrepresentative number of homes (n = 9) in Montreal. No other information on measured concentrations was presented in the published account of this study (Otson and Benoit, 1985).

Information on concentrations of dibutyl phthalate in surface waters in the NAQUADAT/ENVIRODAT database is limited to 73 records for Alberta and two records for British Columbia dating from 1985 to 1988. Concentrations were above the detection limit for only eight records and reported values ranged from <1 to 2 µg/L (NAQUADAT, 1993). The Alberta Ministry of the Environment detected dibutyl phthalate in 3 of 45 samples of raw surface water; the average concentration was below the detection limit (1 µg/L), while the maximum concentration was 4 µg/L (Halina, 1993). The Ontario Ministry of the Environment, under the Municipal and Industrial Strategy for Abatement (MISA) program, reported that dibutyl phthalate was detected in the intake water of one organic chemical manufacturing plant at an average concentration of 1.4 µg/L (plant located on the St. Clair River) (OME, 1992a). For water samples collected in 1988 and 1989 using large-volume sampling methods designed to lower the detection limit, the Niagara River Data Interpretation Group (NRDIG, 1990) reported mean concentrations of 12.2 ng/L at Fort Erie (26 of 26 samples contained dibutyl phthalate concentrations above the detection limit of 0.29 ng/L; max 26.87 ng/L) and 15.16 ng/L at Niagara-on-the-Lake (25 of 25 samples contained dibutyl phthalate concentrations above the detection limit of 0.29 ng/L; max 72.93 ng/L). Germain and Langlois (1988), also using large-volume sampling techniques, reported a mean concentration of 89 ng/L for dibutyl phthalate in the St. Lawrence River in the Montreal area in 1987. In 1979, maximum concentrations of dibutyl phthalate in the range of 10 to 100 µg/L were reported for chemical plant intake water from the St. Clair River (Munro *et al*., 1985).

Only one report was identified concerning the presence of dibutyl phthalate in groundwater. Lesage (1991) reported a concentration of approximately 570 µg dibutyl phthalate/L in a single sample of groundwater beneath a former coke oven plant site at Sidney, Nova Scotia, in 1987.

Dibutyl phthalate was not detected (detection limit = 1 µg/L) in a 1984 survey of an unspecified number of samples of drinking water from seven cities in the Niagara and

Lake Ontario regions (OME, 1984). In a study of 329 samples taken in Alberta in 1985 and 1986, concentrations of dibutyl phthalate ranged from less than or equal to the detection limit (1.0 µg/L) to 7.2 µg/L in 18 surface water supplies, and up to 1.0 µg/L in 10 groundwater supplies; mean concentrations were less than 1.0 µg/L in both surface water and groundwater samples (Spink, 1986). In a more recent survey of 1237 samples taken in Alberta from 1987 to 1992, the mean concentrations were identical to those reported for the 1985 and 1986 period (Halina, 1993). Dibutyl phthalate was not detected in 22 samples of raw drinking water supplies from 11 municipalities in the Lac St-Jean and Charlevoix areas of Quebec (detection limit, 1 µg/L) (MENVIQ, 1993).

In samples of sediment taken from the Detroit River in 1982, concentrations of dibutyl phthalate ranged from <0.1 to 0.65 mg/kg (d.w.) (Fallon and Horvath, 1985). Concentrations of dibutyl phthalate in samples of sediment collected in 1983 downstream from a sewage outfall in the estuary of the Fraser River, British Columbia, ranged from 0.07 to 0.45 mg/kg (d.w.) (Rogers and Hall, 1987). In samples collected in the 1970s, concentrations of dibutyl phthalate up to 0.3 mg/kg were reported in sediments from Lake Superior and Lake Huron (CCREM, 1987).

Concentrations ranging from <0.1 mg/kg to 1.4 mg dibutyl phthalate/kg were detected in 13 out of 30 samples (detection limit = 0.1 mg/kg) of soils in urban areas of Port Credit and Oakville/Burlington, Ontario (Golder Associates, 1987). Levels of 0.027 to 0.175 mg dibutyl phthalate/kg were identified in an unspecified number of samples of soil from an industrial site in Quebec (MENVIQ, 1989).

The concentrations of dibutyl phthalate in aquatic biota from the Great Lakes and other areas in Canada were less than 10 µg/g wet weight (Burns *et al.,* 1981; Glass *et al.,* 1977; Swain, 1978; Williams, 1973). The highest concentrations were reported for skinless fillets from long-nose suckers, *Catostomus catostomus* (8.1 µg dibutyl phthalate/g) and rainbow trout, *Oncorhynchus mykiss* (5.4 µg/g) from Lake Superior (Glass *et al.,* 1977). Concentrations of dibutyl phthalate in fish from various United States Great Lakes harbours and tributary mouths ranged from <0.02 to 35 µg/g wet weight (DeVault, 1985).

Identified data on levels of dibutyl phthalate in wildlife are limited to one study in Atlantic Canada (Zitko, 1972). Reported concentrations of dibutyl phthalate in egg yolks of the double-crested cormorant, *Phalacrocorax auritus,* and herring gull, *Larus argentatus,* were 14.1 µg/g (lipid basis) and 19.1 µg/g (lipid basis), respectively.

In a market basket survey of 98 different food types obtained from Halifax in 1986, dibutyl phthalate was detected in butter (1.5 µg/g), freshwater fish (0.5 µg/g), cereal products (ranged from not detected up to 0.62 µg/g), baked potatoes (0.63 µg/g), coleslaw (0.11 µg/g), bananas, blueberries, and pineapples (0.12, 0.09, and 0.05 µg/g, respectively), margarine (0.64 µg/g), white sugar (0.2 µg/g), and gelatin dessert (0.09 µg/g) (NHW, 1992). In an early Canadian study of 21 samples of fish

(Williams, 1973), dibutyl phthalate was detected in one sample of canned tuna (78 ppb or ng/g) and one sample of canned salmon (37 ppb or ng/g).

Though data on the content of dibutyl phthalate in cosmetics available in Canada specifically were not identified, in 1981, dibutyl phthalate was reported as an ingredient in a total of 590 cosmetic formulations in the United States at concentrations ranging from less than 0.1% to between 10 and 25% (CIR, 1985).

2.4 Effects-related Information

2.4.1 *Experimental Animals and* In Vitro

The acute toxicity of dibutyl phthalate following oral or intraperitoneal administration is low, with reported LD_{50}s following oral administration to rats ranging from approximately 8 g/kg body weight (b.w.) to at least 20 g/kg (b.w.) (Smith, 1953; Lehman, 1955; White *et al.,* 1983; CIR, 1985). In mice, values are approximately 5 g/kg (b.w.) to greater than 13 g/kg (b.w.) (CIR, 1985; Woodward, 1988).

The short-term toxicity of dibutyl phthalate has been investigated in rodents following oral administration. In most of the available studies, animals were exposed to only a single dose level. Effects in rats after oral administration for 5 to 21 days include those on liver enzymes (Aitio and Parkki, 1978; Bell *et al.,* 1978; Kawashima *et al.,* 1983; Barber *et al.,* 1987) and hepatomegaly at doses of 420 mg/[kg (b.w.)·d] and higher (Yamada, 1974; Bell *et al.,* 1978; Oishi and Hiraga, 1980a; Barber *et al.,* 1987), a reduction in the rate of weight gain at doses of 600 mg/[kg (b.w.) ·d] and higher (Barber *et al.,* 1987; Yamada, 1974) and splenomegaly after intragastric intubation of 1.0 mL/[kg (b.w.) ·d] {1047 mg/[kg (b.w.) ·d]} (Yamada, 1974). Peroxisome proliferation in the liver of male F344 rats was observed after administration of 600 mg/[kg (b.w.) ·d] following ingestion in the diet for 21 days (Barber *et al.,* 1987). The lowest no-effect level was that reported in an abstract by Lake *et al.* ; in which the no-observed-adverse-effect-level (NOAEL) reported by the authors was 104 mg/[kg (b.w.)·d] based on induction of hepatic peroxisome proliferation in male F344 rats, as assessed by measurement of cyanide-insensitive palmitoyl-CoA oxidation activity (Lake *et al.,* 1991).

For mice, data identified on short-term toxicity are limited to two investigations. In a study conducted by Ota *et al.* (1973), there was an increase in renal weight and histopathological effects in the kidney of mice ingesting 2.5% in their diet for two weeks (equivalent to 3000 mg/[kg (b.w.) ·d] {No-observed-effect-level, NOEL = 300 mg/[kg (b.w.) ·day] }. In contrast, there was a significant decrease in the relative kidney weight when ICR male mice were fed a diet containing 2% {equivalent to 2400 mg/[kg (b.w.)·d]} dibutyl phthalate for one week (Oishi and Hiraga, 1 980b). Results of histopathological examinations were not reported. A slight but insignificant increase in kidney weight was also observed in JCL:Wistar rats exposed to 1000 mg/[kg (b.w.) ·d] (Oishi and Hiraga, 1980a).

The effects in rats observed following ingestion of dibutyl phthalate for subchronic periods up to seven months included a reduction in the rate of weight gain at doses greater than 2300 mg/[kg (b.w.) ·d] (Radeva and Dinoyeva, 1966 in HSE, 1986; Murakami *et al.*, 1986a; b) and an increase in relative liver weight at doses of 120 mg/[kg (b.w.) ·d] or greater (Nikonorow *et al.*, 1973; Murakami *et al.*, 1986a; b). Peroxisome proliferation in the liver was observed at 2500 mg/[kg (b.w.)·d] after exposure for 34 to 36 days (Murakami *et al.*, 1986b). In the study conducted by Radeva and Dinoyeva (1966 in HSE, 1986) in which male rats (strain unspecified) were fed diets containing levels equivalent to 0.1, 1, and 10 mg/[kg (b.w.) ·d] for seven months, marked venous congestion was observed in some exposed rats at necropsy but the organ and dose group(s) in which it occurred were not specified. In mice, histopathological lesions in the kidney and liver were observed at doses of 500 and 5000 mg/[kg (b.w.)·d] dibutyl phthalate for three months (Ota *et al.*, 1974). The lowest reported lowest-observed-effect-level (LOEL) in an adequately documented subchronic study following ingestion is, therefore, 120 mg/kg (b.w.), based on the increase in relative liver weight in rats reported by Nikonorow *et al.* (1973).

The lowest identified LOEL following inhalation in a subchronic study was that of Kawano (1980) reported on the basis of a study for which only an English abstract is available, namely, 0.5 mg/m^3 based on decreased body weight gain, increases in relative organ weights, and hypolipidemic effects in rats exposed for up to 6 months. In other identified studies, no effects were observed following exposure for 93 days to 1 mg/m^3 (Men'shikova, 1971 in HSE, 1986), whereas effects on body weight gain, organ weights, and hematological parameters were observed at a high concentration (900 mg/m^3) following exposure for 35 days (Antonyuk and Aldyreva, 1973 in HSE, 1986).

Owing to limitations, such as small group sizes, short periods of exposure, and poor documentation, available studies (Smith, 1953; Nikonorow *et al.*, 1973; Krauskopf, 1973) are considered inadequate to assess the chronic toxicity or carcinogenicity of dibutyl phthalate in experimental animals.

Dibutyl phthalate has not been mutagenic in most *in vitro* assays in bacteria (Shahin and von Borstel, 1977; Florin *et al.*, 1980; Kozumbo *et al.*, 1982; Zeiger *et al.*, 1982; 1985), while in mammalian cells, there is some equivocal evidence of chromosome damage (clastogenicity) (Abe and Sasaki, 1977; Ishidate and Odashima, 1977).

Repeated oral exposure to concentrations of dibutyl phthalate for 4 to 90 days {250 to 2600 mg/[kg (b.w.)·d]} affects the reproductive system of male rodents; however, there are considerable interspecies differences in response and the effects of short-term exposure appear to be at least in part, reversible (Tanino *et al.*, 1987). Observed effects in the available studies include marked reductions in the weights of testes and accessory sex glands, decreased numbers of spermatocytes, degeneration of the seminiferous tubules of the testes, a reduction in testicular zinc levels and serum testosterone levels, and increases in testosterone levels in the testes and an increase in urinary zinc excretion at doses of 250 mg/[kg (b.w.) ·d] or higher (Cater *et al.*, 1977; Gray and Butterworth, 1980; Oishi and Hiraga, 1980a; 1980b; Gray *et al.*, 1982;

Ikemoto *et al.,* 1983; Fukuoka *et al.,* 1989; 1990; Srivastava *et al.,* 1990; Killinger *et al.,* 1991; Lake *et al.,* 1991). Though many of these studies involved administration of a single dose level, the lowest reported effect levels for reproductive effects in males in sufficiently well documented studies were observed in a multi-dose investigation in which 250, 500, or 1000 mg/[kg (b.w.) .d] of dibutyl phthalate were administered to young male rats by gavage in groundnut oil (Srivastava *et al.,* 1990). At the two highest doses, decreases in the weight of the testes, effects on testicular enzymes, and degeneration of the seminiferous tubules were observed. At the lowest dose, there were effects on testicular enzymes associated with degeneration of spermatogenic cells {LOAEL = 250 mg/[kg (b.w.)·d]}.

Dibutyl phthalate also adversely affects reproduction in females. Following ingestion by male and female CD-1 mice (11 weeks of age at outset) of 1300 mg/[kg (b.w.) ·d) in the diet seven days before and during a 98-day cohabitation period (Reel *et al.,* 1984; Lamb *et al.,* 1987), there were significant decreases in the number of breeding pairs able to produce at least one litter, the number of live pups per litter, and the proportion of pups born alive {NOEL = 390 mg/[kg (b.w.) ·d] }. In a crossover mating trial with the control and F_0 mice exposed to 1300 mg/ [kg (b.w.) ·d], the proportion of fertile pairs producing offspring was significantly reduced in the control male and exposed female pairing. In addition, the number of live pups per litter, the proportion of pups born alive, and live pup weights were significantly decreased for this pairing. In the F_0 females, absolute and relative liver weights were significantly increased and the uterine weight was significantly decreased at the high dose. In studies reported only as abstracts, pup survival was reduced and body weights decreased following exposure during gestation and lactation to 1000 mg/[kg (b.w.) ·d)] (rats) and 2600 mg/[kg (b.w.) ·d] (mice) (Killinger *et al.,* 1989).

In other studies, there were no adverse effects in rats after short-term exposure following ovulation and continuing through the period of implantation during pregnancy at doses up to 2000 mg/[kg (b.w.) ·d] (Cummings and Gray, 1987). There were no adverse effects on the female reproductive system in an unspecified number of hamsters exposed to 500 or 1000 mg/[kg (b.w.) ·d] from 20 to 55 days of age (Gray *et al.,* 1983). In a second experiment in the same report, however, half of the breeding pairs of rats exposed to 500 mg/[kg (b.w.) ·d] from 20 to 75 days of age did not breed {NOEL = 250 mg/[kg (b.w.)·d]}. There were no effects in female rats exposed to 520 mg/[kg (b.w.) ·d] for six weeks and then mated with unexposed males through several generations (Bornmann and Loeser, 1956 in HSE, 1986).

The developmental effects of dibutyl phthalate have been examined in rats and mice following oral and intraperitoneal administration. Based on the results of available studies, dibutyl phthalate has generally induced fetotoxic effects in the absence of maternal toxicity. In mice, dibutyl phthalate has caused dose-dependent increases in the number of resorptions and dead fetuses at oral doses of 625 mg/[kg (b.w.) ·d] or higher (Hamano *et al.,* 1977; Shiota *et al.,* 1980; Shiota and Nishimura, 1982; Hardin *et al.,* 1987). Dose-dependent decreases in fetal weights and number of viable litters were also observed in mice at these doses. Similarly in rats, oral doses of 600 mg/[kg (b.w.) ·d]

caused an increase in the number of resorptions and decreased fetal body weights when dibutyl phthalate was administered throughout gestation but not when administered before and during mating, although 120 mg/[kg (b.w.) ·d] was without effect (Nikonorow *et al*., 1973). Limited data also indicate that dibutyl phthalate might be teratogenic. In mice administered dibutyl phthalate in their diet on days 0 to 18 of gestation, there was a borderline increase in fetal neural tube defects (exencephaly and myeloschisis) at 2100 mg/[kg (b.w.) ·d] in one study in which a significant reduction in body weight gain of the mothers was observed at day 18 (Shiota and Nishimura, 1982). In another investigation, there was a significant increase in external defects (non-losing eyelid, encephalocele, cleft palate, and spina bifida) at 625 mg/[kg (b.w.) ·d], a dose at which an increase in the weight of the livers of the mothers was observed {NOEL = 62.5 mg/[kg (b.w.) ·d]} (Hamano *et al.*, 1977). Skeletal abnormalities have also been reported in the offspring of rats exposed intraperitoneally to doses of 320 mg/[kg (b.w.) ·d] or greater, although maternal toxicity was not addressed (Singh *et al.,* 1972). Therefore, the lowest reported NOEL for developmental effects of dibutyl phthalate was 62.5 mg/[kg (b.w.) ·d] as reported in JCL:ICR mice (Hamano *et al.,* 1977).

In the study reported by Hamano *et al.* (1977), JCL:ICR mice were administered 0.005, 0.05, or 0.5% dibutyl phthalate in food {equivalent to 6.25, 62.5, or 625 mg/[kg (b.w.)·d] } throughout 18 days of gestation. There were no significant differences in the mortality of maternal mice, the rate of spontaneous abortions, or the rate of premature births between the control and exposed groups. The highest dose was embryotoxic, resulting in a lower number of live offspring. At this highest dose, an increase in kidney weight in mothers was reported, although there were no effects on the weights of other organs, body weight gain, or survival in the mothers. The frequency of offspring having external anomalies was also significantly higher in the high dose group than in controls. The abnormalities consisted mainly of spina bifida, exencephaly, cleft palate, and non-closing eyelids. A small but insignificant increase in skeletal anomalies was also seen in the high-dose group. Therefore, the NOEL in this study was considered to be 62.5 mg/[kg (b.w.) ·d] on the basis of embryotoxic and teratogenic effects.

Data on the neurotoxicity and immunotoxicity of dibutyl phthalate in experimental animals have not been identified.

2.4.2 *Humans*

Three limited epidemiological studies of neurological (Milkov *et al.,* 1973; Gilioli *et al.,* 1978) and reproductive effects (Aldyreva *et al.,* 1975, summarized by Woodward, 1988) in populations exposed to dibutyl phthalate in the occupational environment have been identified. Owing to limitations of these investigations including lack of an appropriate control group (Milkov *et al.,* 1973), the small size of the exposed population (Gilioli *et al.,* 1978), and the lack of adequate documentation of protocol and results (Aldyreva *et al.,* 1975, summarized by Woodward, 1988), these studies are considered inadequate as a basis for assessment of neurotoxic or reproductive effects. In addition, workers were generally exposed to numerous compounds other than dibutyl phthalate.

2.4.3 *Ecotoxicology*

The identified information for dibutyl phthalate includes acute and chronic data for a number of species of various trophic levels in the aquatic environment from bacteria and algae to fish. No information was identified on effects of dibutyl phthalate on amphibians, reptiles, or mammalian wildlife.

Mayer and Ellersieck (1986) reported 96-h LC_{50} values of 350 µg dibutyl phthalate/L for the yellow perch, *Perca flavescens,* and 460 µg/L for the channel catfish, *Ictalurus punctatus,* two freshwater species. The sheepshead minnow, *Cyprinodon variegatus,* for which a 96-h LC_{50} of 600 µg/L has been reported (CMA, 1984), was the most sensitive marine fish species identified.

Slightly higher 96-h LC_{50}s were reported for invertebrate species, including a 96-h LC_{50} of 750 µg/L for the Mysid shrimp, *Mysidopsis bahia* (EG&G Bionomics, 1984). A 48-h EC_{50} of 760 µg dibutyl phthalate/L for the midge, *Chironomus plumosus,* was reported by Streufert *et al.* (1980).

The lowest identified LOEL following chronic exposure was a 99-day value of 190 µg dibutyl phthalate/L for the rainbow trout, *Oncorhynchus mykiss,* with growth reduced by about 27% based on dry weight (Ward and Boeri, 1991). The NOEL in this study was 100 µg/L. A 10-day EC_{50} (decreased cell numbers) of 750 µg dibutyl phthalate/L was reported for the green algae, *Selenastrum capricornutum* (Springborn Bionomics, 1984). For arthropods, Laughlin *et al.* (1978) reported a 28-day LOEL (survival) of 1000 µg/L for the grass shrimp, *Palaemonetes pugio* (NOEL of 500 µg/L), while McCarthy and Whitmore (1985) reported a 16-day LOEL (survival and reproduction) of 1800 µg/L for *Daphnia magna* (NOEL of 560 µg/L).

No toxicological data were identified for sediment-dwelling biota in Canada.

Although the number of studies on the effects of dibutyl phthalate on plants is limited, effects resulting from exposure through atmosphere, soil, and water were identified. Dibutyl phthalate emitted from flexible glazing strips used in greenhouses has been implicated in development of toxic symptoms in greenhouse plants. Hardwick *et al.* (1984) reported a threshold concentration between 141 and 360 ng dibutyl phthalate/m^3 in air for visible damage (growth restriction, chlorosis, and cotyledon death) by dibutyl phthalate in summer cabbage, *Brassica oleracea.* Dibutyl phthalate, at a concentration of 1 g/L (added as a methanol solution), reduced seed germination by 48% in peas, *Pisum sativum,* and by 58% in spinach, *Spinacia oleracea,* grown in tap water, but had no observable effect on subsequent development of the seeds that did germinate (Herring and Bering, 1988). It should be noted, however, that this concentration is about 100 times higher than the saturation concentration of dibutyl phthalate in water. Dibutyl phthalate at soil concentrations of 200 mg/kg and above reduced the germination of soybeans, *Glycine max,* by >33% and decreased the growth of corn and soybeans by 29 to 80% (Overcash *et al.,* 1982).

In a study in which ring doves *(Streptopelia risoria)* were fed a diet containing 10 mg dibutyl phthalate/kg (1.1 mg dibutyl phthalate/[kg (b.w.)·d]} for a period of three weeks before mating through to completion of a clutch of two eggs, there was a 23% increase in water permeability and a 10% decrease in egg shell thickness (Peakall, 1974). (A 15% decrease in shell thickness is considered significant for reproductive effects.) Rapid recovery occurred when exposure was ended. An approximate ED_{50} of 33 µmol (9.19 mg) per egg was calculated for dibutyl phthalate in a chicken embryo toxicity study (Korhonen *et al.*, 1983). Embryotoxic effects included early (within two days of treatment) and late (between 3 and 11 days after treatment) deaths.

3.0 Assessment of "Toxic" under *CEPA*

3.1 CEPA 11(a) Environment

At present, there are no Canadian producers of dibutyl phthalate. In 1991, approximately 540 tonnes of dibutyl phthalate were imported into Canada. Data on releases of dibutyl phthalate to water were limited to a few measurements of industrial effluents, and no data were identified on its release to the atmosphere. In Canada, dibutyl phthalate was detected in air, surface water and groundwater, sediment, biota, sewage sludge and waste effluents. Dibutyl phthalate is relatively non-persistent in air and surface waters, with a half-life of just a few days in these compartments. In soil, dibutyl phthalate may be more persistent, with a half-life sometimes exceeding 26 weeks. Dibutyl phthalate would also be expected to be more persistent in anaerobic sediments.

Airborne concentrations of 360 ng dibutyl phthalate/m^3 have been reported to cause growth restriction, chlorosis, and cotyledon death in some sensitive terrestrial plants grown in greenhouses. The ambient atmospheric concentration of 4.5 ng/m^3 in the Great Lakes region is 80 times less than this value.

The lowest reported chronic effect level for dissolved dibutyl phthalate on freshwater aquatic organisms was 190 µg/L (99-day LOEL on growth) for rainbow trout. This effect level was divided by a factor of 10 to account for differences in sensitivity between species and to extrapolate from laboratory to field conditions, resulting in an estimated effects threshold of 19 µg/L. The highest concentration of dibutyl phthalate reported recently for Canadian waters (4 µg/L) is approximately five times less than this estimated effects threshold, while the highest concentration reported for the Niagara River (73 ng/L) is approximately 260 times less.

No toxicological data were identified for sediment-dwelling biota in Canada. However, since dibutyl phthalate is used in relatively small amounts in Canada and is not manufactured here, exposure to those biota is considered to he minimal.

The potential for adverse effects to wildlife from exposure to dibutyl phthalate through air, water, and food is evaluated with a "worst case" scenario using mink *(Mustela vison),* a terrestrial mammal having a diet consisting in part of aquatic prey. A daily exposure of 1318 µg/[kg (b.w.)·d] was estimated for mink exposed to the highest concentration of dibutyl phthalate recently reported for Canadian waters (Table 1). Reported levels of dibutyl phthalate in the Niagara River area are lower, resulting in mink being exposed to 24 µg/[kg (b.w.) ·d] (Table 1). The intake of dibutyl phthalate from air and water in both calculations is negligible when compared to intake from food.

The lowest reported NOEL for embryotoxic and teratogenic effects in mice was 62.5 mg/[kg (b.w.) ·d]. Using a factor of 10 to account for interspecies differences and to extrapolate from the laboratory to the field, the effects threshold for wild mammals was estimated to be 6250 µg/[kg (b.w.) ·d]. As the worst-case exposure scenario is approximately five times less than this value, while an exposure scenario based on

Table 1 Estimated Total Daily Exposure of a Piscivorous Mammal in Canadian Waters

Exposure Route	Environmental Levels*	Mink Daily Requirements (per kilogram body weight)**	Daily Intake {µg/[kg (b.w.) ·d]}
Air	4.5 ng/m^3	0.55 m^3/d	0.002
Surface water	4 µg/L[1]	0.1 L/d	0.4[1]
	73 ng/L[2]		0.00732
Biota(Fish)	8.5 µg/g[1]	155 g/d	1318[1]
	155 ng/g[2]		24[2]
Total	_____	_____	1318[1]
			24[2]

* The level in air is the maximum level measured in the Great Lakes (Hoff and Chan, 1987); the levels in surface water are [1]the maximum dibutyl phthalate level in Canadian waters (NAQUADAT, 1993) and [2]the maximum concentration of dibutyl phthalate in water samples from Niagara-on-the-Lake, 1988-89 (NRDIG, 1990); the level in fish is the level predicted in fish based on the maximum measured BCF of 2125 for the fathead minnow and the above water concentrations.

** Inhalation rate from Stahl (1967); drinking rate from Calder and Braun (1983); and ingestion rate from Nagy (1987), assuming a diet of 75% fish.

environmental levels found in the Niagara River area is approximately 260 times less, exposure to dibutyl phthalate should not pose a risk to mammalian wildlife.

Therefore, on the basis of available data, dibutyl phthalate is not considered to be entering the environment in a quantity or concentration or under conditions that are having a harmful effect on the environment.

3.2 CEPA 11(b) Environment on Which Human Life Depends

Dibutyl phthalate is estimated to be removed rapidly from the atmosphere (half-life ranging from 7.4 hours to 3.1 days) and will not persist in the troposphere. As such, dibutyl phthalate is not expected to contribute significantly to the formation of ground-level ozone, to global warming, or to the depletion of stratospheric ozone.

Therefore, on the basis of available data, dibutyl phthalate is not considered to be entering the environment in a quantity or concentration or under conditions that constitute a danger to the environment upon which human life depends.

3.3 CEPA 11(c) Human Life or Health

3.3.1 *Population Exposure*

Based on the very limited data on concentrations of dibutyl phthalate in various media (ambient air, indoor air, drinking water, food, and soil) and the reference values for body weights and intakes of these environmental media (EHD, 1992), the average daily intake of dibutyl phthalate for different age groups in the general population has been estimated (Table 2). It should be noted, however, that due to limitations of the available data base, it was not possible to estimate intakes on the basis of mean concentrations in all media, but rather less representative ranges were used for soil and indoor air. Based on these estimates, the principal media of exposure to dibutyl phthalate for the general population in Canada listed in order of their relative importance are as follows: food, indoor air, drinking water, soil, and ambient air. In addition, members of the general population are also exposed to dibutyl phthalate by a dermal route, particularly from cosmetics, though available data were insufficient to estimate intake from this source.

Based on the medium-specific intakes, it is estimated that the average daily intake of dibutyl phthalate for the various age groups in the general population in Canada range from 1.9 to 5.0 µg/[kg (b.w.)·d]. It should be noted that these estimates do not include intake from consumer products. Based on the percentage content of dibutyl phthalate in some cosmetics (0.1 to between 10 and 25%), these products could contribute significantly to the exposure of some members of the general population.

3.3.2 *Effects*

Carcinogenicity is potentially the most sensitive endpoint for assessment of "toxic" under CEPA. The potential carcinogenicity of dibutyl phthalate has not been examined in epidemiological studies in human populations and available data are considered inadequate to assess the carcinogenicity of dibutyl phthalate in experimental animals. The weight of available data in *in vitro* assays indicates that dibutyl phthalate is not genotoxic. Dibutyl phthalate has been classified, therefore, in Group VI ("Unclassifiable with Respect to its Carcinogenicity to Humans") of the classification scheme for carcinogenicity developed for the assessment of "toxic" under Paragraph 1 (c) of CEPA (EHD, 1992). For compounds classified in Group VI, a Tolerable Daily Intake (TDI) is derived on the basis of an NO(A)EL or LO(A)EL for the most relevant route of exposure divided by an uncertainty factor. For dibutyl phthalate, most of the studies have been conducted by the oral route of exposure, and on the basis of limited available data on concentrations in various media, this is believed to be the most important route of intake of this compound for humans.

Table 2 Estimated Daily Intake of Dibutyl Phthalate for the General Population in Canada

Substrate/ Medium[a]	Estimated Intake (µg/[kg(b.w.)·day])				
	Age				
	0 to 0.5 yr[b]	0.5 to 4 yr[c]	5 to 11yr[d]	12 to 19 yr[e]	20 to 70 yr[f]
Ambient air	0.000 2 to 0.000 3	0.000 3 to 0.000 4	0.000 3 to 0.000 4	0.000 3 to 0.0004	0.000 2 to 0.000 3
Indoor air	0.7	0.9	1.1	0.9	0.8
Drinking water	0.1	0.06	0.03	0.02	0.02
Food	1.6	4.1	3.2	1.4	1.1
Soil	<0.000 5 to 0.007	<0.000 4 to 0.005	<0.000 1 to 0.002	<0.000 04 to 0.000 5	<0.000 03 to 0.000 4
Total Estimated Intake	~2.4	~5.0	~4.3	~2.3	~1,9

a Mean concentrations in ambient air based on a small study in a limited region of Ontario were 4.5 to 6.2 ng/m^3 (Hoff and Chan, 1987); the rather high concentrations in ambient air near an incinerator reported by Thomas (1973) were not incorporated into the estimation of total daily intake since they are not likely to be representative for the general population under current conditions and have not been confirmed elsewhere; the maximum concentration in indoor air was 2.85 µg/m^3 based on a small and possibly unrepresentative number (n = 9) of homes in Montreal; mean values were not specified (Otson and Benoit, 1985). It is assumed that people generally spend 4 hours outdoors and 20 hours indoors (EHD, 1992). Dibutyl phthalate was not detected in drinking water (detection limit 1.0 µg/L) in a regional study in Ontario (OME, 1984); mean values in surface water and groundwater supplies in Alberta were 1.0 µg/L (Spink, 1986). Intake of dibutyl phthalate was estimated based on the concentrations in the various food types of a market basket survey (NHW, 1992) multiplied by the age-specific intakes of various food stuffs from the Nutrition Canada survey (EHD, 1992). The dibutyl phthalate content in the soil in urban areas of Port Credit, Oakville, and Burlington, Ontario, ranged from <0.1 to 1.4 µg/g (Golder Associates, 1987). Available data were insufficient to estimate intake from consumer products, though cosmetics may contribute significantly to the exposure of some members of the general population in certain age groups.

b Weighs 7 kg, breathes 2 m^3 air, drinks 0.75 L water, and ingests 35 mg soil/day (EHD, 1992).

c Weighs 13 kg, breathes 5 m^3 air, drinks 0.8 L water, and ingests 50 mg soil/day (EHD, 1992).

d Weighs 27 kg, breathes 12 m^3 air, drinks 0.9 L water, and ingests 35 mg soil/day (EHD, 1992).

e Weighs 57 kg, breathes 21 m^3 air, drinks 1.3 L water, and ingests 20 mg soil/day (EHD, 1992).

f Weighs 70 kg, breathes 23 m^3 air, drinks 1.5 L water, and ingests 20 mg soil/day (EHD, 1992).

The limited data available on effects of dibutyl phthalate in humans are insufficient to serve as the basis for establishment of an effect level for derivation of a TDI. Based on adequately conducted and documented studies in experimental animals, the most sensitive endpoint for establishment of a TDI for dibutyl phthalate is fetotoxic and possible teratogenic effects. The lowest reported NOEL was that observed in the study by Hamano *et al.* (1977) in which the number of live offspring was decreased, incidence of external defects (spina bifida, exencephaly, cleft palate, non-closing eyelid) and skeletal anomalies (insignificantly) were increased in the offspring of mice administered 625 mg/[kg (b.w.) ·d] throughout gestation. At this highest dose, an increase in kidney weight in the mothers was reported. The NOEL in this study was 62.5 mg/[kg (b.w.) ·d].

The possible teratogenic potential of dibutyl phthalate has also been observed in mice and rats exposed to higher doses. A borderline increase in fetal neural tube defects (exencephaly and myeloschisis) was observed in the offspring of mice following oral administration of 2100 mg/[kg (b.w.) ·d] during gestation, a dose that induced a significant reduction in body weight gain by day 18 in the mothers (Shiota and Nishimura, 1982). Increases in skeletal malformations have also been reported in the offspring of rats exposed intraperitoneally to doses of 320 mg/[kg (b.w.)·d] or greater, though maternal toxicity was not addressed in this study (Singh *et al.,* 1972).

On the basis of these data, a TDI has been derived as follows:

$$\text{TDI} = \frac{62.5 \text{ mg/[kg (b.w.) ·d]}}{1000}$$

$$= 0.0625 \text{ mg/[kg (b.w.) ·d]} \{(63 \text{ µg/[kg (b.w.) ·d]}\}$$

where:

- 62.5 mg/ [kg (b.w.) ·d] is the lowest reported NOEL in an adequate study (for fetotoxic and teratogenic effects in mice observed at the next highest dose) (Hamano *et al.,* 1977);

- 1000 is the uncertainty factor (x 10 for intraspecies variation, x 10 for interspecies variation and x 10 for severity of the effect at the LOAEL in the critical study - i.e., teratogenicity and for inadequacies of the data base - i.e., lack of adequate data on chronic toxicity and carcinogenicity); this factor is considered to be quite conservative in view of the rather large variation between the administered doses in the critical study - i.e., the LOAEL is 10 times greater than the NOEL.

The effect level for developmental toxicity on which the TDI is based is less than those reported to induce effects in other identified studies. The lowest no-observed-adverse-effect-level in short-term repeated dose studies was 104 mg/[kg (b.w.) ·d] reported by Lake *et al.* (1991) based on dose-related enlargement of the liver and induction of hepatic enzymes (indicative of peroxisome proliferation) in rats. In long-term (subchronic) studies, the lowest level at which effects were observed

in an adequately documented study was that reported by Nikonorow *et al*. (1973), 120 mg/[kg (b.w.) ·d], which significantly increased liver weight in male and female rats following administration by gavage in olive oil for up to 3 months. Although Radeva and Dinoyeva (1966 in HSE, 1986) reported marked venous congestion in some exposed male rats (strain unspecified) at necropsy following administration of diets containing levels equivalent to 0.1, 1, and 10 mg/[kg (b.w.) ·d] for 7 months, the organ and dose group(s) in which it occurred were not specified. The lowest dose reported to induce reproductive effects was that of Srivastava *et al.* (1990) in which decreases in the weight of the testes, effects on testicular enzymes, and degeneration of the seminiferous tubules were observed in male rats exposed to 500 mg/kg (b.w.)d] or higher. At 250 mg/[kg (b.w.)·d] there were effects on testicular enzymes associated with degeneration of spermatogenic cells {LOAEL = 250 mg/[kg (b.w.)·d]}. Adequate data on the chronic toxicity and carcinogenicity of dibutyl phthalate and information on neuro- and immuno-toxicity of dibutyl phthalate in experimental animals were not identified.

Based on very limited data, the estimated total average daily intakes of dibutyl phthalate for the various age groups in the Canadian population range from 1.9 to 5.0 µg/[kg (b.w.)·d]. These estimated average daily intakes are 13 to 33 times less than the tolerable daily intake derived on the basis of data from bioassays in animal species.

Therefore, on the basis of available data, it has been concluded that dibutyl phthalate is not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health.

3.4 Conclusion

On the basis of available data, it has been concluded that dibutyl phthalate is not entering the environment in a quantity or concentration or under conditions that may have a harmful effect on the environment or that may constitute a danger to the environment upon which human life depends, or to human life or health.

4.0 Recommendations for Research and Evaluation

Several data gaps were identified that limited the assessment of environmental effects of dibutyl phthalate. It is recommended that the following studies be conducted:

1. Monitoring of concentrations of dibutyl phthalate in air, soil, water, aquatic invertebrates (including benthic invertebrates), and fish in areas of suspected dibutyl phthalate contamination under conditions designed to yield interference-free results, is required to better estimate exposure of fish and wildlife to this substance (medium priority).

2. Monitoring of emissions of dibutyl phthalate from incinerators is required to determine the significance of this source of atmospheric dibutyl phthalate (medium priority).

3. Toxicity tests with benthic organisms representative of the Canadian environment are required to determine the effects of sediment-bound dibutyl phthalate (high priority).

In addition, to permit a more complete assessment of the exposure of the general population in Canada to dibutyl phthalate and of its potential effects, the following additional data are desirable:

1. In view of the margin between the estimated total daily intake and Tolerable Daily Intake of dibutyl phthalate, additional data are required on concentrations of dibutyl phthalate in indoor air and information on the absorption of dibutyl phthalate from cosmetics, and continued monitoring of the amount of this compound produced, imported, and used in Canada (high priority).

2. In view of the lack of adequate data on the chronic toxicity or carcinogenicity of dibutyl phthalate, a carcinogenesis bioassay is required in which a wide range of non-neoplastic endpoints are examined, preferably following ingestion in two species (high priority).

3. Additional information is required on the possible teratogenicity of dibutyl phthalate in experimental animals from studies in which maternal toxicity is well examined, and studies on neurotoxic and immunotoxic effects of dibutyl phthalate in experimental animals (high priority).

4. Additional information is required on possible neurotoxic and reproductive effects in populations exposed primarily to dibutyl phthalate in the occupational environment (high priority).

5.0 References

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