Canadian Environmental Protection Act, 1999

Follow-up Report on a PSL1 Substance for Which Data Were Insufficient to Conclude Whether the Substance Was "Toxic" to Human Health

Non-pesticidal Organotin Compounds

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LIST OF ACRONYMS AND ABBREVIATIONS

CEPA 1988	*Canadian Environmental Protection Act*
CEPA 1999	*Canadian Environmental Protection Act, 1999*
kg-bw	kilogram body weight
LOAEL	Lowest-Observed-Adverse-Effect Level
LOEL	Lowest-Observed-Effect Level
NOEL	No-Observed-Effect Level
PSL1	first Priority Substances List
PVC	polyvinyl chloride

SYNOPSIS

Non-pesticidal organotin compounds are imported into Canada mainly for use as poly(vinyl chloride) (PVC) stabilizers and as industrial catalysts. Canadian producers of methyltin heat stabilizers have not been identified; however, since 1995, approximately 400 tonnes of butyltin and octyltin heat stabilizers have been produced domestically each year. During that period, total annual imports of organotins (excluding tributyltin oxide) ranged from 400 to1200 tonnes.

Non-pesticidal organotin compounds were included on the first Priority Substances List (PSL1) under the 1988 *Canadian Environmental Protection Act* (CEPA 1988) for assessment of potential risks to the environment and human health. As outlined in the Assessment Report for these compounds, released in 1993, relevant data identified before June 1992 were considered insufficient to conclude whether non-pesticidal organotin compounds were “toxic” to human health as defined in Paragraph 11(c) under CEPA 1988.

Critical data relevant to both estimation of exposure of the general population in Canada and assessment of effects were identified following release of the PSL1 assessment and prior to December 2000. Based on consideration of this information, the margins of exposure between bounding estimates of exposure of the general public and the Lowest-Observed-Effect Levels in adequate studies are considered sufficient to protect human health.

Based on available data, it is concluded, therefore, that non-pesticidal organotin compounds are not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health. Therefore, non-pesticidal organotin compounds are not considered “toxic” to human health as defined in Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

Based upon current use patterns, therefore, investigation of options to reduce exposure in relation to Paragraph 64(c) of CEPA 1999 is not considered to be a priority at this time. . Future uses of these compounds should continue to be monitored to ensure that exposure does not increase to any significant extent, and relevant data should be considered upon development of more sensitive testing strategies for endocrine disrupting effects.

1.0 INTRODUCTION

A common Introduction, which describes the process for the preparation of the updates of the Assessment Reports for the seven substances (including non-pesticidal organotin compounds) on the first Priority Substances List (PSL1) for which data were considered insufficient to conclude whether the substances were "toxic" to human health under the 1988 *Canadian Environmental Protection Act* (CEPA 1988), is posted on all web sites where the Assessment Reports appear.[1]

The strategy for the literature search to identify critical new data (including commercial activity in Canada, human exposure and effects) on non-pesticidal organotin compounds is presented in Appendix A of this Assessment Report. Only relevant data acquired prior to December 2000 were considered in the determination of whether non-pesticidal organotin compounds are "toxic" to human health under Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

In the PSL1 Assessment Report, the evaluation of effects on human health was limited to a subset of the total of 94 relevant compounds included on the Domestic Substances List (Government of Canada, 1993) for which at least some data on mammalian toxicity were identified, in addition to the following closely related compounds: monomethyltin(mercaptoethyl oleate) sulphide, dimethyltin dibromide, dioctyltin dichloride, dioctyltin oxide and dioctyltin bis(mercaptopropionate).

In each of the other six updates of Assessment Reports for substances for which data were considered insufficient to conclude whether the substances were "toxic" to human health under CEPA 1988, presentation is restricted primarily to critical new data that impact on the earlier outcome. In this update, based on information developed since the PSL1 assessment was released, upper bounding estimates of exposure of the general population in Canada are presented. Margins between these estimates of exposure and the lowest-effect levels for each of the non-pesticidal organotin compounds from toxicological studies, including both those reviewed in the PSL1 assessment and those that have become available since that time, are considered.

A draft follow-up report was made available for a 60-day public comment period (between September 28, 2002 and November 27, 2002). No comments were received.

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[1] See "Introduction to Assessment Reports for Reconsideration of PSL1 Substances for Which Data Were Insufficient to Conclude Whether the Substances Were 'Toxic' to Human Health (Paragraph 11(c), CEPA 1988; Paragraph 64(c), CEPA 1999)" at the following web site: www.hc-sc.gc.ca/hecs-sesc/exsd/ps11.htm

2.0 SUMMARY OF THE HUMAN HEALTH RISK ASSESSMENT FOR NON-PESTICIDAL ORGANOTIN COMPOUNDS CONDUCTED UNDER CEPA 1988 (BASED UPON INFORMATION IDENTIFIED UP TO JUNE 1992) (GOVERNMENT OF CANADA, 1993)

At the time of release of the PSL1 Assessment Report (Government of Canada, 1993), non-pesticidal organotin compounds (notably monomethyl- and dimethyltin, butyltin and octyltin compounds) were not manufactured in Canada. They were imported, however, mainly for use as poly(vinyl chloride) (PVC) stabilizers and as industrial catalysts. In 1984, approximately 290 tonnes of methyltin compounds, 1020 tonnes of butyltin compounds and a much smaller quantity of octyltin compounds were imported into Canada. Relevant data were insufficient to derive quantitative estimates of exposure for the general population in Canada for any of the non-pesticidal organotin compounds. While potential for migration of stabilizers from PVC, which is used fairly extensively in distribution systems in Canada, was recognized (Lister, 1992), only one account of relevant data on concentrations in drinking water was identified. This was a report on levels of monomethyl- and dimethyltin in a limited number of tap water samples collected in Florida in 1977 (Braman and Tompkins, 1979). Identified data on concentrations in foodstuffs in Canada were restricted to detection of monobutyl- and dibutyltin in a limited number of samples of canned and fresh molluscs (Forsyth and Cleroux, 1991), butyltin in some fruit drinks (Forsyth, 1992) and both monooctyl- and dioctyltin in a limited number of edible oils and fruit drinks (Forsyth, 1992).[2]

At the time of release of the PSL1 assessment, identified data on the effects of non-pesticidal organotins were limited to monomethyltin, dimethyltin, monobutyltin, dibutyltin, monooctyltin and dioctyltin compounds. In the only carcinogenicity bioassay identified, there was no evidence of carcinogenicity in male rats and mice and no convincing evidence in female mice exposed to dibutyltin diacetate. Results in female rats were inadequate for assessment (NCI, 1978). Additional data on the carcinogenicity of any of the non-pesticidal organotin compounds considered in the assessment were restricted to inadequate studies on mixtures of monomethyltin and dimethyltin compounds (Mosinger, 1979).

Studies on the genotoxicity of monomethyltin were not identified. Dimethyltin did not bind irreversibly to DNA *in vitro* (Barbieri and Silvestri, 1991). Dibutyltin compounds were not genotoxic in the *Salmonella*/microsome test or in a dominant lethal assay in *Drosophila*; a mutagenic response in ovary cells of Chinese hamsters was reported in a limited study in which there was no positive control or replication (Li et al., 1982). Dibutyltin dichloride was positive in an *in vivo* mouse micronucleus test (Life Sciences Research Ltd., 1991).

Based on preliminary review of available information, data on subchronic repeated-dose toxicity appeared to be adequate for monomethyltin, dimethyltin and dibutyltin compounds. Although subchronic studies on dioctyltin compounds were available, they were considered, on

[2] Subsequently published as Forsyth *et al*. (1993b).

the basis of preliminary review, to be limited in terms of number of dose levels, duration of exposure, group sizes and, possibly, the range of endpoints examined.

Based primarily on limitations of information to serve as a basis for estimation of exposure, therefore, **data were considered insufficient to conclude whether non-pesticidal organotin compounds were "toxic" as defined under Paragraph 11(c) of CEPA 1988.**

3.0 POST-PSL1 ANALYSIS (BASED UPON INFORMATION IDENTIFIED BETWEEN JUNE 1992 AND DECEMBER 2000)

3.1 Production, importation, use and release

No Canadian producers of methyltin heat stabilizers were identified (Camford Information Services, 2001a). However, since 1995, 400 tonnes of butyltin and octyltin heat stabilizers have been produced annually by a company in Brantford, Ontario (Camford Information Services, 2001b).

For all organotin compounds (except tributyltin oxide), there has been an (irregular) increase in importation over time (Camford Information Services, 2001a,b). In 1980 and 1983, 96 and 997 tonnes were imported, respectively. Annual imports were 432, 687, 994, 1168 and 859 tonnes in 1995, 1996, 1997, 1998 and 1999, respectively.

Based on a survey conducted in 1999 of the 35 vinyl processors that account for 80% of the total amount of PVC resin (as 100% resin) consumed in Canada, tin (as methyltin, butyltin and octyltin heat stabilizers) was the metal used in largest quantity in vinyl additives (excluding pigments) (Cheminfo Services Inc., 2000). The consumption of butyltin, methyltin and octyltin was 4241, 1217 and 184 tonnes, respectively.

Octyltin compounds are regulated by Health Canada under Division 23 (Food Packaging Materials) of the Food and Drug Regulations (DNHW, 1986). This limits the proportion either singly or in combination in food packaging that has been manufactured from a PVC formulation containing any or all of the octyltin chemicals — namely, di(n-octyl)tin S,S'-bis(isooctylmercaptoacetate), di(n-octyl)tin maleate polymer and (n-octyl)tin S,S',Stris(isooctylmercaptoacetate) — to 3% of the resin, and the food in contact with the package to not more than 1 ppm total octyltin.

3.2 Population exposure

The following presentation is limited to identified recent data that are considered critical to quantitative estimation of exposure of the general population in Canada to non-pesticidal organotin compounds and, hence, to assessment of "toxic" under Paragraph 64(c) of CEPA 1999. Other less relevant recent data that were also identified include Forsyth *et al.* (1993a), Elgethun *et al.* (2000), Kannan *et al.* (1995, 1999, 2000) and Robinson and Kluck (2000).

As follow-up to the PSL1 Assessment Report (Government of Canada, 1993), Health Canada conducted a survey of organotin compounds in Canadian drinking water. Organotin compounds, mainly monomethyltin and monobutyltin, were detected at concentrations ranging up to 22 ng Sn/L and 43.6 ngSn/L, respectively, in distributed water samples from six municipalities in Canada (Sadiki and Williams, 1996). No organotins were detected in raw water samples, indicating that the organotins were likely leaching into the water from some component of the distribution system.

In 1995, organotin compounds were determined in samples of raw and treated water at treatment plants and tap water from distribution lines where PVC pipes/tubing had been recently installed (Sadiki et al., 1996). Although organotins were not detected in either raw water or treated water sampled at the treatment plants, several were present in the samples from distribution systems. Methyltin and dimethyltin were detected at concentrations ranging from 0.5 to 257 ng Sn/L and from 0.5 to 6.5 ng Sn/L, respectively, in samples from 10 of 22 houses. Butyltin compounds were detected in water at only 3 of the 22 houses. Monooctyltin and dioctyltin were not detected in any samples. The authors noted that the highest concentrations of organotins were present in water from those houses supplied by distribution systems where PVC pipes had been most recently installed. These observations were consistent with the results of earlier studies of leaching from PVC pipe conducted by Health Canada (Forsyth and Jay, 1997).

An additional survey was carried out in 1996, with sampling at 28 sites in winter/spring and 21 sites in autumn in eight provinces (Sadiki and Williams, 1999). At each site, 3–6 samples were collected: raw water at the treatment plant, treated water at the treatment plant and water at one or several points of use (houses, commercial buildings, hydrants) in distribution systems where PVC or polyethylene pipes were recently installed. Additional samples were collected in summer 1996, approximately 4–6 months after the first sampling at the five sites where the concentrations of organotin were highest in the winter/spring survey.

Except for one treated water sample in the winter/spring survey, no organotin compounds were detected in raw or treated water collected at water treatment plants or in distributed water supplied through polyethylene pipes. Organotins were detected in samples of water from distribution systems supplied through PVC pipes in both the winter/spring (25/94; 27%) and autumn (28/70; 40%) surveys.

The maximum concentrations of non-pesticidal organotins were as follows: monomethyltin, 291 ng Sn/L; dimethyltin, 49.1 ng Sn/L; monobutyltin, 28.5 ng Sn/L; and dibutyltin, 52.3 ng Sn/L. It should be noted that only eight samples had quantifiable concentrations of either monobutyltin (5.6–28.5 ng Sn/L, three samples) or dibutyltin (1.3–52.3 ng Sn/L, five samples). Of importance is the observation by the authors that concentrations of methyltins decreased in most water samples throughout the year.

Since the release of the PSL1 assessment, Health Canada has conducted a survey of blended wines for organotin content (Forsyth et al., 1994). Twenty-nine of 90 wines tested (32.2%) had at least one organotin present. Monooctyl- and dioctyltin were present in one sample only, at concentrations of 2.41 and 0.12 ng/mL, respectively. Concentrations of monobutyltin in red wine ranged from <0.05 to 0.11 ng/mL; levels in white wine were from <0.05 to 0.20 ng/mL. Concentrations of dibutyltin in red wine ranged from <0.08 to 1.55 ng/mL; levels in white wine were from <0.08 to 1.04 ng/mL. Method detection limits ranged from 0.04 to 0.05 ng Sn/mL. Methodology is currently being developed for a survey of organotin compounds in seafood (Forsyth, 2001).

Estimates of the total daily intake of non-pesticidal organotin compounds for each of six age groups within the general population of Canada and the assumptions upon which they are based are presented in Table 1. For each of the organotin compounds, upper bounding estimates of daily intake from drinking water were <0.1 μg Sn/kg-bw per day (Table 1). The estimates of daily intake of organotins from drinking water should be considered to be upper bounding, since they are conservative in several respects. Estimated intake from drinking water is based on total consumption of tap water (tap water-amended beverages, reconstituted infant formula) rather than tap water consumed as drinking water alone (EHD, 1998). The estimates of intake of monomethyltin, dimethyltin, monobutyltin and dibutyltin from drinking water are also based on the four maximum concentrations reported by Sadiki and Williams (1999). For monomethyltin and dimethyltin, this represents the total daily intake, as concentrations in other media were not identified. Neither monooctyltin nor dioctyltin was detected in the pilot drinking water survey (Sadiki et al., 1996), which is consistent with the only identified use for octyltins in Canada being heat stabilizers for PVC food packaging (Government of Canada, 1993).

The highest concentrations of each of the four organotins identified in drinking water were determined in drinking water collected in homes or commercial buildings in which the water was supplied by recently installed PVC pipes/tubing. However, data of Sadiki and Williams (1999) indicate that concentrations of monomethyltin and dimethyltin decrease over time, with concentrations of monomethyltin and dimethyltin approaching the limit of detection within 4–6 months. At the 18 sites for which samples were collected at a 4- to 6-month interval, monomethyltin was quantified at all sites in the winter/spring sampling. In the samples collected in summer, concentrations had decreased at 16 sites (levels at 5 were either not detected or not quantifiable). Similarly, dimethyltin was detected at 12 of the 18 sites in the winter/spring sampling; in the summer, concentrations had decreased at all sites (eight were either not detected or not quantifiable).

Data are inadequate to meaningfully characterize total intake of organotin compounds from food. However, maximum intakes for butyltin and octyltin compounds calculated on the basis of the few identified concentrations for a maximum of. seven foodstuffs sampled from 1990 to 1993 are presented in Table 1.

Although the estimated intakes via foodstuffs are based on a few small surveys of only a limited range of foodstuffs, they are considered to be conservative. The analyses were conducted on foodstuffs that were considered to be most highly contaminated with organotins as a result of proximity to sources of these compounds (antifouling organotins for shellfish, PVC plastics containing organotin stabilizers for other foodstuffs). Based upon use patterns of organotins, other categories of foodstuffs would not be expected to be in contact with obvious sources of these substances. In addition, the maximum concentration of each organotin measured in the available surveys was used in estimating intake, whereas the majority of samples contained no detectable residues. Finally, the levels in shellfish, which were determined in samples collected in the late 1980s or in 1990, most likely represent overestimates of current levels. As noted in the PSL1 report, the monobutyltin and dibutyltin in these shellfish samples likely resulted from the antifouling pesticide tributyltin, applied to either boats or nets in aquaculture; however, no organotin products are currently registered for aquacultural uses, and it is likely that there have been substantial decreases in environmental concentrations of butyltins, as is the case in other countries subsequent to the application of such regulations.

These limited estimates have been combined with the intakes from total tap water to provide the upper bounding estimated intake from identified sources of exposure. All upper bounding estimates of total daily intake are <0.1 µg Sn/kg-bw per day.

These estimates do not take into account potential intake from air, since data on concentrations of non-pesticidal organotin compounds in either indoor or ambient air were not identified. However, based on limited data on physical/chemical properties, (including low volatility and relatively high boiling points) (Government of Canada, 1993), they are also unlikely to volatilize to the atmosphere in significant quantities.

3.3 Hazard characterization

3.3.1 Methyltin

The database on the toxicity of monomethyltin is limited. In many of the studies, the test compound was a mixture of monomethyl- and dimethyltin. Some of the studies were poorly reported; in one investigation, the route of administration was by intraperitoneal injection. The most extensive study was a subchronic dietary study in rats in which body weight, food intake, hematological and clinical chemistry parameters, urinalysis, organ weights and histological effects on the liver and kidney were examined.(Til *et al*., 1973). Although the group sizes were small (n = 5), there were three dose levels. No effects were observed at the lowest dose; at the mid dose (Lowest-Observed-Effect Level [LOEL] = 4 mg Sn/kg-bw per day), there was a slight increase in blood urea nitrogen in both sexes. (An increase in weight of thymus was observed at all doses in males, but was significant only at the highest dose.)

Although the database for dimethyltin was more extensive than for monomethyltin, the studies were older; in several, there was only one level of exposure. In several subchronic studies with rats and one with dogs, no effects were observed at the highest level of exposure. The lowest effect level reported was in a subchronic study with rats (ClinTrials BioResearch, 1997),[3] in which neuropathological lesions were observed at 0.78 mg Sn/kg-bw per day (Lowest-Observed-Adverse-Effect Level [LOAEL]) administered in drinking water.

3.3.2 Butyltin

The database for monobutyltin was also limited. However, in a reproductive/developmental assay in rats in which there were four levels of exposure (Noda *et al*., 1992), no effects upon dams, reproductive parameters or fetuses were observed at any dose. The No-Observed-Effect Level (NOEL) was 168 mg Sn/kg-bw per day. In a developmental toxicity assay (Ema *et al.*, 1995) with rats, although maternal weight gain was decreased at 421 mg Sn/kg-bw per day (maternal LOAEL), there were no adverse developmental effects.

There was a comparatively large database of studies in which animals were exposed to dibutyltin compounds. Most were designed to investigate only reproductive/developmental or immunological effects. Three studies were identified with similar LOELs. The lowest effect level was reported by Subramoniam *et al*. (1994), in a study in which rats were orally administered dibutyltin for 2 weeks. There was a decrease in thymus weight at 0.24 mg Sn/kg-bw per day (LOEL). Rats dosed 3 times weekly for 9 weeks had suppressed primary antibody response at 0.39 mg Sn/kg-bw per day (LOEL) (Seinen et al., 1977). In a reproductive/developmental protocol (Noda *et al*., 1992), rats exposed by gavage had decreased absolute and relative weight of thymus at 0.58 mg Sn/kg-bw per day (marginal maternal LOEL; statistical significance of weight decrease unclear). The database for dibutyltin compounds included one adequate subchronic dietary assay in rats (Gaunt *et al*., 1968), in which the concentration of hemoglobin was reduced and body weight decreased (possibly due to palatability of the test diet) in females at 2.11 mg Sn/kg-bw per day (LOEL). There were no effects upon urinalysis, organ weight or histological examination of brain, pituitary, heart, thyroid, liver, spleen, kidney, adrenal or gonads.

3.3.3 Octyltin

There were no adequate studies identified in which effect levels could be designated for monooctyltin compounds. However, data for dioctyltin compounds, which are reasonably expected to be more toxic that the corresponding monoalkyltin, are available.

In studies with dioctyltin compounds, the lowest effect levels were 0.57 mg Sn/kg-bw per day, for immunological effects in guinea pigs following 5 weeks of dietary exposure (Seinen et al., 1977), and 0.79 mg Sn/kg-bw per day, for systemic effects such as bile duct proliferation in rats in a subchronic dietary assay (Hazleton Laboratories Inc., 1971). In the latter investigation,

[3] The test compound consisted of ~90% dimethyltin dichloride, ~10% monomethyltin trichloride and <0.1% trimethyltin chloride.

the endpoints examined included body weight, food consumption, hematology, clinical chemistry, urinalysis, organ weight and histological examination of liver and kidney.

3.4 Human health risk characterization and conclusion

3.4.1 Methyltin

In the most extensive study (Til *et al.*, 1973), the LOEL for monomethyltin was 4 mg Sn/kg-bw per day, based upon a slight increase in blood urea nitrogen in both sexes of rats. This LOEL is 129 000 times greater than the upper bounding estimate of total daily intake of monomethyltin from total tap water, based upon the highest concentration of that species in drinking water reported by Sadiki and Williams (1999). No data on concentrations of monomethyltin in foodstuffs were identified.

The lowest effect level reported for dimethyltin was in a subchronic drinking water study in rats (ClinTrials BioResearch, 1997), in which neuropathological lesions were observed at 0.78 mg Sn/kg-bw per day (LOAEL). This LOAEL is 150 000 times greater than the upper bounding estimate of intake of dimethyltin from total tap water, based upon the maximum concentration reported in the Health Canada drinking water survey (Sadiki and Williams, 1999). No data were identified for concentrations of dimethyltin in foodstuffs.

3.4.2 Butyltin

A NOEL for monobutyltin of 168 mg Sn/kg-bw per day was reported by Noda *et al.* (1992) in a reproductive/developmental assay in rats. This NOEL is.31 million times greater than the upper bounding estimate of intake of monobutyltin from total tap water and food, based upon the highest concentration of monobutyltin reported by Sadiki and Williams (1999) and limited data on concentrations of monobutyltin in six foodstuffs. A maternal LOAEL of 421 mg Sn/kg-bw per day (based upon decreased weight gain) for rats administered monobutyltin (Ema *et al*., 1995) is 78 million times greater than the above upper bounding estimate of intake of monobutyltin from total tap water and food.

Three studies were identified with similar LOELs for dibutyltin (ranging from 0.24 to 0.58 mg Sn/kg-bw per day), based upon effects on thymus and primary antibody response Seinen *et al.*, 1977; Noda *et al.*, 1992; Subramoniam *et al.*, 1994). These LOELs are from. 43 000 to 104 000 times greater than the upper bounding estimate of intake of dibutyltin from total tap water based upon the highest concentration reported by Sadiki and Williams (1999) and concentrations of dibutyltin in five foodstuffs.

3.4.3 Octyltin

Adequate studies as a basis for identification of meaningful effect levels for monooctyltin compounds were not identified. The upper bounding estimate of intake of monooctyltin, based upon reported concentrations in six foodstuffs, is 0.08 µg/kg-bw per day, for infants up to 6 months of age.

In studies with dioctyltin compounds, the lowest effect levels were 0.57 mg Sn/kg-bw per day, for immunological effects in guinea pigs (Seinen *et al.*, 1977), and 0.79 mg Sn/kg-bw per day, for systemic effects such as bile duct proliferation in rats (Hazleton Laboratories Inc., 1971). These LOELs for guinea pigs and rats are 15 000 and 20 800 times greater, respectively, than the upper bounding estimate of intake of 0.038 µg/kg-bw per day for infants, based upon data for only six foods.

These margins of exposure are considered to be conservative, since the upper bounding estimates of exposure are based upon data from studies in which samples of drinking water and foodstuffs were selected because they were expected to contain the highest levels of organotins. These margins of exposure between the effect levels in the toxicity studies and the upper bounding estimates of exposure are considered adequate to address elements of uncertainty dealing with, for example, inter- and intraspecies variation and less than chronic study.

On this basis, non-pesticidal organotin compounds are not considered "toxic" as defined in Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999*.

3.5 Uncertainties and degree of confidence in human health risk characterization

There is a high degree of confidence in the data on concentrations of non-pesticidal organotin compounds in drinking water, as they were based upon the results of extensive sampling by Health Canada. There is a low degree of confidence in data on concentrations of non-pesticidal organotins in foodstuffs. However, it should be noted that, although sampling was not extensive, foodstuffs were targeted in which it would be expected that organotins would be present.

There is a low degree of confidence in the database on health effects of non-pesticidal organotins. Identified studies in laboratory animals were composed, for the most part, of older studies of short-term duration.

3.6 Considerations for follow-up

Based upon current use patterns, investigation of options to reduce exposure is not considered to be a priority at this time. Future uses of these compounds should continue to be monitored to ensure that exposure does not increase to any significant extent. Review of any additional data that become available on monooctyltin compounds is also desirable. In view of the structural similarity with the pesticidal organotins, relevant data should also be considered upon development of more sensitive testing strategies for endocrine disrupting effects

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Table 1: Upper bounding estimates of exposure to organotin compounds

Organotin compound	Age group	Total tap water		Food		Intake from both total tap water and food (µg Sn/kg-bw per day)[b]
		Maximum identified concentration in drinking water (µg Sn/L)[1]	Intake (µg Sn/kg-bw per day)[2]	Concentrations in foods (numerical designation of specific foods reported in EHD [1998])	Intake from food (µg Sn/kg-bw per day)[b]	
Monomethyl	0–6 months[3]	0.291	0.031	no data		
	6 months–4 years[4]		0.0131			
	5–11 years[5]		0.0103			
	12–19 years[6]		0.0059			
	20–59 years[7]		0.0062			
	60+ years[8]		0.0065			
Dimethyl	0–6 months[3]	0.0491	0.0052	no data		
	6 months–4 years[4]		0.0022			
	5–11 years[5]		0.0017			
	12–19 years[6]		0.001			
	20–59 years[7]		0.001			
	60+ years[8]		0.0011			

Organotin compound	Age group	Total tap water		Food		Intake from both total tap water and food (µg Sn/kg-bw per day)[b]
		Maximum identified concentration in drinking water (µg Sn/L)[1]	Intake (µg Sn/kg-bw per day)[2]	Concentrations in foods (numerical designation of specific foods reported in EHD [1998])	Intake from food (µg Sn/kg-bw per day)[b]	
Monobutyl	0–6 months[3]	0.0285	0.003	Monobutyltin, identified concentrations in foods: #47 (shellfish), 1.2 ng/g in fresh clams[9] #48 (canned shellfish), 5.9 ng/g in canned mussels[9] #123 (citrus juice, fresh), 0.2 ng/mL in orange juice[10] #124 (citrus juice, canned), 0.2 ng/mL in orange juice[10] #126 (fruit juice, canned), 0.2 ng/mL in orange juice[10] #130 (grape juice, bottled), 0.2 ng/mL in grape juice[10] #174 (red wine), 0.11 ng/mL in wine[11]	0.0024	0.0054
	6 months–4 years[4]		0.0013		0.0012	0.0025
	5–11 years[5]		0.001		0.0005	0.0015
	12–19 years[6]		0.0006		0.0003	0.0009
	20–59 years[7]		0.0006		0.0004	0.0010
	60+ years[8]		0.0006		0.0002	0.0008
Dibutyl	0–6 months[3]	0.0523	0.0056	Dibutyltin, identified concentrations in foods: #44 (fish, marine), <1 ng/g in cod[9] #45 (fish, fresh), <1 ng/g in trout[9] #47 (shellfish), 4.8 ng/g in fresh clams[9] #48 (canned shellfish), 46.7 ng/g in canned mussels[9] #174 (red wine), 1.55 ng/mL in wine[11]	<0.0001	0.0056
	6 months–4 years[4]		0.0024		0.0003	0.0027
	5–11 years[5]		0.0019		0.0008	0.0027
	12–19 years[6]		0.0011		0.0008	0.0019
	20–59 years[7]		0.0011		0.0016	0.0027
	60+ years[8]		0.0012		0.0007	0.0019

Organotin compound	Age group	Total tap water		Food		Intake from both total tap water and food (µg Sn/kg-bw per day)[b]
		Maximum identified concentration in drinking water (µg Sn/L)[1]	Intake (µg Sn/kg-bw per day)[2]	Concentrations in foods (numerical designation of specific foods reported in EHD [1998])	Intake from food (µg Sn/kg-bw per day)[b]	
Monooctyl	0–6 months[3]	No data		Monooctyltin, identified concentrations in foods: #123 (citrus juice, fresh), 11.7 ng/mL in papaya juice[10] #124 (citrus juice, canned), 11.7 ng/mL in papaya juice[10] #126 (fruit juice, canned), 4.8 ng/mL in apple juice[10] #130 (grape juice, bottled), 4.8 ng/mL in grape juice[10] #155 (vegetable fats and oils), 26.9 ng/g in corn oil[12] #174 (red wine), 2.41 ng/mL in wine[11]	0.0838	
	6 months–4 years[4]				0.0494	
	5–11 years[5]				0.0197	
	12–19 years[6]				0.0116	
	20–59 years[7]				0.0132	
	60+ years[8]				0.0082	
Dioctyl	0–6 months[3]	No data		Dioctyltin, identified concentrations in foods: #123 (citrus juice, fresh), 1.0 ng/mL in kiwi juice[10] #124 (citrus juice, canned), 1.0 ng/mL in kiwi juice[10] #126 (fruit juice, canned), 4.3 ng/mL in apple juice[10] #130 (grape juice, bottled), 4.3 ng/mL in grape juice[10] #155 (vegetable fats and oils), 118.4 ng/g in corn oil[12] #174 (red wine), 0.12 ng/mL in wine[11]	0.038	
	6 months–4 years[4]				0.0249	
	5–11 years[5]				0.013	

Organotin compound	Age group	Total tap water		Food		Intake from both total tap water and food (µg Sn/kg-bw per day)[b]
		Maximum identified concentration in drinking water (µg Sn/L)[1]	Intake (µg Sn/kg-bw per day)[2]	Concentrations in foods (numerical designation of specific foods reported in EHD [1998])	Intake from food (µg Sn/kg-bw per day)[b]	
	12–19 years[6]				0.0095	
	20–59 years[7]				0.0108	
	60+ years[8]				0.0065	

1 All concentrations of organotins in drinking water reported by Sadiki and Williams (1999).

2 Calculated on Excel spreadsheet.

3 Assumed to weigh 7.5 kg and to drink 0.8 L of water per day. Assumed to consume on a daily basis: 9.74 g fresh citrus juice, 19.62 g canned citrus juice, 43.53 g canned fruit juice, 15.8 g bottled grape juice (EHD, 1998).

4 Assumed to weigh 15.5 kg and to drink 0.7 L of water per day. Assumed to consume on a daily basis: 1.59 g marine fish, 1.16 g fresh fish, 0.27 g shellfish, 0.02 g canned shellfish, 34.88 g fresh citrus juice, 8.83 g canned citrus juice, 42.08 g canned fruit juice, 4.11 g bottled grape juice, 1.22 g vegetable fats and oils, 0.02 g red wine (EHD, 1998).

5 Assumed to weigh 31.0 kg and to drink 1.1 L of water per day. Assumed to consume on a daily basis: 4.74 g marine fish, 1.08 g fresh fish, 0.27 g shellfish, 0.37 g canned shellfish, 22.55 g fresh citrus juice, 12.9 g canned citrus juice, 26.68 g canned fruit juice, 2.52 g bottled grape juice, 2.04 g vegetable fats and oils, 0.65 g red wine (EHD, 1998).

6 Assumed to weigh 59.4 kg and to drink 1.2 L of water per day. Assumed to consume on a daily basis: 5.09 g marine fish, 1.09 g fresh fish, 0.15 g shellfish, 0.84 g canned shellfish, 32.74 g fresh citrus juice, 10.62 g canned citrus juice, 9.71 g canned fruit juice, 5.29 g bottled grape juice, 3.83 g vegetable fats and oils, 1.56 g red wine (EHD, 1998).

7 Assumed to weigh 70.9 kg and to drink 1.5 L of water per day. Assumed to consume on a daily basis: 7.67 g marine fish, 1.28 g fresh fish, 0.70 g shellfish, 1.57 g canned shellfish, 42.43 g fresh citrus juice, 14.26 g canned citrus juice, 14.47 g canned fruit juice, 2.92 g bottled grape juice, 5.33 g vegetable fats and oils, 18.52 g red wine (EHD, 1998).

8 Assumed to weigh 72.0 kg and to drink 1.6 L of water per day. Assumed to consume on a daily basis: 3.64 g marine fish, 1.28 g fresh fish, 0.32 g shellfish, 0.62 g canned shellfish, 25.73 g fresh citrus juice, 10.27 g canned citrus juice, 10.78 g canned fruit juice, 0.45 g bottled grape juice, 3.26 g vegetable fats and oils, 10.71 g red wine (EHD, 1998).

9 Forsyth and Cleroux (1991). Date of sampling not reported, but probably 1990.

10 Forsyth et al. (1992). Date of sampling not reported, but probably 1991–1992.

11 Forsyth et al. (1994). Date of sampling not reported, but probably 1992–1993.

12 Forsyth et al. (1993b). Date of sampling not reported, but probably 1991–1992.

Appendix A: Search Strategy — New Information for the Assessment of "Toxic" to Human Health Under Paragraph 64(c) of CEPA 1999"

In an update of the literature carried out under contract by BIBRA International (1995), data published from the period 1992 to 1995 were identified from searches of the BIBRA in-house databank, as well as Toxline (U.S. National Library of Medicine), BIOSIS (Biosciences Information Services, Biological Abstracts) and Medline (U.S. National Library of Medicine).

Subsequently, searches were carried out on Toxline Plus. The subfiles of this database include BIOSIS, CA (Chemical Abstracts), CIS (International Labour Office), CRISP (Computerized Retrieval of Information on Scientific Projects, National Institutes of Health), DART (Developmental and Reproductive Toxicology Database, Environmental Teratology Information Centre), EPIDEM (Epidemiology Information System, Toxicology Information Response Centre), FEDRIP (Federal Research in Progress), HMTC (HMTC Abstracts Bulletin, Hazardous Material Technical Centre), IPA (International Pharmaceutical Abstracts, American Society of Hospital Pharmacists), NTIS (Government Reports Announcements and Indexes, National Technical Information Service), RISKLINE (Swedish National Chemicals Inspectorate) and TSCATS (Toxic Substances Control Act Test Submission to United States Environmental Protection Agency).

In addition, Current Contents (subfiles: Agriculture, Biology and Environmental Sciences; Life Sciences) was searched.