PUBLIC COMMENTS ON AND RESPONSES TO PUBLIC COMMENTS ON THE DRAFT SCREENING HEALTH ASSESSMENT REPORT ON PBDES

Comments on the *Canadian Environmental Protection Act, 1999* (CEPA 1999) Screening Health Assessment Report on Polybrominated Diphenyl Ethers (PBDEs) were provided by K. Martin (Member of Parliament for Esquimalt–Juan de Fuca on behalf of C. Williams-Derry and E. Murray of Northwest Environment Watch), E. MacDonald (Sierra Legal Defence Fund), H. Jones-Otazo and M. Diamond (University of Toronto), B. McElgunn (Learning Disabilities Association of Canada), M.E. Axmith (Canadian Plastics Industry Association) and R.B. Dawson (Bromine Science and Environmental Forum).

As part of its mandate under CEPA 1999, Health Canada strives to prepare defensible screening health risk assessments through a transparent process that includes several stages of internal and external peer review. To ensure the integrity of this process and its timely completion, the process incorporates a cut-off date for addition to the database of information considered in the assessment. Health Canada actively encourages early submission of relevant data; information submitted following the cut-off date is considered primarily to inform decisions regarding risk management, strategic options or priority of the need to update the health risk assessment at a later time.

Comments for which responses have been provided are those related to the basis for the conclusions of the human health risk assessment for PBDEs (see Table 1). Comments related to risk management for PBDEs, which will be considered in subsequent stages of the process, are simply summarized here as part of the complete record (see Table 2). Comments related to the regulatory process, which are not specific to this assessment, are also summarized (see Table 3).

Table 1: Comments on the basis for conclusions in draft Screening Health Assessment Report on PBDEs

Comment	Response
Health Canada should publish the (unpublished) EHD (1998) document, which outlines reference intake values cited in the assessment.	The document containing these reference values will be posted on the Existing Substances Division website (http://www.hc-sc.gc.ca/exsd).
The estimates of exposure for the food groups "cereal products" and "vegetables" were based on data for pizza and french fries, respectively. The uncertainties associated with extrapolation of these data to these food categories should be indicated.	The specific food items included in the exposure estimate were indicated in the text of the Supporting Working Document. This document also contains a discussion of the most significant uncertainties and limitations of the data on which the exposure assessment is based. The uncertainties highlighted by the reviewers, while recognized, contribute less than those highlighted in the report.
If PBDEs were added to the Priority Substances List (PSL) for further assessment because of uncertainties in the database on health effects, such further assessment would take too long and result in delays in implementation of any risk management measures.	As presented in the draft report, Health Canada agrees that the PBDEs should not be placed on the PSL at this time, although it is recognized that uncertainties in the available database that preclude a definitive declaration of "toxic" or not "toxic" to human health under CEPA 1999 could be addressed by additional in-depth evaluation, including likely additional generation of data. However, as is also presented in the draft screening assessment report, in light of PBDEs being considered "toxic" to the environment, measures will likely be introduced to control exposure of environmental organisms to PBDEs. It is expected that these measures will also result in reduction of population exposure in Canada and thus be protective for human health, based on experience in other countries that risk management actions introduced to protect the environment have resulted in a reduction of exposure of humans. Therefore, there will be no delay in taking action as a result of uncertainties in the database concerning health effects.
Children will likely be exposed to PBDEs repeatedly over a long period of time. This exposure scenario is not reflected in the critical study in laboratory animals in which the protocol involved a single exposure.	Health Canada has acknowledged the uncertainties concerning the relevance of the results of the critical study in laboratory animals to the human situation wherein exposure can be continuous on a daily basis. However, this value was selected as the critical effect level in a screening context because it was the lowest level following any period of exposure, including long-term/chronic exposure, observed to induce neurobehavioural or any other effects in the available studies involving specific congeners, congener groups or commercial mixtures.
The opinion was expressed that risks to children were understated by the use of	The "margin of exposure" in screening health assessments is the magnitude of the ratio between the level (dose) at

Comment	Response
the margin of exposure approach rather than a hazard quotient approach involving application of uncertainty factors.	which the critical effect is observed in studies conducted in animals or, in some cases, humans and the upper-bound estimated (or measured) level of human exposure to a substance. Recommendations are based on the adequacy of this margin of exposure, taking into account confidence in the completeness of the identified databases on effects and exposure, within a screening context. The relative uncertainty of and degree of confidence in exposure and effects databases that serve as the basis for decision-making in the assessment of the adequacy of margins of exposure are explicitly delineated and consistent across screening assessments. They are also consistent with similar considerations made for the health risk assessment of Priority Substances under CEPA 1999. Use of the margin of exposure approach obviates the need to develop chemical-specific uncertainty factors, which is considered beyond the scope of a screening assessment (available data for PBDEs would not likely be sufficient to develop such factors). Additional information on the approach to preparation of screening assessments for Domestic Substances List (DSL) substances at Health Canada can be found at http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/exist_substances-substances_existantes_e.pdf.
The potential importance of intake of PBDEs in dust was mentioned, and some recent data on measured concentrations were cited.	While these data were published subsequent to the cut-off date specified in the screening assessment report, the concentrations of PBDEs in dust used to calculate intake in the assessment were greater than those cited in the comments. As well, the estimate of intake of dust for toddlers in the draft report (100 mg/day) was similar to those cited in the comments (113 or 120 mg/day).
A potential link between effects on thyroid hormones and neurodevelopmental effects was mentioned.	While Health Canada is aware of this postulated link, at the present time the mode of action for induction of the neurodevelopmental effects observed in rodents has not been elucidated. This has not precluded their consideration as the critical endpoint for the screening assessment.
Reference was made to information indicating that PBDEs are potent thyroid disruptors, with seven times more binding power than human thyroxine for human transthyretin.	The commenter referenced a secondary account of an *in vitro* investigation of the binding potential of several substances to transthyretin. However, examination of the original source indicated that the secondary account had incorrectly cited the results of the study with respect to PBDEs, as it was another compound tested that displayed "seven times more binding power"; indeed, PBDEs did not bind transthyretin, although two hydroxylated PBDEs did display some binding activity (1.42- and 1.22-fold more active than thyroxine), as did some unidentified

Comment	Response
	metabolites of PBDEs (relative activity was not quantifiable for the metabolites).
Recent data on levels of PBDEs in breast milk of women from Puget Sound were provided.	While these data were published subsequent to the cut-off date specified in the screening assessment report, the upper-bounding estimate of exposure presented in the assessment incorporates values for levels of PBDEs in human breast milk greater than those cited in the comments.
Reference was made to recent data indicating that concurrent exposure to PBDEs and polychlorinated biphenyls (PCBs) may be more potent than exposure to either substance group individually.	While these data were published subsequent to the cut-off date specified in the screening assessment report, additional risks associated with exposure to multiple substances is somewhat accounted for by the conservative approach of using the upper-bound estimate of exposure for all PBDEs and the lowest reported effect level for the most toxic congener based on available data.
The opinion was stated that decabromodiphenyl ether (DeBDE) and commercial decabromodiphenyl ether (ComDeBDE) should not have been included in this screening assessment on PBDEs, based on the differences in exposure and toxicity profiles between DeBDE/ComDeBDE and the other PBDE congeners.	The identical base structure, combination of congener groups within the commercial mixtures, trends in physical/chemical properties with degree of bromination and similarities in toxicological effects support the consideration of PBDEs as a group in a screening context (outlined at http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/exist_substances-substances_existantes_e.pdf). For example, with regard to the critical targets for PBDEs, there is indication of effects on the liver for DeBDE/ComDeBDE in available studies. In addition, the effect levels for developmental neurotoxicity are within the same range (i.e., 0.8 versus 2.22 mg/kg bw per day for pentabromodiphenyl ether [PeBDE] and DeBDE/ComDeBDe, respectively). Moreover, in view of the limited data available on levels of each of the congener groups within the environment and consistent with the conservative approach adopted in screening assessments, a measure of total exposure to all congeners combined was considered appropriate. Also, while a conclusion with respect to potential effects on human health was not presented for DeBDE/ComDeBDE specifically, it was not concluded that this group of PBDEs is considered “toxic” to human health as defined in Paragraph 64(c) of CEPA 1999, based on this conservative approach.
Submission of data on DeBDE/ComDeBDE under the U.S. Voluntary Children’s Chemical Evaluation Program (VCCEP) and the U.S. National Academy of Sciences review (NAS, 2000) contained valuable	If sufficiently well documented, Health Canada makes use of previous reviews as important sources of data identification and expert judgment for some aspects of the assessment. Health Canada is aware of the reviews mentioned in the comments and has considered the information contained therein. Information considered

Comment	Response
information on DeBDE/ComDeBDE's toxicology and risk. These references do not appear to have been referred to by Health Canada.	relevant to the screening health assessment identified from other reviews is cited in the draft assessment.
The opinion was expressed that the absence of DeBDE/ComDeBDE from lists of potential carcinogens (e.g., IARC, 1990; OSHA, 1990; NTP, 2000) should be indicated in the assessment.	The conclusion of a more recent evaluation of the International Agency for Research on Cancer (i.e., IARC, 1999) was indicated in the Supporting Working Document.
Although six Eriksson and Viberg studies are cited in the last paragraph on page 3 of the draft screening health assessment, these publications actually report only three separate studies with respect to the PeBDE congener and neurodevelopment in mice. It was stated that "several reporting errors are evident," and reference is made to the descriptions of these neurodevelopmental studies in the text.	Multiple accounts of a study are often published in different journals, conference proceedings, etc.; all accounts of which Health Canada is aware are indicated, so that the entire database that was considered is clear to the reader. Several different studies involving different protocols are discussed in the paragraph in question. Additional details of the protocols have been included in the tabulated descriptions of these studies for clarification.
The statement in the draft screening assessment report that information on the effects induced by the various congener groups was considered relevant to assessment of the group of PBDEs (including commercial mixtures) since "these congener groups are also present in the commercial mixtures ComPeBDE, ComOcBDE and ComDeBDE" was considered to be erroneous.	The statement in the screening assessment will be revised to read "…are also present in the commercial mixtures ComPeBDE, ComOcBDE ***or*** ComDeBDE."
It was suggested that reference to a critical effect level for DeBDE/ComDeBDE be removed from the summary Table (Table 2) because of limitations of the relevant study.	The limitations of the study in question are recognized and were taken into consideration in determining the adequacy of the margin of exposure; however, it was considered acceptable within the context of a screening health assessment. Additional information on the approach to preparation of screening assessments for DSL substances at Health Canada can be found at http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/exist_substances-substances_existantes_e.pdf.
It was recommended that the lowest-observed-effect level (LOEL) of 80 mg/kg bw per day be deleted from Table 3 based on the 77% purity of that product in contrast to the current 97% purity.	While the purity of the product tested was noted in the assessment report, this is considered to be within the realm of acceptable uncertainties in the context of a screening assessment.
In the last column of Table 3 under	In Table 3, only the study with the lowest reported LOEL

Comment	Response
subchronic toxicity, only mice are mentioned, while National Toxicology Program (NTP) subchronic studies were performed in both rats and mice.	(or, in the absence of a reported LOEL, the highest no-observed-effect level, or NOEL) for each study type is described. The NTP (1986) study in rats will be added to the "additional studies" listed.
It was recommended that the word "adenomas" be deleted from Table 3, as "neoplastic nodules is a term no longer used by the NTP and is not equivalent to adenomas as indicated."	The word "adenomas" will be deleted from Table 3 of the assessment report. The terminology in the original report of the NTP bioassay (i.e., neoplastic nodules) will be presented in the study description in the assessment report. It should be noted, however, that cancer was not considered the critical effect for this congener group.
It was recommended that the statement "increased incidence of hepatocellular adenomas and carcinomas combined" be deleted from Table 3, since the increase was only marginal in male mice compared with controls and may have been due to early deaths in control mice from fighting, and the absolute value was within historical limits.	The Table entry for this study has been modified to read "marginal and statistically significant only at the low dose." The fact that the increase was within historical controls was reported in the Supporting Working Document.
It was questioned whether defining a LOEL for non-neoplastic effects in the NTP two-year bioassay was appropriate, because of the "high" doses at which such effects were observed.	Results reported are those observed by the investigators (i.e., an account of the non-neoplastic effects observed at the lowest dose at which they occurred).
It was suggested that the results of the DeBDE/ComDeBDE developmental study in rats in Table 3 were inaccurately reported in the draft screening health assessment report. The highest dose of 1000 mg/kg bw per day was designated a NOEL by the authors of the study (Hardy et al., 2002), based on the fact that the increase in early resorptions was within historical controls, although this dose was reported as a LOEL in the Table.	The description of the study in question has been modified to be consistent with the study authors' conclusion. The fact that the increase was within historical controls was mentioned in the text of the Supporting Working Document.
A comment was made concerning "Health Canada's focus on DeBDE/ComDeBDE's potential for toxicity from metabolites."	In the draft screening health assessment, Health Canada did not focus on the potential toxicity of DeBDE/ComDeBDE metabolites.
The comment was made that DeBDE/ComDeBDE "does not constitute a danger in Canada to human life or health."	In the draft screening health assessment, it was not proposed that this group of PBDEs be considered "toxic" to human health under CEPA 1999. Further in-depth assessment would be required to definitively conclude with respect to whether these substances would be considered "toxic" to human health under CEPA 1999.
Interest was expressed in meeting with appropriate members of staff to review	Staff of Environment Canada and Health Canada met with industry representatives to provide an opportunity to

Comment	Response
the position on DeBDE/ComDeBDE in the draft screening assessment report on PBDEs.	elaborate on comments provided during the public comment period.
A measured log K_{ow} of 6.265 for DeBDE was provided, along with a reference for this value.	This information was added to the Supporting Working Document for the screening health assessment.

Table 2: Comments relating to risk management of PBDEs

Recommend adding DeBDE/ComDeBDE[1] to the Virtual Elimination List under CEPA 1999 based on its presence in breast milk and potential for debromination into more toxic forms.
Recommend the development of new product designs to decrease the need for chemical fire retardants.
Recommend an interim ban on PBDEs in all consumer products including imports under Section 94 of CEPA 1999.
Recommend initiation of a broad monitoring program of PBDEs to determine if levels in humans decrease after regulatory action and to help identify important exposure pathways for humans.
Recommend developing a strategy for the safe removal of PBDE products already in use or the safe disposal of in-use products at the end of their life cycles in order to decrease exposures.
Recommend testing of potential substitutes for PBDEs for persistence, bioaccumulation and toxicity.
It was suggested that the benefits of using DeBDE/ComDeBDE outweigh the risks of harm and should be given weight in the screening assessment.
Recommend that PBDEs be added to the List of Toxic Substances under Schedule 1 and that PBDEs be eliminated from the environment as quickly as possible.

[1] Discussion of the congener group DeBDE and the commercial mixture ComDeBDE could not be separated due to the similarities between these two (i.e., current formulations of ComDeBDE are approximately 97% DeBDE) and the common practice of referring to them by the same name.

Table 3: General comments on regulatory process

Two submitters provided general commentary on the process of assessment of chemicals in Canada under CEPA 1999, comparing the process with the European Union's proposed REACH (Registration, Evaluation, and Authorization of Chemicals) program; PBDEs are simply used as an example of an environmental contaminant situation that could be avoided under a program similar to REACH.
Request to meet with government officials to discuss implementation of regulatory process similar to REACH.