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BSEF Comments on the draft Risk Profile for OctaBDE

The Bromine Science and Environmental Forum (BSEF, www.bsef.com) is submitting the following comments on the draft Risk Profile for Octabromodiphenyl ether (OctaBDE) (CAS No. 32536-52-0).

BSEF represents three major global suppliers of bromine and brominated chemicals. One or more of these companies have made and/or distributed the two brominated products which are currently being evaluated as candidates for possible addition as POP substances to the Stockholm Convention. These substances are “legacy” products and none of these substances have been made and/or imported in the US for any commercial uses since December 31, 2004.

The Chemical Abstract Service number 32536-52-0 corresponds to the CAS Name “benzene, 1,1'-oxybis-, octabromo”, which generically describes all 12 possible isomers of a diphenyl ether structure having 8 bromine atoms attached at any possible combination of locations on the 2 benzene ring structures. Like commercial PentaBDE, at the time it was made and distributed the commercial product commonly called “OctaBDE” was actually a complex reaction mixture containing a range of congeners. The predominant components had from six to ten bromine atoms (HexaBDE to DecaBDE congeners). Consequently it is more appropriate to use the term “commercial OctaBDE” (c-OctaBDE) when discussing the material distributed in commerce for flame retardant use and reserve the term “Octabromodiphenyl ether” and CAS No. 32536-52-0 for use when referring specifically to diphenyl ether structures having 8 bromine atoms attached.

At POPRC2 it was agreed that sufficient information had been provided in the POP nomination of c-OctaBDE to indicate that it contained certain HexaBDE isomers (e.g. BDE-153) which appeared to have POP characteristics and a Risk Profile was asked to be prepared.

The present draft Risk Profile raises one major area of concern for BSEF that we believe must be addressed before this document can be finalized. This major concern relates to draft Risk Profile’s author attempt to introduce several items that do not appear to be consistent with what was presented to POPRC2 and which do not seem to be well supported scientifically.

Notably, the draft Risk Profile:

- Claims that scientific data demonstrates that BDE components of commercial OctaBDE having 8 or more bromine atoms can be expected to undergo reductive debromination in biota and various environmental compartments and lead to the formation of lower brominated PBDEs (e.g. TetraBDE, PentaBDE etc) some of which could have POP characteristics.
- Makes inappropriate and overly broad conclusions regarding the comparative toxicity of specific PBDE’s in relation to substances such as PCBs and Halogenated Dioxins/Dibenzofurans components.

Comments related to both of these issues were previously provided to the author and the Secretariat but these did not seem to be reflected in the latest draft.

- **Reductive debromination**

Regarding the issue of reductive debromination BSEF questions whether this is an appropriate topic at this stage of the process for evaluating the POP characteristics of the components found in “commercial OctaBDE”. POPRC 2 decided based on the information provided in the screening phase that the basis to move forward on the Risk Profile was the presence of a substantial HexaBDE content. By including BDE 153, a major constituent of c-Octa, in the risk management of c-PentaBDE, commercial OctaBDE would already be managed via c-PentaBDE. The potential for formation of other substances in commercial OctaBDE with POP characteristics was not part of the consideration for moving c-OctaBDE to the Risk Profile stage. Therefore before this reason for concern becomes part of the Risk Profile, we believe the information, evidence and significance of this happening should first be addressed in the POPRC prior to introducing it into a Risk Profile.

Beyond our view on the procedural aspects of introducing into the risk profile concerns that were not part of the original charge given to the author, the information used to support the debromination of components in c-OctaBDE is taken from laboratory studies that used conditions which components of c-OctaBDE would not ordinarily be expected to encounter in the environment. In fact in the few studies of actual environmental fate of highly brominated PBDE (e.g. Octa-DecaBDE) in natural settings, there is little evidence that this debromination proceeds with the rate or to the extent of what has been shown in lab studies. Moreover, many studies quoted on debromination were not even carried out using c-OctaBDE but instead with other PBDE's. We think it is not appropriate to use these results in the context of OctaBDE without first investigating if the use of read across from other PBDE species is appropriate.

For the reasons we point out, it would be best to remove references to debromination in from the Risk Profile and if needed, raise this issue at the next POPRC meeting for consideration in later revision to the Risk Profile.

- **Conclusions on the comparative toxicity of specific PBDE's in relation to substances such as PCBs and Halogenated Dioxins/Dibenzofurans components**

As for the attempts by the draft Risk Profile's author to attribute “PCB-like” effects to c-OctaBDE there is very little if any primary literature citations that have been used to support this as a valid comparison. We have provided references to several recent papers that have pointed out that PCBs and PBDE's seem to have little in common mechanistically and in some cases seem to even exhibit completely opposite mechanisms and/or effects. We believe it would be best if the Risk Profile limited itself to what is known about the toxicological properties of the components of c-OctaBDE and avoid efforts to draw analogies to other substances.

Please find in the table below our detailed comments for the draft Risk Profile for c-OctaBDE:

Page no	Quote	Comment
4	<i>"The bioaccumulation potential ... is well documented"</i>	Please provide the actual BCF values for the relevant PBDE congeners.
4	<i>As debromination into other POP-like chemicals is expected . . .</i>	We think this statement is not supported by evidence. Please see more detailed comments below.
5	<i>It should be noted that hexa BDE 153 concentrations close to these value have been found in several species and geographic sites and total PBDE concentrations frequently exceed largely this threshold.</i>	It is important to indicate where these concentrations were found (e.g. in industrial/urban areas or remote areas).
5	<i>The greatest difficulty appears for the estimation of the potential hazard of the commercial mixture and its components. There are traditional ecotoxicological and toxicological studies where no effects have been observed even at unrealistically high concentrations. However, an in-depth assessment of these studies considering in particular the properties and toxicokinetic of PBDE indicates that the test design, exposure conditions and measured endpoints are not appropriate for a sound assessment of these types of chemicals. Thus, the lack of effects reported in those tests should be considered with care.</i>	The message in this paragraph seems to be a repeat of what is said just 3 paragraphs earlier. One or the other should be deleted or they should be combined.
5	<i>Based on the existing evidence, additional concerns related to the debromination into toxic BDEs, the increasing evidence relating these chemicals with other POPs (similarities between PBDEs and PCBs; relationships with dioxins and furans),</i>	This statement is far too broad. There are also clear dissimilarities between PBDEs and PCBs. From a toxicological perspective, as reported by Van Den Berg, Peters et al, certainly there are clearly mechanistic reasons why this statement is not correct. From a chemical and physical property perspective, the PBDE analog of the corresponding PCB is less volatile, less water soluble and considerably large and heavier.

Page no	Quote	Comment
5	<i>No relevant effects have been observed in aquatic, sediment and soil laboratory studies; however, this information cannot be used to conclude that Hexa to NonaBDE are not toxic for these organisms as the measured endpoints and the exposure conditions, employed in these assays are clearly insufficient for a proper assessment of chemicals such as hexa to nonaBDE.</i>	The ability of the EU to perform a risk assessment on c-OctaBDE as well as Canada's recent (2006) human health and environmental risk assessments of the whole family of commercial PBDE's seems to contradict this statement.
5	<i>it is concluded that the components of c-OctaBDE, Hexa to NonaBDE, are likely, as a result of LRET, to lead to significant adverse human health and/or environmental..</i>	The conclusion at POPRC was only for the selected HexaBDE and HeptaBDE isomers and should be reworded accordingly. This statement expands the actual list of substances that would be listed from only a handful of isomers to well over 50.
11	<i>For instance, Ahn et al. (2006) showed that decaBDE immobilised on specific soil/sediment and mineral aerosols yielded a number of penta to triBDEs, via octaBDE as a intermediate step.</i>	This reference should not be cited because does not deal with OctaBDE or c-OctaBDE. Further the study does not serve as a good predictor of what actually happens in the environment. Ahn's laboratory experiments created artificial conditions which might be useful in providing indicative information of possible degradation routes/mechanisms. However by substantially changing the solubility and adding catalytic metals and reactive solvents or other substances to enhance the degradation, the type and amount of substances formed may not represent that found in the environment. The Ahn study used "unstabilized" THF which acted as a solvent for DecaBDE as well as a proton donor. Furthermore this stepwise debromination to Br4 and Br5 PBDE's occurred only in a specific range of THF:H2O ratios (i.e. no such reactions at 100% THF or 100% H2O). Ahn et al say water itself did not act as the proton donor, nor did the reaction occur when stabilized THF (containing BHT) was used. The work also examined the use of catechol as a surrogate for naturally occurring reductant. Again degradation was only seen at the extreme end of the molar ratios of Catechol to DecaBDE. Further the degradation products were not actually reported in the paper. So the environmental relevance of this work (and much of the other laboratory based work) seems unclear.

Page no	Quote	Comment
11	<i>It's worth noting that degradation of polybrominated diphenyl ethers (PBDEs) can yield byproducts that are lower brominated congeners. For instance, Ahn et al. (2006) showed that decaBDE immobilised on specific soil/sediment and mineral aerosols yielded a number of penta to triBDEs, via octaBDE as an intermediate step. This may pose an additional environmental concern, as these lower brominated diphenyl ethers are usually more toxic and much more bioaccumulative.</i>	As indicated in previous comments, the work of Ahn and many others doing research in degradation of highly brominated PBDEs while providing information on theoretical pathways and products of degradation, few if any laboratory studies have been performed under environmentally relevant conditions. The EU itself in their on going risk assessment of DecaBDE has made this important distinction.
12	<i>Henry's law constant, a key property to determine if there is risk of long-range environmental transport for a substance, is well inside the range set by the other POPs.</i>	Benchmarking of c-OctaBDE or any other substance against other currently listed POPs may give a false impression of the potential for long range transport since the factors shown do not take into account such parameters as Log Koc or other properties that would make a substance less likely to be present in an environmental compartment to begin with. For example substances with high Log Koc will tend to bind tightly to sediment and become essentially immobilized. The table implies that all substances with a HLC of between 0.04 and 3276 will undergo LRT. If studies have been done showing this range of Henry's Law constant values is a good predictor of LRT, a reference should be provided.
11	<i>However, the work of Sellström et al. (2005) shows a noticeable accumulation of these substances (hepta and decaBDE, amongst other BDEs) in wild falcons. Verreault et al. (2005) found accumulation of several octaBDE congeners (both higher and lower brominated) in several environmental samples of two Arctic top predators, and De Wit et al. (2006) reported a variety of PBDEs in the Arctic.</i>	These papers obviously show that these congeners were detected in these animals. The term "accumulation" implies that these species are concentrating the contaminants which may or may not be the case. Without knowing the actual exposure, no conclusion can be drawn. Since the presence of the materials in the animals cannot be disputed, a better way to characterize the findings would be refer to "presence" rather than "accumulation."

Page no	Quote	Comment
13	<p><i>A second aspect of concern is that although the higher brominated BPDEs are persistent, there is evidence that they can degrade under some conditions. Lower brominated diphenyl ether congeners have been identified among the degradation products. Since some of the products may be more bioaccumulative and toxic than the parent compound, any significant formation would be a cause for concern.</i></p>	<p>Review articles by Stapleton and a review by TNO indicate that debromination of DecaBDE is not likely to contribute significantly to the presence of Br4-6 BDEs in the environment or biota. Stapleton summarizes as follows: "The potential for significant formation of BDE 47, BDE 99 and BDE 100 in the environment due to debromination is low as the only study showing this is not environmentally relevant. The formation of hexaBDE has more realistic probability and could be related to debromination of DecaBDE in humans. Photolytic debromination of DecaBDE in dust, soils and sediments, leading to the formation of hepta-, octa- and nonaBDE congeners is environmentally relevant; not withstanding more research on the significance of these lower congeners fate in the environment."</p> <p>Work by Sellstrom et al reinforces the need to back up lab data with field data. Their work published in late 2005 says "Previously, BDE-209 was found to photolytically debrominate when applied artificially to soil with solvent in laboratory and field experiments (13). The photolytic pattern seen was distinctive for nona- and octa-BDEs with increased peak height for the late eluting peaks (13). In soils from the current study, no evidence of photolytic breakdown was seen, i.e., no distinctive photolytic pattern was seen in the chromatograms. Laboratory experiments with Björketorp soil also showed no change in peak patterns with length of UV exposure. Soil aging has been shown to encapsulate and shield contaminants so they are less accessible to microbial breakdown and also probably to sunlight (41). Also, these soils were plowed under and this may also affect accessibility to sunlight. The results with soils collected in the field show the importance of following up laboratory studies with field studies."</p> <p>¹ "Effect of Sewage-Sludge Application on Concentrations of Higher Brominated Diphenyl Ethers in Soils and Earthworms" Sellström, U.; de Wit, C. A.; Lundgren, N.; Tysklind, M., Environ. Sci. Technol.; 39(23) (2005); 9064-9070</p> <p>There is not sufficient evidence that degradation occurs under environmentally relevant conditions to state what substances are actually formed in the environment by OctaBDE and whether or not they are more bioaccumulative or less so than the parent compound itself.</p>

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13	<i>The possible formation of brominated dibenzo-p-dioxins and dibenzofurans during combustion or other high temperature processes involving articles containing c-octaBDE is another cause of concern (European Commission, 2003).</i>	Information developed by the Swedish Fire safety institute (STENA) has shown that over the lifecycle of televisions, the presence of flame retardants actually reduces the environmental footprint by having fewer episodes of water and soil contamination. In other words, using an FR such as OctaBDE is an environmental benefit.
15	<i>Gerecke et al. (2005) in a study on DecaBDE reported the degradation of nonaBDE 206 and 207 under anaerobic conditions using sewage sludge inoculum to OctaBDEs; and this degradation has been confirmed in other studies (Gaul et al, 2006; He et al, 2006).</i>	See TNO's full comments regarding Gerecke's work. This is again another case where unrealistic conditions were used to achieve any evidence of degradation of DecaBDE. For example, TNO states: "In the study reported by Gerecke et al., the incubation lasted 238 days, whereas the retention time in a full scale anaerobic fermentor would be ca. 20 days."
16	<i>The photodecomposition of several BDEs has been studied in different matrices such as methanol/water 80:20 (Eriksson et al. 2001) a sealed polyethylene tube exposed to natural sunlight for up to 120 min (Peterman et al. 2003); or water (Sanchez-Prado et al., 2006); in general degradation was faster for the higher brominated DEs than for the lower brominated congeners. Rayne et al. (2006) suggest a short photochemical half-life for the hexa BDE153 in aquatic systems, with rapid photohydrodebromination to some of the most prevalent penta- and tetra-brominated diphenyl ether congeners</i>	See TNO comments about the relevance of these types of studies to environmental degradation.
16	<i>the BCF for octaBDE would be <9.5 while the BCF for heptaBDE would be about <1.1-3.8 and the BCF for c-octaBDE would be about <10-36 (European Communities 2003).</i>	This demonstrates that OctaBDEs clearly do not meet the B criterion.
16	<i>the BCF for octaBDE would be <9.5 while the BCF for heptaBDE would be about <1.1-3.8 and the BCF for c-octaBDE would be about <10-36 (European Communities 2003).</i>	Please also state the BCF for hexa- and pentaBDE.

Page no	Quote	Comment
16	<i>The potential for biomagnification has been demonstrated for hexa and heptaBDE (Burreau et al., 2004; Sormo et al., 2006), and more recently suggested for the DecaBDE (Law et al., 2006).</i>	This study was cited in a recent update to the DecaBDE EU Environmental Risk Assessment. This work was examined by EURAS a competent and well regarded consultant in the field of environmental risk characterization. They identified a number of shortcomings in this work by Law and concluded it should not be used as evidence that DecaBDE biomagnifies. This evaluation has been provided to the UK as rapporteur to this risk assessment. The reference to DecaBDE should be removed or at least presented to indicate some lack of certainty concerning the findings of Law et al.
17	<i>A recent study (Drouillard et al., 2007) has reported a depuration rate constant for the hexaBDE 0.016 days⁻¹ in juvenile American kestrels (Falco sparverius), with a retention of about 50% of the administered dose</i>	It seems that there needs to be a summary statement here that addresses the fact that data is supportive of uptake for the Br4-6 but that these substances seem to be relatively rapidly eliminated (depuration rates are a matter of a few hours to a few days).
17	<i>A controlled feeding trial assessed transfer and accumulation of PBDEs from feed to farmed Atlantic salmon (Salmo salar). On average, 95% of the total PBDE content in the feed accumulated in whole salmon including heptaBDE 183 (Isosaari, et al. 2005).</i>	The ranges of PBDE's congener families in the food and the range found in the fish should be mentioned here if they include those found in c-OctaBDE.
17	<i>As debromination in the environment and biota has been demonstrated, hypothetically, the presence of hexa to nonaBDEs could be explained by a long range transport of decaBDE and its subsequent debromination, however, it is very unlikely to assume a long range transport for decaBDE and not for the nona to hexa congeners.</i>	This clearly overstates the situation regarding the state of knowledge about DecaBDE and environmentally related debromination. The EU's most recent draft Environmental Risk Assessment (issued in May 2007) does not go this far.

Page no	Quote	Comment
18	<i>Previous model predictions suggested a low potential for long-range atmospheric transport for highly brominated BDEs (e.g. Wania and Dugani, 2004). However, in a recent paper on DecaBDE, Breivik et al., (2006) have reported that chemicals that are both sorbed to particles and potentially persistent in the atmosphere, such as BDE-209, may have a larger potential for LRT than anticipated on the basis of earlier model evaluations. This explanation could be also applied to c-OctaBDE components</i>	The issue of particle bound long range transport is certainly worth consideration. However in doing so, it seems necessary to them also consider the issue of bioavailability of the chemical when it is particle bound. It is well understood that the toxicity of substances can be mitigated when tightly bound to particulate matter. Further, substances that are particle bound can also be much less readily degraded by photolytic processes as has been shown in work by Zetsch et al. These factors should at least be qualitatively considered if particle transport is considered an important mechanism of LRT.
18	<i>PBDEs (ranging from tri- to OctaBDEs) were detected in deposition samples collected from sites in The Netherlands, Germany and Belgium, confirming their presence in precipitation (Peters 2003).</i>	The concentrations should be mentioned .
18	<i>The highest levels were in sediments downstream from a warehouse where c-DecaBDE was stored (Environment Agency 1997).</i>	This reference needs to be checked. Our recollection was that this was an issue associated with the Mersey River near Liverpool and it was later determined that off shore dumping municipal waste water treatment sludge in the Irish Sea lead to the encroachment of contaminated sludge into the estuary area. Further, unless there is other documentation that ties the presence of OctaBDE to the presence of a warehouse containing DecaBDE, why mention this at all? The sediment was probably also downstream of hundreds of other facilities.
19	<i>Martinez et al. (2006) have recently reported concentrations of sum of hexa to nonaBDE in the range of 15.5 to 160 µg/kg dw in sludge from municipal wastewater treatment facilities in Spain, and up to 268 µg/kg dw in industrial facilities</i>	The concentration of these 3 congener families should be mentioned.

Page no	Quote	Comment
21	<i>Exposure to components of c-OctaBDE in remote areas is confirmed and based on the available information should be attributed to a combination of releases and transport of c-OctaBDE, c-pentaBDE (for hexaBDE) and c-DecaBDE (for nonaBDE), and to the debromination of DecaBDE in the environment and biota.</i>	This statement is not supported in the document. Of the 20+ references in this section only 1 mentioned NonaBDE detection (Martinez 2006 in WWTP sludge in Spain) and only 5-6 of the 20 mention detection of OctaBDEs (all from samples collected in fish, sediment, soil, sludge or wash off waters (deposition samples) collected in the EU. This data clearly does not support exposure to "hexa-nonaBDE's in remote areas".
21	<i>In a recent study (Toms et al., 2007) the concentrations of PBDEs found in Australian human milk were lower than those reported from North America but higher than those reported from Europe and Asia</i>	A summary statement regarding presence in biota seems to be appropriate here. Clearly Br4-Br6 (Br7?) BDE's appear with greater frequency and at higher concentration than the higher (Br8-10) BDEs.
21	<i>European Communities (2003) presents some information on the levels of components of c-octaBDE measured in human samples. Large variations among individuals were generally observed, but significant differences between the control population and occupationally exposed groups were also reported.</i> <i>In a recent study (Toms et al., 2007) the concentrations of PBDEs found in Australian human milk were lower than those reported from North America but higher than those reported from Europe and Asia</i>	The congener families should be indicated.

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21	<i>Exposure to components of c-OctaBDE in remote areas is confirmed and based on the available information should be attributed to a combination of releases and transport of c-OctaBDE, c-pentaBDE (for hexaBDE) and c-DecaBDE (for nonaBDE), and to the debromination of DecaBDE in the environment and biota.</i>	Where is the information showing NonaBDEs exposure in this document? This statement is far too definitive considering what is known about c-DecaBDE. There is ~5 times more nonaBDE in the c-Octa than in c-DecaBDE and given relative poor support for environmentally relevant degradation of DecaBDE to lower species it is hard to find good support for this statement.
22	<i>The presence of hexa and heptaBDE in fish from remote alpine lakes in Switzerland (Switzerland info2) reported to be related to atmospheric deposition confirms the potential for atmospheric long-range transport.</i>	Something needs to be said about the location of the samples in order to support LRT. How does the presence of Br6&BR7 BDE's in Swiss lakes prove LRT? Could these have come from regional sources (major cities in the region where the samples were collected)
22	<i>Like for other chemicals with similar properties, aging processes are expected to reduce the bioavailability, and the experiments conducted on sediment dwelling organisms comparing the bioaccumulation in spiked sediments and from contaminated biosolids offer and indirect support for this hypothesis.</i>	This section needs a summary statement – “As the major routes of intake likely via oral routes and the majority of data supports that Br4-6(??) BDEs are commonly found in the highest concentration, these would appear to be the most bioavailable congeners.”

Page no	Quote	Comment
23	<p><i>Delayed neurotoxic effects. Neonatal mice exposed to a single dose of 0.45 mg BDE153/kg bw on postnatal day 10 showed when tested at 2, 4 and 6 months of age altered motor behavior. Spatial learning ability and memory function in the adult mice were also affected Viberg et al. (2001a)</i></p> <p><i>Eriksson et al. 2002a confirmed neurotoxic effects (aberrant behavioral responses) on developing male mice exposed to 0.45 to 9.0 mg/kg bw of BDE153 on day 10 of development. The effects were comparable to those observed for PCB153 leading the authors to speculate that interactive neurotoxic action may be possible between the two compounds.</i></p> <p><i>These neurotoxic effects have also been observed after a single oral dose of nonaBDE 206 or OctaBDE 203 administered on postnatal day 3 or 10 to, or PBDE 183; with disturbances in spontaneous behavior, leading to disrupted habituation and a hyperactive condition in adults at the age of 2 months. (Viberg et al., 2006).</i></p>	<p>It should be noted that the EU as well as other regulatory authorities have repeatedly acknowledged that the limitations and confounding factors associated with the Viberg/Eriksson methodology make it impossible to determine the relevance of this information to assessing risk to human health or the environment. See The EU's comments regarding this topic in the DecaBDE risk assessment.</p>
23	<p><i>Delayed neurotoxic effects. Neonatal mice exposed to a single dose of 0.45 mg BDE153/kg bw on postnatal day 10 showed when tested at 2, 4 and 6 months of age altered motor behavior. Spatial learning ability and memory function in the adult mice were also affected Viberg et al. (2001a)</i></p> <p><i>Eriksson et al. 2002a confirmed neurotoxic effects (aberrant behavioral responses) on developing male mice exposed to 0.45 to 9.0 mg/kg bw of BDE153 on day 10 of development.</i></p>	<p>The two authors were professor and student at the same university. It appears that these two comments are not actually two separately conducted studies of BDE 153, but a restatement of prior work with additional commentary. The original references should be checked.</p>

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23	<p><i>Delayed neurotoxic effects. Neonatal mice exposed to a single dose of 0.45 mg BDE153/kg bw on postnatal day 10 showed when tested at 2, 4 and 6 months of age altered motor behavior. Spatial learning ability and memory function in the adult mice were also affected Viberg et al. (2001a)</i></p> <p><i>Eriksson et al. 2002a confirmed neurotoxic effects (aberrant behavioral responses) on developing male mice exposed to 0.45 to 9.0 mg/kg bw of BDE153 on day 10 of development. The effects were comparable to those observed for PCB153 leading the authors to speculate that interactive neurotoxic action may be possible between the two compounds.</i></p> <p><i>These neurotoxic effects have also been observed after a single oral dose of nonaBDE 206 or OctaBDE 203 administered on postnatal day 3 or 10 to, or PBDE 183; with disturbances in spontaneous behavior, leading to disrupted habituation and a hyperactive condition in adults at the age of 2 months. (Viberg et al., 2006).</i></p>	<p>The EU's position regarding the methodology of Viberg and Eriksson for assessment of potential neurotoxicity is clearly explained in the EU Risk Assessments of c-PentaBDE, c-OctaBDE and DecaBDE. The work is of unknown relevance to humans or animals exposed to these substances and is not adequate for risk assessment purposes.</p>
24	<p><i>Unfortunately, wild populations are co-exposed to a mixture of PBDEs as well as to other related brominated and chlorinated persistent pollutants, and with the current level of knowledge epidemiological investigations can just present associations but no cause-effect relationships between the exposure/accumulation of the components of the commercial OctaBDE mixtures and potential adverse effects observed in wildlife.</i></p>	<p>What single out brominated and chlorinated pollutants? There are a range of man made pollutants that reach wildlife and so a more generic statement seems appropriate.</p>

Page no	Quote	Comment
24	<i>The additional transformation in the environment through debromination, in particular the evidence suggesting a significant role of debromination of Octa to DecaBDE to other PBDE congeners in biota is highly relevant as food is expected to be the main exposure route for these chemicals, although increases the difficulties for quantitative assessments, and</i>	Again, while lab studies have shown indication that transformation in the environment is a possibility, actual field data does not appear to support this. This statement is far to definitive given the present state of knowledge. The environmental transformation remains mainly a laboratory phenomena and those that have tried to find evidence in the field have failed (Sellstrom, DeBoer, etc). The evidence of biotic transformation is still limited to the laboratory and even there, the % of the material actually taken up and transformed is tiny compared to what is eliminated non-transformed.
24	<i>Chlorinated persistent pollutants, and with the current level of knowledge epidemiological</i>	Unless there is specific information that certain families are in some way interacting with PBDEs to change the magnitude or types of effects, it is unnecessary to point to specific families of compounds. Otherwise what is the basis for naming one family but not another?
24	<i>It should be noted that other BDE are also found in commercial mixtures, but those are expected to be covered by the c-penta and c-deca entries.</i>	What are “ c-Deca entries ”?
24-25	<i>It should be noted that theoretically this represent 80 different congeners, while the available information focuses on less than ten congeners and some mixtures.</i>	It is not clear why this statement is made. What is the relevance of the number of theoretical congeners to the decision about whether or not c-OctaBDE and its components are POPs under the Stockholm Convention?
25	<i>The persistence of these PBDE in the environment is well documented. The only relevant degradation pathways identified until now are photolysis, anaerobic degradation and metabolism in biota, acting through debromination and producing other BDE which may have higher toxicity and bioaccumulation potential.</i>	This seems to contradict the concerns raised about potential degradation earlier in the report. How can a substance at the same time be persistent and degrading?
25	<i>The bioaccumulation potential ... is well documented ...</i>	Please provide the actual BCF values for the relevant PBDE congeners.
25	<i>In summary, a bioaccumulation potential is confirmed for at least some isomers,</i>	Please mention for which isomers and mention the corresponding BCF values

Page no	Quote	Comment
25	<i>There is also enough toxicokinetic information demonstrating that elimination rates in some vertebrate and invertebrate species are equivalent to those observed for other POPs, with values in the range of 0.01 to 0.5 days⁻¹, equivalent to a half life of about 14 to 70 days assuming first order kinetic; and therefore, low enough for supporting a justified concern on the bioaccumulation potential of Hexa to NonaBDE. Monitoring programs measuring PBDE concentrations in biota conducted in industrialized and remote areas confirm this potential for bioaccumulation</i>	This comparison is not provided anywhere in the document. Many of the BDE's have half lives in the order of a few hours to a day. So this comparison needs to be shown. There is barely any information in this document or in the published literature indicating that heptaBDE's or higher have any significant bioaccumulation potential. Bioavailability has been demonstrated, but this is not evidence of significant bioaccumulation. In fact on page 30 of the <u>Draft Management Option Dossier for commercial octabromodiphenyl ether (c-OctaBDE)</u> prepared for the UNECE POPs Task Force under direction from DG Environment by BiPRO states "The Task Force on POPs generally concluded that the hazard characteristics of penta and hexa congeners contained in c-octaBDE, together with the monitoring information on these components, were indicative of the potential for environmental and/or human health effects due to long range air transport (ECE/EB.AIR.5/2006/10)" (emphasis added)
25	<i>As debromination into other POP-like chemicals is expected to be a relevant contribution to the dissipation of hexa to nonaBDE, the absence of food-chain biomagnification for a specific congener on a specific taxonomic group does not necessarily decrease the overall concern.</i>	There was essentially no information presented in this document or in the literature indicating that the higher brominated components in c-OctaBDE debrominate to form Br4-6 BDE's under environmental conditions.
25	<i>In fact, biota monitoring data in remote areas offer the best demonstration on the potential for long range transport of c-OctaBDE components, in particular for Hexa and HeptaBDE. Theoretically this presence could also be explained by the transport of DecaBDE and its subsequent debromination. However, the comparative analysis of the available information on the physical-chemical properties of the different PBDE homologues indicates that debromination from DecaBDE might contribute to the process but it is not realistic to assume that this explains the process without additional transport from other congeners. Thus, based on the available information a long-range transport is expected for the c-OctaBDE components, and the role of</i>	The biota monitoring in remote areas cited in this present document (Norstrom et al. (2002) and Wakeford et al. (2002)) do not support this statement. <u>In fact this document states that Br8-Br10 BDE were not found at their limits of detection.</u> Evidence is provided in this document that supports the concern for Br5, Br 6 and possible Br7 BDEs.

Page no	Quote	Comment
	<i>atmospheric transport is confirmed at least for Hexa and HeptaBDE based on its detection in alpine lakes.</i>	
26	<i>In fact, the measured endpoints and the exposure conditions, employed in these assays are clearly insufficient for a proper assessment of chemicals such as hexa to nonaBDE. Ecotoxicity tests on these types of chemicals should cover if possible several generations or at least a full life cycle, and the measured endpoints must include sublethal effects associated to the accumulation and re-mobilization of the PBDEs during critical periods of development and reproduction, as well as the ecologically relevant consequences of metabolic changes. In addition, all environmentally relevant exposure routes must be addressed.</i>	The information that is available is largely the result of industry performing studies at the request of the EU as part of the OctaBDE risk assessment (RA). As originally worded it seemed to diminish the previous efforts of the EU under their RA program.
26	<i>However, the immuno-toxicological effects and particularly the delayed neurotoxic effects observed after a single dose require specific attention. Although a quantitative evaluation of these effects in terms of its potential risk for human health and ecosystem is not possible based on the current level of information, the reported observations must be analyzed with care. Certainly, the doses at which the effect have been observed are well above exposure levels in remote areas estimated from current monitoring data for a single congener. However, the effects have been observed for different congeners, and realistic environmental exposure occurs for a mixture of PBDEs. There is not enough information for considering if these effects may be additive or even more than additive in synergistic exposures. The margins between effects observed in the lab and estimated oral</i>	Far too much weight is given in this paragraph to studies that are insufficient for risk assessment purposes and the hypothesis of additivity or synergism is highly speculative and not supported by any data. Any critical body burden calculations should be based on more relevant and robust toxicological information.

Page no	Quote	Comment
	<p><i>exposure levels in the field (based on monitoring data) are not so high when the different isomers/homologues are sum. McDonald (2005) estimated a critical body burden for hexa BDE 153 of 2000 µg/kg lipid based on the NOEL of 0.45 mg/kg reported by Viberg et al 2003 and gives a margin of safety of 7 between this level and the 95 percentile of total PBDE levels in US human populations. It should be noted that hexa BDE 153 concentrations close to these value have been found in several species and geographic sites (see Canada info 2 for a review) and total PBDE concentrations frequently exceed largely this threshold.</i></p>	
26	<p><i>The available tests do not fulfil these conditions, thus, although no toxicity was reported, no concluding statements on the toxicity of hexa to OctaBDE congeners for aquatic, sediment and soil dwelling organisms can be presented.</i></p>	<p>Why can this information not be used? Most studies were carried out by reputed laboratories under GLP conditions. Almost all of the studies done in regards to c-OctaBDE by industry were conducted at the direction and request of the EU. Certainly at the time the EU must have thought the study plan was adequate. If in recent years the perspective has changed, this does not mean either EU or industry lacked diligence in carrying out their roles. The EU managed to develop PEC/PNEC ratios and MOSs for many relevant scenarios and end points.</p>
26	<p><i>There is not enough information for considering if these effects may be additive or even more than additive in synergistic exposures.</i></p>	<p>There is as much justification for speculation about antagonistic effects as there is additive or synergistic effects. So we should either include all possibilities or exclude all of them.</p>
26	<p><i>First, the reported debromination of highly brominated BDEs in the environment and biota suggests a potential for the formation of congeners with demonstrated POP properties such as those included in the risk profile of c-pentaBDE.</i></p>	<p>See previous comments regarding debromination issues. This is certainly an important area for research, but does not at present seem to be relevant. The <u><i>Draft Management Option Dossier for commercial octabromodiphenyl ether (c-OctaBDE)</i></u> states “The environmental degradation rate by debromination of c-OctaBDE has not been determined and the environmental significance of any degradation pathways remains uncertain. There is currently no evidence that significant degradation of higher brominated compounds to lower brominated diphenyl ether congeners is actually occurring in the environment.” The Risk Profile statement should be removed or substantially modified.</p>

Page no	Quote	Comment
27	<p><i>Second, there is an increasing evidence suggesting similar toxicological profiles and therefore, equivalent hazards and concerns, between PBDEs and PCBs, although the mode of action seems to be better categorized by AhR-independent mechanisms, as PBDEs do bind but not activate the AhR-AhR nuclear translocator protein-XRE complex (Peters et al., 2006) and appear capable of up-regulating CYP2B and CYP3A in rats at doses similar to that for non-dioxin-like PCB153 (Sanders et al., 2005). As the persistence, bioaccumulation potential and long range transport of the c-octaBDE components are well documented, the confirmation of an equivalent level of hazard for these two groups should be sufficient for confirming a long-range transport associated risk</i></p>	<p>This statement is not supported by significant references in this document. In fact it supports that there is no similar toxicological profile and does not support any synergistic effects. Actually several more recent papers have pointed out that contrary to earlier speculation, the analogy between PCB's and PBDE's is a poor one. In fact they environmentally relevant PBDE's seem to have little in common mechanistically to the corresponding PCB's. See recent work by Van den Berg et al <u>Toxicological Sciences</u> (2004, 82(2): p 488-496) and <u>Toxicological Sciences</u> (2006 92(1):133-142) as well as "Polybrominated Diphenyl Ethers (PBDE's) antagonize or inhibit TCDD induced CYP1A1 activity in various in vitro systems" <u>ORGANOHALOGEN COMPOUNDS VOL 67 – 2290</u></p>
27	<p><i>Third, the potential formation of polybrominated ...</i></p>	<p>We agree that it isn't relevant to the risk profile and therefore, it should not be included. Any halogen containing molecule when burned has the potential to form any number of species depending upon particular combustion conditions. So PBDE's as a family and c-OctaBDE specifically is not unique in this respect. Furthermore, recent information indicates that polybrominated Dioxins and Furans are also produced biogenically (see "Brominated Dibenzo-<i>p</i>-Dioxins: A New Class of Marine Toxins?" ES&T 2007, 41, 3069-3074) and in some cases at concentrations higher than PCDD/PCDFs. This would tend to indicate that these compounds are probably far more ubiquitous than any of us might expect.</p>

Page no	Quote	Comment
27	<i>The evaluation of the human and environmental risk of commercial OctaBDE associated to its potential for long range transport is not an easy task as the commercial product is a mixture of components with different properties and profiles, which may also be released to the environment due to its presence as components of other PBDE commercial products and also produced in the environment by debromination of commercial decaBDE.</i>	See previous comments regarding DecaBDE debromination.
27	<i>Second, there is an increasing evidence suggesting similar toxicological profiles and therefore, equivalent hazards and concerns, between PBDEs and PCBs, although the mode of action seems to be better categorized by AhR-independent mechanisms, as PBDEs do bind but not activate the AhR-AhR nuclear translocator protein-XRE complex (Peters et al., 2006) and appear capable of up-regulating CYP2B and CYP3A in rats at doses similar to that for non-dioxin-like PCB153 (Sanders et al., 2005). As the persistence, bioaccumulation potential and long range transport of the c-octaBDE components are well documented, the confirmation of an equivalent level of hazard for these two groups should be sufficient for confirming a long-range transport associated risk</i>	This most recent information points to a different mode of action and differences in potency, so it seems inappropriate to say that PBDEs and PCBs have similar toxicological profiles. This document does not seem to have any information other than what is mentioned here regarding this issue. If this is intended to serve as support for declaring components of c-OctaBDE as POPs, then it requires better supporting information.
27	<i>In addition, specific studies have reported particular hazards such as delayed neurotoxicity and immunotoxicity which may be particularly relevant in the assessment of both human health and ecosystem risks.</i>	The EU, US and Canada have all come to regard the work by Viberg and colleagues as not useful in assessing the hazard presented to human health or the environment. It is indicative of a need for further study using standard OECD guideline methods. See the EU's comments on Viberg's work in the DecaBDE Risk Assessment for example.

Page no	Quote	Comment
28	<p><i>Based on the existing evidence, additional concerns related to the debromination into toxic BDEs, the increasing evidence relating these chemicals with other POPs (similarities between PBDEs and PCBs; relationships with dioxins and furans), and that under Article 8, paragraph 7(a) of the Convention the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the components of c-OctaBDE, Hexa to NonaBDE, are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.</i></p>	<p>In light of the previous comments and documentation found in this report, it is reasonable on the basis stated that action is warranted for BDE's with less than 7 Br atoms. However the issues of debromination, PCB like effects and dioxin/dibenzofurans are not supported by the evidence and should not be used to justify action on c-OctaBDE or any of its components.</p>
28	<p><i>Based on the existing evidence, additional concerns related to the debromination into toxic BDEs, the increasing evidence relating these chemicals with other POPs (similarities between PBDEs and PCBs; relationships with dioxins and furans), and that under Article 8, paragraph 7(a) of the Convention the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the components of c-OctaBDE, Hexa to NonaBDE, are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.</i></p>	<p>For the reasons previously mentioned relating to debromination, PCB-like statements, evidence for exposure to the higher BDE's in remote areas, etc. this concluding statement seems to go too far beyond where the evidence actually exists. It should be more narrow and aimed at those congeners that have been shown to meet these criteria.</p>

Concluding statement

Given the above, BSEF believes that:

- References to the reductive debromination of BDE components of commercial OctaBDE having 8 or more bromine atoms should be removed from the draft Risk Profile for c-OctaBDE.
- The Risk Profile for c-OctaBDE should be amended to focus on those congeners present in this legacy product that have POP characteristics as initially agreed by POP RC2.
- Lastly, because HexaBDE congeners can be addressed through the Annex A listing of c-PentaBDE, it would be appropriate to do so. In doing so, the c-OctaBDE proposal could be withdrawn, thereby reducing the workload for UNEP while still addressing the PBDE substances that have been identified by POPRC as meeting the POP criteria. BDE-153, a HexaBDE isomer is a significant component in c-PentaBDE and therefore should be included in the Risk Management Evaluation of c-PentaBDE.

July 2007
