Comments on the Design for the Environment (DfE) Program Alternatives Assessment for the Flame Retardant Decabromodiphenyl ether

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Aluminum hydroxide, Al(OH)3, CAS: 21645-51-2

SUBJECT MATTER

Aluminum hydroxide has been subjected to an EPA Assessment. The reviewed application was the use of Aluminum hydroxide as an alternative flame retardant for DecaBDE. Aluminum hydroxide was assessed as of "Moderate Hazard" regarding acute and chronic aquatic toxicity and of "Moderate Hazard" regarding neurotoxicity.

The purpose of this paper is to critically appraise the basis for assigning a "Moderate Hazard" for the above mentioned end points.

Environmental concerns

Any anthropogenic sources of aluminum oxides do not significantly contribute to the environmental concentration of aluminum, considering the ubiquitous presence of naturally occurring aluminum oxide minerals in bulk quantities.

Acute and chronic toxicity studies done for different soluble and non-soluble Aluminum salts during the REACH registration process shows no evident for any acute or a chronic toxicity effects for aluminum hydroxide.

Acute ecotoxicity

An acute fish toxicity study for Aluminum hydroxide according OECD 203 conducted by the Norwegian Institute for Water Research *(NIVA,1996 ,Effect of Aluminium hydroxide on the acute toxicity of Salmo trutta under semistatic exposure conditions.)* shows no mortalities with the nominal loading of 100 mg/L observed after 96 hours of exposure by Salmo trutta. The mean measured dissolved Al-ion concentration was 70 µg/L.

The 96 hr LC50 for P.promelas exposed to Al as AlCl3 in unfiltered water was greater than the highest measured concentration tested, 218644.1 µg/L total Al. The NOEC and LOEC in the unfiltered water was 37196.9 and 72890.0 µg/L, respectively. There was no relationship between the amount of dissolved Al and fish mortality. There were no effects on P.promelas survival after 96 hrs in the filtered toxicity test at the highest measured concentration tested 1949.4 µg/L.*(Parametrix, 2009,Acute toxicity of aluminium to the fathead minnow (Pimephales promelas) in filtered and unfiltered test solutions.)*

Chronic ecotoxicity

In August 1988 the US Environmental Protection Agency (EPA) published an ambient water quality criteria report. In this report the NOEC for Al3+-ions was set at 87 µg/l.

Aluminum hydroxide ($Al_{(}OH)_3$) is non-soluble in water (<0.09mg/L) and slowly soluble in mineral acids.

A chronic fish toxicity study for high soluble Aluminum chloride salt was conducted by Parametrix, Albany, Oregon in 2009 according the EPA 2002, Short-term methods for estimating the chronic toxicity of effluents and receiving waters to freshwater organisms. Fourth Edition. Office of Water, USEPA, Washington, DC. EPA-821-R-02-013. As a result of this study the NOEC for Al-ions was set to 0.752 mg Al/l (filtered) and 56.48 mg Al/l (unfiltered).

Long Term Fish Toxicity Literature Review: Four long-term reliable chronic toxicity studies to two species of fish *(Pimephales promelas and Salveninus fontinalis)* were identified as acceptable from the published literature. See Table # "Overview of long-term effects on fish" (below). NOECs and EC10s ranged from 0.088 to 2.3 mg Al/L and 0.078 to 5.19 mg Al/L, respectively. *(REACH-Registration dossier for Aluminum hydroxide)*

The amount of Al3+-ions generated by Al(OH)3 with a solubility of <0,09mg/l will be max 34,6 µg/l. This means, that the maximum available Al3+ ion concentration generated by Al(OH)3 is more than 2.5 times below the NOEC set up by EPA. From this point of view it is clear that there´s no chronic toxicity related to aluminum oxide.

PERSISTENCE

Literally, aluminum oxides are indeed "persistent", keeping in mind that these oxides make up a large part of the earth's crust and as such have been part of the environment for billions of years. However, this is certainly not the type of "persistence" that raises concerns for human or environmental health. An inert mineral cannot be biodegradable - regardless of how benign its ecological profile is. Consequently, the criterion "persistence" should not be applied to such materials at all.

Any anthropogenic sources of aluminum oxides do not significantly contribute to the environmental concentration of aluminum, considering the ubiquitous presence of naturally occurring aluminum oxide minerals in bulk quantities. However, according to the Draft EPA Assessment for Aluminum hydroxide, this inherent inorganic substance will be assessed as of Very High Concern regarding persistency. If this is truly the case, then these criteria should be revised since they systematically stigmatize chemicals that are inherently harmless by virtue of their insolubility and inertness.

SYSTEMIC TOXICITY

Bioavailability

Aluminum hydroxide is practically non-soluble in water (<0,09 mg/L) and slowly soluble in mineral acids.

The uptake of orally ingested metal ions occurs predominantly in the duodenum where the pH value is near-neutral. In addition, Al^{3+} ions associate with the abundant phosphate ion to give insoluble $AlPO_4$.

By virtue of the very low solubility at neutral pH, aluminum is very poorly absorbed from the gastrointestinal tract.

Studies in human volunteers[1] with ^{26}Al (as hydroxide) have demonstrated a negligible uptake (0.01%) following an oral bolus dose of 100 mg Al.

The skin is also a very efficient barrier against uptake of Al. The anti-perspirant Al salt, aluminum chlorohydrate, was tested in human volunteers (^{26}Al was used as tracer)[2]. Occlusively applied for 24 h to an underarm site, only 0.014% of the applied dose were found absorbed. For the much less soluble Aluminum hydroxide, uptake through intact skin can thus be ruled out.

Priest and co-workers[3] studied human inhalation, using ^{26}Al given as aluminum oxide (1.2 µm MMAD). The subjects were studied over a period of 3 months. Concurrent blood, urinary, and fecal measurements indicated a rapid phase of lung clearance. About 45% were cleared one day after exposure, resulting largely from mechanical clearance via the tracheobronchial tract. Deep-lung deposition approximated 60% of these 1.2-µm MMAD particles, hence the pattern of early clearance phase was consistent with the predicted regional deposition of particles of this size. Following this relatively rapid phase – largely due to mechanical clearance – a small (4.5% of the inhaled dose) fraction of aluminum remained in the lung. Over the next 3 months, serial urinary aluminum analyses suggested a considerably reduced but slow, steady clearance from the lungs, calculated at 0.015% per day of the total lung deposition, with a 72-day lung retention half-time. By the end of this period, only about 0.2% of the initially deposited dose remained; the authors suggest that slow mechanical clearance continued as indicated by the presence of ^{26}Al in the feces as long as 300–500 days post inhalation. These data suggested near insolubility of aluminum oxide. The virtual insolubility of aluminum oxide was suggested by its slow internal clearance; specifically, the daily clearance rate – following rapid mechanical removal phase – was 0.025% per day of retained lung dose, equivalent to a half-life of about 5.5 years. This suggests that the lung provides a long-term deposition site rather than a major portal of entry for aluminum oxides into the body economy.

Some examples of natural exposures to Al (reported in: " Toxicological profile for Aluminum; US Department of Health and Human Services, ATSDR, 2008)

1. Inhalation:

Levels of aluminum in the air generally range from 0.005 to 0.18 mg/m³

2 Oral uptake:

Water:	Levels of aluminum in drinking waters range from 0.1 to 1 mg/l	
Food (examples):	Tee:	up to 5 mg/l
	Peaches:	0.51 mg/l
	Green vegetables:	3.1 mg/l
Drugs:	Antacids:	up to 10 mg/l

Regarding this natural occurring concentrations of aluminum in food and beverages the amount of Al3+ generated by Al(OH)3 (34.6 µg/l = 0,034 mg/l) is negligible.

General Effects

An acute oral toxicity study with $Al(OH)_3$ in the rat[4] did not show any clinical signs of toxicity at the limit dose (2000 mg/kg bw). This is in line with negligible gastrointestinal absorption.

Repeated oral absorption of aluminum chlorohydrate over 4 weeks to rats via gavage did not elicit any systemic effects[5]. Only irritation of gastric mucosa was provoked by the irritant test material.

Exposure of rats to γ-AlO(OH) via inhalation over 4 weeks[6] elicited only the typical effects expected for LSLTPs (low-solubility low-toxicity particles), i.e., inflammatory responses evident as changes in BAL parameters. There were no signs of systemic toxicity, which is also in line with the very low systemic uptake via lungs.

Based on the complete absence of systemic effects following oral or inhalation absorption, it is not justified to flag Aluminum hydroxide for "systemic toxicity ".

Neurotoxicity

The neurotoxic potential of Al has been a matter of discussion since 1897 [7]. However, even this first investigator -and almost each successive researcher- has generally found it necessary to introduce various aluminum species directly into or on the tissue or organ of interest in order to replicate most neurological effects.

In most oral feeding studies, pathologic alterations could consistently be induced only through

1. use of large doses
2. concomitant administrations of aluminum absorptive facilitators, such as lactates or citrates; and/or
3. strong irritant aluminum compounds (e.g., aluminum trichloride) that disrupt normal body barriers to uptake.

In effect, the considerable real-world barriers to aluminum absorption largely require experimental strategies directed toward effect production.

Interest in neurological research dealing with possible aluminum toxicity was again stimulated in the mid-1960s, with reports of Klatzo *et al.*[8] that neurofibrillary tangles (NFTs) similar to those seen in Alzheimer's disease (AD) could be produced by introduction of aluminum compounds directly into the CNS. Alfrey[9] later confirmed the etiological association of aluminum with yet another neurological disorder in humans -dialysis encephalopathy (DE) - thus strengthening this association. It is noteworthy that, again, an unusual portal of entry was required to provoke this phenomenon.

Over time, the suggested association of human AD became less clear. For example, progressive encephalopathies characterized by neurotubular disorganization were induced only in immature cats and rabbits in the spinal cord – unlike the anomalies observed in AD – as well as in selected areas of the cortex. Even more problematically, this single hallmark of AD (i.e., the disorganized neurofibrillary tangle NFT) was shown to be dissimilar to the NFT seen in AD. Structurally, the latter NFT consisted of paired helical 20–24-nm tubules whereas the experimentally induced tubules consisted of individual 10-nm neurotubules. Further research demonstrated that the protein constituents of these tubular structures differed.

Likewise, there has been a consistent failure to experimentally produce another hallmark lesion characteristic for AD: myeloid-staining neural plaques. The situation was further confused when reports appeared indicating that aluminum was present in elevated quantities in the brain cortex and the NFT of human cases. Alfrey *et al.* [10] have never seen either of the two structural hallmarks (NFT and amyloid plaques) in cases of DE. Further, memory impairments restrictive to the visual domain are seen in DE in contrast to the generalized memory loss in AD.

In summary, various aspects of neurotoxicity have been experimentally provoked only under conditions that are unrelated to real-life exposure situations. Effects elicited only by artificial introduction of metal ions into tissues that they cannot reach via physiological pathways are interesting from an academic and scientific point of view, but must not be the basis for regulatory decisions.

REGULATORY AND NGO POSITIONS REGARDING ALUMINUM COMPOUNDS

In their "Red List" document[11], Clean Production Action (CPA) and Healthy Building Network (HBN) refer to a review[12] by Grandjean and Landrigan to identify potential "Red List" chemicals. Clearly, listing Al compounds on a panel of "Chemicals known to be neurotoxic in man" is far from being justified, based on the discussion provided in the previous section on neurotoxicity.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has set a tolerable weekly intake of 7 mg Al/kg bw for aluminum and its salts[13]. Concern is only voiced over aluminum intake by individuals with chronic renal failure. Because of their impaired aluminum excretion, critical Al concentrations in tissues and body fluids may build up over time.

Compounds like aluminum sulfate, $Al_2(SO_4)_3$, and sodium aluminum sulfate, $NaAl(SO_4)_2$, are common food ingredients (e.g., in baking powder) and are on the FDA GRAS (generally recognized as safe) list[14]. $Al(OH)_3$ has GRAS status for use in paper or paperboard products with direct food contact.

Under EU regulations, Al compounds (soluble like sulfate or insoluble like Al_2O_3) are not classified for systemic effects.

A clear position regarding an association between Alzheimer's disease and aluminum salts has been published by the German Federal Institute for Risk Assessment (BfR)[15]:

"[...] So far no causal relationship has been proven scientifically between elevated aluminium up-take from foods including drinking water, medicinal products or cosmetics and

Alzheimer's disease. Amyloid deposits in the brain are typical for Alzheimer's. However, an above-average frequency was not observed either in dialysis patients or in aluminium workers – two groups of individuals who come into contact with aluminium on a larger scale. BfR does not, therefore, see any health risk for consumers from aluminium intake from food-contact articles or cosmetics. [...]"

The OSHA Workplace exposure limit for alumina (Al_2O_3, respirable fraction) is 5 mg Al/m³. This value is typical for nuisance dusts without systemic effects. No concern for potential neurotoxicity is included in this limit value.

EXPERIENCE WITH HUMAN EXPOSURE

Aluminum salts, both soluble and insoluble, are found in products which are used such to produce intimate human exposure. One prominent use of $Al(OH)_3$ is in antacids (e.g., Equate™, Maalox™, or Mylanta™). Up to 5,000 mg Al/person/day are ingested from aluminum-containing medicinal products (aluminum hydroxide, aluminum-containing phosphate binders) like antacids. Known side effects comprise moderate laxative effects, but no neurotoxic effects. Individuals with severely impaired renal function may use these drugs; however, close monitoring of serum Al levels is imperative for this subpopulation.

A major source of potential exposure to aluminum is found in the aluminum metal industry, mainly in refining and smelting as well as powder production. It should be emphasized that all such exposures are to aluminum *oxide*. Despite a century's experience, there is relatively little workplace exposure data from this industry since no consistent dust disorders attributable to aluminum oxides have occurred. During the previous 100 years of common usage, subsequent to extreme potentials for human exposure, except for some occupational pulmonary diseases, this ubiquitous metal had not been clearly associated with human disease.

DISCUSSION

The use of Aluminum hydroxide as a flame retardant offers appreciable benefit over the halogen-based flame retardant - like DecaBDE - that have been used widely until today. It is capable of absorbing toxic fumes and thus reduces the emission of hazardous fumes, e.g., from smoldering insulation material. In addition, Aluminum hydroxide releases water when heated and thus serves to cool the smoldering material. The release of polyhalogenated dibenzodioxins and furans is a serious health problem posed by halogenated flame retardants. Substituting these compounds by Aluminum hydroxide is therefore an important step towards greater consumer safety.

The use of Aluminum hydroxide as flame retardant, e.g., in insulation material for electrical wiring, is far less exposure prone than the use of Al salts in deodorants or oral antacids. As far as exposure duration is concerned, lifelong occupational exposures in the Al producing industry have not been associated with neurotoxic events or other signs of systemic toxicity, despite a century of experience.

The search for safer alternatives to an existing flame retardant should be over when a material has been found that fulfills the technical specifications of for a flame retardant while at the same time it is generally recognized as safe by the FDA –for use as food additive or as

packaging material for food. The toxicity and epidemiology of aluminum compound is well-investigated and leaves no uncertainty regarding the safety of these products for man and environment.

Leaving aside the biodegradability criterion which reasonably cannot be applied to an insoluble mineral, the other criteria for assigning a “Low Hazard” for all end-points, like low bioaccumulation potential, low human toxicity and low ecotoxicity, are perfectly fulfilled by Aluminum hydroxide.

CONCLUSION

In the absence of any adverse effects of Aluminum hydroxide on man and environment, the use of Aluminum hydroxide as flame retardant should be assigned "Low” for all end-points.

By Dr. Karl-Heinz Spriestersbach et al.

REFERENCES

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[10] Alfrey *et al.* (1976) The dialysis encephalopathy syndrome. *N. Engl. J. Med.* **294**, 184–188

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BASF

September 19, 2012

From: Raymond Davis
To: Emma Lavoie
Subject: Comments on An Alternatives Assessment For The Flame Retardant decabromodiphenyl Ether (Decabde)

Dear Ms. Lavoie,

BASF is writing to correct misinformation about Red Phosphorous in the Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (decaDBE) published in July of this year.

Incorrect LD_{50} value used for the categoriozation. On page 4-32, the acute toxicity of red phosphorous is characterized as Very High based on oral LD_{50} values of 11.5 mg/kg (rat, mouse), 105 mg/kg (rabbit), and 5 mg/kg (dog) taken from an alternatives assessment written for the Maine Department of Environmental Protection. BASF feels that these values are incorrect and unverifiable. In the Maine DEP report, these values are cited as coming from the MSDS sheets of 2 companies (see attached Maine DEP report), which in turn derived them from a database called RTECS; this database, in turn, derived these values from a secondary source "Vrednie chemichescie veshestva. Neorganicheskie soedinenia elementov V-VII groopp" (Hazardous substances. Inorganic substances containing V-VII group elements), Bandman A.L. et al., Chimia, 1989" with no description of study design or results (see attached listing from RTECS). What the EPA did not indicate is that the Maine DEP report also cited a value of >15,000 mg/kg from an unpublished report provided to ECHA under REACh registration in which male and female rats (10 total) survived a single treatment with 15,000 mg/kg of Red Phosphorous by oral gavage (attached). Furthermore, this value was confirmed in a second study reported to ECHA in which 10 rats (5 male and 5 female) survived treatment with 10,000 mg/kg Red Phosphorous by oral gavage (attached). Thus, the oral LD_{50} values listed in the Alternatives Assessment report (11.5 mg/kg for the rat and mouse), 105 mg/kg for the rabbit, and 5 mg/kg (dog)) are questionable, and these values should be replaced by the verifiable values of > 15,000 mg/kg. This correction results in a classification of Low for Acute toxicity rather than Very High. BASF requests that this value and categorization be corrected in the final document.

We are happy to discuss these comments and the impact that they have on the use of Red Phosphorous. Please feel free to contact me at the number below.

Regards,

Raymond M. David, Ph.D., DABT
Manager, Toxicology

Attachment 1

Pure Strategies Inc. prepared for the Maine Department of Environmental Protection (2010). "Decabromodiphenyl Ether Flame Retardant in Plastic Pallets: A Safer Alternatives Assessment, Appendices."
Accessible at: http://www.maine.gov/tools/whatsnew/attach.php?id=365205&an=3

This attachment is available in a separate document. The attachment provided by BASF was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Attachment 2

Study submitted to ECHA, "Phosphorus: Exp Key Acute toxicity: oral.001."
Accessible at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ebc0201-2545-5adb-e044-00144f67d031/AGGR-6836fe9c-ba96-4882-99ca-1660e305e63b_DISS-9ebc0201-2545-5adb-e044-00144f67d031.html#AGGR-6836fe9c-ba96-4882-99ca-1660e305e63b

This attachment is available in a separate document. The attachment provided by BASF was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Attachment 3

Study submitted to ECHA, "Phosphorus: Exp Supporting Acute toxicity: oral.002." Accessible at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ebc0201-2545-5adb-e044-00144f67d031/AGGR-37cdea8c-c51d-43cc-ae6a-61a364cf9a2f_DISS-9ebc0201-2545-5adb-e044-00144f67d031.html#AGGR-37cdea8c-c51d-43cc-ae6a-61a364cf9a2f

This attachment is available in a separate document. The attachment provided by BASF was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Attachment 4

Registry of Toxic Effects of Chemical Substances (RTECS) entry. "Phosphorus (red)."

This attachment is available in a separate document. The attachment provided by BASF was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Attachment 5

Registry of Toxic Effects of Chemical Substances (RTECS) entry. "Phosphorus (white)."

This attachment is available in a separate document. The attachment provided by BASF was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

GlobalAutomakers

Aston Martin ∘ Ferrari ∘ Honda ∘ Hyundai ∘ Isuzu ∘ Kia ∘ Maserati
McLaren ∘ Nissan ∘ Peugeot ∘ Subaru ∘ Suzuki ∘ Toyota

September 27, 2012

Emma Lavoie
Document Control Office (7407M)
Office of Pollution Prevention and Toxics (OPPT)
Environmental Protection Agency
1200 Pennsylvania Ave. NW.
Washington, DC 20460–0001
ATTN: Docket ID EPA–HQ–OPPT–2010–1039

RE: Environmental Protection Agency Design for the Environment's July 2012 Draft Report on "An Alternatives Assessment for the Flame-Retardant Decabromodiphenyl Ether (DecaBDE)"
(Submitted via Email)

Dear Ms. Lavoie:

The Technical Affairs Committee of the Association of Global Automakers, Inc. (Global Automakers)[1] appreciates the opportunity to provide the enclosed comments to the U.S. Environmental Protection Agency (EPA) on the Design for the Environment's (DfE) draft report, "An Alternatives Assessment for the Flame-Retardant Decabromodiphenyl Ether (DecaBDE)" (July 2012).

Global Automakers and its members have consistently supported the development and use of the safest chemicals and products available for use in the automotive industry. Through the application of green chemistry principles and sound scientific methods, Global Automakers believes that the design and development of new chemistries and technologies will continue to provide innovative solutions to current and emerging environmental challenges. Our goal is to ensure that our members have the opportunity to provide high quality, environmentally sound, and safe products and services. With these goals in mind, we look for ways to provide tools to our members to facilitate continuous improvement and to ensure that wherever possible we assist them to not only meet but exceed safety and environmental standards.

[1] The Association of Global Automakers represents international motor vehicle manufacturers, original equipment suppliers, and other automotive-related trade associations. Our Technical Affairs Committee members include: American Honda Motor Co., American Suzuki Motor Corp., Aston Martin Lagonda of North America, Inc., Ferrari North America, Inc., Hyundai Motor America, Isuzu Motors America, Inc., Kia Motors America, Inc., Maserati North America, Inc., McLaren Automotive Ltd., Nissan North America, Inc. Peugeot Motors of America Subaru of America, Inc., ADVICS North America, Inc., Delphi Corporation, Denso International America, Inc., and Robert Bosch Corporation. We work with industry leaders, legislators, and regulators in the United States to create public policies that improve motor vehicle safety, encourage technological innovation, and protect our planet. Our goal is to foster an open and competitive automotive marketplace that encourages investment, job growth, and development of vehicles that can enhance Americans' quality of life. For more information, visit www.globalautomakers.org.

The automotive industry has worked diligently to develop and implement strategies to successfully eliminate pentabromodiphenyl ether (pentaBDE) and octabromodiphenyl ether (octaBDE) from our products, and we are now working aggressively towards the elimination of decabromodiphenyl ether (decaBDE).

We thank you for consideration of these comments and would welcome the opportunity to provide any additional information you may need. If you have any questions, please contact Julia Rege, Senior Manager, Environment & Energy at jrege@globalautomakers.org or (202) 650-5559.

Sincerely,

Michael J. Stanton
President & CEO, Global Automakers

Comments Submitted by
The Association of Global Automakers, Inc.

Regarding the Draft Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecaBDE)

We appreciate the significant investment that EPA has made in developing this Alternative Assessment (AA) for decaBDE. By engaging a diverse set of stakeholders, EPA through the Design for the Environment (DfE) program has been able to compile a comprehensive listing of potential alternatives for decaBDE and an overview of the potential health and environmental impacts associated with those alternatives. By including the transportation sector in this assessment, EPA has been able to identify many of the current uses for decaBDE in the automotive sector and the critical role that decaBDE plays in achieving safety standards. As recognized in the AA, "DecaBDE is effective in meeting fire safety standards for plastics and textiles that are used for the manufacture of consumer electronics, wire and cable insulation,…paneling for cars, buses and airplanes…" (1-2)

What is clear from the transportation section of the draft report is that decaBDE has a myriad of uses in the automotive sector and serves to provide a critical function in meeting both federal flammability and industry sponsored safety standards. The availability of safe alternatives that provide those same performance and safety characteristics is essential to our industry and to meeting our commitments to our customers.

The context within which we provide these comments is the utility of this draft assessment to assist the automotive sector in making informed choices and substitution decisions for long term design and development of our products. In the automotive sector, the design and development phase of an automobile is a multi-year process. As clearly recognized in the draft decaBDE AA, there are no "drop in" replacements for uses in the automotive sector. Substitution of one chemical or product for another is a time and resource intensive process. Substitution decisions must be informed by performance data, safety tests, health and environmental considerations, economics, and consumer acceptance criteria. Substitution decisions must be made for the long term and must be informed by a strong degree of regulatory certainty and predictability. As stated in the report, "Alternative flame retardants must not only have a favorable environmental profile, but also must provide satisfactory (or superior) fire safety, have an acceptable cost, and attain the appropriate balance of properties…in the final product." (6-1) Our comments focus on three key points:

1. Availability of DecaBDE Substitutes for the Automotive Sector
2. Reliance on the DecaBDE Assessment for Decision Making
3. Market Availability of Substitutes

Availability of DecaBDE Substitutes for the Automotive Sector

One of the overarching questions raised by this AA is how EPA will use the findings of this work to further inform on any regulatory action or program focused on decaBDE. Of the 32 alternatives identified by the DfE partnership, 22 were identified as potentially viable and functional replacements for decaBDE in automotive applications. However, as the assessment correctly points out, "Few potential alternatives to decaBDE are "drop-in" replacements." (1-2)

In the case of the automotive sector, none of the 32 identified alternatives has a hazard profile that is significantly preferable to decaBDE itself. Of the 22 potential alternatives for automotive applications, while many have lower bioaccumulation potential, all are rated as High or Very High for persistence. Some appear to have better aquatic toxicity profiles but less preferable acute and/or chronic health effects profiles. Where human health effects profiles appear to be preferable, aquatic impacts are of concern. In short, there is no clear preferable alternative based on EPA's hazard assessment.

In the absence of an environmentally preferable alternative for what can be considered a critical use, what guidance can EPA provide for sectors that require the continued availability of an effective flame retardant? Switching to any of the alternatives identified in this assessment are likely to only provide a short term solution for the automotive sector. All of the chemicals assessed in this process have hazard profiles that will likely lead to some type of regulatory oversight. Investments made in the redesign and development of automotive components that contain decaBDE to incorporate any of the current alternatives will be short term at best. As EPA continues its focus on flame retardants and PBT chemicals, any alternative chosen today may be the focus of a phase out tomorrow. In short, this is a moving target creating constant market, as well as regulatory, uncertainty. As recognized in the AA,

> Substituting chemicals can involve significant costs, as industries must adapt their production processes, and have products re-tested for all required performance and product standards. Decision-makers are advised to see informed chemical substitution decisions as long term investments, and to replace the use of decaBDE with a chemical they anticipate using for many years to come. This includes attention to potential future regulatory actions motivated by adverse human health and environmental impacts, as well as market trends. (6-11)

Recognizing that there is no preferable alternative for many uses at this time, we recommend that EPA clearly make that point in this AA. As a document that will be used by a diverse stakeholder group, it is important that this assessment recognize where viable alternatives are not currently available. That clear recognition will help to accomplish two important goals. First, it will serve to manage stakeholder expectations in terms of timing relative to decaBDE phase out. Second, and maybe more importantly, it will signal a need to the research and development community that a prime opportunity exists for green chemistry solutions to this challenge.

We also recommend that EPA incorporate the findings of this assessment into its regulatory scheme for decaBDE and defer any further regulatory actions until safer alternatives are available. As the AA concludes, "Unfortunately, chemicals that are closer to being 'drop-in' substitutes generally have similar physical and chemical properties, and therefore are likely to have similar hazard and exposure profiles." (6-10) This finding does not mean that the automotive sector will not continue to make substitutions wherever possible and work with suppliers to develop new alternative technologies to decaBDE. It is important to recognize that if EPA had completed this Alternatives Assessment before proceeding with the proposed decaBDE significant new use rule (SNUR), EPA would have had a more comprehensive understanding of the limited universe of safer substitutes to factor into its decision making and timing considerations. We strongly recommend that EPA conduct an alternative analysis process prior to issuing any additional SNURs for existing chemicals. Understanding alternatives, their hazard profiles and their availability is essential to developing regulations that are practical and effective.

Reliance on the DecaBDE Assessment for Decision Making

EPA lays out a number of issues that should be taken into consideration when using this AA for selecting alternative flame retardants. While we recognize that it is important to understand the limitations of any tool such as this, the number of limitations or considerations that EPA has used to caveat this effort seems to undermine the utility of this particular tool. For example:

> ***The need for additional data***:
> 1) Much of the data used in the individual hazard assessments is modeled data. There is very little reliable information on many of the alternatives for environmental fate and the AA recommends that environmental monitoring data "could bolster the hazard assessments by confirming that environmental fate is as predicted." (6-4)
>
> 2) The assessment also confirms uncertainty associated with high persistence or highly bioaccumulative chemicals and their degradation products. "[They] have high potential for exposure and unpredictable hazards following chronic exposures that may not be captured in the hazard screening process." (6-6)
>
> 3) "Empirical data is needed to confirm low toxicity and bioaccumulation predictions." (6-7)
>
> 4) "In the absence of measured data we encourage users of this alternative assessment to be cautious in the interpretation of hazard profiles." (6-7)

Taken together, these cautions about the availability and reliability of the data used to develop the hazard profiles gives the user concerns about the ultimate reliability that this AA will provide in making informed substitution choices.

Market Availability of Substitutes

While many of the alternatives assessed in this report are commercially available, the report makes it clear that some may not be available in the quantity needed for widespread use. Commercial availability should be a key factor when determining if an alternative is "viable."

Conclusion

We appreciate the significant effort that EPA has invested in developing this Alternatives Assessment for decaBDE. We applaud the open process that has been used in engaging a diverse set of stakeholders and providing a forum for all views to be heard. The result of this process has been to demonstrate that while alternatives are available, none of them are "drop-in" replacements for uses in the automotive sector, and none of the alternatives have a preferable hazard profile when compared to decaBDE. This finding is important in that it signals the need for continued use of decaBDE in certain circumstances and the need for a concerted research and development effort to identify a preferable alternative(s). We urge that there be close coordination between the DfE program and the pending TSCA SNUR regarding decaBDE.

Budenheim

September 27, 2012

Budenheim

Dear Ms. Emma Lavoie,

This letter refers to the *draft report on deca BDE substitutes, July 2012*, and in particular to the qualification of ammonium polyphosphate as a Flame Retardant of VERY HIGH PERSISTENCE.

This qualification is apparently made based on the description of the chemical as it appears in page 4 -62 of the mentioned draft.

We, as experts in the world of phosphates for more than 100 years, and in particular in the ammonium polyphosphates technology, believe that the given description needs to be modified.

The assumption made in page 4-63 is that the solubility had been determined from the suspension and would not reflect the real solubility in water. As a consequence, the ammonium polyphosphates have been qualified as a chemical of a very high persistence.

However, the test method used in the industry and by Clariant and Wanjie when determining solubility is based on using only the *clear phase* of the suspension *after centrifugation* of the suspension. Therefore the solubility values given by Clariant and Wanjie do indeed represent the true solubility in water and can be used for the evaluation of the persistence.

Please find in the annexed document our arguments and proposal for use in page 4-62, and the proposal to change the qualification of the persistence to LOW and VERY LOW (depending on the type of ammonium polyphosphate).

In the hope that this note will contribute to the work and offering our knowledge for any further question you may have, we remain with best regards

Budenheim, Sep 28, 2012

Dr. Moritz Fichtmueller

Vice President BU Material Ingredients

Comments on Ammonium polyphosphate description - Page 4-62

Ammonium polyphosphates (APPs) can be divided in three groups depending on the chain length:

a) Crystal phase II as per XRay diffraction pattern, corresponding to polymers of a chain length > 1000. *(1)*

b) Crystal phase I as per Xray diffraction pattern, corresponding to polymers of a chain length 6<n<1000. *(1)*

c) Polymers with a chain length < 6. Only existing as liquids in a water phase and characterized by Thin Film Liquid Chromatography. They are typically mixtures of tetra, tri, pyro and orthophosphates (the monomer) (5)

Chemical Considerations (2)

APPs are condensation products from dehydration of orthophosphates (monomer), by thermal treatment and/or the use of condensing products. The chain length will depend on the condensation process applied to obtain the particular APP

n ($NH_4H_2PO_4$) -> n ((NH_4PO_3)) + n H_2O

APPs can be hydrolyzed in the same manner as they are condensed, back to the original monomer ammonium orthophosphate.

The shorter the chain length is, the higher the hydrolysis rate.

Solubility will depend on: Chain length, pH of water, concentration in water, time and temperature.

solubility, 10 gr APP in 100 ml of water, 1h, 25ºC

APPII	< 1 gr/100 ml water
APPI	10-1 gr/100 ml water
liquid APP	NA

	solubility, 10 gr APP in 100 ml of water, 24 h., 75ºC
APPII	< 10gr/100 ml water
APPI	>10gr /100 ml water (fully soluble)
liquid APP	NA

Source: APP suppliers, TDS, (4)

The hydrolysis products are fertilizers that can react in alkaline soils (Ca CO3) to form Ca3(PO4)2 (original composition of the natural mined phosphate rock from which orthophosphoric acid is obtained). Ammonia is either absorbed by plant leaves or converted by soil bacteria in nitrates to be absorbed by radicular mechanisms.

Acidic soils will accelerate the hydrolysis of APPs. Once hydrolyzed, bacteria can act on NH4+ groups and orthophosphoric/polyphosphoric acids reacts with soil metal nutrients carrying them to the plant (slow release fertilization) (3).

Our conclusion is that any APPs behave as a N/P fertilizer, and the analysis of the persistence should refer to the same criteria applied to the fertilizer sector.

We recommend dividing the ammonium polyphosphates in the three groups APPII, APPI and liquid APP and assign a persistence qualification as Low, Low and Very Low respectively.

References

(1) Preparation and characterization of Crystalline Long-Chain ammonium polyphosphates. *C.Y: Shen, et al. Journal of the American Chemical Society /91:1 / January 1, 1969)*

(2) *Chapter 5.4: PHOSPHOROUS 2000,D.E.C Corbridge, Elsevier*

(3) Development of a Novel Slow-Releasing Iron-Manganese Fertilizer Compound . *Ishita Bhattacharya et al., Ind. Eng. Chem. Res.* 2007, *46,* 287-2876 ,

(4) Budenheim confidential studies.

(5) 11-37 -0 TDS ex Potash Corp. ,10-30-0 TDS Praypol (Prayon)

International Antimony Association (i2a)

September 28, 2012

To: Dr Emma Lavoie

Concerning: *"An Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecaBDE)" – comments on antimony trioxide hazard assessment*

Brussels, 28 September 2012

Dear Dr Lavoie,

I am submitting this letter on behalf of the members of the International Antimony Association (i2a). We are an international non-profit association whose mission is to gather, study and disseminate information on the safe use of antimony and antimony compounds, especially with regard to the relevant environmental, health and safety regulations.

We highly appreciate you included the data of the ATO Risk Assessment Report (2008) (which was later that year approved by OECD under the SIAP program) in the draft alternative assessment report "*An Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecaBDE)*" released on 30 July 2012. We hereby would like to raise one additional point for your consideration:

Dermal irritation (p99): First, we would like to bring the Gross et al (1955) study with rabbits to your attention. This study has been used in the ATO RAR, and concludes that ATO is not irritating to rabbit skin (Gross P et al. (1955) *Toxicologic study of calcium halophosphate phosphors and antimony trioxide. Acute and chronic toxicity and some pharmacologic aspects*. AMA Arch. Ind. Health 11, 473-478). Second, in the ATO RAR, it was concluded that special conditions, namely substantial heat and sweat, are required in addition to high chemical dermal exposure to ATO in all cases where skin irritation effects were described in the workplace (decision of the Committee for Risk Assessment (RAC) of ECHA of 3 July 2009). This means that the skin irritation is an unspecific phenomenon in which poorly soluble fine powders can block sweat ducts, there causing rashes. This has also been reported with other inert inorganic materials. Furthermore, it was unclear whether ATO was the only chemical substance to which the above mentioned workers had been exposed. We would highly appreciate if this could be addressed in the present draft report as well, and that, based on this, the risk was ranked as 'low' instead of 'moderate'. The dermal irritation of ATO is considered a particle effect rather than an antimony effect.

We hope the above mentioned comments can be considered in the final document.

Should you have any further questions regarding ATO or other antimony compounds, please do not hesitate to contact us.

Kind regards,

Dr. Jelle Mertens
i2a Regulatory Scientist
(+32 (2) 771 26 68; jelle@antimony.be)

Clariant

September 18, 2012

CLARIANT

September 18, 2012
From: Adrian Beard
To: Emma Lavoie
Subject: DfE AA question - Red Phosphorus - acute mammalian tox study from HOECHST, 1975

Dear Emma,

Please find attached an study on acute toxicity of red phosphorus which we also submitted within the dossier for REACH (I thought I had submitted it earlier already …):

- acute tox for female rats: LD50 > 15000 mg/kg bw
- acute inhalation study was not possible due to phys-chem properties of red P and was waived
- because the oral LD50 > 15 g/kg bw and the substance is not sensitising to skin, the acute dermal tox was waived as well. Here, no effects are to be expected.
- because of the high LD50 it can be assumed that red P is not acutely toxic.

Best regards
Adrian

Attachment

This attachment provided by Clariant is *not* provided here or in a separate document because it was claimed confidential.

October 3, 2012
From: Adrian Beard
To: Emma Lavoie
Subject: DfE AA question - Red Phosphorus - workplace safety and handling issues

Dear Emma,

I would like to add a comment on red phosphorus. Whereas we believe that you rate the acute toxicity as much too high compared to our data and legal classification, the EPA report only briefly mentions degradation products on page 4-504:

"**Metabolites, Degradates and Transformation Products:** Phosphine (CASRN 7803-51-2), phosphorus oxides, hypophosphorus acid (CASRN 6303-21-5), phosphoric acid (CASRN 7664-38-2)"

The potential formation of toxic phosphine gas is a serious workplace safety issue which requires special precautions or specially treated product forms. Phosphine may also form under unfavourable conditions in use (high humidity and temperature, large surface area). The oxidation to phosphorus acids can also pose a problem in applications like electrical or electronic equipment. This should be considered in choosing red phosphorus as a flame retardant. Please see the attached Clariant information sheet on handling of red phosphorus powder grades.

Best regards
Adrian

Attachment

Clariant, BU Additives. "Safety Precautions in Handling Red Phosphorus Power Grades."

This attachment is available in a separate document. The attachment provided by Clariant on October 3, 2012 was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

September 28, 2012
From: Adrian Beard
To: Emma Lavoie
Subject: US-EPA decaBDE alternatives assessment - Clariant comments on Ammonium Polyphosphate (APP)

Dear Emma,

I had submitted comments earlier on the PERSISTENCE rating of APP. To summarize, I believe the concept of degradation and persistence is rooted in and makes sense for organic materials which can decompose to CO2 and water (and others oxidation products) eventually. For inorganic materials and metals the concept in terms of a "concern indicator" is difficult to apply.

In this respect we fully support the letter submitted by Budenheim Corp. (Moritz Fichtmueller), suggesting a persistence rating of LOW or even VERY LOW for ammonium polyphosphate types. We agree with your assessment that hydrolysis is the mechanism of chemical degradation in the environment. In dilute solutions (such as used by OECD 111) this should occur rather fast and resulting in a half-life < 180 days. The available solubility data point in this direction.

[For APP the situation is even more strange, because a slow degradation in the environment can only be beneficial, since the only negative effect could be eutrophication of water streams or lakes by direct exposure. This effect would be dampened by a slow degradation.]

Just another point concerning the Hazard Evaluation for APP, on page 4-63 one of the reference states Clariant 1999. Interestingly when you look at the reference list (page 4-75) it directs the reader to the website http://www.kraski-laki.ru/pdf/ExolitAP422.pdf which I believe is not a legitimate reference / use of our copyrighted material. Can you please refer to the current datasheet which is located here on our website:

http://www.additives.clariant.com/bu/additives/PDS_Additives.nsf/www/DS-OSTS-7SHDAQ?open

Best regards
Adrian

September 28, 2012
From: Adrian Beard
To: Emma Lavoie
Subject: US-EPA decaBDE alternatives assessment - Clariant comments on Aluminum Diethylphosphinate (DEPAL)

Dear Emma,

In addition to the comment that Tim Reilly made about the Persistence rating, we compared the rating found the Hazard summary table page 4-33 to the summary from the ENFIRO study (c.f. Table below). Both studies are using the same scaling system however in the ENFIRO study both Acute and Chronic tox are rated as Low whereas DEPAL is rated as Moderate in the EPA table. This might be due to the fact that EPA used a NICNAS report on Exolit OP 1312 (which also contains melamine polyphosphate and zinc borate) not OP 1230 (see attached pdf file). Hence I would tend to argue that this particulate NICNAS report is not appropriate for the EPA Hazard Evaluation of DEPAL - please use the ECHA REACH dossier, which has more up to date and reviewed information (see item 2 below). Links to data sheets of our DEPAL products are here.

In my e-mail of 2012-03-01 on the draft assessment I noted:

DEPAL

1. Please find enclosed a study report from TNO (please treat as CONFIDENTIAL) which shows that the bioavailability / bioaccessibility of the aluminium from DEPAL is very low (0.1%). Therefore, concern levels for developmental and neurological should be re-considered. *From what I see in your latest report, this has not been taken into account. You still speak of a bioavailable metal species (= Al). Please review and consider concern level of LOW for Neurotox and Developmental Tox.*
2. The European Chemicals Authority (ECHA) has posted the REACH dossier on their website. You can find it here
http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances
when you search for ELINCS ********* (please treat this number as CONFIDENTIAL and do not cite it)
There you will find the most recent consolidated data on phys-chem, fate, tox and eco-tox.

Best regards
Adrian

Attachment 1

Hazard summary table page 4-33 to the summary from the ENFIRO study:

	Human health												Ecotox		Fate		ENFIRO tox										Metabolisatio
	Carcinogenic	Mutagenic	Reproduction	Developmental	Endocrine disp	Neurological	Acute toxicity	Systematic/organ effects	Sensitization (skin)	Irritation/corrosion (skin)	Irritation/corrosion (eyes)	Immune system	Acute	Chronic	Persistence	Bioaccumulation	Daphnia	Algae	Cytotoxicity neuronal cells	Cytotoxicity liver cells	Depolarization-Evoked Ca2+	Basal Ca2+	nACh receptor	Cell respiration	Comp. T4 TTR binding	Mutagenicity	Estrogenicity	Metabolites
	M	L	L	M		M	L	L	L	L	L		L	L	vH	M			1	1	1	1	1	1	1		1	Penta-nonaBD
	L	L	*L*	*M*		*M*	L	L	L	L	M		L	L	*H*	L				1				1	1		1	recalcitrant Al

ed: limited data available

1	No potency	Response < 20% of control at 1(
2	Low potency	(EC_{50} or IC_{50}) > 10 µM and respo
3	Moderate potenc	1 µM < (EC_{50} or IC_{50}) < 10 µM
4	High potency	0,1 µM < (EC_{50} or IC_{50}) < 1 µM
5	Very high potency	0,01 µM < (EC_{50} or IC_{50}) < 0,1 µM

Attachment 2

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). "Full Public Report, Chemical in Exolit OP 1312."
Accessible at:
http://www.nicnas.gov.au/publications/car/new/std/stdfullr/std1000fr/std1168fr.pdf

This attachment is available in a separate document. This attachment provided by Clariant on September 28, 2012 was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Attachment 3

This attachment provided by Clariant is *not* provided here or in a separate document because it was claimed confidential.

Albemarle Corporation

September 28, 2012

Albemarle Corporation
Health, Safety & Environment
451 Florida Street

Emma Lavoie
Design for the Environment
U.S. Environmental Protection Agency, East Building
1201 Constitution Avenue, NW; Room 5326A (7406M)
Washington DC 20004-3302
Phone: 202-564-0951
Lavoie.Emma@epa.gov

September 28, 2012

RE: Comments on the draft report "An Alternatives Assessment for the Flame-Retardant Decabromodiphenyl Ether (DecaBDE)"

Dear Ms. Lavoie,

Albemarle Corporation is a specialty chemical manufacturer whose product line includes flame retardants. Certain products manufactured by Albemarle Corporation are included in the above draft Design for the Environment (DfE) report. The enclosed comments pertain to three of the substances included in the report, e.g. decabromodiphenyl ether (CASRN 1163-19-5), decabromodiphenyl ethane (CASRN 84852-53-9) and ethylene bis-tetrabromophthalimide (CASRN 32588-76-4). New information is being submitted on carcinogenicity, metabolism, bioaccumulation, and chemical analysis. Copies of final reports and other information are being provided on a CD submitted via overnight mail.

As a manufacturer, Albemarle Corporation has substantial knowledge on these products, and appreciates the opportunity to comment on the DfE draft. Within the 60-day comment period, we are only able to respond to the summary tables for the above three flame retardants. We are unable to comment on the body of the 812 page report.

I hope these comments are useful in your deliberations. By way of introduction, I have investigated the toxicology of brominated flame retardants, including the above three, for over twenty years. Research efforts include performance of numerous guideline and GLP-compliant mammalian, environmental and physical/chemical studies. I've published on these topics and consistently review the brominated flame retardant literature. I participated in reviews on various brominated flame retardants sponsored by the World Health Organization, the European Union, the Organization for Economic and Community Development, the United States National Research Council, the U.S. Environmental Protection Agency, and other organizations and agencies. I serve as a peer-reviewer for journals and governmental agencies. If I can clarify any of the enclosed information, please do not hesitate to contact me.

For your information, Albemarle Corporation has funded independent comments on the three substances by the consulting organizations TERA, Exponent®, and ENVIRON. Those comments were developed independently and are being submitted separately by each organization.

Respectfully,

Marcia L. Hardy, D.V.M., Ph.D.
Senior Toxicology Advisor

Comments on the DRAFT of July 2012 Design for Environment Screening Level Hazard Assessment of Decabromodiphenyl Ether (DecaBDE); CASRN 1163-19-5.

Comments on the DRAFT of July 2012 Design for Environment Screening Level Hazard Assessment of Decabromodiphenyl Ethane (DBDPEthane); CASRN 84852-53-9.

Comments on the DRAFT of July 2012 Design for Environment Screening Level Hazard Assessment of Ethylene Bis-Tetraromophthalimide (EBTBP); CASRN 32588-76-4.

These comments are available in a separate document. The commenter would not provide an alternate format for their comments to enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

Prepared for:
Albemarle Corporation
Baton Rouge, Louisiana

Prepared by:
ENVIRON International Corporation
Monroe, Louisiana

Comments in Response to EPA's Alternatives Assessment for the flame Retardant Decabromodiphenyl Ether (DecalBDE)

Authors:
P. Robinan Gentry, PhD, DABT
Harvey J. Clewell, III, PhD, DABT
Tracy M. Greene, BS
Date:
September 2012
Project Number:
23-29159A

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List of Tables

Table 1: Criteria Used to Assign Hazard Designations

Table 2: Hazard Summary Table

1 Introduction

ENVIRON International Corporation (ENVIRON), at the request of Albemarle Corporation, has prepared comments in response to the Environmental Protection Agency (EPA) Design for the Environment's (DfE) draft document entitled "An Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (Deca BDE)" (EPA 2012). ENVIRON performed a critical review of previous comments submitted by Albemarle in response to an earlier draft of the Alternative Assessment Document and prepared comments focusing on the bioaccumulation, repeated dose and neurodevelopmental toxicity and carcinogenicity for DecaBDE, decabromodiphenyl ethane (EBP), and Ethylene bis-tetrabromophthalimide (EBPTBP).

The purpose of the alternatives assessment document for DecaBDE prepared by EPA (2012) is to identify functional and viable alternatives for DecaBDE, evaluate their human health and environmental profiles, and inform decision makers in order for organizations to choose safer alternatives to DecaBDE. Initially, EPA developed a list of potential DecaBDE alternatives for use in polyolefins, styrenics, engineering thermoplastics, thermosets, elastomers or waterborne emulsions and coatings. Potential alternatives were not chosen based on environmental preferability but based on their functionality and viability.

DfE's assessment of toxicological and environmental endpoints follows the guidance of the "Alternatives Assessment Criteria for Hazard Evaluation" (EPA 2011). The criteria used for hazard designation as outlined by EPA (2011, 2012) for each endpoint reviewed by ENVIRON is presented in Table 1. Based on these criteria, hazard designations were assigned to the potential alternatives. The hazard designations currently assigned to DecaBDE, EBP, and EBPTBP by DfE (EPA 2012) are presented in Table 2.
The following comments, organized by endpoints, were prepared in bulleted format so Albemarle could easily review ENVIRON's major conclusions of the relevant data. The information presented below reflects both ENVIRON's review of the data, as well as, the opinions of Dr. Harvey Clewell of the Hamner Institutes for Health Sciences.

2 Comments by Endpoint

2.1 Repeated Dose Effects

The screening level classification for potential health effects from repeated dose to DecaBDE is currently classified by DfE as MODERATE; however, this classification should be LOW. According the DfE's criteria (EPA 2011), a flame retardant chemical should be classified as having low potential for repeated dose toxicity if the NOAELs are greater than 100 mg/kg/day (Table 1).

- The only LOAEL below 100 mg/kg/day for DecaBDE is from a 28 day study with a mixture containing only 77.4% DecaBDE (Norris et al. 1973) and the endpoint that is the basis of the LOAEL is an increase in liver weight.

- Longer exposure to a diet containing approximately 96% DecaBDE resulted in NOAELs for the same endpoint (liver enlargement) of approximately 3000 mg/kg/day following 13 weeks of exposure (NTP 1986) and 1120 mg/kg/day following 2 years of dietary exposure.

- Studies conducted with the pure compound for longer durations should be relied upon for the determination of the classification of potential repeated dose toxicity. Therefore, based on the 13 week and 2 year studies conducted by NTP (1986) with 96% DecaBDE, the potential for repeated dose toxicity should be LOW, with NOAELs of greater than 100 mg/kg/day.

2.2 Carcinogenicity

The screening level classification for potential carcinogenicity from exposure to DecaBDE is currently MODERATE, based on DFE's criteria (EPA 2011). The DfE classification is based on the GHS Classification and Labeling of Chemicals (UN 2011) and is limited to how regulatory agencies have characterized potential based on the NTP (1986) bioassay (i.e., limited evidence of carcinogenicity in animals). The GHS Classification (UN 2011) indicates that the weight of evidence of the available data relevant to carcinogenic potential should be considered in classifying a compound. This includes consideration of tumor type and background incidence, multisite response, progression to malignancy, reduced tumor latency, and response reported in a single species or several species.

- *Tumor Type/Multisite Response*. The only statistically significant dose related increase in the incidence of any tumor type was an increase in liver neoplastic nodules in male and female rats (NTP 1986). No statistically significant increase or dose related trend in hepatocellular carcinomas was reported. Regarding the liver neoplastic nodules the EPA (2008) makes the following statement regarding the uncertainty in relying upon this endpoint:

  > At the time the NTP (1986) study was conducted, the term neoplastic nodule was used to describe abnormal cellular masses in the livers of rats, characterized by loss or distortion of normal cellular architecture (Maronpot et al. 1986). Some of those nodules would now be described as benign hepatocellular adenomas in rats (Wolf and Mann, 2005). However, there is no complete equivalency between the neoplastic nodule of the past and hepatocellular adenoma term of today. Some of the neoplastic nodules from the NTP (1986) study might now be classified as foci of cellular alteration or hyperplasia rather than adenomas (Maronpot et al. 1986). Adenomas and foci of cellular alteration are considered to be preneoplastic lesions, whereas hyperplastic lesions represent secondary nonneoplastic changes (Maronpot et al. 1986). The assumption that the hepatic neoplastic nodules from the NTP (1986) bioassay are equivalent to hepatic adenomas under the current NTP lexicon is a conservative interpretation of the data.

- *Progression to malignancy.* There was no statistically significant or dose related increase in the incidence of hepatocellular carcinomas in either male or female rats (NTP 1986)

- *Single species vs. several species*. The only statistically significant increase in the incidence of neoplastic nodules was reported in rats. No statistically significant dose related increase in any endpoint was reported in male or female mice (NTP 1986) • *Negative genotoxicity/mutagenicity data*. DecaBDE was not mutagenic in *Salmonella typhimurium*, negative in the mouse lymphoma assay, and did not produce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells (NTP 1986).
- Statistically significant increases in the incidence of thyroid follicular cell hyperplasia were reported in male mice (no increase observed in female mice) and this endpoint has also been suggested as a stage in the development of thyroid follicular cell tumors (EPA 2008). However, no statistically significant or dose-related trend in the incidence of thyroid follicular cell adenomas or carcinomas was observed in male mice.

- Based in part on its review of this study, the National Academy of Sciences (2000) concluded that DecaBDE is a possible carcinogen in the rat, but that no conclusions could be drawn regarding its potential carcinogenicity in the human. In addition, IARC (1999) determined that, based on the NTP (1986) bioassay, DecaBDE was not classifiable as to its carcinogenicity in humans.

- A two-year feeding study in rats performed prior to NTP (1986) (Kociba et al. 1979), reported no evidence of toxicity or carcinogenicity. This study was conducted at much lower dietary concentrations than the NTP (1986) study and used an earlier DecaBDE formulation (77.4% DecaBDE, 21.8% nonaBDEs, 0.8% octaBDEs) as the test material.

The available data provide evidence of the increase in the incidence of a single benign endpoint in a single species, with no evidence of progression to malignancy or mutagenicity. Based on these data, the weight of evidence for the potential for carcinogenicity of DecaBDE in humans would support a LOW classification, when all of the above factors are taken into consideration.

Although a chronic carcinogenicity study has not been conducted, evaluation of the repeated dose and bioavailability studies for EBP and EBPTBP would be consistent with a classification for potential carcinogenicity of LOW.

- Both EBP and EBPTBP were classified as having LOW potential for repeated dose effects. In repeated dose studies for EBP, NOAELs/LOAELs of > 1000 mg/kg/day were reported in 28 and 90-day oral rat studies (Hardy et al. 2002). In repeated dose studies for EBPTBP, NOAELs were all greater than 1000 mg/kg/day (highest dose tested) (Albemarle 1978; NIEHS 1999, IUCLID 2000, HPV 2008).
- EBP was not detected in the blood, bile, or urine of rats following oral administration, indicating poor absorption from the gastrointestinal tract; with high recoveries of the parent compound (81 to 100%) reported in the feces (Albemarle 2004, Albemarle 2012).
- EBPTBP showed a lack of bioaccumulation in rats following 14 days of dosing (Rabold et al. 1978), with only 0.22% and 0.03% of the total dose present in the liver and kidney, respectively, 24 hours after the last dose.

- Studies suggest that the bioavailability of EBP is even less than that of DecaBDE, which is low. Administration of comparable doses of DecaBDE and EBP (100 mg/kg/day) via corn oil gavage for 90 days resulted in tissue concentrations of EBP 3-5 orders of magnitude lower than those for DecaBDE (Wang et al. 2010).
- Reductive debromination of EBP to lower brominated congeners was not demonstrated to be a significant metabolic pathway in rats (Wang et al. 2010).

2.3 Neurotoxicity\Developmental

The screening level classification for potential neurotoxicity and developmental effects from exposure to DecaBDE should be LOW. DfE relied largely on the EPA (2008) for a review of the available neurotoxicity and developmental studies for DecaBDE and the identification of NOAELs/LOAELs. However, the EPA (2008) summary includes several studies with LOAELs below 1000 mg/kg/day (Viberg et al. 2003, 2007; Rice et al. 2007) for which there are issues that must be considered in evaluating the potential for neurotoxicity or developmental effects following exposure to DecaBDE.

- Williams and DeSesso (2010) have conducted a critical review of the available studies evaluating the potential for neurodevelopmental effects following exposure to DecaBDE noting the following:
  - Those studies identifying LOAELs for changes in locomotor activity in mice and rats were conducted by the same laboratory (Viberg et al. 2003, 2007; Rice et al. 2007). In these studies DecaBDE was applied in a unique vehicle (20% fat emulsion of a 1:10 mixture of egg lecithin and peanut oil) which the authors suggested noted allows for "a more physiologically appropriate absorption and hence distribution of the compounds". However, this suggestion has not been demonstrated in the studies cited as support.
  - Those studies noting LOAELs of less than 1000 mg/kg/day (Viberg et al. 2003, 2007; Rice et al. 2007) were not conducted according to GLP Guidelines or using EPA developmental neurotoxicity guidelines. The only study available at the time of the Williams and DeSesso (2010) review that was conducted according to these guidelines, Jacobi et al. (2009), was negative at the highest dose tested (1000 mg/kg/day) and is now in the published literature (Beisemeier et al. 2011).
- Biesemeier et al. (2011) performed a neurodevelopmental toxicity study, in which exposure to DecaBDE via corn oil gavage occurred during gestation and throughout lactation. No neurodevelopmental effects were reported at the highest dose tested of 1000 mg/kg/day.
- Although EPA (2008) considered the studies conducted by Viberg et al. (2003, 2007) and Rice et al. (2007) in the determination of a NOAEL/LOAEL for the derivation of the Reference dose (RfD) for DecaBDE, EPA (2008) rated the confidence in the principal study (Viberg et al. 2003) as low, raising some of the same concerns as Williams and DeSesso (2010), including:

  > The dosing regimen did not include gestation and lactation exposure; only single doses were given. The study was conducted in male mice only. The protocol was unique and did not conform to health effects test guidelines for neurotoxicity screening battery or developmental neurotoxicity studies. While the study design

appears to identify a developmental window of susceptibility, it is not adequate to determine the effect of longer dosing. Translating the implications of these data to more traditional dosing regimens is problematic; particularly with regard to evaluating the implications of in utero and postnatal exposure.

Another concern is that, based on the data provided in the published report (Viberg et al. 2003), more than one pup per litter was used for the behavioral testing (10 male mice were randomly selected from three to five different litters in each treatment group). Increasing the number of samples from each litter may bias the analyses towards false positive. Another concern regarding the study design was the limited number of neurobehavioral parameters that were assessed; the authors measured only indices related to motor activity (locomotion, rearing, and total activity). The absence of a full functional observation battery (FOB) that evaluated neurological and behavioral signs limits the ability to correlate the reported effects with other FOB parameters. Data for the FOB utilized in the Rice et al. (2007) study, also in mice, mitigate some concern related to its absence in the Viberg et al. (2003) study.

- A weight-of-evidence analysis of Viberg et al. (2003, 2007) and Rice et al. (2007) concluded that the reported effects from these laboratories were in opposite directions, suggest low potential neurotoxicity and developmental toxicity, and were not suitable for establishing an RfD for DecaBDE (Goodman 2009).

The integration of the available data, giving the most weight to those studies conducted according to GLP and EPA Guidelines, suggests that a NOAEL of 1000 mg/kg/day for neurological/developmental toxicity is the most appropriate. This would support a classification of LOW potential for neurological/developmental toxicity for DecaBDE.

By analogy, the screening level classification for potential neurotoxicity and developmental effects from exposure to EBP and EBPTBP should also be LOW.

2.4 Bioaccumulation

The screening level classification for potential bioaccumulation for DecaBDE of HIGH has not been demonstrated based on the available measured data (Table 1). According to the DfE criteria (EPA 2011), measured data should be relied upon first in determining classification, rather than estimated values from models, and the measured data do not support a designation of HIGH. However, there are uncertainties regarding the potential metabolic debromination of DecaBDE that warrant further discussion.

- In drawing conclusions regarding the potential for bioaccumulation, the DfE focused largely on the measured accumulation in fish from an unpublished study (MITI 1998; cited in Hardy 2004a, b) and a large estimated bioaccumulation factor using the EPA EPI Suite program (EPA 2012). While DfE reported one study by Noyes et al. (2011) in juvenile fathead minnows, additional studies reporting data regarding the potential for

bioaccumulation of DecaBDE, other than that reported by DfE (EPA 2012), have been conducted (Stapleton et al. 2004; Kierkegaard et al. 1999).

- EPI Suite (2012) is an EPA program that provides users with ***screening-level*** estimates of physical/chemical and environmental fate properties. The program requires only a single input, a representation of the chemical structure, to use the program. It is noted that before using EPI Suite (2012), users should first determine whether any suitable data are available from the literature. It is generally assumed that the relationship between log Kow and log BAF is linear, with increasing log Kow representing an increase in the potential for bioaccumulation. However, it has been demonstrated that for PBDEs bioavailability and metabolic processes in organisms must also be considered. Parabolic associations were noted between log Kow and log BAF in multiple wild aquatic species (Wu et al. 2008), with log BAFs increasing with increasing Kow up to a value of approximately 7 and then a decrease in log BAF was observed with log Kows >7. The authors noted that this was likely related to the efficiency of debromination and elimination in a given species.

- DecaBDE, EBP and EBPTBP have all been tested using protocols consistent with OPPTS (1996) ecological testing guidelines for the estimation of a BCF in common carp (Hardy 2004). Exposure was continued for 6-8 weeks until equilibrium had been reached in fish tissues. Measured BCFs were <5-<50 for DecaBDE and <25 and <33 for EBP and EBPTBP, respectively, suggesting low potential for bioconcentration.

- Bioaccumulation of PBDEs in the aquatic food web is inversely related to the degree of bromination (ATSDR 2004). Higher brominated congeners, such as DecaBDE are rarely detected in biota. This is a result of their low solubility, high log Kow values, and sorption to soil and sediment (ATSDR 2004).

- With increasing bromination, decreasing water solubility of polybrominated diphenyl ethers (PBDEs) is observed; therefore, studies have been conducted to evaluate the potential for bioaccumulation/bioconcentration of DecaBDE in which fish diets were spiked with the compound (Kierkegaard et al. 1999; Stapleton et al. 2004; Noyes et al. 2011). However, it was not demonstrated that comparable concentrations of DecaBDE have been measured in environmental media or biota.

- In dietary studies, potential bioaccumulation of DecaBDE in fish was dose, duration and possibly species dependent in fish. In carp exposed to 40 µg/kg bw for 60 days, no decaBDE was detected in fish tissue (Stapleton et al. 2004). However, in rainbow trout administered 7.5-10 mg/kg body weight/day for 120 days, low levels of decaBDE were observed in tissues.

- Serum half-lives reported for decaBDE ranged from 2 to 15 days in rats (NTP 1986; Huwe and Smith 2007) and occupationally exposed workers (Thuresson et al. 2006). Half-lives for PBDEs have been demonstrated to increase with decreasing bromination in multiple species. In juvenile carp (Stapleton et al. 2004), no half-life could be calculated for DecaBDE due to its lack of accumulation, but half-lives of approximately 23-50 days were estimated for the penta- and hexa-congeners and half-lives of approximately 19-29

days for the hepta- and octa-congeners. In occupationally exposed workers, apparent half-lives of up to approximately 90 days were estimated for hepta- and octa-congeners (Thuresson et al. 2006).

- DecaBDE is poorly absorbed from the gastrointestinal tract of multiple species following repeated dose exposure (Stapleton et al. 2004; Kierkegaard et al. 1999; Huwe et al. 2008; NTP 1986). In fish, Noyes et al. (2011) reports 5.8% bioavailability in fathead minnows (based on parent and presumed metabolites); however, less than 0.5% bioavailability has been reported in common carp (Stapleton et al. 2004) and rainbow trout (Kierkegaard et al. 1999). A study conducted in conjunction with the NTP (1986) two-year bioassay in which DecaBDE was administered in the diet suggested a bioavailability of less than 1%.

- Some concern has been expressed for the potential for debromination of DecaBDE in the environment or through metabolism and elimination in individual species to result in elevated levels of lower brominated congeners. However, these levels appear to be very small based on the low bioavailability of DecaBDE.

  - Levels of octa- and nona-brominated congeners were observed in rats following dietary exposure to 0.3 µg/g diet of a DecaBDE formulation (98.5% DecaBDE, with trace amounts of octa-, nona-, and hepta-BDEs) (Huwe and Smith 2007). The authors noted that these lower brominated congeners may be forming from metabolic debromination of DecaBDE, but only to a small extent because the excess recovered represented an estimated 1% of the administered dose of DecaBDE.

  - In rainbow trout exposed to dietary doses of 7.5-10 mg/kg body weight/day DecaBDE, concentrations of a hexaBDE (BDE-154) were increased in the muscle tissue during the 49 day exposure period (up to approximately 2 ng/g fresh weight) and increased slightly during the 71 day depurination period (to approximately 3 ng/g fresh weight) (Kierkegaard et al. 1999), suggesting low production of metabolites.

  - In juvenile fathead minnows (Noyes et al. 2011), increasing levels of penta- to nona-substituted congeners were observed corresponding to increasing duration of exposure to DecaBDE and increasing tissue concentrations of DecaBDE. However, no results were reported for a 14 day depurination period to determine if the parent or metabolites were decreasing. The authors did note that the cumulative exposure of DecaBDE was approximately 0.45 nmol/fish, with summed metabolites detected at day 28 of approximately 0.026 nmol/fish, also indicating low production of metabolites.

- Unlike lower brominated PBDEs, higher brominated PBDEs, such as DecaBDE, are mainly distributed to the liver and muscle, rather than the adipose tissue. In rats administered a diet containing household dust "naturally" contaminated with PBDEs, at concentrations of 6-8 µg/kg bw for 21 days (Huwe et al. 2008), all tissues preferentially accumulated the lower brominated congeners (penta to hexa congeners). DecaBDE was not readily distributed to most tissues but was extensively excreted in the feces. Liver and plasma were the two body compartments in which decaBDE were most often detected, with none detected in adipose tissue.

- While tri- to hexa-congener PBDEs appear to distribute rather equally to body compartments, hepta- to nona- and especially deca-congeners behave differently than lower molecular weight compounds (Huwe et al. 2008). Higher molecular weight PBDEs have higher concentrations in muscle than adipose tissue in cows; hexa to deca BDEs also poorly transferred into the milk (Huwe et al. 2008). Studies in cows, humans and seals have shown limited distribution of higher brominated congeners into milk, making milk a poor matrix for predicting exposure to or body burdens of hepta- to deca-BDEs (Huwe et al. 2008).

The available data for DecaBDE suggest LOW potential for bioaccumulation, based on its low bioavailability, lack of distribution into adipose tissue and short half-life (approximately 2-15 days in most species). However, there remain questions regarding its potential to be debrominated in the environment or through metabolism in species to lower brominated congeners that may be more persistent. The available data suggest that although this may be possible, the levels of the lower congeners would not approach levels of concern as it relates to the potential for toxicity or carcinogenicity.

Results from bioaccumulation studies conducted for EBP and EBPTBP also indicate low gastrointestinal absorption. The screening level classification for potential bioaccumulation for both EBP and EBPTBP should be LOW based on the available measured data which should be relied upon first in determining classification.

- EBP and EBPTBP measured bioconcentration in fish is reported to be negligible (BCFs ranging from <0.3 to <25 in carp) (Japan Chemical Ecology-Toxicology and Information Centre 1992, Hardy 2004a,b).
- EBP was not present in the blood, bile, or urine of rats following oral administration and is poorly absorbed from the gastrointestinal tract; with high recoveries of the parent compound (81 to 100%) reported in the feces (Albemarle 2004, Albemarle 2012).
- EBPTBP showed a lack of bioaccumulation in rats following 14 days of dosing (Rabold et al. 1978), with only 0.22% and 0.03% of the total dose present in the liver and kidney, respectively, 24 hours after the last dose.

3 Summary/Conclusions

In determining the potential for toxicity, carcinogenicity and bioaccumulation of DecaBDE and its potential substitutes, it is important that DecaBDE has limited absorption/bioavailability and a relatively short half-life in multiple species. Although the integration of the data for repeated dose toxicity, neurological/developmental toxicity and carcinogenicity suggest a low potential for human health effects, this should be considered in combination with the potential exposure levels in humans to provide additional confidence in these classifications, especially due to the potential concerns being raised regarding the debromination of DecaBDE to more persistent congeners. Recent estimates of exposures from air and diet to ***total*** PBDEs in children are estimated to range from 8-50 ng/kg/day (Costa and Giordano 2011) and in adults are estimated to range from 1-16 ng/kg/day (Costa and Giordano 2007), with 28% of this dose represented by DecaBDE (Costa and Giodano 2011). Not only are these exposures orders of magnitude lower than any posing potential concern for toxicity or carcinogenicity in animals, humans also have

barrier functions of the blood brain barrier and gastrointestinal tract that are more mature in the perinatal phase than those in animals (Williams and DeSesso 2010). These differences would predispose the experimental animals to higher rates of absorption than would be expected in humans. These comparisons and differences should provide increased confidence that the potential for human health effects and bioaccumulation are low.

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Table 1 – Criteria Used to Assign Hazard Designations[a]					
Endpoint	**Very High**	**High**	**Moderate**	**Low**	**Very Low**
Human Health Effects					
Carcinogenicity					
	Known or presumed human carcinogen (equivalent to Globally Harmonized System of Classification and Labeling of Chemicals (GHS) category 1A and 1B	Suspected human carcinogen (equivalent to GHS Category 2)	Limited or marginal evidence of carcinogenicity in animals (and inadequate evidence in humans)	Negative or robust mechanism-based SAR (as described above)	-
Developmental Toxicity					
Oral (mg/kg/day)	-	<50	50-250	>250-1000	>1000
Neurotoxicity					
Oral (mg/kg/day)	-	<10	10-100	>100	-
Repeated Dose					
Oral (mg/kg/day)	-	<10	10-100	>100	-
Environmental Persistence					
Bioaccumulation					
Bioconcentration Factor (BDF)/Bioaccumulation factor (BAF)	>5000	5000-1000	<1000-100	<100	-
Log BDF/BAF	>3.7	3.7-3	<3-2	2	-

Notes:
[a] Excerpt from Table 4-2, Page 4-4 through 4.7 of EPA (2012)

Table 2 – Hazard Summary Tablea						
VL= Very Low hazard L= Low hazard M = Moderate hazard H = High hazard VH = Very High hazard						
Chemical	**CASRN**	**Human Health Effects**				**Environmental Fate**
		Carcinogenicity	**Developmental**	**Neurological**	**Repeated Dose**	**Bioaccumulation**
Decabromodiphenyl Ethane	84852-53-9	M[b]	VL	H[b]	L	H
Decabromodiphenyl Ether	1163-19-5	M	H	H	M	H
Ethylene Bis-tetrabromophthalimide	32588-76-4	M[b]	L	M[b]	L	H
Notes: [a] Excerpt from Table 4-7, Page 4-29 of EPA (2012) [b] Based on analogy to experimental data for a structurally similar compound						

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Comments on the Draft EPA DfE Screening Level Hazard Summary for Decabromyldiphenyl Ether (DecaBDE)

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Comments on the Draft EPA DfE Screening Level Hazard Summary for Decabromyldiphenyl Ether (DecaBDE)

General Comments

- Throughout the draft Design for the Environment (DfE) Screening Hazard Assessment for the Flame Retardant Decabromodiphenyl Ether ("DecaBDE report") [1], there are many entries provided as secondary sources, such as the European Chemicals Bureau or EPA. It would be appropriate and useful for the DecaBDE report to include the actual citation of the primary study that was summarized by the secondary source because this will provide for greater transparency, eliminate potential confusion, and provide a more scientifically useful document.

- The EPA DfE guidelines document (EPA 2011) states that EPA experts will evaluate the quality and reliability of both experimental and estimated toxicological data. Instead of describing the quality and reliability of the data, EPA only listed "Reported in a secondary source" for many of the entries of the DecaBDE report in the column "data quality". Such a statement does not provide any information about the quality of a study, methodological limitations or strengths, appropriateness of data analysis, or whether standard protocol methods were implemented in the studies (e.g., OECD or GLP guidelines). Such variables can significantly influence the evaluation of the validity of data from studies and impacts the overall weight-of-the-evidence analysis of an association between a chemical exposure and health effect. Therefore, it is critical to provide more detail about data quality in the draft DecaBDE report.

Comments on Specific Sections of the DecaBDE Report

- **Hazard and Risk Assessments**: Please include the published review by Hardy et al. (2009) in the list of risk assessments for DecaBDE. The Hardy et al. (2009) risk assessment is a comprehensive critical review of the toxicological and human health literature for DecaDBE to develop a chronic oral reference dose (RfD). This risk assessment was recently reviewed by the Toxicology Excellence for Risk Assessment (TERA) International Toxicity Estimates of Risk (ITER) expert panel and the oral RfD for DecaBDE developed in this publication has been posted in the ITER database[2].

[1] U.S. Environmental Protection Agency (EPA). July 2012. An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE). Draft for Public Comment.
[2] http://iter.ctcnet.net/publicurl/pub_view_l2_non.cfm?crn=1163%2D19%2D5&type=NCO

- **Human Health Effects**: In this section of the report, the relevant endpoints should be added to the first or second column of the table under the heading "Property/Endpoint". For example, in the Toxicokinetics section, there is a single endpoint listed directly below entitled, "Dermal Absorption *in vitro*" which includes one dermal study that is summarized. However, in the rows following that entry, there are several intravenous and oral studies described, but there is no "Property/Endpoint" entry for those studies.

- **Toxicokinetics:** The available scientific studies for DecaBDE do not support EPA's statement in this section: "Although experimental findings in human and animal studies suggest that decabromodiphenyl ether is poorly absorbed following oral and dermal administration, even low levels of decabromodiphenyl ether are physiologically relevant due to its chemical properties". What is meant by "physiologically relevant" and what "chemical properties" is EPA referring to? DecaBDE is poorly absorbed and the available NOELs and NOAELs of ≥1000 mg/kg/day in several mammalian repeated dose studies confirm that DecaBDE is associated with low toxicity (Hardy et al. 2009; Goodman et al. 2009; Williams and DeSesso 2010).

- **Carcinogenicity**: EPA stated that DecaBDE is a "moderate" hazard for this endpoint; however, the weight of the evidence indicates DecaBDE should be considered of "low" carcinogenic hazard because the carcinogenicity studies for DecaBDE support a lack of carcinogenicity. According to the EPA DfE criteria document, "When limited or marginal data on carcinogenicity are present, a designation of moderate will be used." In the case of DecaBDE, EPA's "moderate" rating was based on NTP's determinations of equivocal evidence of carcinogenicity in male mice (increased incidence of hepatocelluar adenomas or carcinomas and thyroid gland follicular cell adenomas or carcinomas) and some evidence of carcinogenicity in male and female rats (increased incidences of non-neoplastic nodules in the liver) and on the IRIS assessment of "suggestive evidence of carcinogenic potential" (NTP 1986). However, the available scientific data do not support a "moderate" rating of carcinogenicity for DecaBDE and instead support a "low" rating. The available scientific evidence supports the conclusion that DecaBDE is not a carcinogen for the following reasons: 1) DecaBDE is not mutagenic; 2) In the NTP (1986) carcinogenicity study with DecaBDE, the authors considered the increased incidence of neoplastic nodules of the liver in male and female rats to be suggestive evidence of carcinogenicity; however, this terminology was abandoned by the NTP in 1986 when "neoplastic nodule" was replaced with "hepatocellular hyperplasia" (a reversible change) and "hepatocellular adenoma" (a nonreversible change); 3) In the NTP (1986) study, the equivocal evidence in male mice, an increase in hepatocellular adenomas or carcinomas (combined), was considered to be related to the early loss of control male mice from fighting, which led to a lower than usual incidence in the control

group (Goodman 2009); 4) the thyroid follicular cell tumors were consistent with a rodent-specific mode of action (MOA) that is commonly observed in male rodents and not relevant for assessing human carcinogenic risk; 5) DecaBDE is not listed by NTP as a known or reasonably anticipated human carcinogen; 6) a 2-year carcinogenicity study in rats treated with up to 1 mg/kg/day of a lower purity DecaBDE product found no evidence of carcinogenicity (Kociba et al. 1975); 6) the chronic studies with DecaBDE suggest that low-dose exposures (e.g., ≤1.0 mg/kg-day) do not induce non-neoplastic or neoplastic changes in cells and excessively high-dose exposures (e.g., 6,650 mg/kg-day) may induce proliferative lesions in select tissues (e.g., thyroid follicular hyperplasia) that may progress to neoplasia via mode of actions that are not relevant to humans (Hardy et al. 2009); and 7) DecaBDE is not listed as a carcinogen by the EU or OSHA, and the International Agency for Research on Cancer (IARC) determined it is "not classifiable as to its carcinogenicity to humans (Group 3)" based on limited evidence in experimental animals. In conclusion, the weight of the evidence indicates DecaBDE should be considered of "low" carcinogenic hazard.

- **Developmental and Neurological Effects:** This section rates DecaBDE as "high" with respect to developmental hazard (neurotoxicity); however, the weight of the scientific evidence indicates that DecaBDE should be considered "low" for neurological developmental effects. EPA or OECD guideline and GLP-compliant prenatal developmental and developmental neurotoxicity studies provide NOAELs of 1,000 mg/kg/d for developmental effects (Hardy et al. 2009; Williams and DeSesso 2010). Only studies from a single laboratory at Uppsala University, Sweden, (Eriksson et al. 2002; Viberg et al. 2003; Viberg et al. 2007; Johansson et al. 2008) have reported results indicating alterations in behavior, habituation, and memory that persisted in adult mice and rats following administration of a single dose of decaBDE (and other PBDE congeners) on postnatal days 3, 10, or 19. These results have not been replicated by other laboratories conducting studies with similar or identical protocols (Health Canada 2012). The team at Uppsala University developed its own methodologies to study post-natal developmental impacts of individual chemicals and mixtures, and these have contrasted sharply with standard, guideline study methods (e.g., OECD, GLP) that have been used by the chemical industry and regulators (Alcock 2011). In studies conducted by Viberg et al. (2003; 2007), administration of a single dose of DecaBDE (20.1 mg/kg) on post-natal day 3 caused alterations in behavior, habituation and memory that persisted in adult mice and rats, based on reduced motor activity data. However, other researchers (Hardy and Stedeford 2008; Hardy et al, 2009; Goodman 2009; Alcock et al. 2011; Williams and DeSesso 2010) have noted several limitations with these studies ranging from issues about the purity of the test compound, single dose administration, the experimental design, very small group sizes, failure to treat littermates as dependent variables in their analysis, the number of dams and offspring included in the analysis, and lack of

information on the motion-measuring device that was used in the studies by Viberg et al. 2003 and 2007.

There are significant differences in the developmental neurotoxicity results between studies conducted according to regulatory guidelines and those conducted in academic settings that were not designed following regulatory guidelines (Alcock et al. 2011). Hardy et al. (2002) conducted a GLP-compliant developmental toxicity in which SD rats were treated with 0, 100, 300, or 1000 mg/kg-day DecaBDE via gavage in corn oil on gestation days 0–19. There were no clinical signs of toxicity observed in the dams and no treatment-related effects were detected in fetal body weights, fetal sex distribution, or from the fetal external, visceral, or skeletal examinations. The no-observed-effect level (NOEL) for maternal and developmental toxicity was 1000 mg/kg-day, the highest dose level tested. A recent developmental neurotoxicity study designed and conducted according to OECD and USEPA guidelines found no evidence of adverse effects at any DecaBDE dose tested(1, 10, 100, 1,000 mg/kg/day) (Biesemeier et al. 2011). Administration of DecaBDE resulted in no maternal toxicity, no effects on offspring survival and growth, and no effects on any of the neurobehavioral endpoints studied at any dose level, compared with the control groups. This study is convincingly negative and does not confirm the developmental effects reported in the non-guideline studies using unusual methods conducted by the Uppsala researchers. An analysis by Goodman (2009) and the additional review of the developmental studies by Williams and DeSesso (2010) supports the conclusion that the weight of evidence indicates DecaBDE is not a developmental neurotoxicant. The lack of consistency across studies precludes establishment of a causal relationship between perinatal exposure to DecaBDE and alterations in motor activity. As such, the developmental hazard designation for DecaBDE should be "very low" based on a NOAEL >1,000 mg/kg-day (U.S. EPA 2011).

- **Repeated dose effects:** This section rates DecaBDE as "moderate" with respect to repeated dose effects; however, however, the weight of the scientific evidence indicates that DecaBDE should be considered "low" with respect to repeated dose effects. This conclusion is based on the following reasons: 1) several repeated dose studies with DecaBDE have determined NOAELs of at least 1000 mg/kg/day (Hardy et al. 2002; NTP 1986); 2) Using different methods, the National Research Council's National Academy of Sciences and Hardy et al. (2009) derived an RfD of 4 mg/kg/day for DecaBDE, a level that is not indicative of a concern for repeated dose effects; 3) ATSDR derived an intermediate exposure RfD for DecaBDE of 10 mg/kg/day, which is not indicative of a concern for repeated dose effects; 4) the basis of the "moderate" concern for repeated dose effects is based on a LOAEL of 80 mg/kg/day derived from a 30-day study by Norris et al. (1975) that evaluated a form of DecaBDE that is not in commercial production and has not been produced since the 1980s (77% versus ≥ 97% DecaBDE); 5)

The NTP 14-day, 90- day, and 2-year studies with NOAELs of ≥1,000 mg/kg/d did not report the effects observed by Norris et al. (1975), and the NTP studies were performed using test material closely resembling more relevant production. Furthermore, the effects observed in the Norris et al. (1975) study were not seen in the NTP studies that were performed at much higher doses; and 5) the EU Risk Assessment recognized the NTP study as the most appropriate for assessing repeated dose effects (EC 2002).

- **Bioaccumulation:** This section rates DecaBDE as "high" with respect to bioaccumulation; however, however, the weight of the scientific evidence indicates that DecaBDE should be considered "low" with respect to bioaccumulation. There have been several studies with DecaBDE that indicate poor oral absorption, and essentially no elimination in the urine with typically greater than 90% of an oral dose eliminated in the feces within 72 h as the parent molecule or bound residues (Hardy et al. 2009). A low uptake from the gut coupled with direct elimination from the liver to the bile results in only a small fraction of an oral dose reaching the systemic circulation and, ultimately, tissues (Hardy et al. 2009). The limited bioavailability of DecaBDE has been considered a factor in its general lack of mammalian toxicity by the National Toxicology Program, EU, UK, and other researchers (NTP 1986; EC 2002; el Dareer et al. 1987; Dungey and Akintoye 2007; Hardy et al. 2009). NTP evaluated the disposition of radiolabeled DecaBDE in several studies, and found that ". . .these studies indicate that, after exposure at all doses in the diet, greater than 99% of the radioactivity recovered was excreted in the feces within 72 hours".

Comments on Specific Sections of the EPA Decabromodiphenyl Ethane (DBDP-Ethane) Screening Level Hazard Summary

- **Hazard and Risk Assessments**: The DPDP-Ethane Summary identifies the risk evaluation conducted by the UK Environment Agency (Dungey et al. 2007). In their evaluation, UK Environment concluded that, "Overall, the risks arising from direct toxic effects of EBP [DPDP-Ethane] are low." Although this conclusion is consistent with the hazard levels assigned by EPA for most endpoints, it differs from the hazard levels assigned by EPA for carcinogenicity (moderate) and neurolgocial effects (High). Because the hazard levels for these endpoints are based on analogy to DecaDBE, the DPDP-Ethane summary should also cite the hazard and risk assessments cited for DecaDBE. In addition, as noted in our comments on DecaDBE, please include the published toxicology and human health risk assessment conducted by Hardy et al. (2009). This risk assessment was independently reviewed by TERA's International Toxicity Estimates of Risk (ITER) expert panel and the oral RfD derived by Hardy et al. (2009) of 4 mg/kg-day has been posted in the ITER database.

- **Carcinogenicity**: EPA designated DBDP-Ethane as having a "moderate" carcinogenicity hazard based on analogy to DecaBDE, noting that no experimental carcinogenicity data are available for DBDP-Ethane. However, as noted in our comments on DecaBDE, the "moderate" hazard designation for DecaBDE should be changed to "low" for the reasons identified. Most specifically, the conclusion of "equivocal evidence" in rodents from NTP (1986) on which the EPA designation is based is inaccurate. As described in our comments on the DecaBDE Summary and elsewhere (Goodman et al. 2009), the increased incidence of liver adenomas or carcinomas in male mice was considered related to the unusually high early mortality in the control group. The increased incidence in "neoplastic nodules" is not relevant because, at that time, that pathological designation included hepatocellular hyperplasia, which is not a neoplasm. In fact, NTP itself does not include DecaBDE on its List of Carcinogens. In addition, an earlier carcinogenesis study on DecaBDE not cited in the Summary found no evidence of carcinogenicity (Kociba et al. 1975).

  EPA noted under Data Quality that the "moderate" designation is partially based on the "high potential for bioaccumulation" of DBDP-Ethane. However, both the basis and relevance of this conclusion is unclear. As stated by EPA in the Summary, and supported by experimental evidence (Hardy 2004), DBDP-Ethane "…is poorly absorbed in the GI tract." The absorption is so low that, even accepting that bioaccumulation is relevant in this case, it is highly unlikely to bioaccumulate to any significant degree, at exposure levels that any person is likely to encounter on an ongoing basis. This is particularly

noteworthy when one considers the extremely high exposure levels used in the NTP (1986) carcinogenicity study for DecaBDE (up to 2,250 mg/kg-day and 7,780 mg/kg-day for rats and mice, respectively). If bioaccumulation were an important factor in this case, then it seems likely that lifetime exposure to 7,780 mg/kg-day of DecaBDE would have resulted in more significant tumor formation. Finally, as noted in our comments on bioaccumulation, below, based on the available data DBDP-Ethane should be considered to have "low" bioaccumulation potential, in any case.

- **Reproduction and Fertility Effects:** EPA assigned a "low" reproductive hazard designation for DBDP-Ethane based on Hardy (2004) and Hardy et al. (2010), and stated, "there was no evidence of treatment-related adverse effects on the reproductive system in two developmental toxicity studies in rats and rabbits" at a NOEL $\geq$ 1,250 mg/kg-day. EPA qualified the designation, stating that it was uncertain because the available prenatal development studies were of short exposure duration and not designed as a reproductive toxicity screen.

  This section should also rely upon the 90-day repeat dose study in rats in which there were no histopathologically evident effects in reproductive organs at any dose level, including the high dose of 1,000 mg/kg-day (Hardy et al. 2002). The prenatal development studies in rats and rabbits, along with the 90-day repeat dose rat study provide adequate evidence that reproductive effects do not occur even at high dose levels (>1,000 mg/kg-day). Under the OECD SIDS program, a prenatal development study and a 90-day repeat dose study that includes histopathologic evaluation of reproductive organs meets the data needs for reproductive hazard assessment (OECD 2012). Thus, the uncertainty expressed in the summary should be removed because adequate data are available.

  In addition, based on EPA's DfE Alternatives Assessment Criteria for Hazard Evaluation (U.S. EPA 2011), an effects level greater than 1,000 mg/kg-day for oral exposures would be assigned a "very low" hazard designation. There were no effects on reproduction in either rats or rabbits at exposures up to and including the highest dose tested of 1,250 mg/kg-day in the prenatal development studies (Hardy et al. 2010). There were no effects on the reproductive organs of rats at exposures up to and including the highest study dose of 1,000 mg/kg-day (Hardy et al. 2002). Thus, as noted in the DPDP-Ethane Summary, the NOAEL for reproductive toxicity is >1,250 mg/kg-day. Thus, the data support a "very low" hazard designation rather than a "low" hazard designation.

- **Neurotoxicty:** EPA designated DBDP-Ethane as having a "high" neurotoxicity hazard based on analogy to DecaBDE. EPA specifically identifies data used for the basis of this designation as "Mice as neonates (day 3, 10, 19), single oral dose; neurobehavioral

effects" and indicates it is estimated by analogy with DecaBDE. EPA does not provide a citation, instead citing "professional judgment." However, this appears to refer to Viberg et al. (2003). As discussed in our comments on DecaBDE, Viberg et al. (2003) reported effects on motor activity (but not other neurological endpoints) in mice following a single exposure to DecaBDE on postnatal day 3 (but not days 10 or 19). Among other issues, Viberg et al. (2003) and other studies from the Uppsala laboratory used an unusual dosing method, used non-standard analysis methods that did not control for litter effects, and the results are not reproducible outside their laboratory. The DecaBDE Summary includes several neurotoxicity studies, but not Viberg et al (2003). The DBDP-Ethane Summary should also be updated to remove the reference to what appears to be the Viberg et al (2003) study and identify the studies used for the DecaBDE designation, including the only guideline compliant developmental neurotoxicity study (Biesemeier et al. 2011). The data quality section should also discuss the uncertainty in the hazard designation based on the large discrepancy between the guideline compliant GLP study (Biesemeier et al. 2011), which found no evidence of neurotoxicity at dose levels up to 1,000 mg/kg-day (indicating a "low" neurotoxicity hazard) and the non-GLP studies that form the basis of the "high" hazard designation. The weight of the scientific evidence indicates that DecaBDE should be considered "low" for neurological developmental effects.

In addition, despite identifying the same basis for the neurotoxicity designation for DBDP-Ethane and EBTBP, DBDP-Ethane was given a "high" hazard designation whereas EBTBP was given a "moderate" designation.

- **Repeated Dose Effects:** EPA designated DBDP-Ethane as having a "low" hazard for repeated dose effects based on no lasting adverse effects in 28-day and 90-day studies. EPA concluded, however, there was a potential for effects in longer term studies because of the "potential for bioaccumulation." We agree with the "low" hazard, but believe the basis for the statement of potential for repeated dose effects at longer durations is inaccurate. As described below, there is no evidence that DBDP-Ethane is bioaccumulative and, thus, no basis for the statement about potential effects with longer term exposures. This statement should be removed.

- **Bioaccumulation:** EPA assigned a "high" bioaccumulation designation for DBDP-Ethane, indicating "monitoring data suggest that decabromodiphenyl ethane may bioaccumulate in aquatic and terrestrial species." EPA specifically cites Betts (2009) for ecological biomonitoring data, indicating that Betts summarizes "detections" of DBDP-Ethane in several species. One cannot, however, conclude just from the presence of a chemical in an organism that the chemical bioaccumulates. It only means exposure has

occurred; it may be the result of a recent exposure, rather than bioaccumulation and in fact, taking into account measured and estimated properties of DBDP-Ethane, it is unlikely that it bioaccumulates. First, as noted by EPA in the Toxicokinetics section of the Summary, DBDP-Ethane is poorly absorbed through all routes of exposure. Thus, uptake would be slow. Second, the measured fish bioconcentration factors (BCFs <2.5 and <25) and the estimated bioaccumulation factor (BAF = 62) identified in the Summary are less than the cutoff criterion associated with "low" bioaccumulation potential (U.S. EPA 2011). Specifically, EPA identifies a BCF or BAF value <100 as "low" bioaccumulation. Therefore, based on its low solubility and low BCF/BAF, DBDP-Ethane should be categorized as having "low" bioaccumulation potential.

Comments on Specific Sections of the EPA Ethylene Bis-Tetrabromophthalimide (EBTBP) Screening Level Hazard Summary

- **Carcinogenicity**: EPA designated EBTBP as having a "moderate" carcinogenicity hazard based on analogy to DecaBDE, noting that no experimental carcinogenicity data are available for EBTBP. However, as noted in our comments on DecaBDE, the "moderate" hazard designation for DecaBDE should be changed to "low" for the reasons identified. Most specifically, the conclusion of "equivocal evidence" in rodents from NTP (1986) on which the EPA designation is based is inaccurate. As described in our comments on the DecaBDE Summary and elsewhere (Goodman et al. 2009), the increased incidence of liver adenomas or carcinomas in male mice was considered related to the unusually high early mortality in the control group. The increased incidence in "neoplastic nodules" is not relevant because, at that time, that pathological designation included hepatocellular hyperplasia, which is not a neoplasm. In fact, NTP itself does not include DecaBDE on its List of Carcinogens. In addition, an earlier carcinogenesis study on DecaBDE not cited in the Summary found no evidence of carcinogenicity (Kociba et al. 1975).

  EPA noted under Data Quality that the "moderate" designation is partially based on the "high potential for bioaccumulation" of EBTBP. However, both the basis and relevance of this conclusion is unclear. As stated by EPA in the Summary, EBTBP "…is estimated to not be absorbed by any route" as a neat material, and "…is expected to have poor absorption for all routes when in solution." The absorption is so low that, even accepting that bioaccumulation is relevant in this case, it is highly unlikely to bioaccumulate to any significant degree, at exposure levels that any person is likely to encounter on an ongoing basis. This is particularly noteworthy when one considers the extremely high exposure levels used in the NTP (1986) carcinogenicity study for DecaBDE (up to 2,250 mg/kg-day and 7,780 mg/kg-day for rats and mice, respectively). If bioaccumulation were an important factor in this case, then it seems likely that lifetime exposure to 7,780 mg/kg-day of DecaBDE would have resulted in more significant tumor formation. Finally, as noted in our comments on bioaccumulation, below, based on the available data EBTBP should be considered to have "low" bioaccumulation potential, in any case.

- **Neurotoxicity:** EPA designated EBTBP as having a "moderate" neurotoxicity hazard based on analogy to DecaBDE. EPA specifically identifies data used for the basis of this designation as "Mice as neonates (day 3, 10, 19), single oral dose; neurobehavioral effects" and indicates it is estimated by analogy with DecaBDE. EPA does not provide a citation, instead citing "professional judgment." However, this appears to refer to Viberg et al. (2003). As discussed in our comments on DecaBDE, Viberg et al. (2003) reported effects on motor activity (but not other neurological endpoints) in mice following a single

exposure to DecaBDE on postnatal day 3 (but not days 10 or 19). Among other issues, Viberg et al. (2003) and other studies from the Uppsala laboratory used an unusual dosing method, used non-standard analysis methods that did not control for litter effects (counting individual pups within a litter independently), and the results are not reproducible outside their laboratory. The DecaBDE Summary includes several neurotoxicity studies, but not Viberg et al (2003). The EBTBP Summary should also be updated to remove the reference to what appears to be the Viberg et al (2003) study and identify the studies used for the DecaBDE designation, including the only guideline compliant developmental neurotoxicity study (Biesemeier et al. 2011). The data quality section should also discuss the uncertainty in the hazard designation based on the large discrepancy between the guideline compliant GLP study (Biesemeier et al. 2011), which found no evidence of neurotoxicity at dose levels up to 1,000 mg/kg-day (indicating a "low" neurotoxicity hazard) and the non-GLP studies that form the basis of the "high" hazard designation. The weight of the scientific evidence indicates that DecaBDE should be considered "low" for neurological developmental effects.

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Toxicology Excellence for Risk Assessment (TERA)

September 28, 2012

TERA

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for public health protection

September 27, 2012
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Design for the Environment
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Phone: 202-564-0951

Dear Dr. Lavoie,

We appreciate the opportunity to provide information to EPA that will enable it to more appropriately select safer alternatives to decabromodiphenyl ether (DecaBDE). We wish to transmit new information and analysis for some of these flame retardant chemicals that EPA might find valuable as it addresses potential environmental risks. The specific new information includes:

- Mode of Action (MOA) information on tumor development, including assistance by staff of the National Toxicology Program staff (letter attached) and Dr. Gene McConnell, a well-known and respected pathologist associated for many years with the NTP,
- A recently developed and reviewed Reference Dose (RfD) for decabromodiphenyl ether on the National Library of Medicine with significantly different findings from previous risk assessments, and
- An independent evaluation of neurotoxicity and bioaccumulation data regarding some of the prominent flame retardant chemicals.

This new information gives EPA an opportunity to relook at some of its findings in the Design for the Environment (DfE) Program, and specifically its text entitled "*Flame Retardant Alternatives for Decabromodiphenyl Ether (DecaBDE).*" This new information might allow a new analysis following EPA cancer guidelines and the International Programme on Chemical Safety (IPCS) Mode of Action (MOA) and Human Relevance (MOA/HR) framework, resulting in a unifying MOA hypothesis that accounts for all tumor findings of decabromodiphenyl ether, to the point where other tumor MOAs, such as mutagenicity, can be credibly excluded.

The newer neurological toxicity data address EPA's concerns raised in its 2008 IRIS evaluation using the non-guideline studies. These newer data allow the use of a different critical effect for the basis of revised RfD, which is similar to that developed by the NAS (2000).

Bioavailability and bioaccumulation modeling and data are disparate, where models generally show high concern for these endpoints and actual data show low concern. We recommend that

EPA work with outside parties to further develop the science in this area, so that more credible judgments can be made.

We have done this work at the request of Albermarle Corporation, but share our final findings and analysis with EPA prior to sending them on to Albermarle. Our comments may or may not reflect their opinions.

As always, thanks for the opportunity to help!

Sincerely,

Michael Leonard Dourson, Ph.D., DABT, ATS
President

Bernard Gadagbui, M.S., Ph.D., DABT, ERT
Toxicologist

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TERA

Alternatives Assessment for Decabromodiphenyl Ether Comments

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1. Findings

EPA's decabromodiphenyl ethane (DBDPEthane) and ethylene bis-tetrabromophthalimide (EBTBP) assessments depend in large part on its decabromodiphenyl ether (DecaDBE) IRIS assessment. EPA's decision to do this is not unreasonable. DecaBDE has a fairly comprehensive database and has been evaluated several times by expert bodies, such as the International Agency for Research on Cancer (IARC, 1999), the US National Academy of Sciences (NAS, 2000), the Agency for Toxic Substances and Disease Registry (ATSDR, 2004), and the U.S. EPA (2008). However, since the time of the last evaluation, significantly new information has been developed, such that all of these previous evaluations should be updated.

Thus, reliance on any older DecaBDE evaluation calls into question the veracity parts of current U.S. EPA DfE text.

2. Mode of Action (MOA) Information under Review with NTP

Existing assessments for DecaBDE are now out of date in two ways. The first way in which these older assessments are out of date is that the carcinogenicity classification and dose response assessment for DecaDBE are not consistent with current understanding of Mode of Action (MOA) using U.S. EPA's (2005) and the International Programme on Chemical Safety (IPCS) (Boobis et al, 2008; Seed et al., 2005) latest guidelines. For example, the description of rat liver tumors at the NTP (1986) is not in keeping with later classifications, and noncancer toxicity, important for understanding MOA, is not well described. Of course, the focus of the older NTP bioassays was focused on hazard identification of the tumor endpoint, and not a MOA understanding of tumor development. Thus, one cannot expect the older bioassays to have recorded all noncancer lesions that might be relevant in today's risk assessment thinking, which leads with an understanding of MOA (U.S. EPA, 2005) and the use of the IPCS MOA/HR frameworks.

We propose working with our NTP colleagues in order to reclassify the liver tumors using modern descriptions, and to further explore the noncancer toxicity in the rodent liver. Furthermore, a review the underlying MOA for the NTP findings of thyroid tumors in mice will also be conducted using U.S. EPA (1998, 2005) guidelines and the use of the IPCS MOA/HR framework.

The fact that DecaBDE is not mutagenic suggests a different mode of action, supporting the collaborative work with NTP and additional MOA investigation.

3. New Reference Dose (RfD) at the National Library of Medicine

The second way these older assessments are out of date is that a newer analysis (Hardy et al., 2009) suggests a 600-fold higher RfD, based in part on a study (Biesemeier et al., 2010, 2011) and related analyses (e.g., Williams and DeSesso, 2010) that resolve several questions left open by the earlier work of Viberg and colleagues (e.g., Viberg, et al., 2003) and Rice and colleagues (e.g., Rice et al., 2007), on which in part U.S. EPA and others based their work. In fact, the Hardy et al. (2009) analysis confirms the earlier RfD developed by the NAS (2000). This newer RfD of Hardy et al. (2009) has been through journal peer review and also a quality assurance

review by 3 independent scientists, prior to be placed on the National Library of Medicine's TOXNET, under the International Toxicity Estimates for Risk (*ITER*) database.

Comments from this quality assurance review of the Hardy et al. (2009) RfD are publicly available.

A synopsis of relevant risk assessment values follows. But in summary, Table 1, based in part on the International Toxicity Estimates for Risk (*ITER*) database on the National Library of Medicine's TOXNET, shows that these various risk values are disparate.

Specifically, from the National Library of Medicine's TOXNET synopsis (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?iter) we find:

> ATSDR, U.S. EPA and Hardy et al. (2009) (under the *ITER* column) have evaluated the noncancer oral toxicity data for decabromodiphenyl ether (DecaBDE). U.S. EPA derived a reference dose (RfD) of 0.007 mg/kg-day based on a NOAEL of 2.22 mg/kg-day for decreased spontaneous motor behavior observed in mice exposed to DecaBDE in a single dose gavage study (Viberg et al., 2003). U.S. EPA used an uncertainty factor of 300 (10 each for intra- and interspecies variability, and 3 to adjust for exposure duration). In a journal publication, Hardy et al. (2009) (under the *ITER* column) derived an RfD of 4 mg/kg-day based on a BMDL10 of 419 mg/kg-day for hepatocellular degeneration observed in rats (NTP, 1986) and an uncertainty factor of 30 (10 for intraspecies variability, and 3 for interspecies uncertainty). A review panel, through TERA's *ITER* Review program, has reviewed the Hardy et al. publication and approved the value for inclusion in this database (see the quantitative estimate section for panel comments and conclusions).
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> U.S. EPA and Hardy et al. selected different studies as the critical study. Hardy et al. did not use the critical study selected by U.S. EPA (Viberg et al., 2003) because they concluded that the study did not follow recommended U.S. EPA protocols and a subsequent study by Biesemeier et al. (2010) suggested that developmental neurotoxicity is not the critical effect. Hardy et al. selected a value of 1 to account for interspecies toxicokinetic variability because dosimetric adjustments were made to the experimental animal dose; 3 was used as the default for toxicodynamic uncertainty. This is compared to U.S. EPA's default value of 10 for interspecies extrapolation. As a result of different choices in critical study, point of departure, and uncertainty factor, the difference between the values derived by U.S. EPA and Hardy et al. is 3 orders of magnitude.
>
> ATSDR did not derive an oral minimal risk level (MRL) for chronic-duration exposure to DecaBDE because in the only available chronic study of high purity DecaBDE, the lowest tested dose of 1,120 mg/kg-day in rats is a LOAEL for a liver lesion (neoplastic nodules) that is precancerous and associated with thrombosis in the same tissue (NTP, 1986). Due to the dissimilar toxicity and environmental chemistry of DecaBDE, ATSDR has evaluated DecaBDE and lower brominated mixtures separately. Please see the *ITER* file for polybrominated diphenyl ethers (PBDEs) for more information on ATSDR's approach for the lower brominated congeners.

From the NAS (2000) report we find:

> The subcommittee derived an oral RfD for DecaBDE by using the chronic NOAEL of 1,120 mg/kg-d, based on liver thrombosis and degeneration observed in rats at the next higher dose (continued on next page)
>
> (NTP 1986), and a composite uncertainty factor of 300, resulting in an RfD of 4 mg/kg-d
>
> (RfD=NOEL÷ 300). The composite uncertainty factor is composed of 3 uncertainty factors: 10 for interspecies extrapolation, 10 for intraspecies variability, and 3 for database uncertainties (10A×10H×3D=300). The RfD is based on a well-designed chronic toxicity study of DecaBDE in two species. Data on chronic, developmental, and reproductive toxicity are available from other studies in rats. However, limitations in these studies (particularly compound purity (77.4%), lack of a second species, and use of low dose levels in the chronic study; lack of longer than one-generation testing in the reproductive study) indicate that there is some uncertainty in the DecaBDE database. Based on these considerations, an uncertainty factor of 3, instead of 10, for database insufficiency was used.

4. An Independent Evaluation of Neurotoxicity

Specific neurotoxicity or neurodevelopmental toxicity studies were not available for the flame retardant alternatives DBDPEthane and EBTBP. However, short term bioassays were available and these do not indicate neurological effects as critical.

In its draft DfE document, U.S. EPA (2012) describes the hazard of DBDPEthane and EBTBP with respect to neurotoxicity as high and medium, respectively (pages 4-29, 4-248, and 4-254), based on analogy to DecaBDE and professional judgment. In this same document, the hazard of DecaBDE is described as high with respect to neurotoxicity. This high rating for DecaBDE is based on an earlier assessment of DecaBDE (U.S. EPA 2008) where a non-guideline study conducted by Viberg et al. (2003) reported functional neurobehavioral effects of single-dose exposures to DecaBDE.

A review of the basis of relevant studies on neurobehavioral effects for DecaBDE follows, but in summary, this review indicates that this toxicity is not the critical effect, and that concerns about Viberg et a. (2003), raised by U.S. EPA (2008), have been addressed with the recently published guideline neurobehavioral studies. Thus, U.S. EPA (2012) should focus more on the chemical-specific DBDPE and EBTBP studies to determine the critical effect(s).

4.1 Review of Relevant Studies

Viberg et al. (2003) investigated neurotoxic effects of DecaBDE on spontaneous motor behavior on postnatal days (PNs) 3, 10, or 19 (i.e., at different stages of neonatal mouse brain development). There were significant dose-related changes in the habituation ratio calculated from three behavior variables (locomotion, rearing, and total activity) in mice exposed to 20.1 mg/kg (the LOAEL) and evaluated at 2, 4, and 6 months of age, but no statistically significant effect was seen at 2.22 mg/kg (the NOAEL). Two other studies (Rice et al., 2007; Viberg et al., 2007) were also evaluated in the U.S. EPA's 2008 assessment. The Rice et al. (2007) study

involved repeated postnatal dosing of a different strain of mice than Viberg et al. (2003) with 0, 6 or 20 mg/kg-day of DecaBDE over PNDs 2–15. The litter was used as the statistical unit and a LOAEL of 6 mg/kg-day, the lowest dose tested, was identified based on decrease in the percent of male and female pups performing palpebral reflex on PND 14, for increased struggling behavior of male mice on PND 20, for decreased T4 levels in male mice (although the T4 levels did not appear to be statistically different in treated vs control mice), and for effects on locomotor activity of male mice on PND 70. In the Viberg et al. (2007) study, a LOAEL of 6.7 mg/kg was identified for significant changes in spontaneous motor behavior (locomotion, rearing, and total activity) in 2-month-old rats given BDE-209 on PND 3.

U.S. EPA (2008) identified several concerns that raised potential issues about the full reliance on the Viberg et al. (2003) as the critical study. Concerns include:

1. Lack of dosing regimen that includes gestation and lactation exposure (U.S. EPA, 1998a);

2. Use of only single doses and male mice only in the study;

3. Lack of conformance of protocol to health effects test guidelines for neurotoxicity screening battery or developmental neurotoxicity studies [U.S. EPA, 1998a, c (both cited in U.S. EPA, 2008)];

4. Use of more than one pulp per litter for the behavioral testing (10 mice were randomly selected from three to five different litters in each treatment group). The increase in number of samples from each litter is likely to bias the analyses towards false positives, with the possibility of attributing the observed neurobehavioral effects to differences in pups born to a single dam rather than related to treatment; and

5. Assessment of limited number of neurobehavioral parameters - only indices related to motor activity (locomotion, rearing, and total activity) were measured - instead of full FOB that evaluates neurological and behavioral signs. However, Rice et al. (2007) study, also in mice, provided data for FOB that mitigate some concern related to its absence in the Viberg et al. (2003) study.

The concerns listed by U.S. EPA above are warranted. Based in part on these concerns newer reviews and studies were conducted, as described below. U.S. EPA's draft DfE document has not fully considered these several reviews and newer data generated since the U.S. EPA (2008) assessment that evaluated the neurotoxicity potential for DecaBDE.

Specifically, Goodman (2009) conducted a weight-of-evidence analysis of developmental neurobehavioral effects. The author reached a different conclusion regarding the evidence provided by four studies from two laboratories (Viberg et al., 2003; Viberg et al., 2007; Johansson et al., 2008; Rice et al., 2007). These are the same studies, with the exception of Johansson et al. (2008), evaluated by U.S. EPA (2008) in their assessment for DecaBDE. According to Goodman (2009), the reported effects from these laboratories were in opposite directions. While mice treated with 20 mg/kg day BDE-209 initially had higher activity and an increased habituation (Rice et al. (2007), mice and rats treated with 20 mg/kg BDE-209 (Viberg et al., 2003, 2007) or mice treated with ≥2 mg/kg DecaBDE (Johansson et al., 2008) had lower initial activity and decreased habituation (although inappropriate statistical methods may have

affected results). Goodman (2009) noted an overall lack of effects in the Functional Observational Battery conducted by Rice et al. (2007). Goodman (2009) concluded that the Viberg et al. (2003b) study, even in conjunction with other studies, is not suitable for establishing an RfD for DecaBDE or the commercial DecaBDE product.

Hardy et al. (2010) reviewed the four studies as in Goodman et al. (2009), in addition to Silverberg et al. (2009) for the potential for DecaBDE to cause developmental neurotoxicity. Hardy and colleagues initially rated these toxicity studies based on the Klimisch criteria (Klimisch et al., 1997), an internationally agreed upon method for ranking studies based on data quality and reliability (ECHA, 2012). Based on these criteria, Hardy et al. (2010) assigned Klimisch scores to each study as shown in Table 2.

Studies receiving a score of 1 "Reliable without Restrictions" or 2 "Reliable with Restrictions" are routinely carried forward and evaluated using the U.S. EPA's general assessment factors in the derivation of an RfD (U.S. EPA, 2003) for any chemical. Based on this rating, Hardy et al. concluded that the Viberg et al. (2003) study is not the most suitable for deriving a reference dose, if developmental neurotoxicity is the most sensitive endpoint for DecaBDE.

Williams and DeSesso (2010) reviewed the published animal studies that investigated perinatal exposure to brominated flame retardants, PBDE congeners (including DecaBDE), hexabromocyclododecane (HBCD), and tetrabromobisphenol A (TBBPA) with specific neurobehavioral evaluations – particularly, assessments of motor activity to assess whether an association exists between perinatal exposure and development of consistent neurobehavioral alterations. These authors evaluated a study by Jacobi et al. (2009) that also examined the neurobehavioral effects of perinatal exposure to DecaBDE. Jacobi et al. (2009) and Silverberg et al (2009) report the same study, in short form that was later published in full as Biesemeier et al. (2011). In all, Williams and DeSesso analyzed 25 motor activity studies on the PBDE congeners, HBCD and TBBPA from 10 different laboratories. Thirteen (13) of these studies were conducted in a single laboratory [Eriksson and Viberg studies; see list of studies in Williams and DeSesso (2010)] using the same experimental design and methods and reported adverse effects for all PBDE congeners tested, as well as HBCD. According to Williams and DeSesso (2010), these studies show effects at similar doses, an observation that these authors describe as somewhat of a surprise and highly unexpected, due to the known differences in their chemical structures, relative bioavailabilities, dispositions, toxicokinetics, and anticipated differences in binding at target sites. Moreover, Williams and DeSesso (2010) found that studies from other investigators contradict the Viberg and Erikssen work. While some of these studies suggest that the effects of exposure are long-lasting, others indicate that untoward effects disappear over time. Williams and DeSesso also provided the following insight regarding the results from these studies: (1) the direction of change in motor activity, if any, appears to depend on the particular study: some studies show overall increased activity with treatment; others show activity levels that are above or below control levels depending on the test interval; and still others show no effects of treatment on motor activity; (2) some studies suggest that perinatal exposure alters locomotor activity specifically; others indicate that the effect is on rearing; and still others show effects on both parameters. Based on the overall lack of consistent findings across the body of studies evaluated, Williams and DeSesso (2010) stated that it is not possible to conclude that perinatal exposure to the substances examined is associated with specific changes in motor activity.

In a GLP-compliant study, conducted according to OECD and U.S. EPA guidelines for developmental neurotoxicity, Beisemeier et al. (2011) dosed rat dams via oral gavage in corn oil) from gestation day 6 to weaning at doses of 0-1000 mg/kg-day of DecaBDE (97.5% DecaBDE plus 2.5% nonaBDE). Clinical signs were observed daily. Neurobehavioral tests (startle response, learning and memory) were conducted on PNDs 20, 22, 60 and 62, while motor activity tests were conducted on PNDs 13, 17, 61, 120 and 180. There were no treatment-related changes in motor activity assessments performed at 2, 4, or 6 months of age and no treatment-related neuropathological or morphometric alterations. The NOAEL for neurodevelopmental toxicity of DecaBDE was 1000 mg/kg-day. This study thus failed to identify such effects in rat pups at doses higher than those used in the other studies.

In 2011, an International Toxicity Estimates for Risk *(ITER)* Review panel was organized by the Toxicology Excellence for Risk Assessment (TERA) to evaluate a recently published RfD by Hardy et al. (2009), discussed briefly earlier in this review. As part of this quality assurance review, the newer neurological data were considered, along with available pharmacokinetic data and human and animal toxicity data for DecaBDE. The panel specifically reviewed the Viberg et al. (2003, 2007) studies and found them to be hypothesis generating (since they do not follow U.S. EPA recommended protocols). The panel found the Rice et al. (2007) study as suggestively-confirming. However, the panel found that the studies conducted by Biesemeier et al. (2010, 2011) were convincingly negative and did not confirm the hypothesized effect. The panel also considered the additional analysis by Goodman (2009) on the statistics of the Rice et al. (2007) work, and the additional analysis of Williams and DeSesso (2010) that the overall dataset for DecaBDE does not indicate developmental neurotoxicity. The panel agreed with these analyses.

Recently Health Canada (2012) has reviewed the available data on the health effects of DecaBDE. TERA staff has not had sufficient time to analyze this work.

5. An Independent Evaluation of Bioaccumulation

In its draft DfE document, U.S. EPA (2012) describes the hazard of DBDPEthane, DecaBDE, and EBTBP with respect to bioaccumulation as high, respectively (pages 4-29, 4-248, 4-268, and 4-311).

Little question exists as to whether DecaBDE and related chemicals are persistent. The use of such chemicals for fire safety demands that they be persistent and resist breakdown. However, mammalian toxicokinetic studies generally show little bioavailability, and the few available bioaccumulation and biomagnification studies also show only modest accumulation or magnification. In contrast, modeling generally suggests high levels for biomagnification. A review of the basis of relevant studies on bioaccumulation and biomagnification for these chemicals follows, but in summary, this review indicates a disparity in available data and models. This disparity suggests that a collaborative effort with multiple parties might be helpful in developing a scientific credible path forward.

5.1 Review of Relevant Studies

An in-depth analysis[1] of the toxicokinetics of DecaBDE indicates that it is poorly absorbed, and rapidly eliminated in the feces predominantly as the parent molecule (U.S. EPA, 2008). If absorption occurs, DecaBDE is eliminated by the liver into the bile as the parent compound. If metabolism occurs, it does so to a very limited extent (e.g. <3% of the dose) (Huwe and Smith, 2007; Huwe et al., 2008a, 2008b). EPA 2008 considered DecaBDE as not bioaccumulative.

U.S. EPA (2008) reviewed several studies that investigated the bioavailability of DecaBDE in mammalian species and concluded that DecaBDE is not bioaccumulative. Other regulatory bodies have also reviewed the extensive literature that has been developed on the bioaccumulation of DecaBDE (see Environment Agency, 2009- the leading public body protecting and improving the environment in England and Wales –; Environment Canada, 2010). Based on the review by Environment Agency (2009), laboratory studies on the uptake of DecaBDE in aquatic organisms, and mammals as well as DecaBDE adsorbed onto dust confirm that DecaBDE is bioavailable to a limited extent. However, data are not considered sufficiently robust to determine the actual BCF/BAF for decaBDE. Several feeding studies show that DecaBDE is absorbed from the diet but the biomagnifications factors (BMF) obtained are generally <1, while there appears to be no evidence of increasing concentrations with increasing trophic level, demonstrating that DecaBDE is not biomagnifying (Environment Agency, 2009).

Environment Canada (2010) also conducted an extensive review of experimental studies and published models that predict bioaccumulation in aquatic food webs and biomagnifications in terrestrial mammals. Environment Canada indicates that no measured or experimental evidence exists that support a conclusion that DecaBDE, as the parent compound, has a significant potential to bioaccumulate or biomagnify in the environment.

Limited data available indicate that bioaccumulation of DBDPEthane and EBTBP is low in fish, thus supporting a low BCF designation. There are not sufficient data to support a conclusion that DBDPEthane and EBTBP has a significant/high potential to bioaccumulate or biomagnify. However, studies (Albermarle, 2012) conducted on DBDPEthane using 14-C test article only detected background levels of 14C-activity in blood, plasma, or tissues, with excellent recovery of 14-C in feces. In these studies, HPLC-BetaRam analyses of fecal extracts provide no evidence of metabolism.

6. Specific Comments

U.S. EPA Text, page 1-2. Rather, the report provides information that will help decision makers consider environmental and human health profiles for available alternatives, so that they can choose the safest possible functional alternative.

> Response: The hazard identification and dose response assessment for DecaBDE has changed by 600-fold in the last several years, due to new scientific studies. Comparison of safety among possible functional alternatives needs to consider this information, now available at the National Library of Medicine's TOXNET.

[1] TERA can provide additional information upon request.

U.S. EPA Text, page 4-252 and also page 4-315. Carcinogenicity ratings for Decabromodiphenyl Ethane or Ethylene Bis-Tetrabromophthalimide.

Response: U.S. EPA's cancer call is different than IARC's and based on combined incidence of liver neoplastic nodules and carcinoma observed in a rat feeding study (NTP, 1986). U.S. EPA used a multistage model with linear extrapolation from the point of departure (LED12) to determine the slope factor of 0.0007 per mg/kg-day. In light of U.S. EPA (2005) and IPCS (Boobis et al, 2008; Seed et al., 2005) guidelines, several issues are now evident with this evaluation, including:

1) The cancer slope is very shallow, indicating low potency, but U.S. EPA's category choice does not reflect this fact.

2) The term neoplastic nodule is no longer used for rat liver tumors. Under current pathology guidelines (Wolf and Mann, 2005---attached), it may be that these neoplastic nodules would now be described as benign hepatocellular adenomas or preneoplastic hyperplasia. Accordingly, there is uncertainty in the calculated slope factor that should be considered when it is applied in a quantitative risk assessment. If any of the neoplastic nodules are described as preneoplastic hyperplasia, then the derivation of a cancer slope factor based on increased incidence of neoplastic nodules would result in an overestimate of risk.

Because of this, TERA has contacted staff of the NTP to develop a rereading of the rat liver slides, since it is now possible to know if previous the categorization of these neoplastic nodules would change. This work with NTP will also assist in understanding the potential MOA for liver tumor development. U.S. EPA (2005) and IPCS guidelines could then be used to determine this through a MOA/Human Relevance analysis.

3) Thyroid tumors in mice might be the result of liver hypertrophy, resulting in loss of thyroid hormone that would cause thyroid hyperplasia and tumors via a threshold mechanism. U.S. EPA (2005) and IPCS guidelines could also be used to determine this through a MOA/Human Relevance analysis.

U.S. EPA Text, page 4-254. Evaluation of neurotoxicity as "HIGH."

Response: But is not this rating internally inconsistent with that for repeat dose toxicity for DBDPEthane on the very next page, 4-255? Part of the effort in a repeat dose study is monitoring neurological effects. Such observations likely occurred in these studies, without positive neurological findings. Moreover, U.S. EPA's evaluation is based by analogy to DecaBDE, the neurological findings of which have now been discounted in a guideline study.

It is necessary for U.S. EPA to fully re-evaluate the whole data set for DecaBDE to consider the appropriate NOAEL for this chemical. Furthermore, we encourage U.S. EPA to use chemical specific data in addition to data by analogy.

U.S. EPA Text, page 4-319. Evaluation of neurotoxicity as "MODERATE."

Response: But is not this rating internally inconsistent with that for repeat dose toxicity on the same page for EBTBP? Part of the effort in a repeat dose study is monitoring neurological effects. Such observations occurred in these studies, without positive neurological findings (including daily clinical observations). Moreover, U.S. EPA's evaluation is based by analogy to DBDE, the neurological findings of which have now been discounted in a guideline study.

We encourage U.S. EPA to use chemical specific data in addition to data by analogy.

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Table 1. Noncancer Oral Risk Values Table: Adapted from *ITER* Noncancer Oral Risk Table for: Decabromodiphenyl Ether (DECABDE)

Risk Value Parameter\ Organization	ATSDR	ITER PR	NAS	U.S.EPA
Risk Value Name	chronic MRL	RfD	RfD	RfD
Risk Value*	NA	4E+0	4 E+0	7E-3
Year	2004	2009	2000	2008
Basis (Experimental)*	NA	$BMDL_{10}$ 419	NOAEL 1120	NOAEL 2.22
Basis (Adjusted)*	NA	$BMDL_{10(HEC)}$ 113	NA	NA
Uncertainty Factor	NA	30	300	300
Critical Organ or Effect	NA	liver	liver	neurobehavioral
Species	NA	rat	rat	mouse
Study	NA	NTP, 1986	NTP, 1986	Viberg et al., 2003
View Specifics:	Click here	Click here	Click here	Click here

**In mg/kg body weight per day, unless otherwise specified.*

Table 2. Summary of developmental neurotoxicity studies for BDE-209 with Klimisch code and rationale (Hardy et al., 2009)

Study	Route; dose; purity; timing	Species; sample size; sex	Reported effects	Klimisch code[a]	Rationale
Viberg et al. (2003)	Oral gavage to pups; single dose of 2.22 or 20.1 mg/kg-bw; purity not stated; PND 3 or 19	Male NMRI mouse pups; 10 mice/group	Spontaneous behavior was altered in mice receiving 20.1 mg/kg-bw on PND 3 only. The effects worsened with age.	3	A code of 3 "not reliable" was assigned because the authors failed to control for litter effects. The authors stated: "[a] total of 10 mice were randomly picked from the three to five different litters in each treatment group." Therefore, between 2 and 4 littermates were used as independent values within each treatment group.
Viberg et al. (2007)	Oral gavage to pups; single dose of 6.7 or 20.1 mg/kg-bw; 98%; PND 3	Male Sprague-Dawley rat pups; 20 rats/group	Disrupted spontaneous behavior in rats of both treatment groups when tested at 2 months of age.	3	A code of 3 "not reliable" was assigned. The authors randomly selected 20 rats from 3 to 5 litters in each treatment group – that is, between 4 and 7 littermates were used as independent values within each treatment group. This study design fails to control for litter effects.
Rice et al. (2007)	Oral pipette to pups; 0, 6, or 20 mg/kg-day; 99.5%; PNDs 2–15	Male and female C57BL6/J mouse pups; 11 control litters, 13 low-dose litters, and 11 high-dose litters	On PND 14, the palpebral reflex in high-dose pups was significantly reduced; On PND 16, the forelimb grip was significantly reduced in high-dose pups; On PND 18, pups in the low-dose group struggled significantly during handling; On PND 21, the slope of the linear trend of serum T4 in males was significantly different	2	A code of 2 "reliable with restrictions" was assigned for the reasons that follow. A summary of the study is published in the peer-reviewed literature. The authors properly used the litter as the experimental unit. The individual animal data are not publicly available, nor was the study conducted in accordance with an international guideline or under GLP standards.

Study	Route; dose; purity; timing	Species; sample size; sex	Reported effects	Klimisch code[a]	Rationale
			from zero; On PND 70, the linear slope of motor activity was significantly different from controls.		
Johansson et al. (2008)	Oral gavage to pups; a single dose of 0, 1.34, 2.22, 13.4, or 20.1 mg/kg-bw; >98%; PND 3	Male NMRI mouse pups; 10–16 mice/ group	Adult mice at 2 and 4 months of age showed a dose-response related change in spontaneous behavior; At 4 months of age, the cholinergic system was affected in a dose-response manner.	3	A code of 3 "not reliable" was assigned because the authors failed to control for litter effects. For each endpoint evaluated, the authors used between 2 and 6 littermates as independent values within each treatment group.
Silberberg et al. (2009)	Oral gavage to dams; 0, 1, 100, or 1000 mg/kg-day; 97.5%; GD6 to lactation day (LD) 21	Sprague Dawley rat pups; 30 litter	No significant maternal or developmental effects reported.	1	A code of 1 "reliable without restriction" was assigned. This study was performed in accordance with international test guidelines and under GLP standards. The protocol was approved by the Rapporteur to the European Union's RAR on DecaBDE prior to study initiation. A copy of the complete report including all individual animal data was submitted to the Rapporteur.

Attachment

Wolf, D. C. and P. C. Mann (2005). "Confounders in interpreting pathology for safety and risk assessment." Toxicol. Appl. Pharmacol. **202**: 302-308

This attachment is available in a separate document. The attachment provided by TERA was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

ARNOLD & PORTER LLP

September 28, 2012

VIA E-MAIL (LAVOIE.EMMA@EPA.GOV)

Emma Lavoie
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Washington, DC 20460

Re: iGPS Comments on Draft DecaBDE Alternatives Assessment

Dear Ms. Lavoie:

On behalf of our client, Intelligent Global Pooling Systems Company, LLC ("iGPS" and the "Company"), we appreciate the opportunity to submit comments regarding the draft document entitled An Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecaBDE) ("Draft Assessment"). iGPS had the opportunity to comment on several pre-publication versions of this document through its involvement in the Flame-Retardant Alternatives for DecaBDE Partnership organized by the United States Environmental Protection Agency ("EPA"). As discussed below, while iGPS appreciates that EPA accepted some of our comments and suggestions, EPA did not incorporate certain key points made through suggested edits or in the attached letter sent to EPA on January 31, 2011. These comments focus on major concerns that iGPS has with the document in its current form.

iGPS's most significant concern is that certain passages of the Draft Assessment are structured and worded in such a way that a reader of the document might draw incorrect conclusions. Specifically, iGPS believes that the document as structured leads a reader to inaccurately conclude that manufacturers that rely on decaBDE as a flame retardant for their products can readily switch to decaBDE alternatives with lesser impacts on the environment and public health. To mitigate these concerns, EPA should be more explicit about the limitations of the Draft's hazard ranking approach and the very limited data set upon which EPA relied for its analysis. Such information should be stated in the forwardmost sections of the document. Moreover, EPA should revise the Draft to remove assertions that the alternative flame retardants are all "functional" replacements for decaBDE in certain plastics when EPA has not examined whether this is the case. Failure to correct these errors could lead governmental agencies, non-governmental organizations, and private parties relying on the final document to reach false conclusions about the comparative risks and benefits of decaBDE and the identified potential alternatives, a result that would thwart the very purpose of the Alternatives Assessment. EPA

should also modify the Draft to clarify certain statements that otherwise would mislead the reader concerning the comparative flammability of plastic versus wood pallets, as well as correct technical inaccuracies in its assessment of brominated polymers.

I. Background on iGPS

iGPS is the operator of the world's first pallet rental service providing lightweight, sustainable plastic shipping pallets. The Company is not itself a chemical manufacturer or processor. iGPS does, however, purchase (and lease to its customers) plastic shipping pallets that are produced using a highly specialized fire-resistant polymeric composite matrix. The polymer blend that was used to form the first commercial fleet of iGPS pallets contained small quantities of the flame retardant decaBDE. The additive enabled the pallets to meet 'national fire safety standards (such as UL 2335 and FM 4996) that apply in warehouses and similar areas where goods packed on shipping pallets can be stored. In addition to meeting fire safety standards, iGPS's pallets also are lighter, stronger, and safer than the traditional heavy wood shipping pallets that remain the predominant type of pallet in commerce to this day. iGPS's pallets also have an environmental profile which an independent life cycle analysis has determined to be far superior to wood pallets. Embedded radio frequency identification devices (RFID technology) enable the iGPS pallets to be traced and tracked throughout the supply chain.

Sustainability is a defining feature of iGPS's pallets and of iGPS's business model. iGPS's pallets remain reusable for a period of time well beyond that of traditional wood shipping pallets. Indeed, iGPS's pallets are never disposed because when damaged beyond repair they are taken out of service and ground or shredded, and then re-molded into new plastic pallets. In this way, iGPS follows the environmentally sound and socially responsible practice of "cradle to cradle" sustainability. These comments seek to ensure that the Draft Assessment furthers iGPS's and EPA's shared commitment to promoting environmentally sustainable practices.

II. Comments on Draft Assessment

A. EPA should modify the Draft Assessment so that its conclusions are not taken out of context and utilized inappropriately by third parties.

The Draft Assessment is intended to promote the selection of alternatives to decaBDE with fewer potential environmental impacts by providing an indication of the relative hazards of decaBDE and selected alternatives that may be appropriate for use in certain products. However, as currently drafted, there is significant risk that a reader of the Draft Assessment could be misled and reach certain erroneous conclusions that could promote the use of alternatives to decaBDE that do not reduce environmental impacts.

1. *EPA should more explicitly highlight the limitations of its relative hazard ranking approach as an indicator of risk at the outset of the document and in Chapter 4.*

Chapter 1 of the Draft Assessment contains a discussion of the differences between risk assessment, life cycle assessment ("LCA"), and the alternatives assessment approach applied in the Draft Assessment. For example, the discussion highlights that risk assessment includes an evaluation of hazard and exposure, while LCA typically examines a broader set of environmental issues than simply human health and environmental hazards. Draft Assessment at 1-6. The Draft only briefly identifies potential limitations of the risk assessment and LCA approaches.

iGPS appreciates the inclusion of this discussion, but believes that it fails to effectively alert readers to the considerable limitations of the alternatives assessment approach, and that failing to do so will lead readers to reach the wrong conclusions about the comparative environmental impacts of the various alternatives. To prevent this result, the more significant deficiencies of the alternatives assessment approach should be brought to the forefront of the document and more readily called to the readers' attention. This could be accomplished by including a specific section in Chapter 1 entitled "Limitations of the Assessment."

In this section, EPA should note that by focusing solely on hazard factors, the Alternatives Assessment omits much of the information required to critically assess and compare the environmental costs and benefits of the alternatives. For example, the Final Assessment should specifically state that the hazard ranking approach does not account for the comparative performance characteristics of the various flame retardants. This is meaningful because comparative efficacy determines the quantity of flame retardant that would be added to a formulation to produce the desired effect, and the quantity used can influence risk just as much as the hazard of a flame retardant. Moreover, the quantity of a flame retardant added to a product also will have a potential effect on environmental loading, especially following disposal.

Similarly, the alternatives assessment approach undertaken by EPA does not examine differential potential for the various flame retardants to migrate from a product. Some flame retardant alternatives may be more compatible and stable in a given plastic matrix, while others may be more likely to escape from a product and potentially contaminate the environment. Absent an understanding of this characteristic for the various alternative flame retardants, the Draft Assessment could lead a reader to conclude that these performance characteristics are similar among all alternatives even though important differences may exist that could influence effects on human health and the environment.

These are just two examples of attributes that could affect both functionality and risk. iGPS understands that a full assessment of comparative efficacy and other performance characteristics of decaBDE and alternative flame retardants was outside of the scope of the Agency's Draft Assessment. Nonetheless, it is essential that EPA highlight at the very beginning of the document, as well as in its discussion of hazards in Chapter 4, that

examining hazards alone, without consideration of these other important factors, will mislead the readers and undermine the document.

2. *EPA should discuss the significant limitations in the data set it relied on at the outset of the document and in Chapter 4.*

iGPS understands the challenges that EPA faced in performing the Alternative Assessment given the limited data available regarding the hazard characteristics of decaBDE and the identified alternatives. EPA discusses some of the limitations of the data set in Chapter 6 in a section entitled "Considerations for poorly or incompletely characterized chemicals." EPA notes the following limitations among others:

- No alternative flame retardants had empirical data for all of the subcategories of endpoints that EPA scored. Draft Assessment at 6-6.

- Nine flame retardants had no empirical data at all -- thus, for these alternatives, all endpoints were predicted using tools such as reference to structural analogies and professional judgment. Id.

- Six flame retardants lacked data for at least 10 endpoints. Id.

Absent more complete information, EPA had to rely on methodologies such as analog analysis, structure activity relationship analysis, and professional judgment to substitute for actual data. In fact, EPA relied on professional judgment in hundreds of instances in the Draft Assessment, particularly in analyzing inorganic substitutes, as other methodologies are poorly suited for this task.[1] Yet, with regard to these significant limitations, the Draft states only, "[s]everal chemicals included in this analysis appear to have more preferable profiles with low human health and ecotoxicity endpoints, although they are highly persistent, a frequent property for flame retardants... However, because most of the hazard designations were based on estimated effect levels, there is less confidence in the results." Id. at 6-6.

The importance of highlighting the limitations of these data sets cannot be understated. It is essential that a reader be alerted early in the document that many of the core methodologies used by EPA in its analyses do not rely on empirical data at all for many of the alternatives. Instead, for such alternatives the Draft draws upon these less reliable inferential methods, including extensive use of professional judgment because data and superior methodologies were not applicable in certain situations. iGPS requests that instead of discussing data limitations solely in Chapter 6, that discussions of data limitations be added prominently to Chapters 1 and 4 of the document.

[1] The sparsity of data with regard to potential human health and environmental impacts of many inorganics makes the utility of an alternatives assessment for these classes of chemicals especially limited.

Further, EPA should clarify how these limited data sets impact the utility of the hazard ranking and the overall Assessment. Currently, EPA indicates that the use of "estimated effect levels" leads to "less confidence in the results." However, EPA does not provide a point of reference for this comparative statement. EPA should clarify what it means by "less confidence" and the implications this has for the value of the Assessment when considering alternatives.

B. The Draft's use of the terms "viable" and "functional" is misleading and should be clarified or deleted.

In the Draft Assessment, EPA indicates that the alternative flame retardant chemicals it examines are "viable and functional" replacements for decaBDE. Draft Assessment at 2. EPA explains its concept of viability as follows: "Viability refers to the functional performance of a chemical as a flame retardant in certain plastics, not the environmental preferability of the chemical nor other product performance criteria." Id. at 1-2 fn. 3. This definition of viability is inherently unclear. On the one hand, the definition indicates that a viable alternative is one that will achieve "functional performance ... in certain plastics." On the other, the definition disclaims the notion that "viability" has implications for "product performance criteria." EPA appears to be trying to create a false distinction between whether a flame retardant can functionally perform as a flame retardant in a plastic versus whether it meets the performance criteria for a product. iGPS does not see the distinction between these two concepts, as the measure of functionality for a plastic is whether the finished product can be used successfully for its intended purpose in a particular application. If an alternative will add excess weight or lessen the strength of a finished product, for example, such that the product no longer is itself functional, then the alternative itself cannot be send to be "functional."

EPA recognizes the limitations of its functionality analysis in other portions of the Draft Assessment. For example, EPA discusses how it has not analyzed whether particular flame retardants are appropriate for use in specific products. EPA further indicates that few potential alternatives to decaBDE are "drop-in" replacements, and that use of alternatives may require changes in the formulation of plastics that are used to make products. Draft Assessment at 1-2. EPA recognizes that flame retardants may change the characteristics of polymers in ways unique to the particular polymer and flame retardant involved. Ways that EPA indicates a polymer may be affected include viscosity, flexibility, density, and strength. Id. at 3-4. Changes in these performance characteristics will *per se* affect the "functional performance" of the plastic/flame retardant combination.

On the basis of the foregoing, iGPS believes it would be misleading for the final Assessment to assert that the alternatives it examines are both "viable and functional." iGPS understands that EPA has performed some screening to eliminate consideration of flame retardants that are clearly inappropriate for use in certain plastics. At best, however, this

screening indicates that the flame retardants considered in the Draft Assessment are potentially viable. Thus, iGPS requests that EPA not make the unqualified assertion that all alternatives considered in the Assessment are "viable and functional." Instead, at the very least, EPA should add a qualifier to indicate that the alternatives considered are only potentially viable. In the alternative, EPA could cease referring to these alternative chemicals as "functional", and change the definition of "viability" so that application of the term does not implicitly assert that a flame retardant is functionally appropriate for use in a certain plastic. Because it is impossible to correctly assert that a chemical is functionally appropriate for use in a plastic without examining more thoroughly products in which it will be used, perhaps such alternatives could be characterized on the basis of the producers' assertion that the alternative is "compatible" with use in certain plastics.[2]

C. EPA's statements regarding the flammability of plastic pallets remain incomplete and misleading.

As part of its general discussion of the uses of flame retardants, EPA discusses the emergence of flame retardant use in plastic pallets. EPA asserts that plastic pallets are more flammable than wooden pallets when plastic pallets do not contain flame retardants. Draft Assessment at 2-11. EPA further indicates that fire safety standards for plastic pallets require plastic pallets to pass tests intended to ensure they are "as safe as" wooden pallets, and makes other statements that could be read to indicate that plastic pallets are less fire resistant than wooden pallets. Id.

Without further qualification, EPA's description is incomplete and misleading because, among other things, it does not compare the flammability of plastic pallets manufactured using a polymer which incorporates a flame retardant to wooden pallets. It is important for a reader of the Draft Assessment who is interested in pallet issues to not walk away with the false impression that plastic pallets that are actually on the market are more flammable than wooden pallets. In fact, plastic pallets with flame retardants added are less flammable than their wood counterparts. To avoid an incorrect inference being drawn from the Draft Assessment, iGPS asks that EPA include in its discussion a clarification that its statements regarding plastic pallet flammability do not relate to plastic pallets that are actually on the market that are manufactured using starting materials that incorporate a flame retardant. EPA should indicate that the evidence suggests that plastic pallets with flame retardants are actually less flammable than wood pallets, or at least that EPA has not performed the comparison itself.

D. EPA inaccurately asserts that certain flame retardants are appropriate for use in pallets.

[2] Further, iGPS believes that EPA's statements could be taken out of context when it states that it has consulted with industry experts in preparing the Draft Assessment. Draft Assessment 3-4. While EPA did allow industry participants to comment on pre-publication drafts (except Chapter 4), EPA did not accept all industry edits to the Draft Assessment, and it seems unlikely that entities that are searching for alternatives could have, at that phase, endorsed every finding of specific viability in each particular use noted in the Draft. It seems likely that predictions on viability came from manufacturers and formulators, rather than processors and users.

EPA's assessment included eight brominated polymeric chemicals as possible decaBDE alternatives — (1) brominated epoxy resin end-capped with tribromophenol, (2) brominated polyacrylates, (3) brominated polystyrene, (4) confidential brominated epoxy polymer #1, (5) confidential brominated epoxy polymer #2, (6) confidential brominated epoxy polymer mixture #1, (7) confidential brominated epoxy polymer mixture #2, and (8) confidential brominated polymer. EPA's characterization of this class of chemicals, however, is flawed and leads to an overestimation of hazards associated with these chemicals.

1. *EPA inaccurately asserts that exposure to brominated polymers is associated with lung overloading, fibrosis, and cancer.*

A common characteristic shared by the seven of the eight brominated polymers evaluated by EPA (all but the eighth polymer delineated above) is that they have an average molecular weight of greater than 10,000. EPA states in the Draft Assessment that materials of this weight "have potential for adverse effects due to lung overloading, fibrosis and or cancer." Draft Assessment at 4-21. However, this statement is poorly justified, and it relies on assumptions related to specific exposures in addition to hazards. For example, EPA asserts that brominated polymers are associated with lung overloading as a consequence of dust-forming operations. However, many applications involving the use of brominated polymers do not result in any dust generation, removing the link between these chemicals and the purported effect. For instance, the use of brominated *polymers* in finished products (e.g., consumer products such as electronics) has not been shown to be a dust-generating application. Even if common household dust were generated during use, it has not been shown that the lung's defense mechanisms would not successfully manage the exposure. Lung overloading from high-molecular weight polymers would only be predicted to occur under extreme circumstances, such as during workplace activities such as grinding or sanding operations conducted in poorly-ventilated areas and without personal protective equipment.

In addition, EPA's assertion that polymers with molecular weight greater than 10,000 can cause fibrosis and cancer is contrary to EPA's own assertion that polymerics with weights greater than 1,000 display low bioavailability. Draft Assessment at 4-21. Cancer effects in particular are predicated on the basis of bioavailability, or the propensity of a substance to gain entry to the cells and tissues where the disease subsequently can develop. If high molecular weight polymers are not bioavailable, it is not clear how they would result in cancer or fibrosis, especially during uses involving finished articles.

Given these flaws in EPA's analysis, the assertion that brominated polymers with average molecular weight greater than 10,000 are presumed, in the absence of data, to potentially could cause lung overloading, fibrosis, and cancer should be eliminated from the draft document or modified to reflect the low possibility of occurrence in anything other than a workplace scenario with inadequate health and human hygiene practices. For these reasons, the hazard designation should be changed from "moderate" to "low" for these compounds.

2. *EPA inappropriately characterizes risks associated with unnamed lower molecular weight components and impurities that are purportedly present in commercial mixtures of certain brominated polymers*.

In the hazard analyses for brominated epoxy polymer #2, confidential brominated epoxy mixture #1, and confidential brominated epoxy mixture #2, EPA indicates that a small percentage of these commercial products consists of an unidentified mixture of low molecular weight components. Draft Assessment at 4-201, 4-212, and 4-223. EPA also indicates that unidentified impurities could be present in the confidential brominated polymer. Id. at 4-234. EPA describes the hazards associated with "lower MW components" and "impurities" at the top of page 4-30 in Table 4-4. EPA characterizes these hazards as moderate to very high for various endpoints, a generally more hazardous profile than that associated with the actual polymers being evaluated. This is misleading on many levels including because it implies that a minor constituent that may be permanently and irretrievably embedded in a polymer matrix could present a hazard. Unfortunately, EPA provides no basis for these characterizations. EPA does not identify the lower molecular weight chemicals or impurities it is evaluating. It also does not cite to any studies, data, or methodology that were used to derive the asserted hazard profiles. iGPS requests that EPA provide a detailed basis for these hazard characterizations based on the presence of components and impurities or delete them from the assessment.

E. <u>EPA inappropriately excluded certain alternatives from the assessment.</u>

EPA excluded certain alternatives from the Draft Assessment without sufficient justification. Table 3-3 lists the chemicals that were excluded from the assessment as well as EPA's reasoning for their exclusion. Draft Assessment at 3-16. For example, tetrabromobisphenol A (TBBPA) was excluded because, according to Table 3-3, it was not identified as a "prevalent alternative" to decaBDE. Although it is unclear what EPA meant by designating TBBPA as not a "prevalent alternative", it has been reported as recently as 2006 that the total amount of TBBPA produced globally was greater than 150,000 tons per year, that the global demand for TBBPA was expected to grow by 8-9% per year, and that the primary use of TBBPA is in flame-retarded epoxy, polycarbonate, acrylonitrile-butadiene-styrene (ABS), high impact polystyrene (HIPS), and phenolic resins and printed circuit boards.[3] Given this information, consideration should also be given to including TBBPA in the final version of the assessment.

Further, EPA included certain brominated polymers in the Draft Assessment while excluding others without explanation. For example, EPA included in the assessment the brominated epoxy resin end-capped with tribromophenol (also known as F-2400) but did not include the closely-related brominated epoxy resin without the tribromophenol end cap (also known as F-2016). No explanation for the exclusion of the brominated epoxy resin without the tribromophenol end cap (F-2016) was given. Also excluded from the assessment was a styrene/butadiene co-polymer

[3] See http://esis.jrc.ec.europa.eu/doc/risk assessment/REPORT/tbbpaHHreport402.pdf.

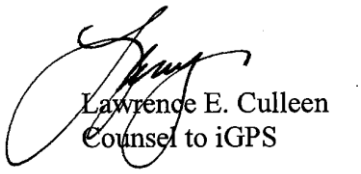
(produced by Dow) that is a very large (150,000 molecular weight) brominated polymer. Again, EPA offered no explanation for the exclusion of this brominated polymer. It is expected that the polymer alternatives not considered in the draft assessment would behave similarly to the alternatives that were considered by EPA in the draft assessment. For example, data for the brominated epoxy resin without the tribromophenol end cap (F-2016) show it to behave identically to the end-capped resin (F-2400)[4]. Prior to issuing the final Assessment, EPA my wish to reassess and carefully characterize which brominated polymers are commercially available and ought to be considered in the final document.

* * *

[4] Compare MSDS for F-2016, available at http://www.icl-industrial.com/brome/brome.nsf/viewAllByUNID/FC1F9A8F82E8D18942256DD6001FBF14/$ file/9239_enF-2016.pdf, with MSDS for F-2400, available at http://www.icl-industrial.com/brome/brome.nsf/viewAllByUNID/D0A8C5A69FB878F4C22572F900349845/$file/9227_enF-2400.pdf (last accessed Sep. 27, 2012).

iGPS appreciates the opportunity to comment on the Draft Assessment. We hope that EPA will modify the document in accordance with these comments to maximize its value as a tool for planning for sustainable alternatives to decaBDE and avoiding incorrect conclusions that could lead to environmentally undesirable consequences.

Sincerely,



Lawrence E. Culleen
Counsel to iGPS

January 31, 2011

Elizabeth Sommer
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Dear Ms. Sommer:

Intelligent Global Pooling Systems (iGPS) appreciates the opportunity to submit these comments in response to the U.S. Environmental Protection Agency's (EPA's) request for comments concerning its draft DfE *Alternatives Assessment Criteria for Hazard Evaluation*. iGPS is a leader in its field as the operator of a shipping pallet rental pool that is comprised of a revolutionary, lightweight, discretely traceable and 100% recyclable plastic pallet which provides an alternative to platforms made of wood. The iGPS pallet has shifted the paradigm for the pallet pooling industry because of the iGPS pallets' many positive attributes, not the least of which is the way in which the iGPS pallet has significantly enhanced the environmental profile of plastic pallets. Among the many positive features of the iGPS pallet is its ability to meet the strict technical standards for performance during both use and storage, including flammability standards. The iGPS pallet historically has incorporated low-levels of decaBDE to provide the flame retardancy necessary for a plastic pallet to meet those standards. Thus, iGPS has been an active and supportive stakeholder in EPA's on-going DfE Alternatives Assessment for decaBDE.

As discussed during the Stakeholder's meetings, iGPS is concerned that the draft Assessment Criteria, when applied, will give persons who make use of any assessments performed using the Criteria an overly simplistic understanding of the potential risks associated with assessed chemicals and the possible alternatives. Moreover, the limited nature of the draft Criteria will ensure that persons making use of the Criteria, and reviewing Hazard Assessments performed while using the Criteria, will fail to gain insight into other factors that affect risk associated with use of assessed chemicals and the possible alternatives; specifically, factors such as exposure during use and the impacts that other alternatives may have by potentially diminishing the performance and functionality of a product in which the alternatives are used. In any final version of the Criteria, the Agency should clearly articulate the importance of a more robust assessment (that goes beyond mere hazard ranking comparisons) when evaluating potential chemical substitutions. Further, EPA also should publish and seek comments on the manner in which the Agency intends to implement the results of assessments performed using its DfE Assessment Criteria. These concerns are described more fully below.

Undue Emphasis on Hazard Implies Hazard is the Sole Criteria in Selecting Substitutes

iGPS supports efforts to consider critically and carefully alternative chemicals when evaluating potential substitutes for another chemical in a specialized use. There are a multitude of factors that should be considered carefully, in order to avoid an outcome whereby a substitute is selected that does not serve to improve the safety and environmental profile of the end product

in which it will be used. This requires careful consideration of all aspects of the potential impacts of use of a substitute chemical throughout the lifecycle of the product in which it would be used -- commencing with the product's manufacture, and carrying through its use and ultimately its disposal.

The Hazard Assessment Criteria proposed by EPA instead focuses primarily on 9 health effects end-points and 3 environmental fate and effects observations and assigns rudimentary scores to the various chemicals under consideration on the basis of these 12 hazard-based criteria. Thus, by applying the Hazard Assessment Criteria, crude comparative "rankings" of various alternatives might become possible (especially comparisons within the Criteria of a specific end point or group of endpoints). In many cases, such as with decaBDE, the hazards posed by many proposed alternatives have never been as comprehensively tested as decaBDE. In which case, Structure Activity Relationships will be used and other professional judgments made to provide estimates of results for certain hazard endpoints. This allows for the possibility that an alternative chemical, which has not been as thoroughly tested, might appear to be a "favorable" alternative to a well-studied chemical with known toxicity -- even one for which exposures can be safely controlled during use (e.g., by limiting its content in a product, thereby limiting its potential for release): The use of ranking systems and estimates means that imprecision is inherently built in to the draft Criteria. Care must be taken that the Hazard Assessment Criteria are not misinterpreted as being a definitive risk assessment or the results might be used erroneously to justify or encourage substituting untested alternatives for well-studied chemicals.

Adding to the inherent imprecision of the Hazard Assessment Criteria rankings is the fact that the current protocol was developed to evaluate only organic chemicals. Since many proposed alternatives to decaBDE are inorganic in nature, using a ranking system that fails to consider the unique attributes of inorganic substances may lead to ill-founded conclusions regarding the suitability of alternatives as safer chemicals.

The Agency apparently has not, however, provided similar simplified ratings for other factors that affect risk, such as the likelihood of there being greater or lesser exposure to an alternative during the manufacture, use and disposal of a product containing an alternative. It also is not clear from the draft document that was made available for comment how the Hazard Assessment Criteria will be balanced against and factored into what EPA previously has stated are the seven steps in conducting a full Alternatives Assessment. http://www.epa.gov/dfe/alternative_assessments.html. By failing to make reference to or acknowledge these other factors and their equal importance to a Hazard Assessment when evaluating substitutes, EPA might unintentionally mislead users of Hazard Assessment documents who may conclude that hazard is the key area of focus for the Agency when determining the appropriateness of a potential chemical alternative. Along these lines, the Agency has also neglected to articulate how it might compare or prioritize all the relevant attributes of sustainability that are impacted by use of a chemical and its substitutes (e.g., Will human health risk be weighed more heavily than ecological risks? Will climate change effects such as greenhouse gas generating potential be considered? How will the impacts of substitution or solid waste production be weighed?).

The draft Hazard Assessment Criteria inadvertently implies that all potential substitutes will perform similarly, and are equally "viable". However, use of the Hazard Assessment Criteria alone will fail to assess fully other potential impacts of each substitute. For example, if the use of a particular substitute will make an end use product inherently weaker than the predicate product, or heavier (thus more energy consumptive during shipment and use), these factors also will have a potential health, safety, and environmental impact that should be considered and evaluated before use of the substitute is commenced. Significantly, the use of certain chemicals in a product might enhance or discourage the product's ability to be re-used repeatedly and perhaps even be recycled. EPA's final Criteria document should be written such that users are made aware that failing to take other important attributes (e.g., performance) into consideration could lead to decisions about substitutes that have unintended consequences that would run counter to the basic aspirations of the pollution prevention ethic that drives an alternatives evaluation such as the DfE program.

iGPS encourages EPA to enhance the Criteria to add references to such other factors and to publish for comment similar tools for assessing and taking them into account in the context of an overall Alternatives Assessment. Previously, EPA has stated that alternatives must satisfy a number of criteria that are not mentioned or referenced in the draft Criteria EPA has released. These include:

a) commercial availability;
b) technological feasibility;
c) delivery of the same or better value in cost and performance;
d) the potential for an improved health and environmental profile;
e) economic and social factors;
f) ability to provide lasting change; and
g) being of interest stakeholders.

iGPS believes such a list of criteria also should include consideration of: comparison of any impacts on worker and consumer exposures to a particular chemical and the alternatives under consideration if substitution were to occur; comparisons of energy consumptiveness; end-of-life and recycling impacts; and additional "life cycle" factors that should be evaluated.

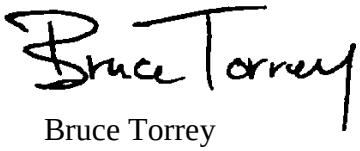
Procedural and Implementation Concerns

Seeking input on the draft Hazard Assessment Criteria is an important mechanism for improving Agency efforts. iGPS encourages EPA to make clear and solicit comments on the ways in which EPA intends to make use of the results of the various Alternatives Assessments that are being performed using the Hazard Assessment Criteria. The Agency has acknowledged that Alternative Assessment results will carry great weight both within the Agency and with interest groups, consumers, as well as state and local governments. Moreover, reference to such Assessments as critical components of EPA regulatory undertakings announced in various "Action Plans" conveys the Agency's apparent intent to rely on the results of such Assessments to inform regulatory decision making. Notably, actions taken pursuant to Section 6 of TSCA require that an assessment of substitutes be made by the Agency in the course of determining appropriate options for regulatory actions to mitigate chemical-related unreasonable risks.

However, the unsophisticated nature of the Hazard Assessment Criteria is likely to generate results that might provide false impressions about the viability and availability of substitutes to Agency staff and others who seek to make use of the results in critical regulatory efforts. Before implementing the Criteria in the context of an overall Alternatives Assessment, iGPS requests that greater effort be given to discussion in public, and with the opportunity for review and comment, of the ways in which the Criteria and any results of their use will inform EPA decision makers in the context of Risk Management Programs.

iGPS intends to remain an enthusiastic participant in the DecaBDE Alternatives Stakeholders' Process, and to work with EPA to develop appropriate criteria for fully assessing chemicals-related risks and to identifying alternative chemistries which provide an effective means to reduce such risks. Please contact me at 407-367-4459 if you would like to discuss these comments.

Sincerely,



Bruce Torrey
Vice President, Technology

26 September 2012

Hewlett-Packard Comments on "AN ALTERNATIVES ASSESSMENT FOR THE FLAME RETARDANT DECABROMODIPHENYL ETHER (DecaBDE) Draft for Public Comment July 2012"

HP would like to thank the EPA DfE team for providing this valuable report that will be very useful in the alternative selection process for HP and the electronics industry in general. We have two comments on the report that we feel need to be addressed and will hopefully lead to a more robust assessment process. We would appreciate your response in any format that is convenient.

1. Combinations of highest hazard designations in the hazard summary table.

Chemical (for relevant trade names see the synonym section of the individual profiles in Section 4.8)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Organic Phosphorus or Nitrogen Flame Retardants (PFRs or NFRs) Alternatives																
Discrete PFR, NFR and P/NFR Alternatives																
Substituted Amine Phosphate Mixture [1]	Confidential	*H*	*M*	*M*	*M*	*M*	*L*	*M*	*M*	*M*[§]	*M*[§]	*VH*	*M*	*L*	*H*	*L*

[1]Hazard designations are based upon the component of the salt with the highest designation, including the corresponding free acid or base.

- The table above was copied from page 4-31 of the report and the footnote was re-typed for clarity.
- The footnote suggests that a hazard table was (or could be) created for each component and that the highest hazard score from any component was used in the summary table above. We believe this practice can lead to misinformed alternative selection by eliminating otherwise acceptable alternatives. Consider the following example:

	GS Benchmark	Persistence	Bioaccumulation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity
Component 1	2	vH	L	L	L
Component 2	2	L	L	vH	vH
Combined	1	vH	L	vH	vH

In this hypothetical example component 1 has very high persistence and component 2 has very high acute and chronic toxicity. When the hazard table is used to determine the GreenScreen™ benchmark scores, these chemicals individually score a benchmark 2. When combined however, the combination of very high persistence and very high aquatic toxicity result in a benchmark 1 score. Ultimately, two individual components do not act like the combined score so merging the hazard tables doesn't accurately predict the true hazard. The combined score is not correct, not predictive and not useful.

- We would propose the creation and maintenance of separate, complete hazard summaries for the individual components, especially for mixtures and salts.
- As a side note, not related to the report, we have been in conference calls where this practice was discussed for transformation products as well. It has been mentioned that DfE will use endpoint scores from metabolites and degradation products to fill data gaps. While we understand the need to fill data gaps with proxy data, in some cases this may result in the same problem discussed above. For example, there may be a intermediate degradation product that has high toxicity but quickly degrades to a less toxic chemical. If the highest endpoint score from the degradation byproducts is used it may paint the wrong picture.

2. Endocrine activity for BAPP

				component.
Endocrine Activity		**BAPP is not expected to affect endocrine activity based on expert judgment. BAPP does not release bisphenol A. No data located.**		
		Low potential for endocrine activity. (Estimated)	Expert judgment	Estimated based on expert judgment.
Immunotoxicity		**Estimated to have low potential for immunotoxicity based on expert judgment. No data located.**		
	Immune System Effects	Low potential for immunotoxicity. (Estimated)	Expert judgment	Estimated based on expert judgment.
ECOTOXICITY				
ECOSAR Class		Esters, Esters (phosphate)		

- The table above was copied from page 4-143 in the report.
- The report "Flame Retardant Alternatives" Conducted by Syracuse Research Corporation for the Washington State Departments of Ecology and Health, February 2006 lists bisphenol-A as a degradation product.

- Bisphenol-A is also listed as a contaminant and a degredation product of BAPP in the Clean Production Action report "The Green Screen for Safer Chemicals: Evaluating Flame Retardants for TV Enclosures."
- We would appreciate more explanation of "BAPP does not release biphenol-A." Why are you saying BPA is not a breakdown product of BAPP?

Great Lakes Solutions, A Chemtura Business

October 1, 2012

Location in the Report	Comment
Page 3-8, Table 3-2 **Chemical: Bisphenol A bis-(diphenyl phosphate)(reaction products), BAPP, BDRP, DPADP**	Why is there a notation "synergist"? This substance is not a synergist.
Page 3-13, Table 3-2 **Chemical: Red Phosphorous**	Why is there a notation "synergist"? This substance is not a synergist.
Page 4-30; Table 4-4 **Header Row: text which symbolizes that the alternative may contain impurities**	Consider adding the phrase "for this endpoint" after the word "order".
Page 4-30; Table 4-4 **Chemical: Brominated Polystyrene**	Add the CAS number 148993-99-1 (Benzene, ethenyl-,ar-bromo derivs., homopolymer) which is the CAS number used for PBDS-80 and the other Chemtura products.
Page 4-31; Table 4-5 **Chemical: Bisphenol A bis-(diphenyl phosphate), BAPP**	The fish bioconcentration factor studies looked for n=1 and determined the BCF was very low. While the predicted BAF is barely over the 1000 threshold, based on the AA Criteria for Hazard Evaluation Version 2.0 it should not have been used for classification of the hazard as "High". The guidance states "If a measured log BAF or BCF is available and the value is >2 then apply the bioaccumulation criteria in Table 13." The results of 2 good quality BCF studies were submitted. There is a one measured log BCF >2 (our data shows <159, the log of which is <3-2) so this is the value to use from Table 13. This means "Moderate" as opposed to "High" for bioaccumulation. We further refer you to the dossier submitted by the UK to ECHA in Sept 2011 which states on Page 29 "Two bioconcentration studies have been conducted on the test substance (from two sources). Different analytical methods were used in the studies and both are considered valid. In one study (Noguchi S (1999)) the BCF values are reported to be less than or equal to the limits of detection determined i.e.

Location in the Report	Comment
	no detectable test item was found in the fish. In the other study (Hori K (1996)) BCF values have been calculated and the low, variable results are typical of a low BCF substance. Based on the two study results it is considered that the substance does not bioaccumulate.
Page 4-31; Table 4-5 **Chemicals: Phosphonate Oligomer and Polyphosphate**	Because these two substances have the same CAS number but different hazard assessments, these entries need to be differentiated more clearly (i.e., molecular weight?).
Page 4-132 **Hazard Profile for Bisphenol A Bis-(diphenyl phosphate), BAPP**	The experimental BCF is in the low to moderate range and the estimated BAF (1100) is just slightly over the "high" cut off. Under these circumstances, it would seem EPA may want to consider a "moderate" rating and show it in color (indicating that actual data exist).
Page 4-134 **Hazard Profile for Bisphenol A Bis-(diphenyl phosphate), BAPP – In regards to the oligomers**	It would be more accurate to use a range of 80-85%.
Page 4-134 **Hazard Profile for Bisphenol A Bis-(diphenyl phosphate), BAPP – In regards to the risk phrases**	It should be noted here that the UK supported the removal of the R53 classification and a request to remove the classification is currently being evaluated.
Page 4-177 **Hazard Profile for Brominated Polystyrene – In regards to the CASRN**	Should include 148993-99 as an additional CAS number (corresponding CAS name should be in the synonyms).
Page 4-177 **Hazard Profile for Brominated Polystyrene – In regards to the synonyms**	2-Propenoic acid (2,3,4,5,6-pentabromophenyl)methyl ester, homopolymer clearly does not belong in this list of synonyms. It is a completely different chemical.
Page 4-233 **Hazard Profile for Confidential Brominated Polymer – In regards to the chemical name**	We have suggested alternative description that should satisfy everyone. Contact Bob Campbell.
Page 4-234 **Hazard Profile for Confidential Brominated Polymer –In regards to U.S. EPA TSCA regulatory status**	We have no objection to state that the substance is on the TSCA inventory (you don't have to say whether it is on the confidential or non-confidential). We say on public documents that Emerald 1000 is on the TSCA inventory.
Page 4-235 **Hazard Profile for Confidential Brominated Polymer –In regards to water solubility**	We now have a GLP study showing water solubility is well below 1 ppb. This will be provided to the EPA shortly.
Page 241 **Hazard Profile for Confidential Brominated**	EPA is in the process of modifying the consent order. Please consult with the PMN manager

Location in the Report	Comment
Polymer – In regards to chronic aquatic toxicity	for the latest status
Page 241 **Hazard Profile for Confidential Brominated Polymer – In regards to daphnid ChV**	Our GLP chronic daphnid study is complete and will be submitted. Results indicate that this endpoint can be classified as "L".
Page 245 **Hazard Profile for Confidential Brominated Polymer – In regards to bioaccumulation**	Was the analog a substance >1,000 MW? If not, then it really is not a suitable analog. In addition, the lowest MW species in our product is well above 1,000 and impurities <1,000 are essentially absent. The EPA polymer exemption allows for up to 25% of species below 1,000 MW and still be considered a polymer of low concern.
Page 245 **Hazard Profile for Confidential Brominated Polymer – In regards to BAF**	What analog substances with MW >1000 have a BAF factor above 100? Above 10?
Page 5-1 **Figure 5-1**	Use of a fire for recycling without control seems out of place. The fire is more appropriate for incineration. Is the recycling (without control) supposed to represent re-use/re-purposing. If the fire is intended to represent illegaly/illicit uncontrolled burning, that should not be characterized as recycling since the purpose of this activity is no to recycle/re-use the FR, it is to recover metals. Perhaps "uncontrolled metal recovery" would be a more appropriate caption under the flames.

October 1, 2012

Ms. Emma T. Lavoie, PhD
Design for the Environment Program
Office of Pollution Prevention and Toxics
United States Environmental Protection Agency
1201 Constitution Avenue, N.W.
Washington, D.C. 20004

Dear Ms. Lavoie:

On behalf of The Boeing Company ("Boeing"), I am pleased to provide comments on the draft Alternatives Assessment for the flame retardant chemical decabromodiphenyl ether (decaBDE).

Boeing is the world's largest manufacturer of commercial jetliners and defense, space and security systems. Boeing products and tailored services include commercial and military aircraft, satellites, weapons, electronic and defense systems, launch systems, advanced information and communication systems, and performance-based logistics and training. Boeing employs more than 171,000 people across all 50 U.S. states and in 70 countries, with major manufacturing operations in eight U.S. states. As a top U.S. exporter, Boeing has customers in more than 150 countries around the world, and supports airlines and U.S. and allied government customers in more than 90 countries.

We appreciate the commitment of EPA's Design for the Environment (DfE) program to providing manufacturers and other stakeholders with the best available information on potential chemical alternatives. As a manufacturer of complex durable goods, Boeing uses materials which contain a wide range of chemicals to ensure that its products are safe and effective. As more and more chemicals are identified for scrutiny and potential restriction, it is increasingly important to have the best available information concerning possible alternatives.

In that regard, we urge EPA's DfE office and the Agency's Chemical Control Division to work as closely together as possible to ensure that the DfE Assessment analyses are timely and useful. The DfE program's work will be most useful to chemical users if reports are available well in advance of market-based or regulatory restrictions. In the case of the draft report on decaBDE, the urgency created by the US manufacturers' unilateral phaseout schedule has forced users to make decisions about alternatives without the benefit of the DfE's final report. While we recognize that EPA has limited, if any, authority regarding the decisions by manufacturers to make (or not make) a certain chemical, the Agency certainly can control the timing of regulatory restrictions, and so we urge the Agency to recognize that a chemical user's ability to use the

work of the DfE program is diminished if regulatory deadlines force chemical users to select alternatives before DfE reports are available.

As the draft Alternatives Assessment makes clear throughout, decaBDE has been used in a number of applications in a number of sectors. We understand that the decaBDE Alternatives Assessment cannot focus in detail on any particular sector's use of decBDE. Nonetheless, we appreciate the efforts of the authors to solicit information on specific uses of decaBDE in the aerospace sector and we are gratified that the information we provided is included in the report. To the extent that Boeing can and does know where decaBDE is used in parts and components it uses to manufacture aerospace products, we believe the representations in Table 2-1 and Section 2.2.4 are accurate. However, we cannot endorse the representation in Figure 2-7 of the volumes of decaBDE used in various sectors. Although decaBDE is used in a number of parts and components in aerospace manufacturing, the volumes are generally low. Furthermore, given the concerted efforts in the aerospace industry over the past several years to identify and implement alternatives, it is difficult to know whether this characterization, if once accurate, is still timely. We would ask the authors to consider whether this information is sufficiently reliable and material to warrant inclusion in the final Assessment.

Boeing appreciates the work that has gone into creating this document, and we encourage EPA to continue to commit resources to assisting manufacturers with the task of identifying chemical alternatives. With the intent of encouraging this work and possibly making it more useful to manufacturers at all levels in the supply chain, we offer the following specific comments.

First, for the results of any Alternatives Assessment to be most useful, it must be available to – and written for -- those who have the authority and the responsibility to select and implement chemical alternatives. As the discussion in Section 5.4 of this draft Assessment indicates, the authors understand that the supply chain for the use of decaBDE in both textiles and plastic materials is complex. For these materials, decisions concerning the use of flame retardant chemicals are typically made by formulators, finishers, compounders and/or moulders. Indeed, the supply chains for many complex durable goods may be even more complicated than that diagramed in Figure 5-3 if materials or parts containing decaBDE are used to build subcomponents or subassemblies which are ultimately aggregated into final products.

As a producer of many complex aerospace products, Boeing has a strong interest in ensuring that the materials used to build parts, components and assemblies are effective and safe. When chemical substitutions are required, Boeing works closely with its suppliers to assist them in evaluating the performance of materials containing chemical alternatives; in the past several years, we have increased our commitment dramatically to help our suppliers evaluate materials containing alternatives to certain brominated flame retardants. However, Boeing does not buy any decaBDE as a raw material, and it does not have the responsibility or the authority to identify alternatives for materials, parts and components it may procure. Indeed, as we attempted to outline in our comments on EPA's recent proposed Significant New Use Rule and Test Rule for PBDEs, 77 Fed. Reg. 19862 (April 2, 2012), Boeing and other final assemblers often have limited visibility concerning the use of specific flame retardant chemicals, and limited

authority to effect changes.[5] Therefore, the primary audience for this Alternatives Assessment is the universe of companies which are incorporating flame retardant chemicals into textiles, resin systems and plastic materials that become the parts and components used to manufacture aircraft and many other products.

Boeing has more than 3,400 Tier 1 suppliers, many of whom are supplying materials, parts or components that must meet flammability standards. It is these manufacturers (and in some cases, their suppliers) which must make determinations about alternatives for decaBDE. While each of these companies has earned the right to provide materials to Boeing by meeting rigorous standards for quality and performance, some of these businesses are small and may not have resources that allow a thorough familiarity with EPA regulatory processes. In addition, a number of Boeing's suppliers are located outside of the United States and may not be fully conversant in US regulatory practices.

For these reasons, we believe that the information and guidance provided in the decaBDE Alternatives Assessment should be as clear and as accurate as possible. We are concerned that in a number of instances, the information provided is not sufficiently complete to support final decisions by our suppliers concerning alternatives to decaBDE. As one example, the analysis of Confidential Brominated Epoxy Polymer #2 (page 258) provides estimated values, professional judgment opinions, references to "no data collected," and lacks information on basic parameters, such as pH values, that a formulator would need to effectively evaluate this alternative.

Following are several other examples of instances in which Boeing believes the information provided concerning specific alternatives warrants clarification or elaboration:

- Aluminum diethylphosphinate (CAS 2257890-38-8) is not listed on the non-confidential TSCA Inventory. EPA should clarify if it is in the PMN process or if it is on the confidential inventory.
- Brominated Epoxy Resin End-Capped with Tribromophenol (CAS 135229-48-0). The TSCA note indicates that the CAS number is not on the non-confidential Inventory; however it also states that it is listed on the Inventory as CAS 534584-61-7 (ACC. No. 153958). Searches of databases do not associate either CAS Number with the Accession Number. This is confusing and EPA should provide further clarification for users to determine if the chemical is a viable candidate for production purposes.
- Confidential CASRN and MF – Polyquel 240, 241,145,146, and Emerald Innovation 1000. It is of no value to a user to hold the CASRN confidential as well as the formula. There is no information presented beyond EPA's professional judgment,

[5]For all of the materials, parts, and components that Boeing procures for aircraft manufacturing, it has varying levels of ability to identify the chemical composition, including the use of flame retardant chemicals, of such materials. In some cases, Boeing may control the design of the part and will work closely with suppliers to identify potential alternatives and ensure that materials containing those alternatives will meet all applicable requirements. In other cases, Boeing may procure components or assemblies based on performance standards, and therefore may have limited knowledge of the materials used to manufacture those components or assemblies. In yet other cases, parts or components or assemblies may be procured by third parties, and Boeing is obligated is to install those parts or components; but in such cases, Boeing has little ability to know or acquire information concerning the chemical composition of such components or assemblies.

leaving a potential user with no information to make an independent assessment as to the viability of these chemicals for production processes.

- Decabromodiphenyl ethane (CAS 84852-53-9). There is mention of the SNUR and the requirement that the chemical cannot be released into U.S. waters. EPA should list the regulatory citation for the SNUR in the text. The SNUR (40 CFR 721.536) also has a requirement under *Industrial, commercial and consumer activities* as specified in 40 CFR 721.80q that EPA does not address. 40 CFR 721.80q states that a significant new use of the substance is "Aggregate manufacture and importation volume for any use greater than that allowed by the section 5(e) consent order……..". Realistically, a chemical with a production volume cap that is unknown/confidential automatically raises questions for the formulator/processor/user as to the chemical's long term availability as a decaBDE substitute. EPA needs to make all information about a chemical public to facilitate informed decisions by downstream users.
- Resorcinol Bis-Diphenylphosphate (CAS 125997-21-9 and CAS 57583-54-7) according to the summary this chemical has CAS numbers that are used interchangeably, one on the inventory and one not. Can a downstream user safely assume then that this chemical is considered by EPA to be on the inventory?
- Tetrabromobisphenol A Bis(2,3-dibromopropyl)ether (CAS 21850-44-2) – The TSCA regulatory status indicates that this chemical is subject to a Section 4 test rule. EPA should list the regulatory citation for the test rule in the text, indicate if testing requirements have sunset, indicate who is subject to the test rule and list the tests required to be performed.
- Triphenyl phosphate (CAS 115-86-6) - The TSCA regulatory status indicates that this chemical is subject to a Section 4 test rule. EPA should list the regulatory citation for the test rule in the text, indicate who is subject to the test rule and list the tests required to be performed.

In summary, to make this Alternatives Assessment most useful to manufacturers in the aerospace industry, EPA should recognize first that decisions concerning alternatives to decaBDE are made by suppliers and others well upstream in the supply chain, including many small businesses and companies located outside of the United States. To be most useful, the Assessment should identify where information is incomplete and what additional information is required to resolve significant uncertainties. Similarly, where EPA is exercising its professional judgment, it should provide information it relies upon to make such judgments. Together, these improvements would facilitate a company's ability to assess the viability of various alternatives, and would likewise assist Boeing as it works with its suppliers to ensure that materials containing flame retardant chemicals meet all applicable requirements.

Lastly, we have several comments concerning the discussion in Section 6.6, "Moving Towards a Substitution Decision." We commend the authors for recognizing that because decaBDE is used in a range of polymers and end products, it is unlikely that a single alternative evaluated by this report will fulfill all of the current applications of decaBDE. The report also acknowledges that the search for chemical alternatives often involves the consideration of trade-offs, especially when there is imperfect information on the endpoints of certain alternatives.

Indeed, in the aerospace industry, decaBDE has been used in a wide variety of materials, parts and components, each with unique requirements and specifications. Therefore, the search for an alternative flame retardant solution for each of these applications must be conducted independently with attention to the specific requirements of each material, part or component. We believe this requirement makes the search for replacements for decaBDE in the aerospace industry more complicated than in other manufacturing sectors.

Furthermore, while we acknowledge that the search for, and selection of, alternatives chemicals may involve tradeoffs, we urge the report to reflect that at least for the aerospace industry, and for other transportation sectors as well, the primary purpose of using flame retardant chemicals is to ensure passenger and crew safety. Either by regulatory directive or by internal standards for product quality and stewardship, certain minimum standards for safety must be met. We urge the discussion in Section 6.6 of the report to reflect that while certain tradeoffs may be contemplated, these types of minimum standards for safety cannot be compromised and this may make the selection of alternatives for decaBDE in the aerospace sector even more challenging.

Thank you again for the opportunity to present these comments. Please do not hesitate to contact us if you should have questions or require additional information.

Sincerely,

Charles L. Ingebretson
The Boeing Company

PUBLIC COMMENT TO

AN ALTERNATIVE ASSESSMENT FOR THE FLAME RETARDANT DECABROMODIPHENYL ETHER (DecaDBE) – EPA – June 2012

Sponsored by

Italmatch Chemicals S.p.A.

September 2012

1. INTRODUCTION

Italmatch Chemicals S.p.A. is an Italian producer of Red Phosphorus, used as Flame Retardant and submitted a Joint Registration in the REACH framework (Regulation EC 1906/2007) for Red Phosphorus in 2010. The Lead Registrant for the substance in Europe is Clariant GmbH, who contributed to finalise the final dossier currently disseminated on the ECHA website, who is the actual main data owner.

We found some discrepancies in the published document and we want to comment about the assessment of Red Phosphorus, proposing as a conclusion to modify it as followings:

1) Acute mammalian toxicity: from VERY HIGH to LOW
2) Dermal irritation: from HIGH to LOW

In Table 4-6 on page 4-32 of the alternatives assessment report there is evidence of the assignment to Red Phosphorus of "VH very high hazard" to Acute Toxicity and "H high hazard" for Dermal irritation.

Table 4-6 Screening Level Hazard Summary for Inorganic Flame Retardant Alternatives

This table only contains information regarding the inherent hazards of flame retardant chemicals. Evaluation of risk considers both the hazard and exposure associated with substance including combustion and degradation byproducts. The caveats listed in the legend and footnote sections must be taken into account when interpreting the hazard information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard —Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics (*VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.

[d] This hazard designation is driven by potential for lung overloading as a result of dust forming operations.

[R] Recalcitrant: Substance is comprised of metallic species that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions.

* Ongoing studies may result in a change in this endpoint

Chemical (for relevant trade names see the synonym section of the individual profiles in Section 4.8)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Inorganic Flame Retardant Alternatives																
Aluminum Diethylphosphinate	225789-38-8	L	*L*	L	*L*	*M*	*M*	L	L		L	VL	M	M	*H*[R]	*L*
Aluminum Hydroxide	21645-51-2	L	*L*	L	*L*	L	M	L	L		VL	VL	*M*	*M*	*H*[R]	*L*
Ammonium Polyphosphate	68333-79-9	L	*L*	*L*	*L*	*L*	*L*	*M*[d]	L		VL	L	*L*	*L*	*VH*	*L*
Antimony Trioxide[1]	1309-64-4	L	L*	L	*L*	*L*	*L*	M*	L		L	M	M	M	*H*[R]	*L*
Magnesium Hydroxide	1309-42-8	L	L	L	*L*	*L*	*L*	L	*L*		M	*M*	*L*	*L*	*H*[R]	*L*
Red Phosphorus	7723-14-0	VH	*L*	*M*	*L*	*L*	*L*	*L*	L		M	H	L	L	H	*L*
Zinc Borate	1332-07-6	L	*L*	*H*	*M*	*M*	*H*	*L*	L		L	L	*H*	*H*	H[R]	*L*

[1] This compound is included in the ongoing EPA Work Plan evaluation for Antimony and Compounds

The conclusions used for the assignment of VH are explained in Chapter 4.8, in the Table Red Phosphorus on page 4-503 of the alternatives assessment report:

Acute Mammalian Toxicity : VERY HIGH: Based on oral LD50 value of 5 and 11,5 mg/kg in cats and dogs, and, rats and mice, respectively. In addition mild histological changes in the respiratory tract, respiratory distress, laryngeal lesions and pulmonary congestion have occurred in several animals studies (including human) following exposure to red phosphorus/butyl rubber (RP/BR) smoke at concentrations between 0,1-5,3 mg/L,

Both oral LD50 and the inhalation LC50 values are considered for the assignment of VH for acute toxicity of Red Phosphorus according to the criteria described in Table 4-2: Criteria used to assign hazard designations of the, on page 4-4 of the alternatives assessment report.

Regarding the inhalation studies, the exposure to Red Phosphorus and Red Phosphorus/butyl rubber combustion smoke is included.

For Dermal irritation it is stated that "Prolonged contact with red phosphorus may cause severe skin irritation."

2. ACUTE ORAL TOXICITY

Data assessment

2.1 In Chapter 4.8 "Hazard evaluation", for each endpoint related to Red Phosphorus, data, reference and data quality are listed.

Red Phosphorus CASRN 7723-14-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Acute Lethality	**Oral**	Rat, mouse LD_{50}: 11.5 mg/kg	RTECS; Maine DEP, 2007	Reported in secondary sources.
		Rabbit LD_{50}: 105 mg/kg	RTECS	Reported in a secondary source.
		Cat, dog LD_{50}: 5 mg/kg	RTECS	Reported in a secondary source.
		Rat LD_{50} > 10,000 mg/kg-bw - 15,000 mg/kg-bw	NRC, 1997; Maine DEP, 2007	Reported in secondary sources.
		Single dosage of 0.66 mg/kg did not produce mortality in rabbits or guinea pigs. Cirrhosis-like symptoms were observed.	ERMA; Maine DEP, 2007	Reported in secondary sources.

2.2 Starting from an evident discrepancy between the two data reported for Rats (LD50 on Rat > 10000 – 15000 mg/kg-bw [NRC, 1997] and LD50 on Rat= 11.5 mg/kg [RTECS]), the objective was to evaluate the type and variability of data available and contextualize them: first comprehend what substances were tested, their purity (keeping in mind the impact that, even in small percentages, white phosphorus can have on toxicity), how the studies have been performed and finally to establish the reliability of the data used for the alternatives assessment. We concluded with the following table (Table 1).

2.3 The following data, which reliability is not confirmed, seem to have been considered for "VH" classification:

Table 1

Tested species	type of endpoint	value
Rat, mouse	LD50	11,5 mg/kg
Rabbit	LD50	105 mg/kg
Cat, dog	LD50	5 mg/kg

2.4 Since the column "Data quality" states that the data were "Reported in secondary sources", apparently no original report was retrieved for confirmation of these values, thus no indication of the tested substance, no indication of year, test method, tested substance or its purity are provided; furthermore the secondary reference indicated in the EPA document (RTECS) does not seem to report any of this three LD50s.

The RTECS number is not specified in Chapter 4.8, in fact the number for Red Phosphorus RTECS is TH 3495000 in which these data are not reported, while the second reference that has been cited is a Maine DEP report, which actually derived these values from MSDS sheets from 2 companies, which in turn derived them from the earlier mentioned RTECS.

In the RTECS database, we traced the mentioned values to be retrieved from a secondary source in russian [Vrednie chemichescie veshestva. Neorganicheskie soedinenia elementov V-VII groopp" (Hazardous substances. Inorganic substances containing V-VII group elements), by Bandman A.L. et al., Chimia, 1989" with no description of study design or results. Therefore, to establish the reliability of these studies seems to be difficult and based on the alternatives assessment report not verifiable.

2.5 The reported Rat LD50 values of >10.000 mg/kg-bw - 15.000 mg/kg-bw seem to be considered by EPA as less reliable than the three previously mentioned results and the regulatory decision has obviously been based on the whole set of data without taking into account the reliability of the studies.

These two values have been presented as key studies in the European Registration dossier of Red Phosphorus (actually EC 918-594-3). [HOECHST Aktiengesellschaft, Pharma Forschung, Toxikologie, _Akute *Orale Toxizitat von Phosphor Rot an Weiblichen SPF-Wistar Reatten*, Study Report 131/75, 1975], [Henry, M.C., J.J. Barkley, and C.D. Rowlett.. *Mammalian Toxicological Evaluation of hexachloroethane Smoke Mixture and Red Phosphorus*. Final Report. AD-A109593. Conducted as Contract DAMD17-C-78-C-8086 by Litton Bionetics, Inc., Kensington, MD, for the U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD, 1981)] The original studies are available and can be provided on request for confirmation. The original studies, although dated, describe the tested substance and the procedures in full detail and their reliability has been fully assessed.

Table 2, reported below, summarizes the results of our research into the availability of the studies mentioned in the alternatives assessment report.

Table 2

Acute Mammalian Toxicity					
Acute Lethality	Oral	Rat, mouse LD50: 11.5 mg/kg	√ **Secondary source:** RTECS. Registry of Toxic Effects of Chemical Substances (RTECS). National Institute for Occupational Safety and Health (NIOSH).	X *DATA NOT FOUND IN THE REPORT RTECS TH4395000 - Red Phosphorus*	
			√ **Secondary source:** Maine DEP. Decabromodiphenyl ether flame retardant in plastic pallets. A safer alternatives assessment. Prepared for: Maine Department of Environmental Protection. By: Pure Strategies, Inc. Gloucester, MA, 2007.	√ **Secondary source**: ChemCAS. 2004. MSDS for Phosphorus Red Amorphous. X Original source: NOT MENTIONATED, MSDS are not considered reliable references.	
		Rabbit LD50: 105 mg/kg	√ **Secondary source:** RTECS. Registry of Toxic Effects of Chemical Substances (RTECS). National Institute for Occupational Safety and Health (NIOSH).	X *DATA NOT FOUD IN THE REPORT RTECS TH4395000 - Red Phosphorus*	
		Cat, dog LD50: 5 mg/kg	√ **Secondary source:** RTECS. Registry of Toxic Effects of Chemical Substances (RTECS). National Institute for Occupational Safety and Health (NIOSH).	X *DATA NOT FOUD IN THE REPORT RTECS TH4395000 - Red Phosphorus*	
		Rat LD50 > 10000 mg/kg-bw - 15000 mg/kg-bw	√ **Secondary source:** NRC (National Research Council). Toxicity of military smokes and obscurants, Volume 1. Committee on Toxicology, Commission on Life Sciences, National Research Council. 1997.	√ **Secondary source**: Mitchell, W.R., and E.P. Burrows. 1990. Assessment of Red Phosphorus in the Environment. Tech Rep. 9005. AD-A221704. U.S. Army Biomedical Research and Development Laboratory, Frederick, Md. √ **Original source**: Henry, M.C., J.J. Barkley, and C.D. Rowlett. 1981. Mammalian Toxicological Evaluation of hexachloroethane Smoke Mixture and Red Phosphorus. Final Report. AD-A109593. Conducted as Contract DAMD17-C-78-C-8086 by Litton Bionetics, Inc., Kensington, MD, for the U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.	Total phosphorus content mean: 98.75% (Phosphorus white under 0.01%)
			√ **Secondary source:** Maine DEP. Decabromodiphenyl ether flame retardant in plastic pallets. A safer alternatives assessment. Prepared for: Maine Department of Environmental Protection. By: Pure Strategies, Inc. Gloucester, MA, 2007. (LD50 of > 15,000 mg/kg-bw was determined for red phosphorus in the rat)	√ **Secondary source**: European Chemical Substances Information System (ESIS). 2000. IUCLID Dataset for phosphorus. European Commission Joint Research Centre. √ **Original source**: Clariant study: HOECHST Aktiengesellsch aft, Pharma Forschung, Toxikologie (1975)	TS Phosphorus Red
		Single dosage of 0.66 mg/kg did not produce mortality in rabbits or guinea pigs. Cirrhosis-like symptoms were observed.	√ **Secondary source:** ERMA (Environmental Risk Management Authority). Phosphorus, amorphous (red) New Zealand. (Accessed on March 25, 2011)	√ **Secondary source:** HSDB (Hazardous Substances Data Bank). √ **Source**: Hayes, W.J. and E.R. Laws (eds). 1991. Handbook of Pesticide Toxicology. Volume 2. Classes of Pesticides. New York, NY: Academic Press, Inc.	
			√ **Secondary source:** Maine DEP. Decabromodiphenyl ether flame retardant in plastic pallets. A safer alternatives assessment. Prepared for: Maine Department of Environmental Protection. By: Pure Strategies, Inc. Gloucester, MA, 2007.	√ **Source**: Hayes, W.J. and E.R. Laws (eds). 1991. Handbook of Pesticide Toxicology. Volume 2. Classes of Pesticides. New York, NY: Academic Press, Inc. As described in HSDB.	

√ Original document available

X Original reference can not be retrieved

2.6 In the case of Red Phosphorus the evaluation of the tested substance, and the contextual verification of the original report, is of utmost importance since Mitchell et al. 1990 reported that: "*Little if any significant toxicity appears to be associated with elemental red phosphorus unless it is contaminated with the white allotropic form"* [Uhrmacher, J.C., P.P. Werschulz, D.O. Schultz, and D.O. Weber. 1985. A Health and Environmental Effects Data Base Assessment of U.S. Army

Waste Material,Phase II. Final Report. AD-A175274. Contract No. DAMD17-84-C-4133. Carltech Associates, Columbia, MD].

Therefore small impurities of white phosphorus in the tested sample can significantly impair the results.

Furthermore it is reported in the Hazardous Substances Data Bank (HSDB) that "*Red phosphorus is non-volatile, insoluble, unabsorbable, and thus non-toxic when ingested, unless it is contaminated with traces of yellow phosphorus* .." [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. III-348] **PEER REVIEWED**

In fact Red Phosphorus is manufactured converting White Phosphorus into the allotropic form of Red Phosphorus; the residual content of White Phosphorus in Red Phosphorus will influence the toxicity of Red Phosphorus; but Red Phosphorus producers, especially in Europe, have developed recent technologies to reduce the residual traces of White Phosphorus, from historical values in excess of 1000 ppm, to the present values well below 100 ppm, especially driven by the flame Retardant Industry.

Further considerations on data assessment

It is also known that both in the USA and in Europe there is often a misunderstanding on the identification of the tested substance Red Phosphorus and related data. In this case, there is indeed often some confusion between White Phosphorus and Red Phosphorus and the two substances are in fact almost always reported with the same CAS: 7723-14-0, even though the two allotropic forms have very different toxicological patterns.

Acute lethal toxicity values between 1 and 200 mg/kg are in fact reported in the RTECS TH350000 for White Phosphorus for different species (see Table 3 below)

For rabbits a value of 105 mg/kg is reported as lethal dose for intravenous application of White Phosphorus [AEXPBL Archiv fuer Experimentelle Pathologie und Pharmakologie. (Leipzig,Ger. Dem. Rep.) V.1-109, 1873-1925. For publisher information, see NSAPCC.Volume(issue)/page/year: 64,274,1911]

Given that the toxicity of Red Phosphorus is considered to be less than the toxicity of White Phosphorus, as stated by Mitchell et al and by Gosselin et al, included in the HSDB, the choice of LD50 values for Red Phosphorus in the current alternatives assessment seems odd, since the chosen LD50 values for Red Phosphorus are in the same range as the toxicity values of White Phosphorus.

Table 3

LDLo	Oral	human – woman	22 mg/kg	AHJOA2 American Heart Journal. (C.V. Mosby Co., 11830 Westline Industrial Dr., St. Louis, MO 63146) V.1- 1925- Volume(issue)/page/year: 84,139,1972
TDLo	Oral	Human – woman	11 mg/kg	AJMSA9 American Journal of the Medical Sciences. (Slack Inc., 6900 Grove Rd., Thorofare, NJ 08086) New series: V.1- 1841- Volume(issue)/page/year: 209,223,1944
LDLo	Oral	Human	1.4 mg/kg	PCOC** Pesticide Chemicals Official Compendium, Association of the American Pesticide Control Officials, Inc., 1966. (Topeka, KS)Volume(issue)/page/year: -,901,1966
LDLo	**Oral**	**Human – woman**	**4.6 mg/kg**	AIMDAP Archives of Internal Medicine. (AMA, 535 N. Dearborn St., Chicago,IL 60610) V.1- 1908- Volume(issue)/page/year: 83,164,1949
TDLo	Oral	Human – woman	2,6 mg/kg	NEJMAG New England Journal of Medicine. (Massachusetts Medical Soc., 10 Shattuck St., Boston, MA 02115) V.198- 1928- Volume(issue)/page/year: 232,247,1945
LD50	Oral	Rodent – rat	3.03 mg/kg	NTIS** National Technical Information Service. (Springfield, VA 22161) Formerly U.S. Clearinghouse for Scientific & Technical Information.Volume(issue)/page/year: AD-B011-150
LD50	Oral	Rodent – mouse	4.8 mg/kg	NTIS** National Technical Information Service. (Springfield, VA 22161) Formerly U.S. Clearinghouse for Scientific & Technical Information.Volume(issue)/page/year: AD-B011-150
LDLo	Oral	Mammal – dog	10 mg/kg	YKYUA6 Yakkyoku. Pharmacy. (Nanzando, 4-1-11, Yushima, Bunkyo-ku, Tokyo,Japan) V.1- 1950- Volume(issue)/page/year: 28,329,1977
LDLo	Oral	Mammal – cat	4 mg/kg	YKYUA6 Yakkyoku. Pharmacy. (Nanzando, 4-1-11, Yushima, Bunkyo-ku, Tokyo, Japan) V.1- 1950- Volume(issue)/page/year: 28,329,1977
LDLo	Oral	Mammal – pig	160 mg/kg	28ZEAL "Pesticide Index," Frear, E.H., ed., State College, PA, College Science Pub., 1969 Volume(issue)/page/year: 4,321,1969
LDLo	Oral	Bird – duck	3 mg/kg	JAPMA8 Journal of the American Pharmaceutical Association, Scientific Edition. (Washington, DC) V.29-49, 1940-60. For publisher information, see JPMSAE. Volume(issue)/page/year: 39,151,1950
LDLo	Oral	Mammal - species unspecified	200 mg/kg	28ZEAL "Pesticide Index," Frear, E.H., ed., State College, PA, College Science Pub., 1969 Volume(issue)/page/year: 4,321,1969

3. ACUTE INHALATION TOXICITY

Data assessment

3.1 In Chapter 4.8 "Hazard evaluation", for each endpoint related to Red Phosphorus, data, reference and data quality are listed.

For the Acute Inhalation toxicity of Red Phosphorus the following study results are presented on pages 4-507 to 4-510 of the alternatives assessment report.

		observed.		
	Inhalation	Rat, rabbit LC_{Lo} = 0.15 mg/L (150 mg/m^3) Cardiac: EKG changes not diagnostic of specified effects; liver: fatty liver, degeneration; kidney/ureter/bladder - other changes	RTECS	Reported in a secondary source.

Red Phosphorus CASRN 7723-14-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Rat LC_{50} (1 -hour exposures): 2.32-4.3 mg/L (2,320 – 4,300 mg/m^3)	NRC, 1997; Maine DEP, 2007	Reported in secondary sources.
		Sprague Dawley rats and Beagle dogs exposed to RP-BR and black powder mixture at 1.128-1.882 mg/L (1,128-1,882 mg/m^3). Exposure: 60-240 minutes (rats) or 30-240 minutes (dogs) Respiratory distress (leading to prostration and death in some cases). Transient hypoactivity, salivation, conjunctivitis	EPA, 2010	Adequate; however, study details are not available; reported in a secondary source.
		Sprague Dawley rats exposed to an aerosol generated by combustion of RP/BR for 1 or 4 hours. 1 hour exposures: 3.15, 4.33, 5.36 or 8.46 mg/L (3,150, 4,330, 5,360, 8,460 mg/m^3) 4 hour exposure: 1.53 mg/L (1,530 mg/m^3) 1-hour LC_{50} = 4.597 ml/L (4,597 mg/m^3) Slightly-moderately deformed epiglottis (blunted tip or partially to virtually absent, ulceration, edema); laryngeal lesions (severe ulceration and edema with fibrin substance on the mucosal surface of the ventral larynx); moderate-severe pulmonary congestion, edema, hemorrhage.	EPA, 2010	Reported in a secondary source.

Red Phosphorus CASRN 7723-14-0				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Porton Wistar rats exposed to combustion aerosols of red phosphorus at 3.1 or 3.2 mg/L (3,100 or 3,200 mg/m^3) for 30 minutes. Laryngeal inflammation, blood in tracheal lumen, severe pulmonary congestion and edema, hepatic congestion.	EPA, 2010	Reported in a secondary source.
		Rats, mice, and rabbits exposed to unformulated pure red phosphorus for 1 hour Rat 1-hour LC_{50} = 1.217 mg/L (1,217 mg/m^3) Mouse 1-hour LC_{50} = 0.856 mg/L (856 mg/m^3) Rabbit 1-hour LC_{50} = 5.337 mg/L (5,337 mg/m^3) Death, necrosis and inflammation in the larynx and trachea, pulmonary congestion, hemorrhage, edema, pneumonitis, congestion in liver and kidney (rats, mice guinea pig), cortical necrosis in kidney (mice)	EPA, 2010	Reported in a secondary source.
		Guinea pigs exposed to RP-BR smoke at 120-2.277 mg/L (2,277 mg/m^3) for 5-150 minutes. Death, respiratory distress	EPA, 2010	Reported in a secondary source.

Red Phosphorus CASRN 7723-14-0				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Mild histological changes in the respiratory tract of rabbits and rats (abnormalities in the larynx and trachea, alveolitis, frank pneumonia) exposed to pyrotechnic mixtures containing red phosphorus	Marrs, 1984	Adequate. Histological effects seem to be a result of orthophosphoric acid aerosol.
		Reversible symptoms of respiratory distress in workers exposed to 0.1-0.7 mg/L (100-700 mg/m^3) red phosphorus smoke for <15 minutes	EPA, 2010	Reported in a secondary source.

3.2 First it should be mentioned that Red Phosphorus seems to be the only substance for which inhalation studies were performed using combustion products, the inhalation studies for all other substances were either performed using **dust of the substance, or inhalation studies are lacking.**

It is also relevant to underline then that the classification of the substance seems not to consider the substance in itself **but a very specific application**, **which falls outside the scope of Flame Retardants.**

3.3 Regarding the included inhalation studies for Red Phosphorus, as one can see in the column "Data" of the above Table, the majority of data for the inhalation studies was generated using a mixture of Red Phosphorus/butyl rubber, one study was performed with a mixture of Red Phosphorus/butyl rubber and black powder, while yet another study was performed using unformulated Red Phosphorus for exposure. One correction should be made, the study performed using Porton Wistar rats exposed to aerosols of Red Phosphorus as mentioned in the above table, is actually performed using combustion aerosols of either 95% Red Phosphorus and 5% butyl rubber, or 97% Red Phosphorus and 3% butadiene styrene [Marrs, T.C., Colgrave, H.; Edginton, J.; et al. The toxicity of a red phosphorus smoke after repeated inhalation. J. Haz. Mat. 1989, 22:269-282.].

For one study (RTECS) the exposure substance is unclear since we could not retrieve the reference.

Additional information for some of these studies could be retrieved from the ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) PROPOSED-document as found on the EPA – website (http://www.epa.gov/oppt/aegl/pubs/red_phosphorus_proposed_mar_2010_v1.pdf)

3.4 The above mentioned studies have been performed to establish the effects of Red Phosphorus smoke in formulations **used as a military screen (smoke generating device).** Therefore, these studies are not relevant for the exposure to Red Phosphorus used as a flame retardant.

3.5 Red phosphorus as such (and not mixtures of Red Phosphorus with butyl/rubber) have been used, are used or will be used as flame retardants. While for smoke generating devices the content of Red Phosphorus is intentionally high (>90%) since it is the smoke generated by Red Phosphorus that exerts the intended effect, flame retardants containing Red Phosphorus have a relatively low Red Phosphorus content.

A standard flame retardant product (master batch) would contain 50% Red Phosphorus and 50% resin, which is subsequently used in the production of the final flame retardant product resulting in a Red Phosphorus content between 5-10%. The formulations used in the alternatives assessment report normally have a high Red Phosphorus content (up to 97%)

3.6 For flame retardants, Red Phosphorus (or microencapsulated Red Phosphorus coated with special resins) is used mixed with polyamide thermoplastic resins.

The function of Red Phosphorus in Polyamide is to produce phosphoric acid derivatives which produce a glassy layer over the heated plastic. This glassy layer will then prevent further flame propagation. In this way the generated phosphoric acid derivatives remain on the heated resin as the glassy layer instead of being transported within smoke as is the case for smoke generating devices. As reported above, the phosphoric acid is necessary for the formation of intumescent char which will act as a barrier for the flame and prevent passage of combustible gas.

3.7 At this regard we have conducted test according to CEI EN 50267-2-2: 1999 and CEI EN 50267-1: 1999, to determine the acidity and conductivity of the smoke generated burning a polyamide resin containing Red Phosphorus Flame Retardant. The results are reported in attachment V. and clearly indicate a pH of 7,3 proving the absence of Phosphoric Acid in the smoke.

3.8 The inhalation toxicity of Red Phosphorus from a smoke generating device is reported as related to the exposure of the respiratory tract to the phosphoric acid generated by combustion**.** The phosphoric acid is transported within the smoke, possibly inhaled and responsible for the irritation and subsequent inflammation of the respiratory tract tissues.

However, the efficacy of Red Phosphorus containing flame retardants specifically depends on the release of phosphoric acid in order to form the glassy layer that will prevent flame propagation at the site of combustion. The released phosphoric acid is then contained within the intumescent char, and is not present in the smoke.

3.9 Therefore, the studies which are currently used for determination of inhalation toxicity in the alternatives assessment are not suitable for a fair assessment of alternatives for DecaBDE.

As explained above, both the content of Red Phosphorus and the possible mechanism and presence of phosphoric acid differ substantially between the currently included studies and the real situation for the use of Red Phosphorus containing flame retardants. Also in the context of performing a fair assessment, it should be taken into account that the inhalation studies for the other flame retardant substances were performed with dust instead of combustion material or that inhalation studies are lacking.

3.10 In addition, and for more exhaustive and complete information, we attach to the present document the Study conducted by Fraunhofer Institute, to evaluate the toxicity of smoke according to European Railway Standards CEN/TS 45545-2, comparing the CIT (Conventional Index of Toxicity), of different Flame Retardated Polyamide, some of which containing Red Phosphorus. The toxicity (CIT) of Red Phosphorus containing Polyamide is 3-4 times lower than Halogenated FR.

4. DEMAL IRRITATION

4.1 In Chapter 4.8 "Hazard evaluation", for each endpoint related to Red Phosphorus, data, reference and data quality are listed.

For Dermal irritation of Red Phosphorus the following study results are presented on page 4-519 of the alternatives assessment report.

		phosphorus smoke for <15 minutes		
Dermal Irritation		**HIGH: Prolonged contact with red phosphorus may cause severe skin irritation.**		
	Dermal Irritation	Negative, guinea pigs (0.5 g on application site)	NRC, 1997	Reported in a secondary source.
		Severe irritation, rabbits Application of RP-BR residue	NRC, 1997	Reported in a secondary source.
		Prolonged or repeated contact may cause skin irritation	Maine DEP, 2007	Reported in a secondary source.

4.2 Chapter 4.8 mentions that application to skin resulted in no dermal irritation, based on the NRC, 1997 reference. Some further clarification is necessary for the information provided in the above table from the alternatives assessment report, since the NRC, 1997 reference actually states that:

"*No dermal irritation was noted when red phosphorus was applied to the skin of rabbits at doses of 0.5 g per site. Similarly, dermal application of the element to guinea pigs resulted in no skin irritation or sensitization.*"

Therefore, not only for guinea pigs, the most sensitive species from the inhalation studies but also for rabbits, no dermal irritation could be established.

4.3 Regarding the other studies mentioned in the above table, the application of precipitates of air samples of combusted Red Phosphorus with butyl/rubber resulted in dermal irritation for rabbits. As for the studies provided to determine inhalation toxicity, it needs to be stressed that the composition of Red Phosphorus with butyl/rubber used for smoke screen purposes differs significantly from Red Phosphorus used for flame retardant purposes. Both the content and the release mechanism of phosphoric acid into the smoke of the two different uses are not comparable. Therefore, the inclusion of this study means that no fair alternatives assessment can be performed for Red Phosphorus.

4.4 The final reference to skin irritation after prolonged or repeated contact originates from a secondary source in the Maine DEP, 2007 report which is actually a Material Safety Data Sheet (MSDS) from 2000, which does not contain experimental data on dermal irritation.

4.5 In conclusion, the assessment for dermal irritation needs a re-evaluation since the decisive study in the alternatives assessment was performed with the combustion production of a Red Phosphorus with butyl/rubber mixtures used for smoke screens, and there is no observed dermal irritation when elemental Red Phosphorus was applied to rabbits nor when applied to Guinea pigs.

5. CONCLUSIONS

5.1 In conclusion, the data on Red Phosphorus reported in the document "AN ALTERNATIVE ASSESSMENT FOR THE FLAME RETARDANT DECABROMODIPHENYL ETHER (DecaDBE) – EPA – June 2012" appear not to be consistent, therefore it is of primary importance to characterize all data with reference, test substance, purity, method, and all necessary details in order to establish their reliability and evaluate them for their real contribution to the risk assessment of the substance.

5.2 Based on the previous reported fact that when Red Phosphorus is contaminated with traces of yellow/white phosphorus, assumes significantly different toxicological characteristics, it seems straightforward that only studies where the tested sample can be verified and of good reliability, have to be taken into account for the classification of Red Phosphorus for acute oral toxicity, which in this specific case, would be the Hoechst study with a reported LD50 >15.000 mg/Kg and the Henry et al. study with a derived LD50 > 10.000 mg/Kg.

5.3 Therefore, according to the earlier mentioned criteria used to assign hazard designations on page 4-4 of the alternatives assessment report, Red Phosphorus has to be considered of Very Low Concern for the Acute Oral Toxicity end point.

5.4 The inhalation toxicity of Red phosphorus as a flame retardant cannot be assessed fairly with the currently provided studies in the alternatives assessment based on:

a) the differences in test methods used for the other flame retardant alternative substances (i.e. dust exposure vs combustion smoke exposure),
b) differences in Red Phosphorus content of the formulations used for smoke screen purposes (current assessment, high content) and for flame retardant purposes (not assessed, low content),
c) more important, the described mode of action for Red Phosphorus inhalation toxicity which requires the release of phosphoric acid into smoke, whereas Red Phosphorus used as Flame retardant, generates smoke where Phosphoric Acid is not present, but contributes to the formation of the glassy layer on the plastic.
d) test according to CEI EN norms, to determine pH of smoke generated by red Phosphorus in polyamide, equal to 7,3

5.5 The dermal irritation of Red Phosphorus needs to be re-evaluated since no dermal irritation was observed in rabbits and Guinea pigs after application of elemental Red Phosphorus, and the decisive study was performed with the combustion production of a Red Phosphorus with butyl/rubber mixtures used for smoke screens, i.e. not relevant for the use of Red Phosphorus in flame retardants.

The final proposal is to modify the assessment for Red Phosphorus as following:

1) Acute mammalian toxicity: LOW (hazard)
2) Dermal irritation: LOW (hazard)

ANNEX I

Robust Study Summaries presented within the REACH Registration dossier for acute oral toxicity: HOECHST Aktiengesellschaft, Pharma Forschung, Toxikologie, _Akute *Orale Toxizitat von Phosphor Rot an Weiblichen SPF-Wistar Reatten*, Study Report 131/75, 1975

The original report of HOECHST is in german language and it will be provided on request

This attachment is available in a separate document. The attachment provided by REACH Mastery s.r.l. was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

ANNEX II

Robust Study Summaries presented within the REACH Registration dossier for acute oral toxicity: Henry, M.C., J.J. Barkley, and C.D. Rowlett.. *Mammalian Toxicological Evaluation of hexachloroethane Smoke Mixture and Red Phosphorus*. Final Report. AD-A109593. Conducted as Contract DAMD17-C-78-C-8086 by Litton Bionetics, Inc., Kensington, MD, for the U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD, 1981)

Extracts from the original paper are following

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ANNEX III

Vrednie chemichescie veshestva. Neorganicheskie soedinenia elementov V-VII groopp" (Hazardous substances. Inorganic substances containing V-VII group elements), by Bandman A.L. et al., Chimia, 1989

Original front page of the text book and extract related to toxicity data of Red Phosphorus, page 58

This attachment is available in a separate document. The attachment provided by REACH Mastery s.r.l. was provided in a format that did not enable 508 compliance. If you require an alternate format, please contact Emma Lavoie at lavoie.emma@epa.gov or 202-564-0951.

English rough translation:

Acute poisoning. Animals. When *kormleini* mouse and rat LD50 = 11.5 mg / kg (Krasoysky, etc.), for rabbits 0.21 g (in oil), Cat 10-30 mg for dogs 50-100 mg. If inhaled 0,15-0,16 mg / l vapor F. mice, rats and blood *pogigbali* faces. Marked prolongation of systole, increased con Jania fat and water in the brain, heart, *iechepi*, kidneys, and persistent pirovinogradpoy increase in acid in the blood.

Krasovskid GN et al / / Hygiene and sanitation. 1979. N4 5. Pp. 74-75.

ANNEX IV

Robust Study Summaries presented within the REACH Registration dossier for skin irritation

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ANNEX V

ISRIM: evaluation of the acidity and conductivity of the smoke generated burning a polyamide resin containing Red Phosphorus Flame Retardant according to CEI EN 50267-2-2: 1999 and CEI EN 50267-1: 1999

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ANNEX VI

Fraunhofer Institute: evaluation of the toxicity of smoke according to European Railway Standards cen/ts 45545-2

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