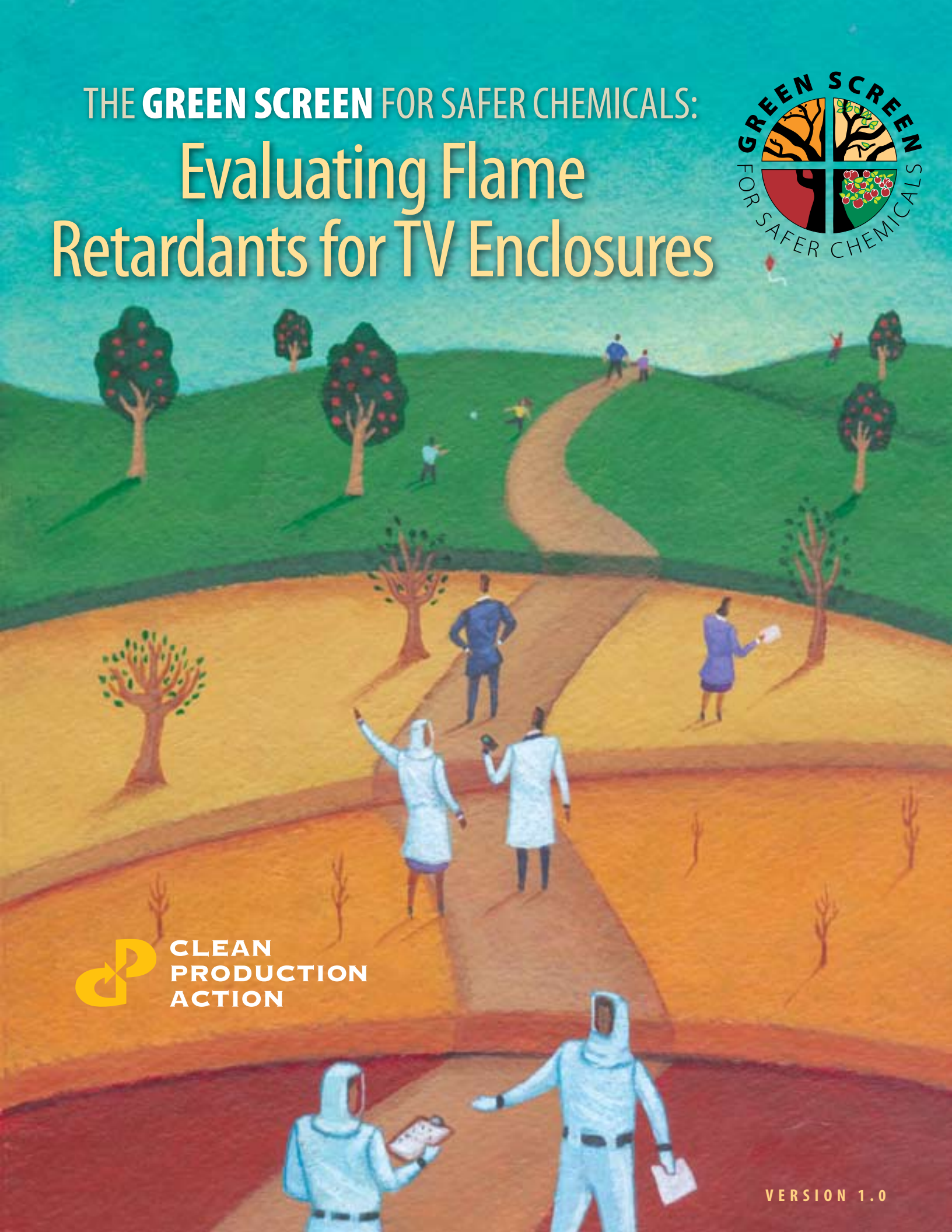
THE **GREEN SCREEN** FOR SAFER CHEMICALS:

Evaluating Flame Retardants for TV Enclosures



CLEAN PRODUCTION ACTION

VERSION 1.0

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Evaluating Flame Retardants for TV Enclosures

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CLEAN PRODUCTION ACTION

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Acknowledgments

The Green Screen for Safer Chemicals emerged over time and with the input of individuals who have spent their careers working the in the field of chemistry, toxicology, and the promotion of safer alternatives. Many have raised challenging and significant questions about the Green Screen. It is through the feedback of critics as well as supporters that the Green Screen reached this point of development and will continue to evolve into a method that is useful in helping to make better, more scientifically robust decisions about chemical selection in a timely fashion. Thank you to Richard Denison, Ken Geiser, Jack Geibig, Kim Hooper, Inez Hua, Denise LaFlamme, Tom Lent, Thomas Osimitz, Heather Stapleton, Joel Tickner, Laurie Valeriano, Kathleen Vokes, and William Waugh for providing critical feedback on earlier versions of this report. Additionally we want to thank Tim Greiner, John Peterson Myers, David Santillo, and Ted Schettler for providing guidance to us on particularly vexing questions. It is important to note that those who reviewed or commented on the report did so as individuals. Their listing here is out of our respect and appreciation for their feedback, not to imply that they or their organization endorse the report and its findings. As the authors, we bear full responsibility for the contents of the report.

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CLEAN PRODUCTION ACTION

Clean Production Action promotes the use of products that are safer and cleaner across their life cycle for consumers, workers, and communities. Our mission is to advance clean production, which we define as the design of products and manufacturing processes in harmony with natural ecological cycles, the elimination of toxic waste and inputs, and the use of renewable energy and materials.

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Executive Summary

The Green Screen for Safer Chemicals defines a path to chemicals that are safer for humans and the environment. It is a rigorous, hazard-based screening method that is designed to inform decision making by businesses, governments, and individuals concerned with the risks posed by chemicals and to advance the development of green chemistry. The Green Screen defines four benchmarks on the path to safer chemicals, with each benchmark defining a progressively safer chemical:

- Benchmark 1:
  Avoid—Chemical of high concern
- Benchmark 2:
  Use but search for safer substitutes
- Benchmark 3:
  Use but still opportunity for improvement
- Benchmark 4:
  Prefer—Safer chemical

Each benchmark includes a set of criteria that a chemical, along with its known and predicted breakdown products and metabolites, must pass. To progress from Benchmark 1 to Benchmark 2, a chemical (and its breakdown products and metabolites) must pass all the criteria specified under Benchmark 1. For example, a chemical (along with its breakdown products and metabolites) that is persistent, bioaccumulative and toxic would not pass beyond Benchmark 1. Similarly, to progress from Benchmark 2 to Benchmark 3 and from Benchmark 3 to Benchmark 4, the chemical (along with its breakdown products and metabolites) must pass all criteria specified under each respective benchmark. The criteria become increasingly more demanding for environmental and human health and safety for each benchmark, with the hazard criteria of Benchmark 4 representing the safest chemical. All of the hazard and benchmark criteria developed for the Green Screen are presented in this report, along with information on government and other precedents for classification that were used to help establish the thresholds.

In order to test the Green Screen, three flame retardants that currently meet performance criteria for use in the external plastic housing of televisions (TVs) were evaluated. With the European Union restricting decabromodiphenyl ether (decaBDE) in electronics and with similar legislative initiatives under consideration at the state level in the United States, a recurring question emerges: are the alternative flame retardants safer than decaBDE from the perspective of human and environmental health and safety? Flame retardant use in TVs is of particular interest

because TVs represent the largest end use for decaBDE.

We use the Green Screen to evaluate three flame retardants: decaBDE and two phosphorous-based alternatives, resorcinol bis (diphenylphosphate) (RDP) and bisphenol A diphosphate (BAPP or BPADP). Of the three flame retardants, RDP was the only flame retardant to pass all criteria under Benchmark 1 of the Green Screen. An integral element of the Green Screen is taking into account potential degradation products and metabolites. This is important given that chemicals in the environment are not static, they integrate into human and natural environments. Both decaBDE and BPADP scored lower on the Green Screen because of their degradation products. While RDP is not a "green chemical" per se, based on assessment via the Green Screen for Safer Chemicals, it achieves a higher level of human and environmental health and safety than the alternatives. Thus RDP (and its breakdown products), based upon a Green Screen assessment, is a safer chemical.

Version 1 of the Green Screen is intended for public use and dissemination. We hope that as the Green Screen is applied, further refinements and improvements will be made. The Green Screen for Safer Chemicals represents a needed building block on the path to sustainable material flows in our economic and ecological systems. It is our goal that companies, government agencies, academia, and nonprofits will use the Green Screen to selec inherently safer chemicals, thereby reducing the risks of exposure to toxic chemicals and increasing the availability of safer, healthier products.

1. Consumers and Citizens Want Safer Chemicals

Examples now abound of how individuals as consumers and as citizens are demanding safer chemicals. The Campaign for Safe Cosmetics is a coalition of organizations and individuals advocating to "phase out the use of chemicals linked to cancer, birth defects and other health problems and replace them with safer alternatives."[1] The City of San Francisco passed a resolution in 2006 to ban the manufacture, sale, and distribution of child care articles and toys that contain bisphenol A or phthalates.[2] Meanwhile across the Atlantic, the European Union enacted in December 2006 a monumental piece of legislation that regulates for the first time the vast majority of chemicals used to manufacture products.[3] In short, people want products and the chemistry behind them to be safe and healthy for their children, communities, and themselves.

Chemicals in general are not the problem. Manufactured chemicals are essential ingredients in the products of the twenty first century economy. Today global production of chemicals totals over 300 million tons per year,[4] there are over 80,000 chemicals in commerce,[5] and global chemical sales approach two trillion dollars per year.[6] Carpets, cars, trains, buses, televisions, computers, fabrics, lights, and even food are among the many products made with manufactured chemicals.

But some chemicals are bad actors: they pose serious risks to human health and the environment. Lead, cadmium, DDT, CFCs, and PCBs are examples of hazardous chemicals that should not be in products. Chemicals that persist, bioaccumulate, and are toxic are dusted across the globe. The vast majority, if not all, humans and mammals, are contaminated with human-made chemicals. Literally, there is no human control group—every person on the planet carries industrial chemicals that were not present 100 years ago. Some of these chemicals have the potential to cause cancer or adverse effects to the brain, normal development, or the endocrine, reproductive, or immune system. The result is a vast chemical experiment with unknown consequences.

How do we know which chemicals are to be preferred and which are to be avoided?

Paul Anastas and John Warner sketched the terrain for defining safer chemicals in 1999 with the publication of their concise and influential book, *Green Chemistry: Theory and Practice*.[7] Their 12 principles of green chemistry provide a rough guide to safer chemicals

(see Box 1 for definitions of "green chemistry" and "safer chemicals"). Of especial interest to defining the path to safer chemicals are these three principles:

- Principle #2. "Design safer chemicals and products: Design chemical products to be fully effective yet have little to no toxicity."
- Principle #10. "Design chemicals and products to degrade after use: Design chemical products to break down to innocuous substances after use so that they do not accumulate in the environment."
- Principle #12. "Minimize the potential for accidents: Design chemicals and their forms (solid, liquid or gas) to minimize the potential for chemical accidents including explosions, fires and releases to the environment."[7]

The success of green chemistry will hinge on changing the intrinsic nature chemicals so that they are inherently safer for human health and the environment.

BOX 1: **Defining the Terrain of "Chemicals" & "Chemistry"**

Chemical *noun*
"a substance (as an acid, alkali, salt, synthetic organic compound) obtained by a chemical process, prepared for use in chemical manufacture, or used for producing a chemical effect."[1]

Chemical *adjective*
- "relating to applications of chemistry: as
  a) acting or operated by chemical means <a ~ extinguisher>
  b) treated with or performed by the aid of chemicals <~ development in photography>
  c) produced by chemical means or synthesized from chemicals <~ fiber> <~ rubber>
  d suitable for use in or used for operations in chemistry <a ~ laboratory> <a ~ plant>"
- "having reference to or relating to the science of chemistry."[1]

Chemistry *noun*
- "a science that deals with the composition, structure, and properties of substances and of the transformations that they undergo"
- a) "the composition and chemical properties of a substance"; b) "chemical processes and phenomena."[1]

Green Chemistry *noun*
- "an approach that provides a fundamental methodology for changing the intrinsic nature of a chemical product or process so that it is inherently of less risk to human health and the environment" and
- "the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products"[2]

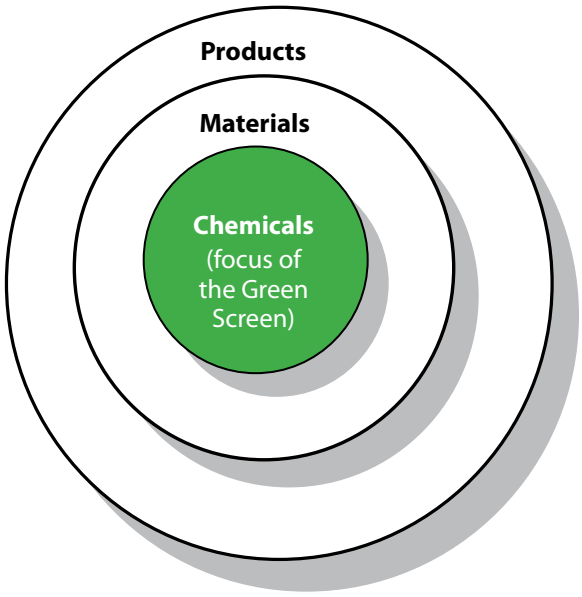
Safer Chemical *noun*
a chemical whose toxicity and hazard are reduced to the lowest possible level while achieving desired performance and function.[3]

SOURCES:
1 G. & C. Merriam Company. 1976. *Webster's Third New International Dictionary of the English Language Unabridged*. Springfield, MA: G. & C. Merriam Company.
2 PT Anastas and J Warner. 1999. *Green Chemistry Theory and Practice*. New York: Oxford University Press, pp.8 and 11.
3 Paraphrased from: PT Anastas and J Warner. 1999. *Green Chemistry Theory and Practice*. New York: Oxford University Press, p.36.

This paper translates the toxicity principles of green chemistry into a method for identifying safer chemicals: the Green Screen for Safer Chemicals. The Green Screen is a chemical assessment method that is designed to be scientifically robust, transparent, and protective of human health and the environment. In addition, it is designed to identify safer chemicals based upon the best available data (be it experimental or analog data) and to inform decisions by businesses, governments, as well as individuals concerned with the risks posed by chemicals. At the heart of the Green Screen are four benchmarks that define a path to preferred chemicals that are safer and healthier for humans and the environment.

The Green Screen for Safer Chemicals fits within the context of the alternatives assessment framework developed by the Lowell Center for Sustainable Production. It is a necessary *module* for evaluating the human health and environmental concerns of chemicals. The Lowell framework outlines three core components of a comprehensive alternatives assessment method. It has a *foundation* that defines goals, guiding principles and decision making rules. It has a *process* for: identifying targets for action; characterizing end uses and functions; identifying alternatives; evaluating and comparing alternatives; and selecting the preferred alternative. Finally it has *modules* or tools for evaluating alternatives based on concerns for: human health and the environment, social justice, economic feasibility or technical performance.[8] As part of an alternatives assessment framework, the Green Screen is designed, as illustrated in Figure 1, for benchmarking chemicals (not materials or products).

FIGURE 1: **Nested Relationship among Chemicals Materials, and Products (and focus of the Green Screen)**



Source: M. Rossi, J. Tickner, K. Geiser 2006, *Alternatives Assessment Framework*, Lowell Center for Sustainable Production

The remainder of this report is divided into five sections. Section 2 defines the need for a transparent chemical assessment method like the Green Screen for Safer Chemicals. Building from the Lowell Alternatives Assessment Framework, Section 3 specifies the *foundation* or guiding principles that informed the design of the Green Screen. Section 4 details the inner workings of the Green Screen and describes how the method operates. In Section 5, we apply the method to three chemicals (and their breakdown products) used to flame retard television casings to illustrate how the Green Screen works in practice and to learn its strengths and challenges. Section 6 concludes with a summary of the challenges to using the Green Screen, how the method addresses these challenges, and findings from the application of the Green Screen to flame retardants.

2. Transparent Method Needed for Identifying Safer Chemicals

The flame retardants, polybrominated diphenyl ethers or PBDEs, exemplify both the benefits and downsides of the modern chemical economy. Every year manufacturers of TVs, computers, furniture, electrical wires, draperies, and other products add chemical flame retardants to their products to protect the public from the dangers of fire. But in adding PBDE flame retardants to their products they have created, however unintended, another public hazard—exposing humans and animals across the globe to hazardous chemicals.

PBDEs are a class of 209 chemicals that are distinguished by the average number and arrangement of bromine atoms in the molecule—ranging from one bromine atom (monobromodiphenyl ether or monoBDE) to ten bromine atoms (decabromodiphenyl ether or decaBDE). Until recently, the PBDE flame retardant formulations on the market were pentaBDE (five bromine atoms), octaBDE (eight bromine atoms), and decaBDE. PentaBDE and octaBDE were voluntarily removed from the market in 2003 (pentaBDE) and 2004 (octaBDE) by the manufacturer, Chemtura (formerly Great Lakes Chemical),[9] when it became clear that these chemicals were targeted for elimination in Europe and certain states in the US.

The first signs of trouble with PBDEs in general, and pentaBDE and octaBDE in particular, emerged in the 1980s when PBDEs were found in fish in Sweden.[10] As researchers expanded their search they found PBDEs widely dispersed in the environment—from homes and cars to fish, seals, polar bears, and humans, from industrial cities to the pristine arctic.[11] PBDEs are effective at contaminating our environment because they are very persistent—meaning they are very slow to degrade in the environment.

Additionally some PBDEs, like pentaBDE, bioaccumulate in animals—meaning the chemicals collect in the fatty tissue of animals—and biomagnify—increase in concentration as they move up the food chain. Persistent and bioaccumulative chemicals such as pentaBDE and octaBDE are of high concern to animals at the top of the food chain, like humans, because they receive the highest exposures. The combination of long life and collecting in tissue means even small releases of persistent and bioaccumulative chemicals matter: the chemicals will be active in the environment and our bodies for long periods of time.

Today PBDEs are sprinkled across the globe. Unfortunately, Americans have the distinction of being the population with highest concentrations of PBDEs in their bodies.[12] PBDEs are of high concern to human health because they adversely affect the thyroid system and neurological development.[13]

With pentaBDE and octaBDE no longer manufactured, decaBDE is now the sole PBDE chemical still in production, with global consumption at 56,418 metric tons per year.[14] Similar to its lower brominated cousins, decaBDE is found widely in the environment: in houses, cars, humans, and wildlife.[11] DecaBDE degrades into lower PBDE congeners.[15] And there are health hazards associated with commercial decaBDE and its breakdown products.[16] The European Union, for example, recently banned decaBDE use in electrical and electronic equipment because decaBDE formulations contain significant concentrations of nonaBDE (nine bromine atoms).[17]

Barriers to deciding whether to continue or discontinue the use of decaBDE include knowing whether alternatives to decaBDE are available and having criteria for determining whether the alternatives are safer for humans and the environment. The 12 principles of green chemistry provide general guidelines to environmentally preferable chemicals. Principle #2, for example, states, "Design chemical products to be fully effective, yet have little or no toxicity."[7] That's the goal, but by what criteria do we evaluate when "little to no toxicity" is achieved?

A number of protocols have been developed to evaluate and identify safer chemicals and materials and to help define the path to safer, healthier chemicals in product design. Notable examples include propriety systems such as the Cradle to Cradle Design Protocol developed by McDonough Braungart Design Chemistry (MBDC),[18] the Greenlist™ developed by SC Johnson and Son, Inc.,[19] and the Dye and Chemistry Protocol developed by Interface Fabrics.[20]

In the public sector, the Canadian government recently completed a human health and ecological categorization of the 23,000 substances on its Domestic Substances List in order to identify chemicals that need further research and possible control.[21] The U.S. Environmental Protection Agency's Design for the Environment Program (DfE) developed a method for assessing chemical alternatives to pentaBDE flame retardants in polyurethane foam[22] and is currently working on assessing flame retardants used in electronic circuit boards.[23] While the DfE method made significant advances in providing needed information on chemicals in a format that supports decision making, it stopped short of providing specific guidance on how to interpret and apply that information.

In this paper we propose a transparent and publicly available method for evaluating chemicals and identifying those that are preferable with respect to human and environmental health and safety. This method is the Green Screen for Safer Chemicals (Green Screen). The Green Screen represents a pragmatic approach to using chemical hazard information that supports alternatives assessment and movement toward the goal of green chemistry and sustainable product design. It builds on the growing availability of publicly accessible data and resources for assessing and communicating chemical hazard information. It is a response to the growing desire of the public for assurance by manufacturers that the human and environmental health and safety aspects of commercial products have been assessed and optimized.

A publicly accessible, transparent, and broadly supported method is needed to help provide guidance on comparing chemical alternatives

and to clearly signal the desirable chemical attributes. This paper details the guiding principles, design, and operation of the Green Screen. The Green Screen is open to comment and improvement.

To better understand how the Green Screen will function in practice, we used it to evaluate decaBDE and other flame retardant chemicals that are applied to TV casings (the plastic housing on the outside of a TV). TV casings, also called enclosures, were chosen as the end use of decaBDE to evaluate because they represent the largest use of decaBDE.[24]

3. Guiding Principles for the Green Screen for Safer Chemicals

In designing the Green Screen we were guided by the following principles:

- transparency,
- highly protective of human health and the environment,
- focus on hazards (not risks),
- robust decision-making method,
- life cycle thinking, and
- continuous improvement.

Transparency. As noted in the previous section, a handful of what seems like sophisticated, intelligent, and thoughtful methods have been designed and used for evaluating the hazards posed by chemicals and selecting safer alternatives. However, a transparent and publicly accessible method for categorizing the hazards of chemicals and benchmarking their progress to being safer is needed in order to support alternatives assessment and to send a market signal to chemical manufacturers and users of their products about what is desirable from the public perspective. In presenting the Green Screen we clearly specify the criteria used for categorizing chemicals based on their hazards and make them available for public review.

Highly protective of human health and the environment. In 1999, the Swedish Parliament defined a sweeping set of fifteen generational objectives (to be achieved in 20 years) for the environment. The objective most relevant to chemical selection is this one: "a non-toxic environment" by 2020. The Swedes define "a non-toxic environment" as: "The environment must be free from man-made or extracted compounds and metals that represent a threat to human health or biological diversity."[25] It is this vision of the future that animates the design and use of the Green Screen: to achieve a non-toxic environment by 2020.

The vision of a non-toxic environment is embedded into the Green Screen through: the focus on hazards (and not risks), the setting of threshold values for defining levels of concern for chemical hazards, the setting of benchmarks, and in the interpretation of evidence of harm from experimental data. Our goal is to promote the development of products made from chemicals and materials that meet the highest levels of environmental health performance.

Focus on Hazards. "Hazard," as defined by the Organisation for Economic Co-operation

and Development (OECD), is the "inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent."[26] And "risk" is the "probability of an adverse effect in an organism, system or (sub) population caused under specified circumstances by exposure to an agent."[26] Risk then, is a function of hazard and exposure.

The fundamental premise behind green chemistry is that the most reliable way to reduce risk is to reduce hazard (rather than reduce exposure).[7] The effectiveness of hazard reduction as a means for reducing risk has been known for decades. Writing in the 1970s, Dr. Joseph Ling (former vice president of environmental engineering and pollution control at 3M) concluded that "conventional controls [that is, controls to reduce exposure], at some point, create more pollution than they remove and consume resources out of proportion to the benefits derived. What emerges is an environmental paradox. It takes resources to remove pollution; pollution removal generates residue; it takes more resources to dispose of this residue and disposal of residue also produces pollution."[27] When Dr. Ling's conclusion is translated into risk language, it reads: "reducing exposure to chemicals [his term is 'pollution'] creates more exposure to chemicals than it prevents because of the resources consumed in collecting and disposing of the sources of exposure." Therefore reducing exposures (or controlling pollution) is inefficient and ultimately ineffective.

The recognition of the superiority of preventing exposure through hazard reduction is embodied in the Pollution Prevention Act of 1990, in which Congress "declares it to be the national policy of the United States that pollution should be prevented or reduced at the source whenever feasible." In pollution prevention, as with green chemistry, the goal is to move from more hazardous to less hazardous (and ideally to environmentally beneficial) chemicals, processes, materials, and products. In taking a hazard-based approach (rather than an exposure-based approach) to reducing chemical risks the focus shifts from reducing exposure through control measures to reducing hazards by selecting chemicals whose inherent properties are safer than the chemicals of concern.

In the search for solutions to chemical risks a hazard-based approach looks upstream for inherently safer chemicals rather than downstream for methods for reducing exposure. The properties of inherently safer chemicals include reduced human and environmental toxicity, reduced physical hazards, such as explodability and corrosivity, and reduced concern for the environmental fate of a chemical (which equals rapid degradation into benign chemicals and low bioaccumulation potential).

Robust, Decision-Making Method. Our goal for the Green Screen is to create a method that is scientifically-based and facilitates relatively quick chemical assessments. We do not want a method that is too complicated and too costly such that no one ever uses it. The end users of the Green Screen are likely to be people with some expertise in chemistry and organizations who want to evaluate a chemical and identify more environmentally preferable chemicals. Users may be businesses, government agencies, or non-governmental organizations (NGOs). In the business community, the Green Screen will be useful to both manufacturers and users of products who want to continually improve the profiles of the chemicals they make and use in commerce.

Life cycle thinking. While understanding a chemical's inherent hazard characteristics is critical, it is also necessary to consider the

chemical within its full life cycle. Ideally it is desirable to know the full life cycle of a chemical, including: resource extraction and feedstock production at its beginning; energy inputs, chemical intermediaries, and chemical releases during manufacturing; emissions to the environment during use; and finally, its breakdown products, from both environmental degradation and metabolism in bodies.

For example, a toxic intermediary used in the manufacture of another chemical can be problematic if it remains as a residual in the product, such as the presence of bisphenol A in polycarbonate. And manufacturing byproducts present in the final product may be hazardous even if the product is not. A chemical that is not inherently toxic may involve worker hazards during its manufacture. And a chemical product that is not persistent may degrade in the environment or within organisms to a persistent compound. Obtaining this kind of information can range from feasible to nearly impossible due to confidentiality or lack of study.

The Green Screen incorporates some life cycle components of a chemical, including: a) manufacturing and use hazards through i) inherent hazards, including flammability and explodability and ii) considering chemical formulations as individual constituents rather than as a single chemical (thus any formulation is only as good as its worst component); and b) end of life concerns through environmental fate, by considering metabolites and environmental degradation products.

Continuous Improvement. We recognize that the Green Screen will have flaws, missing components, and decision criteria in need of revision. In addition, as scientific knowledge is gained, new hazard endpoints may be developed such as in the area of nanotoxicology. For these reasons, this is Version 1.0. Reviewers of Version 1.0 (see acknowledgments) have already provided many insightful and clarifying comments that led to significant changes in the method. As we and others benchmark chemicals using the Green Screen, opportunities for improvement will arise. We are committed to the open development and improvement of the Green Screen by those whose goal is to move the economy to safer chemicals.

As a whole, these principles articulate our commitment to developing a method that promotes the development and use of inherently safer chemicals.

4. The Green Screen: Setting Benchmarks to Safer Chemicals

The Green Screen for Safer Chemicals defines a path to chemicals that are healthier for humans and the environment. It is designed to inform decisions by businesses, governments, and individuals concerned with the risks posed by chemicals. The Green Screen defines four significant benchmarks on the path to safer chemicals:

- Benchmark 1: **Avoid—Chemical of high concern**
- Benchmark 2: **Use but search for safer substitutes**
- Benchmark 3: **Use but still opportunity for improvement**
- Benchmark 4: **Prefer—Safer chemical**

Each benchmark includes a set of benchmark criteria that a chemical must pass. For a chemical—along with its known and predicted breakdown products (i.e., degradation products and metabolites)—to progress from Benchmark 1 to Benchmark 2, it must pass all the criteria specified under Benchmark 1. Similarly to progress from Benchmark 2 to Benchmark 3 and from Benchmark 3 to Benchmark 4 the chemical must pass the criteria specified under each respective benchmark. The criteria become increasingly more demanding for environmental and human health and safety for each benchmark, with the hazard criteria of Benchmark 4 representing a safer chemical.

The development of the Green Screen method involved three major steps:

1. Establish the list of hazards that are critical to evaluating the safety of a chemical in the Green Screen.
2. Define the levels of concern—high, moderate, and low—for each hazard.
3. Specify the hazard criteria for each of the four benchmarks.

4.1. The Green Screen List of Hazards

The Green Screen evaluates a chemical—along with its known and predicted breakdown products—based upon its hazards. Including the known and predicted breakdown products of a chemical into the Green Screen is important: it addresses the potential impacts of a chemical once released into the environment. A precedent for including breakdown products into a chemical assess-

ment is the US Environmental Protection Agency (EPA) Design for the Environment's (DfE) assessment of alternatives to pentaBDE in furniture foam. In its assessment of pentaBDE alternatives, the US EPA noted the likelihood of persistent degradation products for each chemical alternative.[28]

In the Green Screen the hazards of a chemical are defined by: its potential to cause acute or chronic adverse effects in humans or wildlife, its fate in the environment, and certain physical/chemical properties of concern to human health. Acute mammalian toxicity (lethality) and irritation of the skin or eye are examples of acute adverse effects that can result from inhalation, ingestion, or dermal contact with a chemical. Chronic effects occur after repeated exposures and include cancer and adverse effects to the reproductive, neurological, endocrine, or immune systems. The fate of a chemical in the environment—"environmental fate"—is strongly determined by its rate of degradation (defined as persistence) and its tendency to accumulate in tissues and organs (bioaccumulation). The physical/chemical properties of concern in the Green Screen are flammability and explodability.

The Green Screen list of hazards tracks the hazards government agencies are incorporating into their chemical assessments, includ-ing the: US EPA, Environment Canada, International Joint Commission (a commission established by the US and Canada to protect transboundary waters), OSPAR Commission (a regional commission of European countries established to protect the marine environment of the northeast Atlantic Ocean), Washington State Departments of Ecology and Public Health, European Union's recently enacted chemicals policy legislation (Registration, Evaluation and Authorization of Chemicals—REACH), and Stockholm Convention on Persistent Organic Pollutants (an international treaty signed in 2001 and convened by the United Nations Environment Programme).

Chemicals that persist (are slow to degrade), bioaccumulate in animals (collect in animal tissue, or organs), **and** are toxic to humans or animals are especially problematic because their concentrations in the environment increase over time, increasing the opportunities for exerting their toxic effects. Chemicals with these properties of persistence (P), bioaccumulation potential (B), and toxicity (T) are known as PBTs. The Stockholm Convention on Persistent Organic Pollutants (POPs)—which is designed to phase-out very persistent, very bioaccumulative, and toxic chemicals—reflects the widespread recognition of the risks posed by PBTs (POPs are synonymous with PBTs).

Table 1 summarizes the threshold values used by the Stockholm Convention and other government institutions to classify chemicals as P, B, and/or T. "Threshold values" are the cut-off points used for a) determining whether a chemical poses a certain type of hazard (such as, P or B or T) and b) assigning levels of concern (typically high, moderate, or low) for a particular hazard (such as P). On the x-axis of Table 1 are the governmental institutions and on the y-axis are the hazards (P, B, and T) as well as levels of concern associated with persistence and bioaccumulation (very high, high, moderate, or low). In Table 1, "Toxicity – T" is not divided into levels of concern because only one of the governmental organizations has done that—the US EPA. The criteria used by the US EPA to divide toxicological concerns into high, moderate, and low are discussed below in section 4.2.

The list of toxicity concerns incorporated into definitions of PBTs and high hazard chemicals varies by institution and (as reflected in Table 1) includes a wide range of adverse effects to

TABLE 1: **Threshold Values Used by Government Institutions and the Green Screen to Categorize Chemicals as Persistent, Bioaccumulative, and/or Toxic**

Hazard	State Criteria	National Criteria—US EPA		Regional Criteria					International	Green Screen for Safer Chemicals
	Washington State PBT[1]	PBT Chemicals Final Rule[2]	Design for Environment (DfE)[3]	International Joint Commission[4]	OSPAR PBT Definition[5]	European Union (EU) REACH[6]—Substances of Very High Concern			Stockholm Convention on POPs[7]	
						vPvB	PBT	Toxicity		
Persistence—P (half-life in days)										
Very High (v)	na	na	na	na	na	>60 water; or >180 soil or sed.	na	na	>60 water; or >180 soil or sed.; + long-range transport	>60 water; or >180 soil or sed.
High (H)	≥60 water, soil, or sed.	>60 water, soil, or sed.; or >2 air	>180 water, soil, or sed.	>56 water	>50 water	na	>60 mw, >40 fw, >180 m sed., or >120 fw sed./soil	na	na	>40-60 water; or >60-180 soil or sed.
Moderate (M)	na	na	60-180 water, soil, or sed.	7-56 water	na	na	na	na	na	7-40 water; or 30-60 soil or sed.
Low (L)	na	na	<60 water, soil, or sed.	<7 water	na	na	na	na	na	<7 water; or <30 soil or sed.
Bioaccumulation—B (bioconcentration factor—BCF; bioaccumulation factor—BAF; or log octanol-water coefficient—log Kow)										
Very High (v)	na	na	na	na	na	BCF >5000	na	na	BCF/BAF >5000 (or log Kow ≥5)	BCF/BAF >5000 (or log Kow>5)
High (H)	BCF/BAF >1000 (or log Kow >5)	BCF/BAF >1000	BCF >5000	BAF >5000	BCF ≥500 (or log Kow ≥4)	na	BCF >2000	na	na	BCF/BAF >1000-5000 (or log Kow >4.5-5)
Moderate (M)	na	na	BCF 1000-5000	BAF 1000-5000	na	na	na	na	na	BCF/BAF 500-1000 (or log Kow 4-4.5)
Low (L)	na	na	BCF <1000	BAF <1000	na	na	na	na	na	BCF/BAF <500 (or log Kow <4)
Toxicity—T (includes: carcinogen-C; developmental-D or reproductive-R toxicant; mutagen-M; neurotoxic-N; or no observed effect concentration-NOEC)										
	Human: C/D/R/N; or RfD <0.003 mg/kg/day. Aquatic: chronic NOEC <0.1 mg/l; acute NOEC <1.0 mg/l	Human: C/M/R/N; other chronic effects; or effects from site releases	Human: chronic effects. Aquatic: chronic/acute toxicity (see EPA 2005 for details)[3]	Aquatic: chronic NOEC: High: <0.1 µg/l; Moderate: 1.0 µg/l	Human: C/M/R; or other chronic. Aquatic: Acute LC/EC_{50} <1 mg/l; chronic NOEC <0.1 mg/l	na	Human: C/M/R; or other chronic toxicity. Aquatic: Chronic NOEC <0.01 mg/l	Human: C/M/R; endocrine disruption; or equivalent concern	Toxicity/ecotoxicity data with potential adverse effects to humans or environment	see Table 3

ABBREVIATIONS:
EC_{50}=median effective concentration; **fw**=freshwater; **LC_{50}**=median lethal concentration; **m**=marine; **mw**=marine water; **na**=not applicable; **OSPAR**=Oslo and Paris Convention for the Protection of the Marine Environment of the Northeast Atlantic; **PBT**=persistent, bioaccumulative, and toxic; **POPs**=persistent organic pollutants; **RfD**=reference dose; **sed.**=sediment; **US EPA**=US Environmental Protection Agency; **vPvB**=very persistent, very bioacumulative.

SOURCES:

1 Washington State. 2006. Chapter 173-333 WAC - Persistent Bioaccumulative Toxins, January 13, 2006 (http://www.ecy.wa.gov/pubs/wac173333.pdf).
2 US EPA. 1999. Federal Register, Part VII, 40 CFR Part 372 Persistent Bioaccumulative Toxic (PBT) Chemicals; Final Rule, Vol. 64, No. 209, Friday, October 29, 1999.
3 US EPA. 2005. Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam (http://www.epa.gov/dfe/pubs/flameret/ffr-alt.htm).
4 International Joint Commission, Virtual Elimination Task Force. 1993. A Strategy for Virtual Elimination of Persistent Toxic Substances, Vol. 1 (http://www.ijc.org/php/publications/pdf/ID1052.pdf).
5 OSPAR. 2005. Cut-Off Values for the Selection Criteria of the OSPAR Dynamic Selection and Prioritisation Mechanism for Hazardous Substances (http://www.ospar.org/documents/dbase/decrecs/agreements/05-09e_Cut-off-value%20agreement.doc).
6 EU. 2006. Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_396/l_39620061230en00010849.pdf).
7 United Nations. 2001. Stockholm Convention on Persistent Organic Pollutants (http://www.pops.int/documents/convtext/convtext_en.pdf).

humans and wildlife. For ecotoxicity, aquatic toxicity is typically used as the primary basis for the threshold values for practical purposes, i.e., there are common test methods for evaluating effects on aquatic life (fish, daphnia, and algae) and data based on these test methods are available. Ideally test data that represent a broader scope of wildlife will become available in the near future. For human toxicity, the human health effects of most concern for government institutions (and listed in Table 1) are: cancer, developmental effects, reproductive effects, neurological effects, mutagenicity/genotoxicity, and endocrine disruption.

The Green Screen list of hazards most closely tracks the hazards incorporated into the US EPA Design for Environment (DfE) Program's summary assessment of alternatives to the brominated flame retardant, pentaBDE.[28] Table 2 lists the hazards included in both the US EPA DfE program's summary assessment of pentaBDE alternatives and the Green Screen. For definitions of the hazards in Table 2 see Appendix 1.

The most notable difference in hazard lists between the Green Screen and government chemical assessments listed in Table 1 is the inclusion of hazards that relate to the

TABLE 2: **List of Chemical Hazards Presented in the US EPA DfE Program's Chemical Assessment of PentaBDE Alternatives and the Green Screen**

Hazards	US EPA Design for Environment (DfE) Program[1]	Green Screen List of Hazards
Human Health		
Acute	No	Yes
Cancer	Yes	Yes
Developmental	Yes	Yes
Endocrine Disruption	No	Yes
Genotoxicity / Mutagenicity	Yes	Yes
Immune System	No	Yes
Irritation/Corrosion—Skin or Eyes	No	Yes
Neurological	Yes	Yes
Reproductive	Yes	Yes
Sensitizer—Respiratory	No	Yes
Sensitizer—Skin	Yes	Yes
Systemic Toxicity / Organ Effects	Yes	Yes
Ecological		
Acute Aquatic	Yes	Yes
Chronic Aquatic	Yes	Yes
Environmental		
Bioaccumulation Potential	Yes	Yes
Persistence	Yes	Yes
Physical/Chemical Properties		
Explodability	No	Yes
Flammability	No	Yes

1 US Environmental Protection Agency. 2005. *Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam*, Table 4-1.

physical/chemical properties of a chemical, specifically: flammability and explodability. These hazardous properties are included in the Green Screen to ensure that the method addresses chemical hazards that are of concern to workers and communities that neighbor industrial facilities. While many companies have excellent safety programs, chemical accidents still happen on a regular basis and workers and neighboring communities still remain among the most highly exposed populations to hazardous chemicals.[29]

Another notable difference between the Green Screen and US EPA's summary assessment of pentaBDE alternatives is the inclusion of endocrine disruption. While endocrine disruption is not considered an adverse effect per se—"but rather a potential mechanism of action,"[30] particularly for developing organisms—changes in hormone levels and/or disruption of hormonally-regulated processes, such as those caused by endocrine disrupting chemicals can lead to severe health effects. And there is precedent for using endocrine disruption in assessing the risks posed by a chemical. For example, in the US EPA's revised draft risk assessment for dibutyl phthalate (DBP), the Agency proposes to use changes in hormonal levels caused by DBP (which is an anti-androgen - it blocks or interferes with action of male sex hormones) to set the reference dose (RfD) for DBP. Specifically, the US EPA has identified reduction in fetal testosterone as the critical effect for the regulation of DBP. Despite the reduction being reversible, the Agency concluded that it can cause irreversible effects if it occurs during a critical window of development.[31] Because chemicals that are endocrine disruptors pose serious risks to the health of humans or wildlife, endocrine disruption is included among the Green Screen list of hazards. Note that the European Union's REACH legislation includes endocrine disrupting properties among the list of hazards to be used when identifying chemicals of very high concern (see Table 1—European Union— toxicity column).

4.2. Define Levels of Concern—Low, Moderate, and High—for Each Hazard

Each hazard in the Green Screen is divided into three levels of concern: high, moderate, and low. Two hazards, persistence and bioaccumulation, have an additional level of concern of very high, which reflects the growing international consensus in defining very persistent and very bioaccumulative (vPvB) chemicals. Each level of concern (for each hazard) is defined by threshold values that are quantitative, qualitative, or based on expert references. The threshold values developed for the Green Screen build on the existing work cited above and reflect our goal of defining values that harmonize with existing hazard classification and labeling systems and will lead to the use of chemicals that meet the principles of green chemistry.

Two initiatives were especially helpful in defining threshold values: 1) the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) and 2) the US EPA DfE program's assessment of alternatives to pentaBDE. The GHS is an initiative to create an international system for classifying chemicals by types of hazard and communicating hazard elements through labels and safety data sheets. The goal of the GHS is to ensure the availability of information on the physical hazards and toxicity of chemicals in order to "enhance the protection of human health and the environment during the handling, transport, and use of these chemicals."[32]

The GHS defines hazard categories for many, but not all, chemical hazards. Immune system effects and neurotoxicity, for exam-

ple, are not classified in the GHS. The hazard categories are defined from most to least hazardous characteristics. For example, the hazard categories for "skin corrosion/irritation" are: Category 1—causes severe skin burns; Category 2—causes skin irritation; and Category 3—causes mild skin irritation. Appendix 2 lists the GHS hazard categories for acute human toxicity, flammability, and explosiveness.

The US EPA DfE Program defined threshold values for high, moderate, and low levels of concern for environmental fate, ecotoxicity, and human health effects (as part of its assessment of alternatives to pentaBDE).[22] These threshold values were the starting point for defining many of the Green Screen threshold values. Table 3 summarizes the Green Screen threshold values for each level of concern for each hazard. The details and rationale behind each threshold value are described below.

Environmental Fate: Persistence and Bioaccumulation. As Table 1 reveals, there is wide variation in setting threshold values for high persistence and high bioaccumulation potential, even within the US EPA. These differences reflect specific organizational goals, interpretations of science, as well as points in time when the values were developed. The threshold values in the Green Screen for persistence and bioaccumulation are set to be highly protective of human health and the environment.

vP and vB. The Green Screen thresholds for very high persistence (vP) and very high bioaccumulation (vB) are the same thresholds used to identify Stockholm Convention POPs and vPvB chemicals in the European Union (see Table 1).

High Persistence. The threshold values for high persistence in the Green Screen are within the range of values set by Washington State, US EPA PBT Chemicals Final Rule, IJC Virtual Elimination Task Force, OSPAR PBT definition, and the EU REACH legislation: half-life >40-60 days in water (fresh or marine) and >60-180 days in soil or sediment. The longer degradation time for soil and sediment reflects the slower degradation rates for chemicals in these media. In addition, high persistence in the Green Screen includes potential for long-range environmental transport. The Stockholm Convention on POPs, for example, includes the potential for long-range transport among its list of hazards that must be met for a chemical to be a POP.[33]

Moderate and Low Persistence. The Green Screen threshold values for moderate persistence are: half-life 7-40 days in water and 30-60 days in soil sediment. The water value is in the range of the IJC Virtual Elimination Task Force's moderate persistence value for water. The Green Screen threshold values for low persistence are set to reflect the ability of a chemical to rapidly degrade: half-life <30 days in soil or sediment or <7 days in water; or ready biodegradability (defined in Appendix 1).

High/Moderate/Low Bioaccumulation. The preferred data for determining bioaccumulation potential are: bioconcentration factor (BCF), bioaccumulation factor (BAF), or biomonitoring data that indicates bioaccumulation in humans or wildlife data. In the absence of such data, log-octanol water partition coefficient (log K_{ow}) tests are sufficient for determining the level of concern. The high bioaccumulation threshold is set at the same level as Washington State and the US EPA PBT Chemicals Final Rule: BCF/BAF>1000 (with a log K_{ow}>4.5, which is roughly equivalent to a BCF>1000). The moderate bioaccumulation values are set at the same value used by the OSPAR Commission and by GHS in defining criteria for

TABLE 3: **Threshold Values for Each Chemical Hazard Included in the Green Screen**

Hazard	Very High (v)	High (H)	Moderate (M)	Low (L)
Environmental Fate				
Persistence—P (half-life in days)[1]	• Soil or sediment >180 days; or • Water >60 days	• Soil or sediment >60 to 180 days; • Water >40 to 60 days; or • Potential for long-range environmental transport	• Soil or sediment 30 to 60 days; or • Water 7 to 40 days	• Soil or sediment <30 days; • Water <7 days; or • Ready biodegradability
Bioaccumulation Potential—B[1]	• BCF/BAF >5000; or • Absent such data, log K_{ow} >5	• BCF/BAF >1000 to 5000; • Absent such data, log K_{ow} >4.5-5; or • Weight of evidence demonstrates bioaccumulation in humans or wildlife	• BCF/BAF 500 to 1000; • Absent such data, log K_{ow} 4-4.5; or • Suggestive evidence of bioaccumulation in humans or wildlife	• BCF/BAF <500; or • Absent such data, log K_{ow} <4
Ecotoxicity				
Acute Aquatic Toxicity[1]		• $LC_{50}/EC_{50}/IC_{50}$ <1 mg/l; or • GHS Category 1	• $LC_{50}/EC_{50}/IC_{50}$ 1-100 mg/l; or • GHS Category 2 or 3	• $LC_{50}/EC_{50}/IC_{50}$ >100 mg/l
Chronic Aquatic Toxicity[1]		• NOEC <0.1 mg/l; or • GHS Category 1	• NOEC 0.1-10 mg/l; or • GHS Category 2, 3 or 4	• NOEC >10 mg/l
Human Health				
Carcinogenicity*		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • NTP known or reasonably anticipated to be human carcinogen; • OSHA carcinogen; • US EPA known/likely; • California Prop 65; • IARC Group 1 or 2A; • EU Category 1 or 2; or • GHS Category 1A or 1B	• Suggestive animal studies; • Analog data; • Chemical class known to produce toxicity; • US EPA possible; • IARC Group 2B; • EU Category 3; or • GHS Category 2	• No basis for concern identified or • IARC Group 3 or 4
Mutagenicity/ Genotoxicity*		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • EU Category 1 or 2; or • GHS Category 1A or 1B	• Suggestive animal studies; • Analog data; • Chemical class known to produce toxicity; • EU Category 3; or • GHS Category 2	No basis for concern identified
Reproductive toxicity*		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • NTP Center for the Evaluation of Risks to Human Reproduction; • California Prop 65; • EU Category 1 or 2; or • GHS Category 1A or 1B	• Suggestive animal studies; • Analog data; • Chemical class known to produce toxicity; • EU Category 3; or • GHS Category 2	No basis for concern identified
Developmental toxicity*		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • NTP Center for the Evaluation of Risks to Human Reproduction; or • California Prop 65	• Suggestive animal studies; • Analog data; or • Chemical class known to produce toxicity	No basis for concern identified
Endocrine Disruption*		• Evidence of adverse effects in humans; or • Weight of evidence demonstrates potential for adverse effects in humans	• Suggestive animal studies; • Analog data; • Chemical class known to produce toxicity; • EU Draft List—Category 1 or 2; or • Japanese list	No basis for concern identified

TABLE 3: **Threshold Values for Each Chemical Hazard Included in the Green Screen** continued

Hazard	Very High (v)	High (H)	Moderate (M)	Low (L)
Neurotoxicity*		• Evidence of adverse effects in humans; or • Weight of evidence demonstrates potential for adverse effects in humans	• Suggestive animal studies; • Analog data; or • Chemical class known to produce toxicity	No basis for concern identified
Acute Toxicity (oral, dermal, or inhalation)		• LD_{50} <50 mg/kg bodyweight (oral); • LD_{50} <200 mg/kg bodyweight (dermal); • LC_{50} <500 ppm (gas); • LC_{50} <2.0 mg/l (vapor); • LC_{50} <0.5 mg/l (dust or mist); • US EPA Extremely Hazardous Substance List; or • GHS Category 1 or 2	• LD_{50} 50-2000 mg/kg body-weight (oral); • LD_{50} 200-2000 mg/kg bodyweight (dermal); • LC_{50} 500-5000 ppm (gas); • LC_{50} 2-20 mg/l (vapor); • LC_{50} 0.5-5 mg/l (dust or mist); or • GHS Category 3 or 4	No basis for concern identified
Corrosion/Irritation of the Skin or Eye		• Evidence of irreversible effects in studies of human populations; • Weight of evidence of irreversible effects in animal studies; or • GHS Category 1 (skin or eye)	• Evidence of reversible effects in humans or animals; • GHS Category 2 or 3—skin irritation; or • GHS Category 2A or 2B —eye	No basis for concern identified
Sensitization of the Skin or Respiratory System		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • GHS Category 1—(skin or respiratory); or • Positive responses in predictive Human Repeat Insult Patch Tests (HRIPT) (skin)	• Suggestive animal studies; • Analog data; or • Chemical class known to produce toxicity	No basis for concern identified
Immune System Effects		• Evidence of adverse effects in humans; or • Weight of evidence demonstrates potential for adverse effects in humans	• Suggestive animal studies; • Analog data; or • Chemical class known to produce toxicity	No basis for concern identified
Systemic Toxicity/Organ Effects (via single or repeated exposure)		• Evidence of adverse effects in humans; • Weight of evidence demonstrates potential for adverse effects in humans; • GHS Category 1—organ/systemic toxicity following single or repeated exposure	• Suggestive animal studies; • Analog data; • Chemical class known to produce toxicity; • GHS Category 2 or 3 single exposure; or • Category 2 repeated exposure	No basis for concern identified
Physical/Chemical Properties				
Explosive		• GHS Category: Unstable explosives or Divisions 1.1, 1.2, or 1.3	• GHS Category: Divisions 1.4 or 1.5	No basis for concern identified
Flammable		• GHS Category 1—Flammable Gases; • GHS Category 1—Flammable Aerosols; or • GHS Category 1 or 2—Flammable Liquids	• GHS Category 2—Flammable Gases; • GHS Category 2—Flammable Aerosols; or • GHS Category 3 or 4 —Flammable Liquids	No basis for concern identified

*=Priority Human Health Effect. [1]= Experimental data are preferred. Absent experimental data, values based on structure activity relationships are sufficient.

ABBREVIATIONS:
BAF=bioaccumulation factor; **BCF**=bioconcentration factor; **EC_{50}**=median effective concentration; **EU**= European Union; **GHS**=Globally Harmonized System of Classification and Labelling of Chemicals; **IARC**=International Agency for Research on Cancer; **IC_{50}**=mean inhibitory concentration; **LC_{50}**=median lethal concentration: the concentration at which 50% of test animals died after exposure; **LD_{50}**=median lethal dose: the dose at which 50% of test animals died during exposure; **log Kow**=log-octanol water partition coefficient; **NOEC**=no observed effect concentration; **NTP**=National Toxicology Program; **OSHA**=Occupation Safety and Health Administration

chronic hazards to the aquatic environment: BCF/BAF 500-1000 (with a log K_{ow} 4.0-4.5).[34,35] The low bioaccumulation threshold of BCF/BAF<500 is below the OSPAR and GHS thresholds.

QSARs for P and B. Since experimental data for persistence and bioaccumulation (as well as ecotoxicity) are often unavailable, quantitative structure activity relationship (QSAR) models are commonly used by Environment Canada,[36] the US EPA,[37] and other government agencies to predict values for these hazards. For the purposes of assigning levels of concern in the Green Screen for persistence and bioaccumulation, when measurable data are absent, QSARs are considered acceptable (for further discussion of the use and limits of QSARs to fill data gaps see section 4.4).

Ecotoxicity. Lacking reliable test methods for other wildlife, the Green Screen ecotoxicity threshold values are based upon acute and chronic aquatic toxicity. The threshold values of high/moderate/low for chronic/acute ecotoxicity effects are the same in both the Green Screen and the US EPA DfE Program (see Table 3). Reflecting the broad convergence on threshold values for ecotoxicity, the high for chronic/acute ecotoxicity values for the Green Screen are the same as in Washington State, US EPA DfE, OSPAR, and the European Union (see Table 1). In addition to the quantitative thresholds, the Green Screen incorporates GHS hazard categories for the high and moderate levels of concern for acute and chronic aquatic toxicity. As noted above under persistence and bioaccumulation, QSARs are considered appropriate for predicting acute and chronic aquatic toxicity values for some substances.

Human Health Hazards. The Green Screen threshold values for human health hazards consist primarily of qualitative values and expert references, with quantitative values only used for acute toxicity. The quantitative values used for acute human toxicity are based on GHS hazard category thresholds.

Qualitative Values. The Green Screen qualitative values are derived primarily from the US EPA DfE Program's threshold values. As detailed in Table 4, the Green Screen adopts the US EPA's values for moderate and low levels of concern. For high, however, we changed the second part of the US EPA's value from "conclusive evidence of severe effects in animal studies" to "weight of evidence demonstrates potential for adverse effects in humans." The reasons for this change are better alignment with equivalent descriptions for specific toxic effects such as cancer and to emphasize the importance of including more than just animal studies when evaluating the hazards posed by a chemical.

Government agencies like the US EPA and government-sponsored institutions like the International Agency for Research on Cancer (IARC) have spent decades developing and refining classification systems for carcinogens. While the US EPA, National Toxicology Program (NTP), European Union, IARC, and GHS all have crafted their own language for describing the human carcinogenicity potential of a chemical, they also have (with the exception of NTP) defined three equivalent levels of carcinogenic potential: a) known; b) probable/likely/presumed/reasonably anticipated; and c) possible/suspected/suggestive (see Appendix 3 for a summary of the different classification systems and their terms for classifying the carcinogenicity potential of chemicals).

At the highest degree of confidence are the "known" human carcinogens, which are labeled as such based on epidemiological evidence of carcinogenicity in humans. In the US EPA DfE Program and the Green Screen, known carcinogens meet the qualitative

TABLE 4: **US EPA DfE Program and Green Screen Qualitative Description Threshold Values for Human Health Hazards**

Concern Level	US EPA DfE Program Threshold Values	Green Screen Threshold Values	Equivalent Cancer Classification
High (H)	a) Evidence of adverse effects in human populations or b) **conclusive evidence of severe effects in animal studies**	a) Evidence of adverse effects in human populations or b) **weight of evidence demonstrates potential for adverse effects in humans**	a) Known b) Probable / likely
Moderate (M)	a) Suggestive animal studies, b) analog data, or c) chemical class known to produce toxicity	a) Suggestive animal studies, b) analog data, or c) chemical class known to produce toxicity	Possible
Low (L)	No basis for concern identified	No basis for concern identified	Not likely

ABBREVIATIONS:
DfE=Design for Environment; **IARC**=International Agency for Research on Cancer;
US EPA=United States Environmental Protection Agency

value of "evidence of adverse effects in human populations" and therefore would be classified "high" for cancer concern.

Chemicals for which the data are insufficient to conclude they are "known" to cause cancer in humans, but are sufficient to conclude they are "likely" (US EPA) or "probable" (IARC) carcinogens, or "reasonably anticipated" (NTP) to cause cancer in humans, are also classified as "high" for cancer in the Green Screen. The US EPA defines an agent as "Likely to Be Carcinogenic to Humans" "when the ***weight of the evidence is adequate to demonstrate carcinogenic potential to humans*** *[emphasis added]* but does not reach the weight of evidence for the descriptor 'Carcinogenic to Humans.'" [38] The supporting data necessary for the US EPA to conclude, "Likely to Be Carcinogenic," include a mixture of animal, human, and other biological evidence that support a plausible association between human exposure and cancer.[38] The use of the phrase, "weight of evidence demonstrates potential for adverse effects in humans," in the Green Screen is designed to have a similar intention as the aforementioned US EPA precedent.

The third level of carcinogenic potential, which includes terms like "possible" (IARC) and "suggestive evidence of" (US EPA), falls within the moderate level of concern in the Green Screen and is captured by the term: "suggestive animal studies."

Expert References. Another type of threshold value used in the Green Screen is a reference to another source of data developed by an organization with expertise in that area. The expert reference lists included in the Green Screen are: IARC (carcinogenicity),[39] Occupational Safety and Health Administration (carcinogenicity),[40] National Toxicology Program (carcinogenicity and reproductive toxicity),[41] California Prop 65 (carcinogenicity and reproductive/developmental toxicity),[42] European Union (carcinogenicity, mutagenicity, reproductive toxicity, and endocrine disruption), [43,44] Japan (endocrine disruption),[45] and the US EPA (acute toxicity and carcinogenicity).[46]

The Green Screen also references GHS hazard categories for specific human health effects. The GHS does not provide lists of chemicals, but rather develops threshold values for assigning a chemical to a hazard category.[35]

Priority Effects. The Green Screen establishes a set of priority human health effects based on a value system that prioritizes concern for chemical effects that can be triggered at low doses, have the potential to cause irreversible effects, are difficult to manage through conventional control measures, or are included as priorities in existing government chemical assessment programs. The priority effects are: carcinogenicity, mutagenicity/genotoxicity, developmental toxicity, reproductive toxicity, endocrine disruption, and neurotoxicity. Being a "priority effect" in the Green Screen means more stringent treatment in the benchmarks (described in section 4.3).

Physical/Chemical Properties. Certain properties of chemicals lend them to be particularly hazardous to workers and communities because they are flammable or explosive. Threshold values for flammability and explodability are set in the Green Screen using the GHS hazard categories (see Table 3 and Appendix 2 for details).

4.3. Specify Hazard Criteria for Each Benchmark in the Green Screen

The Green Screen defines four benchmarks on the path to safer chemicals:

- Benchmark 1: **Avoid—Chemical of high concern**
- Benchmark 2: **Use but search for safer substitutes**
- Benchmark 3: **Use but still opportunity for improvement**
- Benchmark 4: **Prefer—Safer chemical**

Each benchmark consists of a set of hazard criteria. The hazard criteria encompass a combination of hazards (section 4.1) and threshold values (section 4.2). Figure 2 details the hazard criteria a chemical (along with its known or predicted degradation products and metabolites) needs to pass for each benchmark.

It is critical to include a chemical's metabolites and degradation products in a hazard assessment because they may be more hazardous than the parent compound. The final benchmark for a parent chemical is the lowest benchmark achieved by either it or its breakdown products. For example, if parent chemical Z achieved Benchmark 2, but its breakdown product Y achieved Benchmark 1, the final benchmark for parent chemical Z is Benchmark 1. Thus the degradation product or metabolite of a chemical is equivalent to the parent compound with respect to its benchmark. The burden of proof in this case lies with those who would demonstrate that the degradate or metabolite is insignificant (i.e. transient, not actually formed, etc.).

Benchmark 1: Avoid —High Concern encompasses the hazard criteria that are leading governments to restrict the use of a chemical: high/very high persistence (P), high/very high bioaccumulation (B), and/or high toxicity (T). The European Union's new REACH legislation, for example, targets chemicals that are PBTs, vPvBs, or highly toxic to humans (carcinogenic, mutagenic, reproductive toxicant, or endocrine disruptor—see Table 1). Similarly Washington State, IJC, OSPAR, and the Stockholm Convention on POPs are targeting chemicals that are PBTs. And Canada is prioritizing chemicals that are not only PBTs, but also P+T or B+T for further assessment.

The four hazard criteria for Benchmark 1 are:

- 1(a) PBT—high P + high B + high T (high human toxicity or high ecotoxicity); **or**
- 1(b) vPvB—very high P + very high B; **or**
- 1(c) vPT (vP + high T) **or** vBT (vB + high T); **or**

- 1(d) high human toxicity for any priority effect.[47]

The chemicals that stop at Benchmark 1 are those for which any release into the environment and exposure to humans is viewed as problematic and not amenable to management through pollution control measures.

Benchmark 2: Use but Search for Substitutes. The hazard criteria for Benchmark 2 are:

- 2(a) moderate P **+** moderate B **+** moderate T (moderate human toxicity **or** moderate ecotoxicity); **or**
- 2(b) high P **+** high B; **or**
- 2(c) (high P **+** moderate T) **or** (high B **+** moderate T); **or**
- 2(d) moderate human toxicity for any priority effect **or** high human toxicity; **or**
- 2(e) high flammability **or** high explosiveness.

Benchmark 2 continues the emphasis on persistence, bioaccumulation, and toxicity, but at lower threshold values. In addition, Benchmark 2 includes flammability and explosiveness. It is anticipated that many chemicals will not move past Benchmark 2 because of the broad scope of hazards and challenging threshold values included in the Green Screen.

Benchmark 3: Use but Still Opportunity for Improvement. The hazard criteria for Benchmark 3 are:

- 3(a) moderate P **or** moderate B; **or**
- 3(b) moderate ecotoxicity; **or**
- 3(c) moderate human toxicity; **or**
- 3(d) moderate flammability **or** moderate explosiveness.

These hazard criteria are designed for chemicals that are on the cusp of being highly benign: they have some hazard characteristics of modest concern, but no characteristics of high concern.

Benchmark 4: Prefer—Safer Chemical. Only chemicals with low inherent toxicity to humans and wildlife, that do not bioaccumulate, and rapidly and completely degrade to benign degradation products or metabolites reach Benchmark 4. These are chemicals that would meet the Principles of Green Chemistry (that relate to hazards). It is anticipated that relatively few chemicals would reach Benchmark 4.

If comprehensive hazard data were available for the 80,000-plus chemicals on the market and these chemicals were evaluated based on the Green Screen method, we would predict a normal distribution curve of chemicals along the benchmarks. Our hope is that the use of green chemistry and supporting tools such as the Green Screen will shift that distribution curve away from Benchmark 1 and toward Benchmark 4.

4.4. Using the Green Screen

In the ideal scenario, comprehensive hazard data as well as complete knowledge of all the metabolites and degradation products would be available for all chemicals. Unfortunately the ideal data scenario is seldom attained because comprehensive hazard data are the exception rather than the norm. To date chemical manufacturers have not been required to provide test data to the US EPA before registering a chemical for commercial use, with the outcome that the vast majority of the 80,000 chemicals on the market have limited to no publicly available test data.[48] Thus we live in a world of imperfect and incomplete chemical safety data.

This creates a challenge to using the Green Screen: how to benchmark chemicals with

FIGURE 2:

Green Screen for Safer Chemicals

Start at Benchmark 1 (red) and progress to Benchmark 4 (green)

This chemical passes all of the criteria.

BENCHMARK 4

ready biodegradability (low P) + low B + low Human Toxicity + low Ecotoxicity (+ additional ecotoxicity endprints when available)

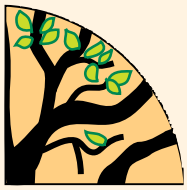
Prefer—Safer Chemical

If this chemical and its break-down products pass all of these criteria, then move on to Benchmark 4

BENCHMARK 3

a. moderate P or moderate B
b. moderate Ecotoxicity
c. moderate Human Toxicity
d. moderate Flammability or moderate Explosivenesness

Use but Still Opportunity for Improvement



If this chemical and its break-down products pass all of these criteria, then move on to Benchmark 3

BENCHMARK 2

a. moderate P + moderate B + moderate T (moderate Human Toxicity or moderate Ecotoxicity)
b. high P + high B
c. (high P + moderate T) or (high B + moderate T)
d. moderate Human Toxicity for any priority effect or high Human Toxicity
e. high Flammability or high Explosiveness

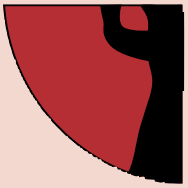
Use but Search for Safer Substitutes

If this chemical and its break-down products pass all of these criteria, then move on to Benchmark 2

BENCHMARK 1

a. PBT: high P + high B + high T[1] (high Human Toxicity[2] or high Ecotoxicity)
b. vPvB: very high P + very high B
c. vPT (vP + high T) or vBT (vB + high T)
d. high Human Toxicity for any priority effect[3]

Avoid—Chemical of High Concern



If this chemical and its break-down products pass all of these criteria, then move on to Benchmark 2

FOOTNOTES:

1 Toxicity – "T" = human toxicity and ecotoxicity
2 Human Toxicity = priority effects (see below) or acute toxicity, immune system or organ effects, sensitization, skin corrosion, or eye damage
3 Priority Effects = carcinogenicity, muta-genicity, reproductive or developmental toxicity, endocrine disruption, or neurotoxicity

ABBREVIATIONS:

B = bioaccumulation **P**=persistence
T=human toxicity and ecotoxicity
vB=very bioaccumulative **vP**=very persistent

limited or no experimental data.[49] Below are four approaches for using the Green Screen in a data-constrained environment.

Comprehensive Data Approach. The preferred approach is to use existing experimental data to determine levels of concern for as many hazards as possible, then to use structure activity relationship (SAR) analyses to fill as many remaining data gaps as possible. This combination of experimental data followed by SAR analysis is common practice at the US EPA, Environment Canada, and other government agencies. A SAR approach calculates or infers a physical/chemical property, environmental fate attribute, and/or specific effect on human health or an environmental species of a chemical based on an analysis of its molecular structure. These correlations may be quantitative or qualitative.[37] Quantitative predictions—known as quantitative SAR or QSAR—are based on validated data sets and have been applied to environmental fate and aquatic toxicity.[50] The US EPA's Office of Pollution Prevention and Toxics has computerized QSARs for persistence, bioaccumulation, and aquatic toxicity.[37] QSARs have their limits, however, with certain types of substances difficult to model, including: pigments and dyes, high log K_{ow} substances, ionizable substances, surfactants, and polymers.[36] Qualitative predictions compare the chemical to one or more closely related chemicals, or *analogs,* and use the analog test data in place of testing the chemical. Qualitative predictions are best done on an endpoint-by-endpoint and case-by-case basis because of the complexity of health endpoints.[50] OncoLogic is an example of a qualitative model developed by the US EPA to provide qualitative SARs for cancer.

The US EPA DfE Program in its report on alternatives to pentaBDE used in low-density foam has developed a useful protocol for presenting which hazard levels of concern are based on experimental data and which were based on SAR/QSAR or professional judgment. Hazard evaluations based on experimental results were presented with bold/colored letters while those based on estimated/predicted results were presented with black/italic font.[28] The Green Screen continues this practice of transparency (see section 5).

The SAR/QSAR strategy has the advantage of providing a comprehensive set of hazard information for a chemical. The downsides include: predicted data are less preferable than experimental data, the models and analogs have their limits (as noted above), and it is resource-intensive—the SAR strategy depends on the expertise of toxicologists and chemists to properly use and interpret the results of the models.

While the benchmarking of chemicals based upon a mixed data set (experimental and SAR) is not ideal, it is often the best that can be achieved given the usually limited experimental data. In fact, the US EPA New Chemicals Program often relies solely on QSAR/SAR data and expert judgment to evaluate new chemicals.[37] Companies concerned by the use of SAR data need to invest in experimental data.

Common Data Source Approach. Another approach is to use a common source of data for benchmarking a set of chemicals. Examples of potential data sources include: Material Safety Data Sheets (MSDSs) from product manufacturers, the Hazardous Substances Data Bank (HSDB), the Integrated Risk Information System (IRIS),[51] the International Uniform ChemicaL Information Database (IUCLID),[52] the High Production Volume Information System (HPVIS),[53] the Organisation for Economic Cooperation and Development (OECD) Screening Information Dataset (SIDS),[54] and the Canadian Domestic Substances List

(DSL) database.[55] The common data source approach has the advantage of using a similar data set for benchmarking of the chemical. The disadvantages will depend on the data source. MSDSs, for example, illustrate some of the common disadvantages to any one data source, including: wide variability in data quality, missing available experimental data (because it is not included in the data source), and inaccurate and incomplete data.[56]

Limited Set of Hazards Approach. A third approach would be to benchmark chemicals based on a few hazards for which experimental and QSAR data are readily available. For example, persistence, bioaccumulation potential, and ecotoxicity are three hazards for which experimental and QSAR data, as well as a QSAR tool (the PBT profiler)[57] are readily available for many chemicals.[58] This type of approach would be useful where one is concerned with only certain types of hazards, such as PBTs (with the "T" only including ecotoxicity) or carcinogenicity. A significant downside to the limited set of hazards approach, by design, is it intentionally excludes potentially serious adverse effects of a chemical. For example, if the limited set of hazards is only PBTs (with "T" only including ecotoxicity) human health effects such as carcinogenicity or reproductive toxicity would be excluded.

Moving Forward. The comprehensive data approach is the best option when resources permit. In the next section we apply the comprehensive data approach and the Green Screen to decaBDE and competing non-halogenated alternatives.

5. Applying the Green Screen to Flame Retardants for TV Enclosures

We have chosen the use of flame retardants in TV enclosures—the external plastic housing of a TV—as a test case for applying the Green Screen. With the European Union restricting decabromodiphenyl ether (decaBDE) in electronics[59] and with states considering similar legislative initiatives, a recurring question emerges in the discussions to restrict decaBDE: are the alternative flame retardants safer? Flame retardant use in TVs is of particular interest because TVs represent the largest end use for decaBDE.[24]

This section benchmarks the environmental preferability of three chemicals used as flame retardants in TV enclosures: decaBDE, bisphenol A diphosphate (BPADP), and resorcinol bis(diphenylphosphate) (RDP). Each flame retardant chemical, along with known breakdown products (i.e. degradation products and metabolites), will be benchmarked through the Green Screen. The method for applying the Green Screen to decaBDE and the other flame retardants involved the following three steps:

1. Identify alternatives to decaBDE in TV enclosures.
2. Assess the hazards of the phosphorous-based and decaBDE flame retardants, including their breakdown products.
3. Apply the Green Screen benchmarks to phosphorous-based and decaBDE flame retardants.

5.1. Identify Alternatives to DecaBDE in TVs

The plausible universe of alternatives to decaBDE for achieving fire safety in TV enclosures includes: chemical substitutes, inherently flame resistant materials that eliminate the need for added flame retardant chemicals (for example, steel or aluminum), and TV re-design options that eliminate the need for flame retardants by separating the enclosure from the heat source. Alternative enclosure designs that eliminate the need for added chemical flame retardants and meet or exceed performance specifications (including flame retardancy) are considered inherently preferable alternatives, particularly if they are derived from benign chemicals (and safe processes) and are recyclable or compostable at end of life.

However, surveys of alternatives to decaBDE in TVs—most notably the Washington State PBDE Chemicals Action Plan[11] and the Lowell Center for Sustainable Production's report on alternatives to decaBDE in electronic enclosure and textile applications[24]—have concluded

that the principal alternatives to decaBDE are other chemical-based flame retardants. The alternative flame retardants for use in TV enclosures are based on both halogen and non-halogen chemistries. Our assessment focuses on the non-halogen alternatives because the market trajectory in electronics overall is toward halogen-free chemistry. Dell, Samsung, and LG Electronics have all, for example, made commitments to eliminate their use of all halogenated flame retardants.[60] Additionally there are concerns with the formation of brominated dioxins and furans across the lifecycle of brominated chemicals.[61]

The two most widely used non-halogen alternatives in TVs are the phosphorous-based alternatives: resorcinol bis(diphenylphosphate) (RDP) and bisphenol A diphosphate (BAPP or BPADP).[11,24] Both BPADP and RDP are mixtures of chemicals.[62] The three major components of BPADP (CAS# 181028-79-5) are:

- ~85% phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (CAS #5945-33-5),
- ~11% phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester (CAS #83029-72-5), and
- less than 3% triphenyl phosphate (CAS #115-86-6).

Commercial BPADP also typically contains 0.07% phenol and <0.01% bisphenol A as contaminants.[63]

The three major components of RDP are:

- ~65-80% phosphoric acid, 1,3-phenylene tetraphenyl ester (CAS #57583-54-7),
- ~15-30% phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester (CAS #98165-92-5), and
- ~<5% triphenyl phosphate (CAS #115-86-6).[63]

DecaBDE, like the phosphorous-based flame retardants, is also a mixture of chemicals:

- ~97% decaBDE and
- ~3% nonabromodiphenyl ether (nonaBDE).

The following section evaluates the hazards associated with the BPADP and RDP formulations as well as decaBDE.

5.2. Hazard Assessment of Phosphorous-based and DecaBDE Flame Retardants

RDP and BPADP. The Syracuse Research Corporation (SRC) completed hazard assessments for RDP and BPADP under contract to the Washington State Departments of Health and Ecology.[63] SRC did not evaluate the hazards of decaBDE because Washington State had already concluded that decaBDE is a PBT.[64]

Appendix 4 contains the summary table (Table 2-1) for BPADP and RDP as presented by SRC in its report to Washington State. The full report contains approximately 140 pages of hazard review information. In developing Table 2-1 the SRC followed the precedent set in its prior work for the US EPA on the report, *Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam*.[28]

SRC compiled data from the literature as well as industry test data. Data were judged for adequacy and excluded if considered inadequate. Inadequate data could result from conflicting studies, poorly designed studies, or studies performed with poor laboratory practices. SRC supplemented test data with estimated results based on QSAR models for aquatic toxicity and certain physical properties. In addition, endpoints for the chemical products with little or no

data were estimated by analogy to triphenyl phosphate. SRC provided predictive information on degradation products which is helpful in considering lifecycle impacts. However, no information on potential metabolites was provided.

Experimental data were only available for triphenyl phosphate. And for triphenyl phosphate, experimental data were missing for cancer hazard and chronic ecotoxicity (see Appendix 4 for details). The potential to cause cancer in humans was estimated using OncoLogic and chronic ecotoxicity was estimated using the QSAR program—Ecological Structure Activity Relationships (ECOSAR). The hazard endpoints for the two other constituents that are part of BPADP and RDP were estimated using analog data from triphenyl phosphate.

This report uses the results of the SRC chemical assessments with the following modifications:

- Added more hazard data into the summary table.
- Modified the thresholds for persistence and bioaccumulation potential to make them consistent with the Green Screen threshold values defined in Table 3.
- Incorporated hazards associated with breakdown products into the assessment.
- Deleted the levels of concern assigned to the formulated compounds of BPADP and RDP.

The summary table in the report by SRC (which is included here as Appendix 4) did not list all the human health effects included in the text of the report, including: acute human toxicity, systemic/organ effects, skin sensitization, skin or eye irritation/corrosion, and immune system effects. SRC's conclusions for these hazards, as well as the hazards included in the summary table (Appendix 4), are incorporated into Table 5. Thus the levels of concern for human health effects and ecotoxicity in Table 5 are the same as SRC's.

An additional hazard, endocrine disruption, was added to Table 5 because it is on the Green Screen list of hazards. A literature search of triphenyl phosphate, which is the principal analog used to evaluate the other phosphoric chemicals, revealed no data on the endocrine disrupting properties of these chemicals.

The levels of concern for persistence (P) and bioaccumulation (B) for the BPADP and RDP constituents differ somewhat in Table 5 from SRC's (see Appendix 4) because of the different threshold values for P and B in the Green Screen.[65] For the primary chemical constituents of BPADP, the level of concern for P for CAS# 83029-72-5 changed from high to very high because the model estimated a half-life of approximately 180 days (recalcitrant biodegradation). For RDP constituents, the level of concern for P for: CAS# 57583-54-7 changed from low to moderate (due to estimated ultimate biodegradation of 37.5 days) and CAS# 98165-92-5 changed from low to high (due to estimated ultimate biodegradation of approximately 60 days). The levels of concern for bioaccumulation (B) potential for: CAS# 57583-54-7 changed from moderate to high (due to a BCF of 3000) and CAS# 115-86-6 changed from low to moderate (due to BCF estimate of less than 1000 by SRC).

SRC also identified degradation products (observed and predicted) for each constituent of BPADP and RDP (see Table 5—"degradation products" column).[63] SRC did not, however, evaluate the hazards posed by the degradation products. The degradation products associated with RDP are: phenol, resorcinol, and diphenyl phosphate. And the degradation products associated with BPADP

constituents are: phenol, diphenyl phosphate, and bisphenol A. Phenol and bisphenol A were also identified as contaminants in the BPADP formulation. Lacking data from SRC, the hazards of each of the degradation products were evaluated based upon a literature review that included:

- risk and hazard assessments by government agencies, including Washington State, European Union, and Agency for Toxic Substances Disease Registry (ATSDR);
- peer reviewed research (often compiled on TOXNET, in particular the Hazardous Substances Data Bank, and the US EPA's Integrated Risk Information System (IRIS); and
- published research articles.

In vivo studies (mostly animal) and *in vitro* studies are widely available for assessing many of the hazards of phenol, bisphenol A, and resorcinol. The levels of concern for these breakdown products of BPADP and RDP are included in Table 5 and referenced in Appendix 5. Data were insufficient, however, for evaluating the hazards of diphenyl phosphate, which was identified as breakdown product from triphenyl phosphate.

A weakness of the SRC report is that it did not explain how the estimated levels of concern for BPADP (CAS# 181028-79-5) and RDP (CAS# 125997-21-9) were derived (see Appendix 4). In the text of the report, SRC provided detailed chemical hazard reviews on each of the three chemical constituents of BPADP and RDP, which included some data for the formulated products. They summarized that data into short summary assessments. However, SRC did not provide similar assessments for the formulated products BPADP (CAS# 181028-79-5) and RDP (CAS# 125997-21-9). Thus it is unclear how SRC derived the levels of concern (H, M, or L) for each of the hazard endpoints shown in Appendix 4 for the formulated products.

DecaBDE. The same method used to assess the hazards of the BPADP and RDP breakdown products was applied to decaBDE and two of its breakdown products, octaBDE and pentaBDE. DecaBDE is breaking down through environmental degradation and metabolism into molecules with fewer bromine compounds.

Depending on the environmental or experimental conditions, a number of breakdown products have been observed from decaBDE. Studies have demonstrated that decaBDE breaks down into more toxic PBDEs (with fewer bromine molecules) through photodegradation, microbial degradation, and metabolism.[66] Photolytic (sunlight) degradation studies have observed the degradation of decaBDE into: tri-, penta-, hexa-, hepta-, octa-, and nona-BDE.[67] Microbial degradation studies of decaBDE degradation under anaerobic conditions have observed the formation of: hepta-, octa-, and nona-BDE.[68] And the metabolic break down products of decaBDE in fish and birds include: penta-, hexa-, hepta-, octa-, and nona-BDE.[69] Ahn, et al. (2006), for example, recorded the photodegradation of decaBDE into the lower brominated congeners—ranging from tri- to nona-BDE—on clay minerals.[70] After a review of the literature on the degradation products from decaBDE the Departments of Ecology and Health in Washington State concluded:

> Research has shown that deca-BDE degrades. Considerable uncertainty remains, however, about the exact degradation products and the relative ratios in which these products are formed. Laboratory studies have shown degradation of deca-BDE into lower congeners including the congeners found in the Penta, Octa and Deca-BDE commercial mixtures. Many of

these same studies indicate, however, that other degradation products are also formed including congeners not commonly found in the commercial mixes. Due to lack of standards for all 209 PBDE congeners and the emphasis placed upon the congeners found in the commercial mixes, research often has not attempted to identify all degradation products. Research has shown that products other than PBDEs are formed from the degradation of deca-BDE. The most commonly mentioned are brominated phenols where a bromine atom is replaced by an alcohol (OH) group. Others degradation products often mentioned in the scientific literature are methyl (CH3), ethyl (CH2CH3) and brominated dioxins and furans. The lack of knowledge about the toxicity of these unidentified congeners and degradation products increases the concern of additional impacts to human health and the environment.

In conclusion

Concern has been raised that deca-BDE will remain a long-term source of lower substituted PBDEs. Potential degradation products include other PBDEs such as lower brominated congeners found in Penta-BDE which have been proven to have a greater environmental impact and are known to bioaccumulate, biomagnify and have greater toxicity. As it has been shown that deca-BDE does degrade readily under laboratory conditions, deca-BDE will also degrade in the environment with time. Therefore it is likely deca-BDE will remain a constant source of lower substituted PBDEs and other degradation products over time.

Given the evidence that decaBDE degrades into the lower congeners, Table 5 includes the hazard profile of a common degradation product and metabolite, octaBDE, as well as pentaBDE, for which there is emerging evidence for environmental degradation. Both octaBDE and pentaBDE have been phased out of production. Appendix 5 references how the levels of concern (in Table 5) were assigned to octaBDE and pentaBDE. Data were not collected on the other PBDE breakdown products or the brominated furans and dioxins, which have also been identified as another set of breakdown products of decaBDE. If the brominated dioxins and furans are similar to the chlorinated dioxins and furans in their hazard profiles (which are already targeted for reduction through the Stockholm Convention on POPs), then they will be of very high concern.

Table 5 summarizes the results of the hazard assessments of BPADP, RDP, decaBDE, and their respective breakdown products. The levels of concern are: low (L), moderate (M), or high (H), and in the case of persistence and bioaccumulation potential, or very high (vH). If the level of concern is noted in **colored bold text**, then the evaluation was based on experimental data. If the level of concern is noted in ***black italic text***, then the evaluation was based on models or expert judgment. Only SRC generated data based on models or expert judgment.

5.3. Apply the Green Screen Benchmarks to Phosphorous-based and DecaBDE Flame Retardants (and their breakdown products)

Translating the hazard profiles of Table 5 into benchmarks involved two steps. First, benchmark each chemical in Table 5 using the Green Screen. Second, assign each formulated compound—RDP, BPADP, and decaBDE—to a benchmark.

5.3.1. Benchmarking each Chemical in Table 5

In this section, each chemical listed in Table 5 is benchmarked according to the Green Screen.

TABLE 5: **Hazard Profiles of Phosphorous-based and DecaBDE Flame Retardants (and their breakdown products)**

Chemical	Chemical Abstract Servies Registry Number (CAS#)	% in Formulation	Human Health Effects													Ecotox.		Fate		Breakdown Products	
			Priority Effects																		
			Carcinogenic	Mutagenic	Reproductive	Developmental	Endocrine Disruption	Neurological	Acute Toxicity	Systemic/Organ Effects	Sensitization (skin)	Sensitization (respiratory)	Irritation/Corrosion (skin)	Irritation/Corrosion (eyes)	Immune System Effects	Acute	Chronic	Persistence	Bioaccumulation	Metabolites	Degradation Products
Bisphenol A diphosphate (BPADP/BAPP) - CAS# 181028-79-5																					
Phosphoric acid, (1-methylethylidene) di-4, 1-phenylene tetraphenyl ester	5945-33-5	~85	*L*	*L*	*L*	*L*	nd	*L*	*L*	*M*	*L*	nd	*L*	*M*	*L*	*L*	*L*	*H*	*L*	nd	phenol + bisphenol A
Phosphoric acid, bis[4-[1-[4-[(diphenoxyphos-phinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester	83029-72-5	~11	*L*	*L*	*L*	*L*	nd	*L*	*L*	*M*	*L*	nd	*L*	*M*	*L*	*L*	*L*	*vH*	*L*	nd	phenol + bisphenol A
Triphenyl Phosphate	115-86-6	<3	*L*	**L**	**L**	**L**	nd	**L**	**L**	**M**	**L**	nd	**L**	**M**	**L**	**H**	*H*	**L**	**M**	nd	diphenyl phosphate + phenol
Breakdown Products																					
Bisphenol A: contaminant and degradation product	80-05-7		**L**	**L**	**M**	**M**	**H**	nd	**L**	**M**	**M**	**M**	**L**	**H**	**M**	**M**	**M**	**L**	**L**		
Phenol: contaminant and degradation product	108-95-2		L	M	L	L	**L**	**M**	**M**	**H**	**L**	**L**	**H**	**H**	**M**	**M**	**M**	**L**	**L**		
Diphenyl phosphate	838-85-7	*insufficient data for evaluation*																			
Resorcinol bis(diphenylphosphate) (RDP) - CAS# 125997-21-9																					
Phosphoric acid, 1, 3-phenylene tetraphenyl ester	57583-54-7	65-80	*L*	*L*	*L*	*L*	nd	*L*	*L*	*M*	*L*	nd	*L*	*M*	*L*	*L*	*H*	*M*	*H*	nd	phenol + resorcinol
Phosphoric acid, bis[3-[(diphenoxy-phosphinyl)oxy]phenyl] phenyl ester	98165-92-5	15-30	*L*	*L*	*L*	*L*	nd	*L*	*L*	*M*	*L*	nd	*L*	*M*	*L*	*L*	*L*	*H*	*L*	nd	phenol + resorcinol
Triphenyl Phosphate	115-86-6	<5	*L*	**L**	**L**	**L**	nd	**L**	**L**	**M**	**L**	nd	**L**	**M**	**L**	**H**	*H*	**L**	**M**	nd	diphenyl phosphate + phenol
Breakdown Products																					
Phenol	108-95-2		**L**	**M**	**L**	**L**	**L**	**M**	**M**	**H**	**L**	**L**	**H**	**H**	**M**	**M**	**M**	**L**	**L**		
Resorcinol	108-46-3		**L**	**L**	**L**	**L**	**M**	**M**	**M**	nd	**M**	nd	**M**	**M**	nd	**M**	**M**	**L**	**L**		
Diphenyl phosphate	838-85-7	*insufficient data for evaluation*																			
Decabromodiphenyl ether (decaBDE) - CAS# 1163-19-5																					
DecaBDE	1163-19-5	97	**M**	**L**	**L**	**M**	**M**	**M**	**L**	**L**	**L**	nd	**L**	**L**	nd	**L**	**L**	**vH**	**M**	penta-to nona-BDE	tri-to nona-BDE
Breakdown Products																					
PentaBDE	32534-81-9		nd	**L**	**M**	**M**	**H**	**M**	**L**	**H**	**L**	**L**	**M**	**M**	nd	**H**	**H**	**vH**	**vH**		
OctaBDE	32536-52-0		nd	**L**	**M**	**H**	**M**	**M**	**L**	**H**	**L**	nd	**L**	**L**	nd	**L**	**L**	**vH**	**M**		

ABBREVIATIONS: **nd**=not determined/unknown; **vH**=very high concern; **H**=high concern; **M**=moderate concern; **L**=low concern. **Colored bold text** = based on experimental data. ***Black italics text***= based on analog data or expert judgment.

SOURCES: BPADP and RDP constituents: Syracuse Research Corporation, 2006, *Flame Retardant Alternatives* (prepared for Washington State). All other chemicals: see Appendix 5.

The benchmark each chemical attains depends on the level of concern it triggers for environmental fate, ecotoxicity, and human health effects; and how those levels of concern compare with the Green Screen hazard criteria detailed in Figure 2. Table 6 summarizes the hazards and levels of concern (high, moderate, low) that are most relevant to the benchmark achieved (see the "Reason for Benchmark" column). In addition, the "Benchmark Achieved/ Stopped by" column in Table 6 shows the benchmark achieved by the chemical and the benchmark criteria (e.g., "1(a)-PBT") that caused the chemical to stop at that benchmark. Below is a more detailed discussion of the reasons why each chemical attained its benchmark.

RDP and its Breakdown Products. For the most part the constituents of RDP are chemicals of moderate concern. Both CAS# 57583-54-7 and CAS# 98165-92-5 reached Benchmark 2—"Use but Search for Safer Substitutes." CAS# 57583-54-7 was stopped at Benchmark 2(c) by the combination of high bioaccumulation and high chronic ecotoxicity (or moderate systemic effects or moderate eye irritation). CAS# 98165-92-5 was also stopped at Benchmark 2(c) by the combination of high persistence and moderate systemic effects (or moderate eye irritation). Triphenyl phosphate, with low persistence, moderate bioaccumulation, and moderate to low human toxicity (for all toxicity endpoints) made it to Benchmark 3—"Use but Still Opportunity for Improvement."

The degradation products for RDP are resorcinol, phenol, and diphenyl phosphate. Resorcinol,[71] with moderate to low levels of concern for all hazards, achieved Benchmark 3. Moderate concerns with resorcinol include irritation, sensitization, and acute toxicity (see Appendix 5 for details on hazards and sources). Phenol, with high levels of concern for irritation/corrosion of skin and eyes, and high systemic effects, achieved Benchmark 2.[72] Neither phenol nor resorcinol is considered endocrine disrupting (see Appendix 5 for details on hazards and sources). Diphenyl phosphate lacked sufficient data for evaluation. An evaluation of diphenyl phosphate would require the use of analog data.

BPADP/BAPP and its Breakdown Products. The constituents of BPADP are mostly chemicals of moderate concern. Both CAS# 5945-33-5 and CAS# 83029-72-5 reached Benchmark 2 but were stopped at Benchmark 2 by the combination of high or very high persistence and moderate systemic effects (or moderate eye irritation). Triphenyl phosphate, as noted above, progressed to Benchmark 3.

The degradation products of BPADP are: phenol, bisphenol A, and diphenyl phosphate.[63] In addition, BPADP contains bisphenol A (~<0.01%) and phenol (~0.07%) as contaminants in some commercial formulations.[11] Phenol reached Benchmark 2 where it was stopped for its high irritancy to skin and eyes and high systemic toxicity. Data were insufficient for evaluating diphenyl phosphate. Bisphenol A, with high concern for endocrine disruption, did not progress beyond Benchmark 1. It is important to note that the emerging trend in low dose experimental research indicates that bisphenol A may be of high concern for reproductive and developmental toxicity. If this trend in independent, low dose research (discussed below) continues to be validated, it would warrant changing the level of concern from moderate to high for reproductive and/or developmental toxicity (for bisphenol A).

The European Union risk assessment on bisphenol A (2003) concluded that the key human health effects to the chemical are: "eye irritation, respiratory tract irritation, skin sensitisation, repeated dose toxicity to the respiratory tract, effects on the liver and

TABLE 6: **Green Screen Benchmarks for the Constituents and Breakdown Products of Phosphorous-based and DecaBDE Flame Retardants**

Chemical	Reasons for Benchmark	Benchmark Achieved / Stopped by
RDP Constituents and Breakdown Products		
CAS# 57583-54-7	• high bioaccumulation • moderate persistence • high chronic ecotoxicity • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 2 / stopped by 2(a),(c)
CAS# 98165-92-5	• high persistence • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 2 / stopped by 2(c)
CAS# 115-86-6 (triphenyl phosphate)	• moderate bioaccumulation • high acute and chronic ecotoxicity • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 3 / stopped by 3(a),(b),(c)
CAS# 108-95-2 (phenol)	• high systemic effects, and irritation/ corrosion of eyes and skin	Benchmark 2 / stopped by 2(d)
CAS# 108-46-3 (resorcinol)	• moderate acute and chronic ecotoxicity • moderate endocrine disruption, neurological effects, acute toxicity, skin sensitization, and irritation/corrosion of eyes and skin	Benchmark 3 / stopped by 3(a),(b),(c)
CAS# 838-85-7 (diphenyl phosphate)	insufficient data for evaluation	
BPADP (BAPP) Constituents and Breakdown Products		
CAS# 5945-33-5	• high persistence • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 2 / stopped by 2(c)
CAS# 83029-72-5	• very high persistence • high chronic ecotoxicity • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 2 / stopped by 2(c)
CAS# 115-86-6 (triphenyl phosphate)	• moderate bioaccumulation • high acute and chronic ecotoxicity • moderate systemic effects and irritation/ corrosion of eyes	Benchmark 3 / stopped by 3(a),(b),(c)
CAS# 108-95-2 (phenol)	• high systemic effects, and irritation/ corrosion of eyes and skin	Benchmark 2 / stopped by 2(d)
CAS# 80-05-7 (bisphenol A)	• high endocrine disruption (and emerging evidence of potentially high concern for reproductive and developmental effects)	Benchmark 1 / stopped by 1(d)
CAS# 838-85-7 (diphenyl phosphate)	insufficient data for evaluation	
DecaBDE and Breakdown Products		
CAS# 1163-19-5 (decaBDE)	• very high persistence • moderate bioaccumulation • moderate cancer, reproductive, developmental, neurological, and systemic effects; and endocrine disruption	Benchmark 2 / stopped by 2(a),(c),(d)
CAS# 32536-52-0 (octaBDE)	• very high persistence • high developmental effects	Benchmark 1 / stopped by 1 (c)
CAS# 32536-52-0 (pentaBDE)	• very high persistence and bioaccumulation • high acute and chronic ecotoxicity • high systemic organ effects • high endocrine disruption	Benchmark 1 / stopped by 1(a),(b),(c)

reproductive toxicity (effects on fertility and on development)."[73] For aquatic organisms, the most sensitive effects appear to be related to endocrine disruption.[73]

Bisphenol A has been identified as estrogenic both through *in vivo* and *in vitro* studies.[74] While there is debate over the strength of bisphenol A's endocrine disrupting capacities, bisphenol A is widely acknowledged to be estrogenic. Research following publication of the EU's risk assessment in 2003 indicates that bisphenol A is significantly more estrogenic than previously acknowledged. Vom Saal and Welshons, for example, conclude that: "Taken together, there is now a large 'low-dose' literature that demonstrates that in many tissues in many species, BPA [bisphenol A] is a chemical with a much higher estrogenic potency than has been acknowledged by chemical corporations and regulatory agencies, since BPA elicits a wide range of effects at doses many orders of magnitude below doses previously predicted to cause no effect."[75]

Bisphenol A causes adverse reproductive and developmental effects in animal studies. But, is the weight of evidence sufficient to consider bisphenol A of high or moderate concern for reproductive and/or developmental toxicity? In 2003, the European Union concluded that bisphenol A may adversely affect fertility (reproductive toxic) and that low dose studies indicate bisphenol A may be a development toxicant.[73] Since the EU risk assessment of bisphenol A, a significant body of experimental data has been published evaluating the toxicity potential of bisphenol A at low doses. There is considerable debate on which studies are relevant for evaluating low dose effects of bisphenol A. Issues in the debate include: the type of animal studied (the Charles River-Sprague Dawley rat, for example, is the least sensitive test animal to estrogenic chemicals), the animal feed used (concerns with contamination with endocrine disrupting compounds), the absence of positive controls (for example, evaluating whether adverse effects result from exposure to other estrogenic chemicals such as DES as well as from bisphenol A), and funding source (no industry funded, low dose, *in vivo* study has found adverse effects, while 94% of government-funded studies did find low dose, *in vivo* adverse effects).[74]

The adverse effects from low dose exposure to bisphenol A include changes in: "Rate of growth and sexual maturation, hormone levels in blood, reproductive organ function, fertility, immune function, enzyme activity, brain structure, brain chemistry, and behavior"; with many of "these effects due to exposure during early development (gestation and/or lactation)."[76] The trend in low dose research indicates that bisphenol A, as an endocrine disruptor, can cause a range of adverse effects, including developmental and reproductive effects. Yet the low dose studies, which produce results counter to those predicted by the older toxicological studies (develop a dose-response curve based on adverse effects at high doses) of bisphenol A exposure, remain to be validated by a government body such as the National Toxicology Program or the European Union. Given the nascent state of research on low doses, we list the level of concern for bisphenol A as a reproductive or developmental toxicant as moderate, with the recognition that the data may shift in a direction to lead to a clear conclusion that BPA is of high concern for these (or other toxic) effects.

DecaBDE and its Breakdown Products. The primary hazard of concern with decaBDE as a homogenous chemical (and excluding its breakdown products) is very high persistence. Beyond persistence there are moderate concerns with decaBDE for many priority effects, including cancer, reproductive toxi-

city, endocrine disruption, and neurotoxicity. The Washington State Action Plan, for example, concluded that: "Results from animal studies provide some evidence of toxic effects associated with exposure to BDE-209 (decaBDE) including neurotoxicity, thyroid hyperplasia, liver toxicity and carcinogenicity at high doses."[11] On carcinogenicity, the US Agency for Toxic Substances and Disease Registry (ASTDR) has identified decaBDE as a possible carcinogen.[77] For bioaccumulation, decaBDE is of moderate concern. While it does not have the BCF value of a bioaccumulative chemical, it is highly persistent and its presence identified via biomonitoring in wildlife, e.g., peregrine falcons[78] and humans is concerning. DecaBDE has been found in human breast milk[13] and blood, including umbilical cord blood.[79] And emerging evidence, for example, from animal studies indicate that decaBDE is bioaccumulating in animal tissue.[80] DecaBDE as a homogenous chemical and excluding its breakdown products reaches Benchmark 2.

While decaBDE is of moderate concern for bioaccumulation potential, it breaks down into a variety of lower brominated congeners and related products that are of high concern (see discussion under decaBDE in section 5.2 above). The lower brominated PBDEs, including pentaBDE, are of very high concern for bioaccumulation and persistence, and high concern for aquatic toxicity. Table 5 evaluates the hazards for octaBDE and pentaBDE as representative of decaBDE breakdown products. PentaBDE is a PBT, being very persistent, very bioaccumulating (with a BCF value of 27,400), and highly toxic to aquatic organisms. OctaBDE is also very persistent and is listed as Category 2 developmental toxicant by the EU. As a PBT, pentaBDE is stopped at Benchmark 1 in the Green Screen. And octaBDE is also stopped at Benchmark 1 because it is very persistent and of high concern for reproductive toxicity (for further details on the levels of concern and their references see Appendix 5).

5.3.2. Benchmarking RDP, BPADP, and DecaBDE

The benchmark achieved by each of the formulated flame retardant chemicals—RDP, BPADP, and decaBDE—is based upon the lowest benchmark achieved by the chemical's constituents and breakdown products. This is to address concerns with the hazards associated with the use of the chemical constituents in manufacture (both due to worker exposure and releases to the environment and into local communities) and with the degradation of the formulated chemical into more hazardous byproducts.

As shown in Table 7, RDP was the only flame retardant—including chemical constituents and breakdown products—among BPADP/BAPP and decaBDE to progress to Benchmark 2—Use but Search for Substitutes. The other two flame retardants, decaBDE and BPADP did not progress beyond Benchmark 1—Avoid Chemical of High Concern.

Both decaBDE and BPADP stopped at Benchmark 1 because of their breakdown products. DecaBDE's breakdown products include pentaBDE as a PBT (Benchmark 1(a)) and octaBDE as very persistent and toxic. BPADP degrades into bisphenol A (and contains the chemical as a contaminant in formulations), which is of high concern for endocrine disruption (and potentially high for its reproductive and developmental effects).

TABLE 7: **Green Screen Benchmarks for Phosphorous-based and DecaBDE Flame Retardants**

Chemical	CAS #	Reasons for Benchmark	Benchmark Achieved
DecaBDE and its breakdown products	1163-19-5	Breakdown products stop decaBDE at Benchmark 1: • pentaBDE is a PBT, vPvB, vPT, and vBT —Benchmarks 1(a),(b),(c) • octaBDE is a vPT—Benchmark 1(c)	Benchmark 1: Avoid—Chemical of High Concern
BPADP/BAPP and its breakdown products	181028-79-5	Breakdown product and formulation conta-minant, bisphenol A, is of high concern for endocrine disruption—stopping BPADP at Benchmark 1(d)	Benchmark 1: Avoid—Chemical of High Concern
RDP and its breakdown products	125997-21-9	• Chemical constituents have: high persistence or high bioaccumulation and moderate/high toxicity (but not for priority effects)—stopping RDP at Benchmarks 2(a) and 2(c) • Breakdown product, phenol, has high systemic effects—stopping RDP at Benchmark 2(d)	Benchmark 2: Use but Search for Safer Substitutes

6. Conclusion

Stating that one chemical is safer than another is fraught with challenges and that is why many avoid it. It would be simpler to state that a chemical such as decaBDE should be avoided because of the hazards it poses, period, with no discussion of whether the alternatives are safer. Yet avoiding the question of whether the alternatives are safer may result in a decision to substitute a known problem chemical with an unknown problem chemical—to move from the proverbial, "frying pan, into the fire."

Once on the path to identifying safer chemicals, another challenge soon arises: lack of experimental data. Since most chemicals lack a comprehensive set of experimental data for all hazards, the question is how best to fill the data gaps. The approach taken in the Green Screen is to fill the data gaps using structure activity relationships (SARs). The SAR strategy has the advantage of providing a more comprehensive set of hazard data for a chemical. The downsides include: the data are less preferable than experimental data, the models and analogs have their limitations, and it is resource-intensive—the complexity of the SAR strategy to filling data gaps means that it is limited to organizations with the resources to access toxicologists and chemists.

The Green Screen approach to data collection is to first, fill all the hazard data points with experimental data when available, then fill the remaining data gaps with SAR/QSAR data when possible. This is the approach taken by the US EPA DfE Program. While the benchmarking of chemicals may be done based upon a mixed data set (experimental and SAR), it is often the best that can be achieved given the limited experimental data. Companies concerned with the use of SAR data need to invest in experimental data. The robustness of the Green Screen results will improve as more comprehensive test data are collected on chemicals. For the Green Screen, it is sufficient and often necessary to benchmark chemicals based on a combination of experimental and SAR data.

Based upon the principles of green chemistry and designed to evaluate the inherent hazards posed by chemicals, the Green Screen method proved to be useful in evaluating the hazards posed by decaBDE and the phosphorous-based flame retardants (and their breakdown products) and relatively simple to apply once the hazard endpoints and levels of concern were established. Of the three flame retardant compounds commonly used in TV enclosures and evaluated in the Green Screen, bisphenol A diphosphate (BPADP) and decaBDE only

reached Benchmark 1: Avoid—Chemical of High Concern. In contrast, resorcinol bis-(diphenylphosphate) (RDP) reached Benchmark 2: Use but Search for Safer Substitutes. According to the Green Screen method, RDP is a preferred alternative to decaBDE. RDP is not a green chemical—it did not achieve the status of a Prefer—Safer Chemical, but it is safer based on its inherent persistence, bioaccumulation potential, and toxicity to humans and the environment than decaBDE, BPADP, and their breakdown products.

An integral element of the Green Screen is taking into account potential degradation products and metabolites. This is important given that chemicals in the environment are not static, they integrate into human and natural environments. Both decaBDE and BPADP scored lower on the Green Screen because of their breakdown products.

In creating the Green Screen we have strived for a method that is transparent, that is scientifically based, and that promotes rather than discourages taking action away from chemicals of very high concern to safer chemicals via informed substitution. This is version 1.0 of the Green Screen because we recognize that the method will need to evolve and change over time as people use it. For example, future directions in revising the Green Screen may involve incorporating nanotoxicology, including reaction byproducts from the use of a chemical, or tweaking the threshold values for the levels of concern for some hazards.

The Green Screen for Safer Chemicals represents a needed building block on the path to sustainable material flows in our economic and ecological systems. It is our goal that companies, government agencies, academia, and nonprofits will use the Green Screen to select inherently safer chemicals, thereby reducing the risks of exposure to toxic chemicals and increasing the availability of safer, healthier products.

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APPENDIX 1: **Glossary of Hazards (included in the Green Screen)**

Term	Definition[1]
Acute Effect	Short-term, in relation to exposure or effect. Exposures are typically less than 96 hours.
Acute Human Toxicant	Chemical that causes harm to humans after short-term exposures. Harm can occur when chemical is inhaled, swallowed, or comes in contact with skin or eye.
Bioaccumulation	An increase in concentration of a pollutant from the environment to the first organism in a food chain based on all sources of input.[2]
Bioconcentration	The specific process by which the concentration of a chemical in an organism becomes higher than its concentration in the air or water around the organism
Biomagnification	An increase in concentration of a pollutant from one link in a food chain to another
Cancer	Any growth or tumor caused by abnormal and uncontrolled cell division.
Chronic	Effects observed after repeated exposures.
Developmental Effect	Adverse effects on the developing organism (including structural abnormality, altered growth, or functional deficiency or death) resulting from exposure prior to conception (in either parent), during prenatal development, or postnatally up to the time of sexual maturation.[2]
Ecotoxicity	Adverse effects observed in living organisms that typically inhabit the wild. The assessment focused on effects in aquatic organisms (fish, invertebrates, algae).
Endocrine Disruption	An endocrine disruptor is an exogenous chemical substance or mixture that alters the structure or function(s) of the endocrine system and causes adverse effects at the level of the organism, its progeny, populations, or subpopulations of organisms, based on scientific principles, data, weight-of-evidence, and the precautionary principle.[3]
Genotoxicity / Mutagenicity	Induction of genetic changes in a cell as a consequence of gene sequence changes (mutagenicity) or chromosome number/structure alterations.
Hazard	"Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent."[4]
Hazard Assessment	"A process designed to determine the possible adverse effects of an agent or situation to which an organism, system or (sub) population could be exposed."[4]
Hazard Identification	"The identification of the type and nature of adverse effects that an agent has as inherent capacity to cause in an organism, system or (sub) population."[4]
Mutagen	Any agent that can induce a genetic mutation or can increase the rate of mutation.
Neurological Effect	Adverse effects on the central or peripheral nervous system.
Persistence	Attribute of a substance that describes the length of time that the substance remains in the environment before it is physically removed by chemical or biological transformations.
Ready Biodegradability (Readily Biodegradable)	Stringent screening tests, conducted under aerobic conditions, in which a high concentration of the test substance (in the range of 2 to 100 mg/L) is used and the biodegradation rate is measured by non-specific parameters like Dissolved Oxygen Carbon (DOC), Biochemical Oxygen Demand (BOD) and CO2. In these tests, a positive result can be considered as indicative of rapid ultimate degradation (i.e., degradation of the substance to CO_2, biomass, H_2O and other inorganic substances like NH_3) in most environments including biological sewage treatment plants.[6]
Reproductive Effect	Adverse effects on the reproductive systems of females or males, including structural/functional alterations to the reproductive organs/syste6m, the related endocrine system, mating, or fertility/reproductive success.
Skin Sensitizer	Chemical that causes an allergic skin reaction characterized by the presence of inflammation; may result in cell death.
Systemic Effect	Adverse effect that is of either a generalized nature or that occurs at a site distant from the point of entry of a substance: a systemic effect requires absorption and distribution of the substance in the body.

SOURCES:

1 Unless otherwise noted, all definitions from: US Environmental Protection Agency, Design for the Environment. 2005. Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam (http://www.epa.gov/dfe/pubs/flameret/ffr-alt.htm—accessed January 11, 2007).

2 International Union of Pure and Applied Chemistry, Clinical Chemistry Division Commission on Toxicology. 1993. Glossary for Chemists of Terms Used in Toxicology.

3 US EPA. 1998. Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) Final Report (http://www.epa.gov/scipoly/oscpendo/edspoverview/edstac.htm—accessed February 12, 2007).

4 Organisation for Economic Co-operation and Development (OECD). 2003. Descriptions of Selected Key Generic Terms Used in Chemical Hazard/Risk Assessment. Paris: OECD.

5 Biology-Online.org, http://www.biology-online.org/dictionary/Mutagen (accessed January 19, 2007).

6 OECD. 2003. Introduction to the OECD Guidelines for Testing of Chemicals Section 3 (http://www.oecd.org/dataoecd/38/2/5598432.pdf—accessed February 12, 2007).

APPENDIX 2: **Globally Harmonized System of Classification and Labeling of Chemicals: Examples of Hazard Categories**

Hazard Class	Hazard Category	Hazard Statement
Explosives	Unstable explosive	Unstable explosive
	Division 1.1	Explosive; mass explosion hazard
	Division 1.2	Explosive; severe projection hazard
	Division 1.3	Explosive; fire, blast or projection hazard
	Division 1.4	Fire or projection hazard
	Division 1.5	May mass explode in fire
Flammable gases	1	Extremely flammable gas
	2	Flammable gas
Flammable aerosols	1	Extremely flammable aerosol
	2	Flammable aerosol
Flammable liquids	1	Extremely flammable liquid and vapour
	2	Highly flammable liquid and vapour
	3	Flammable liquid and vapour
	4	Combustible liquid
Acute toxicity	1,2	Fatal if swallowed (oral). Fatal in contact with skin (dermal). Fatal if inhaled (gas, vapour, dust, mist)
	3	Toxic if swallowed (oral). Toxic in contact with skin (dermal). Toxic if inhaled (gas, vapour, dust, mist)
	4	Harmful if swallowed (oral). Harmful in contact with skin (dermal). Harmful if inhaled (gas, vapour, dust, mist)
	5	May be harmful if swallowed (oral). May be harmful in contact with skin (dermal). May be harmful if inhaled (gas, vapour, dust, mist)
Skin corrosion/irritation	1	Causes severe skin burns and eye damage
	2	Causes skin irritation
	3	Causes mild skin irritation
Serious eye damage / eye irritation	1	Causes serious eye damage
	2A Irritant	Causes serious eye irritation
	2B Mild irritant	Causes eye irritation
Skin sensitizer	1	May cause an allergic skin reaction

SOURCE: United Nations Economic Commission for Europe. 2005. Globally Harmonized System of Classification and Labeling of Chemicals (GHS) (http://www.unece.org/trans/danger/publi/ghs/ghs_rev01/01files_e.html - accessed February 12, 2007).

APPENDIX 3: **Systems for Classifying the Carcinogenicity Potential of Chemicals**

Human Carcinogenicity Potential of a Chemical	European Union[1]	Globally Harmonized System (GHS)[2]	International Agency for Research on Cancer (IARC)[3]	National Toxicology Program (NTP)[4]	US EPA[5] revised in 2005
Known	Category 1—known to be carcinogenic to man	Hazard Category 1A —known to have carcinogenic potential for humans	Group 1— carcinogenic to humans	Known to be human carcinogen	Carcinogenic to humans
Probable / Likely	Category 2—which should be regarded as if carcinogenic to man	Hazard Category 1B —presumed to have carcinogenic potential for humans	Group 2A— probably carcinogenic to humans	Reasonably anticipated to be human carcinogen	Likely to be carcinogenic to humans
Possible	Category 3—which cause concern for man owing to possible carcinogenic effects	Hazard Category 2 —suspected human carcinogen	Group 2B— possibly carcinogenic to humans	*not applicable*	Suggestive evidence of carcinogenic potential
Unknown— not enough data	*not applicable*	*not applicable*	Group 3— not classifiable as to is its carcinogenicity to humans		Inadequate information to assess carcinogenic potential
Not likely			Group 4— probably not carcinogenic to humans		Not likely to be carcinogenic to humans

SOURCES:

1 European Union. 1993. Guidelines for Setting Specific Concentration Limits for Carcinogens in Annex I of Directive 67/548/EEC: Inclusion of Potency Considerations (http://ec.europa.eu/environment/dansub/pdfs/potency.pdf—accessed February 13, 2007).

2 United Nations Economic Commission for Europe. 2005. Globally Harmonized System of Classification and Labeling of Chemicals (GHS) (http://www.unece.org/trans/danger/publi/ghs/ghs_rev01/01files_e.html—accessed February 12, 2007).

3 World Health Organization, International Agency for Research on Cancer. 2006. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Preamble* (http://monographs.iarc.fr/ENG/Preamble/index.php—accessed February 13, 2007).

4 US Department of Health and Human Services, Public Health Service, National Toxicology Program. 2005. *Report on Carcinogens, Eleventh Edition* (http://ntp.niehs.nih.gov/ntp/roc/toc11.html - accessed February 12, 2007).

5 US Environmental Protection Agency. 2005. *Guidelines for Carcinogen Risk Assessment* (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283—accessed February 12, 2007).

APPENDIX 4: **Screening Level Toxicology and Exposure Summary —Table 2-1: from *Flame Retardant Alternatives* prepared by Syracuse Research Corporation for Washington State (2006)**

Chemical	CASRN	Human Health Effects							Ecotoxicity		Environmental		Potential Routes of Exposure						
													Worker			General Population			
		Cancer Hazard	Skin Sensitizer	Reproductive	Developmental	Neurological	Systemic	Genotoxicity	Acute	Chronic	Persistence	Bioaccumulation	Inhalation	Dermal	Ingestion	Inhalation	Dermal	Ingestion	Aquatic
Phosphoric trichloride, reaction products with bisphenol A and phenol (BPADP or BAPP)	181028-79-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***H***	***M***	***H***	***L***	N	Y	Y	N	Y	Y	Y
Phosphoric acid, (1-methylethylidene)di-4, 1-phenylene tetraphenyl ester	5945-33-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***H***	***L***	Y	Y	Y	N	Y	N	N
Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy] phenyl]-1-methylethyl]phenyl] phenyl ester	83029-72-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***H***	***L***	Y	Y	Y	N	Y	N	N
Triphenyl Phosphate	115-86-6	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***H***	***H***	***L***	***L***	Y	Y	Y	Y	Y	Y	Y
Phosphoric trichloride, polymer with 1, 3-benzenediol, phenyl ester (RDP)	125997-21-9	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***H***	***M***	***L***	***M***	Y	Y	Y	Y	Y	Y	Y
Phosphoric acid, 1,3-phenylene tetraphenyl ester	57583-54-7	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***H***	***L***	***M***	Y	Y	Y	N	Y	N	N
Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy] phenyl] phenyl ester	98165-92-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***L***	***L***	Y	Y	Y	N	Y	N	N
Triphenyl Phosphate	115-86-6	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***H***	***H***	***L***	***L***	Y	Y	Y	Y	Y	Y	Y

KEY:
L = Low hazard concern; **M** = Moderate hazard concern; **H** = High hazard concern
L, M,* or *H = endpoint assigned using structure activity relationships (SARs)
N = No; Y = Yes

SOURCE: Syracuse Research Corporation. 2006. *Flame Retardant Alternatives* (prepared for Washington State Department of Health and submitted to Washington State Department of Ecology).

APPENDIX 5:

Hazard Review Summaries of Bisphenol A, Phenol, Resorcinol, PentaBDE, OctaBDE, and DecaBDE

Lacking data from the Syracuse Research Corporation (SRC) report to Washington state (SRC 2006), the hazards of each of the breakdown products were evaluated based upon a literature review that included:

- risk and hazard assessments by government agencies, including Washington State, European Union, and the Agency for Toxic Substances Disease Registry (ATSDR);
- peer reviewed research (often compiled on TOXNET, in particular the Hazardous Substances Data Bank, and the US EPA's Integrated Risk Information System (IRIS); and
- published research articles.

In vivo studies and *in vitro* studies are widely available for assessing many of the hazards of phenol, bisphenol A, resorcinol, and the polybrominated biphenyl ethers — pentaBDE, octaBDE, decaBDE. Hazard reviews of these chemicals are included below.

HAZARD PROFILE SUMMARY

Bisphenol A (BPA) — CAS# 80-05-7

Potential Human Health Effects

Carcinogenicity — Low Concern

EU risk assessment (2003):

"Taking into account all of the animal data available the evidence suggests that bisphenol-A does not have carcinogenic potential" (p.196).

Mutagenicity / Genotoxicity — Low Concern

EU risk assessment (2003):

"Considering all of the available genotoxicity data, and the absence of significant tumour findings in animal carcinogenicity studies, it does not appear that bisphenol-A has significant mutagenic potential in vivo. Any aneugenic potential of bisphenol-A seems to be limited to in vitro test systems and is not of concern. The relevance of the finding that bisphenol-A can produce rat hepatic DNA adduct spots in a postlabelling assay is not entirely clear. However, given the absence of positive results for gene mutation and clastogenicity in cultured mammalian cell tests, it seems unlikely that these are of concern for human health" (p.193).

Reproductive Toxicity — Moderate Concern (potentially High Concern given emerging evidence)

The European Union (EU 2003a), based on evidence compiled prior to 2002, identified bisphenol A as a moderate reproductive toxicant. The EU lists bisphenol A as a Category 3 — Reproductive Toxicant. Classifying bisphenol A as "R62": Possible risk of impaired fertility (ECB 2004).

In its 2003 risk assessment, the EU concluded:

- "The key health effects are reproductive toxicity (effects on fertility and on development) and liver effects following repeated exposure" (EU 2003a, p. 261).
- "The effects of bisphenol-A on fertility and reproductive performance have been investigated in three good quality studies: two generation and multigeneration studies in the rat, and a continuous breeding study in the mouse. In the multigeneration study, an effect on fertility (reduction in litter size) was seen in all three generations at the top dose of 500 mg/kg. Although this effect was seen only at a dose level causing parental toxicity (a reduction in body weight gain (>13%) in both sexes and renal tubule degeneration in females only), it is not clear whether or not the finding could be a secondary consequence of parental toxicity, or a direct effect of bisphenol-A. In the light of this uncertainty, and given that an adverse effect on fertility has been seen in the mouse, it is prudent to assume that bisphenol-A may be having a direct effect on fertility in this study" (pp.240-241).

But emerging evidence indicates that bisphenol A may be of high concern for reproductive toxicity. For example, as cited in the review article by vom Saal and Hughes (2005, p.928):

- "Early onset of sexual maturation in females occurred at maternal doses between 2.4 and 500 µg/kg/day (Honma et al. 2002; Howdeshell et al. 1999; Nikaido et al. 2004)."
- "An increase in prostate size in male offspring occurred at maternal doses between 2 and 50 µg/kg/day (Gupta 2000; Nagel et al. 1997; Timms et al. 2005)."

- "A decrease in daily sperm production and fertility in males was also reported at doses between 0.2 and 20 µg/kg/day due to developmental or adult exposure (Al-Hiyasat et al. 2002; Chitra et al. 2003; Sakaue et al. 2001; vom Saal et al. 1998)."
- "Stimulation of mammary gland development in female offspring occurred at the very low maternal dose of 0.025 µg/kg/day delivered tonically by an Alzet pump (Markey et al. 2001a).
- "Disruption of adult estrous cycles occurred at maternal doses between 100 and 500 µg/kg/day (Nikaido et al. 2004; Talsness et al. 2000)."

These findings lead vom Saal and Hughes (2005) to conclude: "there is now overwhelming evidence demonstrating that these different experimental approaches lead to very different conclusions of safety with regard to the current reference dose for BPA of 50 µg/kg/day" (p.927).

Developmental Toxicity — Moderate Concern (potentially High Concern given emerging evidence)

The European Union (EU 2003a), based on evidence compiled prior to 2002, identified bisphenol A as potentially of concern for developmental toxicity:

> "Overall, in standard developmental studies in rodents, there is no convincing evidence that bisphenol-A is a developmental toxicant. However, the available and apparently conflicting data from studies conducted using low doses (in the µg/kg range) do raise uncertainties. Overall, the majority of EU member states felt that the studies reporting effects at low doses could not be dismissed. However, the member states disagreed on how these studies should be used, if at all, in the risk characterisation for this endpoint. The disagreements were based on differing views about the uncertainties surrounding the reproducibility of the findings and their biological significance, if any, to human health" (EU 2003a, p.242).

But emerging evidence indicates that bisphenol A may be of high concern for developmental toxicity. For example, as cited in the review article by vom Saal and Hughes (2005, p.928):

> "Behavioral effects include hyperactivity at 30 µg/kg/day (Ishido et al. 2004), an increase in aggressiveness at 2–40 µg/kg/day (Farabollini et al. 2002; Kawai et al. 2003), altered reactivity to painful or fear-provoking stimuli at 40 µg/kg/day (Aloisi et al. 2002), and impaired learning at 100 µg/kg/day (Negishi et al. 2004). Developmental exposure to BPA also resulted in a significant change in the locus coeruleus, where BPA at 30 µg/kg/day reversed the normal sex differences in this brain structure and eliminated sex differences in behavior (Kubo et al. 2003). Developmental exposure decreased maternal behavior at 10 µg/kg/day (Palanza et al. 2002), altered play and other sociosexual behaviors at 40 µg/kg/day (Aloisi et al. 2002; Dessi-Fulgheri et al. 2002), and enhanced the behavioral response to drugs such as amphetamine at 40–300 µg/kg/day (Adriani et al. 2003; Suzuki et al. 2003)."

Endocrine Disruption — High Concern

The European Union in its 2003 risk assessment concluded that bisphenol A is weakly estrogenic.

- "Bisphenol-A has been shown to have endocrine modulating activity in a number of in vitro and in vivo screening assays" (EU 2003a, p.231).
- "The study concluded that bisphenol-A acts as a weak estrogen in vivo to fathead minnow exposed to bisphenol-A via water" (EU 2003a, p.74).

Yet the low dose research clearly indicates that bisphenol A is estrogenic at very low doses and causes a wide range of adverse effects at low doses that are related to endocrine disruption. Vom Saal and Hughes (2005, p.927) summarize the data on low dose estrogenic activity for BPA:

> BPA is often described as a very "weak" estrogen because in a few assay systems, such as MCF-7 breast cancer cells in culture, the dose of BPA required to stimulate cell proliferation (~ 10–7 M or 23 ppb) is roughly 100,000 times higher relative to estradiol, which stimulates cell proliferation at approximately 10–12 M (Welshons et al. 1999). This contrasts, however, with the stimulation by BPA of calcium influx in MCF-7 cells that was significant at the lowest dose tested, which was 10–10 M or 23 ppt (Walsh et al. 2005). BPA also stimulated calcium influx and prolactin secretion in rat pituitary tumor cells at the lowest dose tested (10–12 M or 0.23 ppt), and the magnitude of the response to BPA was similar to the response to the same dose of estradiol (Wozniak et al. 2005). It is difficult to conceive how a chemical that can alter cell function at concentrations < 1 ppt can be characterized as a "weak" endocrine disruptor.

Similarly, there is the evidence of adverse effects from endocrine disruption at low doses. As vom Saal and Welsons (2006) conclude: "Taken together, there is now a large 'low-dose' literature that demonstrates that in many tissues in many species, BPA is a chemical with a much higher estrogenic potency than has been acknowledged by chemical corporations and regulatory agencies, since BPA elicits a wide range of effects at doses many orders of magnitude below doses previously predicted to cause no effect (IRIS, 1988)."

Neurotoxicity — not determined

Acute Toxicity — Low Concern

EU risk assessment (2003):

> Bisphenol A "is of low acute toxicity by all routes of exposure relevant to human health" (p.165).

Systemic / Organ Effects — Moderate Concern

EU risk assessment (2003):

> "The key health effects are reproductive toxicity (effects on fertility and on development) and liver effects following repeated exposure" (p.261).

Sensitization — Skin — Moderate Concern

The EU classifies BPA under the risk phrase, "R43," which means it may cause sensitization by skin contact (ECB 2004). And the EU risk assessment concluded that BPA has some potential "cause sensitisation or to trigger sensitisation" (EU 2003a, p.171).

Sensitization — Respiratory — Moderate Concern

EU risk assessment (2003) concluded that BPA:

> "has the potential to cause respiratory irritation" (p. 167).

Irritation/Corrosion — Skin — Low Concern

EU risk assessment (2003):

> Bisphenol A exposure results in "negligible skin irritation" (p.165).

Irritation/Corrosion — Eyes — High Concern

The EU classifies BPA under the risk phrase, "R41," which means is poses a risk of serious damage to eyes (ECB 2004). And the EU risk assessment concluded that BPA has the "potential to cause serious damage to the eyes" (EU 2003a, p.166).

Immune System Effects — Moderate Concern

There are indications that BPA adversely effects the immune system. The EU risk assessment concluded that: "Overall, the studies involving exposure of mice to UV light together with supporting mechanistic data suggest that bisphenol-A can induce a photosensitising reaction that appears to be mediated by the immune system" (EU 2003a, p. 173). And in vom Saal and Hughes' (2003) review of low dose studies, they note studies have found "Altered immune function occurred at doses between 2.5 and 30 µg/kg/day (Sawai et al. 2003; Yoshino et al. 2003, 2004)."

Ecotoxicity

Acute — Moderate Concern

The lowest acute toxicity values — LC50, 96 hour test — for BPA range from 4.6 mg/l in freshwater fish to 7.5 in saltwater fish (see EU 2003a, pp. 69; and HSDB).

Chronic — Moderate Concern

The no observed effect concentration (NOEC) for growth rate in fish range from 0.64 to 3.64 mg/l (EU, 2003, p.69).

Environmental Fate

Persistence — Low Concern

Readily biodegradable (EU 2003a, pp.42 and 47).

Bioaccumulation -- Low Concern

Bioaccumulation factor (BCF) = 67 fish (EU 2003a, p.50).

HAZARD PROFILE SUMMARY

Phenol — CAS# 108-95-2

Potential Human Health Effects

Carcinogenicity — Low Concern

EU risk assessment (2006) conclusion:

"Oral long term studies on rats and mice revealed no effect of phenol on tumour induction. A medium-term study on a transgenic mouse model did not give any indication on treatment related proliferative responses. Phenol was shown to act as a promoter in skin cancer bioassays in mice. A weak carcinogenic effect was observed after long-term skin application of a 10% solution of phenol in benzene (without initiation), but was considered less relevant. The test solution was strongly irritative, and contained the carcinogen benzene. However, there is some concern on the basis of weakly positive in vivo mutagenicity data and from the phenol metabolite hydroquinone classified as a suspected carcinogen (Category 3). This concern is considered to be of minor significance, as long term studies revealed no relevant indication for carcinogenicity. However, in conclusion, phenol is considered not to be a carcinogen in animals.

There are no data revealing an association of phenol exposure to increased tumour rates in humans. No firm conclusion on risk levels could be drawn from a case-control study on respiratory cancer of workers exposed to phenol" (p.128).

Mutagenicity / Genotoxicity — Moderate Concern

EU risk assessment (2006) conclusion:

"The EU Classification and Labelling Working Group decided in 2001 to classify phenol as a category 3 mutagen.

Based on the available evidence, it is considered that this classification still stands and that phenol should still be regarded as a somatic cell mutagen. It is noted that although the high dose positive micronuclei results being secondary to phenol-induced hypothermia is a plausible hypothesis, no definite conclusions about this mechanism can be drawn due to the limited nature of the available data (abstract form and lack of a confirmatory test showing that prevention of hypothermia by maintaining the animals body heat also prevents the induction of micronuclei).

Furthermore, it is deemed that the available in vivo genotoxicity data are unable to address remaining concerns about mutagenicity at the initial site of contact following inhalation or dermal exposure" (p.111).

Reproductive Toxicity — Low Concern

EU risk assessment (2006) conclusion:

"Phenol was investigated for impairment of reproductive performance and fertility in a two-generation (drinking water) reproductive toxicity study in rats. At the highest tested concentration level, according to a mean daily uptake of 300 to 320 mg phenol/kg body weight, which led to reduced water intake and consequently decreased body weight and body weight gain including organ weight impairment in the animals, no adverse effects on reproductive capability and fertility were revealed for either sex across the two generations. Furthermore, sperm parameters and estrous cyclicity had not been affected by phenol treatment. Any effects as revealed during this study were confined to the observation of impaired offspring viability and body weight gain during the pre-weaning period for the

5,000 ppm treated groups for both generations. No such effects had been revealed for the lower tested dosage levels. From the evaluation of this study no adverse effects on reproductive capability and fertility could be revealed up to and including the highest dosages tested (5,000 ppm in drinking water according approximately 301 (males) respectively 320 (females) mg phenol/kg bw/day. Thus it can be concluded for fertility that this endpoint has been adequately examined" (pp.135-136)

Developmental Toxicity — Low Concern

EU risk assessment (2006) conclusion:

"Phenol was evaluated for developmental toxicity in studies with mice and rats. From these studies there are no indications for an embryotoxic or teratogenic potential of phenol. When pregnant rats or mice had been exposed to phenol during gestation (and lactation) indications of prenatal growth retardation and impaired peri-postnatal viability and postnatal growth had been revealed. These effects had been induced at exposure levels that obviously induced systemic toxic effects in the dams and therefore are considered to be secondary and not an indication for a specific fetotoxic potential of phenol. From the overall evaluation of the available studies, for risk characterisation of reproductive toxicity with respect to development a NOAEL/developmental toxicity for phenol of 93 mg/kg body weight is recommended. This NOAEL/developmental toxicity is based on the observations upon offspring performance and development from the 2-generation study" (p.136).

Endocrine Disruption — Low Concern

ATSDR (2006):

"Based on the available information, there is no clear evidence that phenol is an endocrine disruptor in humans or in animals. Long-term studies in rats and mice treated with phenol in the drinking water did not report alterations in the gross or microscopic appearance of the reproductive organs (NCI 1980). In the 13-week experiment, rats and mice received approximately up to 1,700 and 2,700 mg phenol/kg/day, respectively. In the 2-year study, rats received estimated doses of phenol of up to 600–700 mg/kg/day and mice received 1,100–1,200 mg/kg/day. Similar observations were made in a more recent two-generation reproductive study in rats (Ryan et al. 2001). In the latter study, the highest doses of phenol, 301–321 mg/kg/day, had no significant effect on fertility, estrus frequency, testicular sperm count, or sperm motility or morphology. Significant reductions in prostate and uterine weights in all F1 treated groups were not considered adverse effects of phenol by Ryan et al. (2001) on the basis of the absence of histological alterations and functional reproductive effects, and based on the fact that only a few animals had organ weights outside the range of concurrent control values" (p.125).

Neurotoxicity — Moderate Concern

ATSDR:

"An increase in the number of headaches was reported by persons exposed to phenol in drinking water following an accident, but chlorophenols may have contributed to the observe effects (Kim et al. 1994). As reported in a retrospective review (Spiller et al. 1993), 11 patients with oral exposures to phenol-based disinfectants experienced rapid central nervous system depression, but no seizures occurred. Neurological effects (muscle tremor, loss of coordination) have been reported in laboratory animals after single exposures to high concentrations of phenol in the air (Flickinger 1976), continuous exposure in the air (Dalin and Kristoffersson 1974), repeated intermittent exposures in the air (Deichmann et al. 1944), and oral gavage dosing (Deichmann and Witherup 1944; Liao and Oehme 1981; Moser et al. 1995; NTP 1983b). In contrast, no such effects were observed in rats and mice in drinking

water studies of longer durations and with higher doses of phenol (Beyrouty 1998; NCI 1980). These neurological effects correlate with peak blood concentrations of phenol achieved during gavage dosing. Drinking water studies suggest that the nervous system is not a sensitive target for phenol toxicity by this route of exposure. A need to conduct additional toxicity studies is not apparent, but studies aimed at elucidating the mechanism(s) of phenol neurotoxicity are needed" (p.142).

EU risk assessment (2006):

"Although the quality of exposure data are limited, there are human data indicating that phenol adversely affects the nervous system after prolonged oral, dermal or inhalation exposure. Reduction of spontaneous activity, muscle weakness and pain, disordered cognitive capacities were observed in case reports (Merliss, 1972; Kilburn, 1994)" (p.100).

Acute Toxicity — Moderate Concern

EU risk assessment (2006) conclusion:

"Signs and symptoms of acute toxicity in humans and experimental animals are similar regardless of the route of administration. Absorption is rapid, as illustrated by the fact that acute doses of phenol can produce symptoms of toxicity within minutes of administration: Oral toxicity of phenol in humans leading to the death of the victim is reported for doses as low as 140-290 mg/kg body weight (Bruce et al., 1987). Absorption from spilling phenolic solutions on the skin of humans may be very rapid, and death results from collapse within 30 minutes to several hours. Death has resulted from absorption of phenol through a skin area of 64 inch2 (Kania, 1981). For animals, dermal and oral LD50 values are given in the literature: An oral LD50 of 340 mg/kg bw for rats (Deichmann and Witherup, 1944), of approximately 300 mg/kg bw for mice (von Oettingen and Sharpless, 1946) and of less than 620 mg/kg bw for rabbits (Deichmann and Witherup, 1944) are reported. A dermal LD50 value of 660-707 mg/kg bw was determined for female rats (Corning and Hayes, 1970). Although LC50 values are not available in the literature, rats are reported to tolerate phenol concentrations as high as 236 ppm (900 mg/m3) for 8 hours, resulting in ocular and nasal irritation, loss of co-ordination, tremors, and prostration. Based on the frequent reports on human experience with occupational exposure to phenol in earlier times (since 1871), phenol has been classified as 'toxic' and labelled with 'R 23/24/25 (Toxic by inhalation, in contact with skin and if swallowed)'" (p.85).

Systemic / Organ Effects — High Concern

EU risk assessment (2006) conclusion:

"There is sufficient consistency of phenol induced toxic effects on the haematopoietic system, nervous system, the kidney, the liver and skin. The myocard degeneration reported by Deichmann et al. (1944) needs further clarification. There were case reports on the occurrence of arrhythmia after single therapeutic use of phenol (Morrison et al., 1991) giving more weight of evidence that the heart is a target organ. In summary, several animal studies with subacute, and subchronic phenol administration via different routes resulted in relevant toxic effects on function and/or morphology of several organs and organ systems. Although all studies showed deficiencies with respect to the quality of the methodics and documentation or were focussed only on special aspects, the described effects can be considered as sufficiently predictive as relevant risks for human health. At least, the following effects (see Table 4.12) occurring at dosages below the critical dose/concentration for classification and labelling gave arguments for the classification as harmful and labelling with Xn, R 48. The doses or concentrations tested were below the level of the critical dose for classification. Under the assumption that higher doses/concentrations reaching the critical dose would have been used an aggravation of toxic effects would be expected" (p.105).

Sensitization — Skin — Low Concern

EU risk assessment (2006) conclusion:

"Phenol did not cause any signs of skin sensitisation in tests conducted with guinea pigs (modified Buehler Test, Itoh 1982) and mice (Mouse Ear Swelling Assay, Descotes 1988), and there is no evidence of allergic contact dermatitis in humans. Therefore, labelling with R 43 is not warranted" (p.88).

Sensitization — Respiratory — Low Concern

EU risk assessment (2006) conclusion:

"No concern is reached for respiratory tract irritation," (p.viii).

Irritation/Corrosion — Skin — High Concern

EU risk assessment (2006) conclusion:

"Phenol causes severe chemical burns, occasionally skin necrosis is seen with solutions as dilute as 1% (Kania, 1981)" (p.88).

Irritation/Corrosion — Eyes — High Concern

EU risk assessment (2006) conclusion:

"Eye irritation in rabbits caused by a 5% aqueous phenolic solution was irreversible after an observation period of 7 days (Murphy et al., 1982)" (p.88).

Immune System Effects — Moderate Concern

EU risk assessment:

"Phenol-induced suppression of the response to T- and B-cell mitogens was observed in CD-1 mice treated on 28 days with 95.2 mg/l phenol in drinking water. T-cell dependent humoral immune response and antibody levels were reduced at phenol concentrations from 19.5 mg/l (6.2 mg/kg bw/day) (Hsieh et al., 1992). In contrast, rats exposed to phenol containing drinking water did not show any alteration of the T-cell dependent humoral response up to 5,000 ppm (301 mg/kg bw/day) (IITRI, 1999). Spleen cellularity was not affected by phenol treatment in both studies. Atrophic changes of the thymus or spleen were related to a gavage administration of phenol at doses of 12 mg/kg (1/8 female rats) and 40 mg/kg (2/8 females) on 14 days (Berman et al., 1995, Moser et al., 1995, MacPhail et al., 1995). A small appearance of the thymus and the spleen (suggestive for atrophic changes) were noted in the early death on day 14 of treatment with drinking water containing 5,000 ppm phenol (360 mg/kg bw/day) (CMA, 1998b). Chronic studies (NIH, 1980) did not confirm any major effect on the histomorphology of the immune organs (rats and mice: spleen, lymph nodes; mice; bone marrow) related to phenol. The immune system was not addressed in repeat-dose studies on the inhalation or dermal route either because examinations on testing parameters or organ tissues of the immune system were not conducted or due to the lack of any data reported hereon" (p.102).

Ecotoxicity

Acute — Moderate Concern

EU risk assessment (2006):

The 96 hour LC50 values for fish range from 5.02 mg/l to 47.5 mg/l (p.37).

Chronic — Moderate Concern

EU risk assessment (2006):

NOEC values for growth range from 0.1 mg/l to 1.83 mg/l for fish (p.39).

Environmental Fate

Persistence — Low Concern

EU risk assessment (2006):

"The biodegradability of phenol in water has been shown in a number of investigations under the most varied conditions. Only two standardised tests for ready biodegradability are available. In these MITI-I-tests, levels of degradation amounting to between 60 and 70% (after 4 days) and to 85% (after 14 days) were determined (Urano and Kato 1986, MITI 1992). With these results phenol can be classified as readily biodegradable. The results from the other available tests also points toward ready biodegradability. However, on account of the ubiquitous occurrence of phenol, adaptation is to be assumed in the case of all of the inocula. Since this also applies to WWTPs, a degradation rate constant of k = 1 h-1 can be used for them" (pp.11-12).

Bioaccumulation — Low Concern

EU risk assessment (2006):

"As a conclusion from the available test results it can be stated that phenol has only a low bioaccumulation potential. This is also supported by the log Pow of 1.47. According to the equation of Veith et al. (1979) given in the TGD a BCF fish of 3.5 can be calculated from this value. For the further assessment the BCF of 17.5 found by Butte et al. (1985) is used" (p.17).

HAZARD PROFILE SUMMARY

Resorcinol — CAS# 108-46-3

Potential Human Health Effects

Summary of health concerns from the Concise International Chemical Assessment Document (CICAD) on Resorcinol (CICAD 2006):

- "In humans, dermal exposure to resorcinol has been reported to be associated with thyroid effects, CNS disturbances, red blood cell changes, and a low incidence of skin sensitization" (p.34).
- "In animal studies, the toxicological effects reported to be caused by administration of resorcinol include thyroid dysfunction, irritation to skin and eyes, CNS effects, and altered adrenal gland relative weights. In high-dose groups, a decrease in body weight and decreased survival were noted" (p.35).

Carcinogenicity — Low Concern

"Not classifiable as to its carcinogenicity to humans (Group 3)" (IARC 1999).

Mutagenicity / Genotoxicity — Low Concern

CICAD (2006) conclusion:

"Resorcinol is not considered to be genotoxic. In in vitro genotoxicity tests, resorcinol showed mostly negative results. Results from all reported in vivo tests for genotoxicity were negative" (p.35).

Reproductive Toxicity — Low Concern

CICAD (2006) conclusion:

"Resorcinol caused no adverse effects in several reproduction and developmental toxicity studies in rats and rabbits" (p.35).

Developmental Toxicity — Low Concern

CICAD (2006) conclusion:

"Resorcinol caused no adverse effects in several reproduction and developmental toxicity studies in rats and rabbits" (p.35).

Endocrine Disruption — Moderate Concern

Suggestive evidence of concern (CICAD 2006):

In vitro and in vivo data indicate that the antithyroidal activity of resorcinol is caused by inhibition of thyroid peroxidase enzymes, resulting in decreased thyroid hormone production and increased proliferation due to an increase in the secretion of TSH (see section 8.8). The iodination process is catalysed by a haemcontaining enzyme. Resorcinol is known to form covalent bonds with haem (Sessler et al., 1988).

Neurotoxicity -- Moderate Concern

Suggestive evidence of concern (CICAD 2006):

"Resorcinol in animals and humans is reported to affect the CNS. The only investigation into this endpoint is that from the dose range-finding study reported in sections 8.6.1, 8.7, and 8.8.1 (RTF, 2003). Significant increases in locomotor activity were noted for F1 males in the

40, 120, and 360 mg/l groups (4, 13, and 37 mg/kg body weight). However, owing to missing correlating histopathological changes in the three levels of the brain examined and in the absence of a dose–response relationship, other indicators of developmental delay, or other changes in CNS function, these effects were not considered as conclusive evidence of a change in CNS function" (p.29).

Acute Toxicity — Moderate Concern

CICAD (2006):

"After topical use of high concentrations of resorcinol [on humans], CNS disturbances, such as dizziness, vertigo, confusion, disorientation, amnesia, or tremors, or red blood cell changes, such as methaemoglobinaemia, haemolytic anaemia, haemoglubinuria, or cyanosis, have been reported. In most cases, these effects disappeared within several days after discontinuing the resorcinol treatment. In some single case-reports, after exposure to high dermal/oral concentrations, fatal outcomes have been reported. One factor increasing potential toxic effects is the application of resorcinol to injured skin" (p.34).

Systemic / Organ Effects — Moderate Concern

Suggestive evidence of concern (CICAD 2006):

- "Effects on the thyroid gland have been reported both in animal studies and in case-reports in humans" (p.29).
- "Effects on the thyroid gland, such as increased thyroid gland weights and decreased ability of the thyroid to incorporate 125I into the active thyroid hormones T3 and T4, were reported in female rats fed a low-iodine, low-protein diet after oral dosing via drinking-water with resorcinol at about 5–10 mg/kg body weight over 30 days (Cooksey et al., 1985; see section 8.2.1). Changes in thyroid histopathology (increased mean follicular epithelial cell height, decreased mean follicle diameters, and decreased follicle epithelium indices) were noted over 12 weeks with resorcinol at about 5 mg/kg body weight (assuming 35 ml of 0.004% solution/day and 0.275 kg body weight) in drinking-water (Seffner et al., 1995)" (p.25).

Sensitization — Skin — Moderate Concern

Resorcinol "may cause sensitization by skin contact" (CICAD 2006, p.5).

Sensitization — Respiratory — not determined

Irritation/Corrosion — Skin — Moderate Concern

"Resorcinol is irritating to eyes and skin" (CICAD 2006, p.5).

Irritation/Corrosion — Eyes — Moderate Concern

"Resorcinol is irritating to eyes and skin" (CICAD 2006, p.5).

Immune System Effects -- not determined

Ecotoxicity

Acute -- Moderate Concern

CICAD (2006):

"There are several studies available on acute toxicity to different fish species. In general, the 96-h LC50 values for resorcinol were in the range between 26.8 and >100 mg/l" (p.31).

Chronic -- Moderate Concern

CICAD (2006): NOEC estimated at 10 mg/l (p.34).

Environmental Fate

Persistence -- Low Concern

CICAD (2006):

"Resorcinol is readily biodegradable under aerobic conditions and is likely to be biodegraded under anaerobic conditions" (p.4).

Bioaccumulation -- Low Concern

CICAD (2006):

"Experimental test results on bioaccumulation are not available. Based on a log octanol/water partition coefficient of <1 and an estimated BCF of 3.2 (log BCF = 0.5; BCFWIN v.2.15; Fh-ITEM, 2004), a low bioaccumulation is to be expected" (p.14).

HAZARD PROFILE SUMMARY

Pentabromodiphenyl Ether (PentaBDE) — CAS# 32534-81-9

Potential Human Health Effects

The lowest observed effect levels for pentaBDE congeners in animal toxicity studies are for: developmental neurotoxicity, decreased thyroid hormone (endocrine disruption) and developmental reproductive effects (WA 2006, p.23).

Carcinogenicity -- not determined

Washington State PBDE Chemical Action Plan (WA 2006):

"No animal cancer studies have been conducted on the commercial Penta-BDE product or the congeners present in the commercial mixture" (p.21).

Mutagenicity / Genotoxicity -- Low Concern

EU risk assessment (2001):

"given the negative results obtained in vitro and the apparent limited matabolism of pentaBDE, it would be expected that pentaBDE would not be genotoxic in vivo" (p.148).

Reproductive Toxicity -- Moderate Concern

Washington State PBDE Chemical Action Plan (WA 2006):

"Recent animal studies report impacts on both male and female reproduction, occurring at doses as low at 0.06 mg/kg. Effects seen in these studies include changes in both male and female reproductive systems" (p.21).

Developmental Toxicity -- Moderate Concern

Agency for Toxic Substances and Disease Registry (2004):

"Information on the developmental toxicity of PBDEs is available from studies of commercial mixtures of deca-, octa- and pentaBDE. None of the commercial BDE mixtures have been shown to be overtly teratogenic in animals, although neurobehavioral tests, summarized in Section 5.2.2.4 (Neurological Effects), indicate that the developing nervous system is a potential target of some individual lower brominated congeners, including 2,2′,4,4′-tetraBDE (BDE 47), 2,2′,4,4′,5-pentaBDE (BDE 99), and 2,2′,4,4′,5,5′-hexaBDE (BDE 153)" (p.212).

Endocrine Disruption -- High Concern

Agency for Toxic Substances and Disease Registry (2004) has established Minimal Risk Levels (MRLs) for pentaBDE for:

- intermediate inhalation exposure of 0.006 mg/ m3 based on endocrine effects and
- oral intermediate exposure of 0.007 mg/kg/day based on endocrine effects.

Washington State PBDE Chemical Action Plan (WA 2006):

"Exposure to Penta-BDE commercial products and BDE-99 has been shown to decrease thyroid hormone levels in rodents exposed in utero and after birth at doses of 1 mg/kg. Adequate thyroid hormone levels are necessary for normal brain development in utero and post-natally. In humans, the critical time of rapid brain growth occurs during the final trimester of pregnancy and extends after birth until the age of two years. However, similar impacts on thyroid hormone levels have not been observed in humans and scientists are continuing to evaluate the relevance of rodent studies for predicting human health hazards.

Penta-BDE may also impact other hormone systems, with estrogen-like activity being one possible mechanism" (p.21).

Maine (2007):

"In a study in American kestrels, eggs were injected with a mixture of PBDEs-47, -99, -100 and -153 at an environmentally relevant concentration (Fernie et al., 2005). Chicks had lower thyroid hormone levels and liver vitamin A levels, as well as an increase in measures of oxidative stress and decreased metabolic capacity. Injection of PBDE-99 into eggs reduced liver vitamin content in duck hatchlings (Murvoll et al., 2005), indicative of oxidative stress. Increased oxidative stress may lead to cancer and other pathological changes in multiple organ systems in the body, by producing reactive oxygen species that react with lipids, proteins, and DNA. PBDEs-47 and -99, and DE-71 (a penta mixture) all delayed metamorphosis of tadpoles into frogs (Balch et al., 2006), an event which is thyroid-hormone dependent" (pp.14-15).

Neurotoxicity -- Moderate Concern

Washington State PBDE Chemical Action Plan (WA 2006):

"Impacts on brain function (including changes in behavior, learning and memory) have been observed in rodents exposed to Penta- BDE products either in the womb (in utero) or soon after birth (post-natally). Some of these effects persisted and worsened into adulthood. The lowest dose that produced developmental neurotoxic effects in these studies is 0.8 mg/kg" (p.21).

Acute Toxicity — Low Concern

EU risk assessment (2001) conclusion:

"The effects of single inhalation exposures to pentaBDPE have not been adequately investigated in animals, although no deaths occurred following a one-hour exposure to an aerosol of 200 mg/l, suggesting pentaBDPE is of low acute toxicity following inhalation exposure. Studies in rats with commercial preparations containing pentaBDPE indicate that these preparations are of low acute toxicity via the oral and dermal routes of exposure, with LD50 values >2000 mg/kg for these preparations, in both cases" (p.137).

Systemic / Organ Effects — High Concern

Agency for Toxic Substances and Disease Registry (2004) has established
Minimal Risk Levels (MRLs) for pentaBDE for:

chronic oral exposure of 0.0008 mg/kg/day based on liver toxicity.

EU risk assessment (2001):

"at 10 mg/kg/day there was evidence for functional disturbance, with two-fold increases in liver porphyrin levels, accompanied by increases in liver weight and histopathological changes of uncertain character in enlarged parenchymal liver cells of both sexes. At 100 mg/kg/day (the next highest dose used) the liver disturbance was more pronounced, including a 400-fold increase in liver porphyrin levels. Overall, it is predicted that the effect on rat liver at the cut-off for application of R48/22 would constitute serious damage to health" (p.14).

Sensitization — Skin — Low Concern

EU risk assessment (2001):

"does not possess significant skin sensitisation potential" (p.140).

Sensitization — Respiratory — Low Concern

EU risk assessment (2001):

Unlikely to produce significant respiratory tract irritation (p.139).

Irritation/Corrosion — Skin — Moderate Concern

EU risk assessment (2001):

Minimal to mild signs of dermal and eye irritation (p.139).

Irritation/Corrosion — Eyes — Moderate Concern

EU risk assessment (2001):

Minimal to mild signs of dermal and eye irritation (p.139).

Immune System Effects — not determined

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Several acute-duration studies with commercial pentaBDE mixtures and the single congener, 2,2′,4,4′-tetraBDE (BDE 47), suggest that immune suppression might be another important health end point for lower brominated BDEs, although comprehensive immunological evaluations have not been performed on any congener or commercial mixture" (p.40).

Ecotoxicity

Acute — High Concern

EU risk assessment (2001):

The EU classifies pentaBDE as R50/50, "Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment." This decision is based on the EC50 value of 0.014 mg/l seen in a 48-hour Daphnia study, the lack of biodegradation, and the high bioconcentration factor (p.15).

Chronic — High Concern

EU risk assessment (2001) conclusion:

"In summary, therefore, the overall NOEC from the study was determined to be 8.9 µg/l [0.0089 mg/l], with statistically significant effects being seen on juvenile fish length and weight by day 60 post-hatch at a concentration of 16 µg/l [0.016 mg/l]" (p.96).

Environmental Fate

Persistence — Very High Concern

EU risk assessment (2001):

No degradation "was seen in 29 days in an OECD 301B ready biodegradation test carried out to GLP" (p.32).

Bioaccumulation — Very High Concern

ATSDR (2004):

"The commercial pentaBDE product undergoes bioconcentration with a BCF of approximately 14,000 (Hardy 2002b)" (p.399).

"In a laboratory study of Baltic blue mussels (Mytilus edulis L), BCFs from water absorption were found to be 1,300,000 for BDE 47, 1,400,000 for BDE 99, and 1,300,000 for 2,2′,4,4′,5,5′-hexabromodiphenyl ether (BDE 153) (Gustafsson et al. 1999)" (p.399).

HSDB (2007):

"A BCF value of more than 10,000 for carp suggests bioconcentration in aquatic organisms is very high."

HAZARD PROFILE SUMMARY

Octabromodiphenyl Ether (OctaBDE) — CAS# 32536-52-0

Potential Human Health Effects

"Octa-BDE and/or congeners present in the commercial mixture have been shown to be neurotoxic and are able to disrupt the endocrine system (thyroid hormone levels) in animals. Fetal toxicity has been identified as a sensitive toxic endpoint in rat and rabbit studies involving Octa-BDE. Exposure in the womb resulted in bone malformations and decreased fetal weight in rat and rabbit offspring beginning at doses of 2 mg/kg with fetal death occurring at higher doses. Liver changes were also observed in animal studies following exposure to Octa-BDE products at 10 mg/kg or higher" (WA 2006, p.22).

Carcinogenicity — not determined

EU risk assessment (2003):

"No chronic or carcinogenicity studies in animals are available. Only subchronic studies area available to anticipate carcinogenic potential of the substance, thus no firm conclusion can be drawn on carcinogenicity" (p.199).

Mutagenicity / Genotoxicity — Low Concern

EU risk assessment (2003b):

"On the whole, results from different Salmonella tests can be considered as negative. OBDPO [octaBDE] did not induce UDS or SCE in vitro neither cytogenetic effects in vitro. It is noticeable that some of these tests present some limitations in particular the UDS and SCE assays. However, given the negative results obtained in recent Ames and cytogenetic assays conducted in compliance with GLP procedures and the negative results obtained in the mutagenicity tests with PeBDPO [pentaBDE] and DBDPO [decaBDE], no concern for mutagenicity may be assumed" (p.119).

Reproductive Toxicity — Moderate Concern

EU risk assessment (2003b):

"In summary: the only information concerning the potential effects of OBDPO on fertility comes from sub-acute or sub-chronic studies in rats involving administration of commercial OBDPO by oral or inhalation routes. No specific fertility studies have been conducted. The oral sub-chronic study indicates a reversible increase of the absolute and relative testes weight (Great Lakes, 1977). However in recent sub-acute and sub-chronic inhalation studies (Great Lakes, 2000 and 2001), no treatment-related effects on testes and epididymis weights nor microscopic evidence of cell loss or inappropriate cell presence in the seminiferous tubules were shown up to 202 mg/ m3 or 250 mg/ m3. Since this recent sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs, no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown at 202 mg/m3 in the recent 90-day inhalation study. This effect is taken into account although only observed in the one study well conducted and specifically designed to investigate reproductive organs and a NOAEC for female fertility of 16 mg/ m3 is assumed for this end-point. With respect to this effect, it was deemed cautious to apply a classification toxic for reproduction Cat. 3 R62" (p.120).

Developmental Toxicity — High Concern

EU risk assessment (2003b):

"In summary, developmental effects are observed in rats in two studies and they do not seem to be related to maternal toxicity (only decrease in maternal body weight gain during days 16-20 of gestation or decrease in body weight gain interrelated with resorptions and small fetal body weights). These developmental effects are not confirmed in a third assay in rats which was conducted with a test article containing a lesser percentage of octabrominated-diphenyl oxide component. In rabbits, the substance produces only slight foetotoxicity along with a decreased bodyweight gain of the dams at the highest dose. However it must be noticed that this decrease had already happened before the treatment. The lowest identified NOAEL is considered for the risk characterisation i.e. 2 mg/kg/day as obtained in the rabbit. Some of the above mentioned results are considered as borderline but since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, it was deemed cautious to apply a classification: Toxic for reproduction cat. 2 R61" (pp.123-124).

Washington State PBDE Chemical Action Plan (WA 2006):

"Fetal toxicity has been identified as a sensitive toxic endpoint in rat and rabbit studies involving Octa-BDE. Exposure in the womb resulted in bone malformations and decreased fetal weight in rat and rabbit offspring beginning at doses of 2 mg/kg with fetal death occurring at higher doses" (p.22)

Endocrine Disruption — Moderate Concern

Maine (2007):

"Specific PBDE congeners interfere with thyroid hormone, and research is ongoing to elucidate the mechanisms responsible for this effect (Hamers et al., 2006a,b; Richardson et al., 2006)" (p.14).

Washington State PBDE Chemical Action Plan (WA 2006):

"Octa-BDE and/or congeners present in the commercial mixture have been shown to be neurotoxic and are able to disrupt the endocrine system (thyroid hormone levels) in animals" (p.22)

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Inhalation studies of commercial octaBDE dust in rats showed no histopathological changes in the thyroids, parathyroids, adrenals, or pituitary following chamber exposure to 174 mg/ m3 as powdered dust for 8 hours/day for 14 consecutive days (Great Lakes Chemical Corporation 1978), or in the adrenals (only endocrine tissue examined) following nose-only exposure to ≤250 mg/ m3 as dust aerosol for 6 hours/day, 5 days/week for 14 days (Great Lakes Chemical Corporation 2000). Rats that were nose only exposed to commercial octaBDE at levels of 1.1, 16, or 202 mg/m3 for 6 hours/day, 5 days/week for 13 weeks similarly showed no histological changes in the adrenals, pancreas, parathyroids, pituitary, or thyroids (Great Lakes Chemical Corporation 2001a, 2001b). Measurements of serum levels of thyroid hormones in the 13-week rat study, however, showed exposure-related decreases in mean thyroxine (total T4) at ≥16 mg/ m3 in both sexes, and increases in thyroid stimulating hormone (TSH) at ≥16 mg/ m3 in males and 202 mg/ m3 in females. The changes were usually statistically significant ($p<0.05$ or $p<0.01$) compared to controls and were considered by the investigators to be consistent with chemical-induced hypothyroidism. There were no serum T3 changes, thyroid-attributable clinical signs or body weight effects, or gross or histopathological changes in the thyroid. The 1.1 mg/ m3 LOAEL for thyroid effects was used as the basis for the intermediate-

duration MRL for inhalation exposure to octaBDE, as indicated in the footnote to Table 5-1 and discussed in Chapter 4 and Appendix A" (pp.75-76).

Neurotoxicity — Moderate Concern

Washington State PBDE Chemical Action Plan (WA 2006):

"Octa-BDE and/or congeners present in the commercial mixture have been shown to be neurotoxic and are able to disrupt the endocrine system (thyroid hormone levels) in animals" (p.22)

Acute Toxicity — Low Concern

EU risk assessment (2003b):

"The acute toxicity of OBDPO [octaBDE] is very low" (p.107).

Systemic / Organ Effects — High Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"No significant changes in relative or absolute liver weight or gross pathological effects were reported in groups of four rabbits after application of a single dose of up to 10,000 mg/kg of octabromobiphenyl mixture in corn oil to abraded and occluded dorsal skin over a 24-hour period (Waritz et al. 1977). It was unclear if histopathological examinations were performed. Using the same protocol in rabbits, these investigators reported a significant increase ($p<0.01$) in relative and absolute liver weight, distinct lobular markings, and necrotic foci with doses ≥1,000 mg/kg of a commercial hexachlorobiphenyl mixture. A dose of 100 mg/kg was without effect. A significant increase ($p<0.01$) in relative liver weight was reported in rabbits after application of 1 mg/kg/day of a commercial mixture of octabromobiphenyl in corn oil to the intact and occluded shaved dorsal skin on 5 days/week for 2 weeks (Waritz et al. 1977)" (p.229).

Washington State PBDE Chemical Action Plan (WA 2006):

The lowest observed effect levels for octaBDE in animal toxicity studies are for: fetotoxicity and liver changes (p.23).

Liver changes were "observed in animal studies following exposure to Octa-BDE products at 10 mg/kg or higher" (p.22).

Sensitization — Skin — Low Concern

EU risk assessment (2003b):

"OBDPO is not considered as a skin sensitiser" (p.108).

Sensitization — Respiratory — not determined

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Transient signs of respiratory distress that included tachynpea or dyspnea developed in rats that were chamber-exposed to pentaBDE aerosol (compound dissolved in corn oil), octaBDE dust, or decaBDE dust in very high concentrations of 200,000, 60,000, and 48,200 mg/m3, respectively, for 1 hour (IRDC 1974, 1975a, 1975b). Confidence in these effect levels is low due to a small number of tested animals and lack of control data" (p.70).

Irritation/Corrosion — Skin — Low Concern

EU risk assessment (2003b):

"OBDPO is not a dermal or an ocular irritant" (p.108).

Irritation/Corrosion — Eyes — Low Concern

EU risk assessment (2003b):

"OBDPO is not a dermal or an ocular irritant" (p.108).

Immune System Effects — not determined

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Several acute-duration studies with commercial pentaBDE mixtures and the single congener, 2,2',4,4'-tetraBDE (BDE 47), suggest that immune suppression might be another important health end point for lower brominated BDEs, although comprehensive immunological evaluations have not been performed on any congener or commercial mixture" (p.40).

Ecotoxicity

Acute — Low Concern

EU risk assessment (2003b):

"The available toxicity data for octabromodiphenyl ether show that no acute effects in fish or longer-term effects in Daphnia would be expected to occur at concentrations of octabromodiphenyl ether up to its solubility limit. QSAR predictions are also consistent with this" (p.73).

Chronic -- Low Concern

EU risk assessment (2003b):

"The available toxicity data for octabromodiphenyl ether show that no acute effects in fish or longer-term effects in Daphnia would be expected to occur at concentrations of octabromodiphenyl ether up to its solubility limit. QSAR predictions are also consistent with this" (p.73).

Environmental Fate

Persistence — Very High Concern

EU risk assessment (2003b):

"No biodegradation, as determined by oxygen uptake, was seen over the 28-day period and so octabromodiphenyl ether is not readily biodegradable" (p.37).

Bioaccumulation — Moderate Concern

HSDB (2007):

"An estimated range of BCF's from 160 to 910 were calculated for octabromodiphenyl ether(SRC), using log Kow's ranging from 8.35 to 8.90 and a regression-derived equation. According to a classification scheme, these BCF's suggests the potential for bioconcentration in aquatic organisms is high (SRC). However, a single study on mixed polybromodiphenyl ethers ranging from hexabromodiphenyl ether to decabromodiphenyl ether indicated little bioaccumulation in carp with a BCF of <4, after 8 weeks of exposure."

But, biomonitoring data indicate that octaBDE (BDE-203) is bioaccumulating in the foodweb, as Johnson-Restrepo (2005) found:

"Occurrence of BDE-183, BDE-203, and BDE-209 in addition to other major congeners such as BDE-47, BDE-99, and BDE-100 suggests exposure to all technical PBDE formulations (penta-, octa-, and deca-BDE mixtures) for marine fish. Predominance of BDE-209 relative to otherPBDE congeners in sharks is unique and suggests exposure to deca- BDE mixtures. Biomagnification of ∑PBDEs and ∑PCBs in the fish-shark-dolphin foodweb indicates the potential for elevated accumulation of these contaminants by apex predators. åPBDE and åPCB concentrations have increased exponentially, with a doubling time of 2–3 years for bull sharks, and 3-4 years for bottlenose dolphin."

HAZARD PROFILE SUMMARY

Decabromodiphenyl Ether (DecaBDE) — CAS# 1163-19-5

Potential Human Health Effects

Washington State classifies decaBDE as a PBT (WA 2006, p.52).

Carcinogenicity — Moderate Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Based on the limited evidence of carcinogenicity in animals in the NTP bioassay (significantly increased incidences of neoplastic liver nodules in rats and combined hepatocellular adenomas and carcinomas in mice), as well as the lack of human data, decaBDE has been classified in EPA Group C (possible human carcinogen) and IARC Group 3 (not classifiable as to its carcinogenicity to humans)" (p.45).

"Information on carcinogenic effects of PBDEs in animals is limited to results of chronic bioassays of decaBDE mixtures in rats and mice (Kociba et al. 1975; Norris et al. 1975b; NTP 1986). As summarized below, these studies provide limited evidence for the carcinogenicity of decaBDE in animals. No carcinogenicity studies of octaBDE or pentaBDE were located in the available literature" (p.224).

Mutagenicity / Genotoxicity — Low Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Cytogenetic examination of bone marrow cells showed no increase in aberrations in maternal and neonatal rats following maternal oral exposure to ≤100 mg/kg/day of a 77.4% decaBDE mixture (containing 21.8% nonaBDE and 0.8% octaBDE) for 90 days prior to mating and during mating, gestation, and lactation (Norris et al. 1973, 1975a). In vitro assays found that decaBDE did not induce gene mutations in bacterial cells (S. typhimurium TA98, TA100, TA1535, or TA1537) or mammalian cells (mouse lymphoma L5178Y cells), and did not induce sister chromatid exchange or chromosomal aberrations in Chinese hamster ovary cells (NTP 1986)" (p.241).

EU risk assessment (2002):

"On the whole, results from different Salmonella tests can be considered as negative. DBDPO does not exhibit any cytogenetic effects in vitro nor in vivo. It is noticeable that some of these tests present some limitations. However given the absence of alert-structure for genotoxicity according to Tenant and Ashby (1991), the negative results obtained in the mutagenicity tests with DBDPO and also with OBDPO and PeBDPO, no concern about mutagenicity may be assumed" (p.143).

Reproductive Toxicity — Low Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Information on the reproductive toxicity of PBDEs is limited to a one-generation study of a low-purity decaBDE product (77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE) in rats that found no exposure-related functional effects" (p.40).

Developmental Toxicity — Moderate Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"No prenatal developmental toxicity was found in a comprehensive study of commercial decaBDE product (Hardy et al. 2001, 2002)" (p.212).

"A lower purity commercial decaBDE product (77% decaDBE, 22% nonaBDE, 0.8% octaBDE) used in the 1970s was fetotoxic in rats at high dose levels that were not maternally toxic. Developmental effects were investigated in rats that were exposed to doses of 10, 100, or 1,000 mg/kg/day by gavage on GDs 6– 15 and examined on GD 21 (Dow Chemical Co. 1985; Norris et al. 1975b). No treatment-related maternal toxicity was observed. The numbers of fetuses with subcutaneous edema and delayed ossification of normally developed skull bones were significantly increased at 1,000 mg/kg/day. Resorptions were significantly ($p<0.05$) increased at ≥10 mg/kg/day compared to controls as indicated by resorption/implantation site percentages [1% (3/288), 9% (12/141), 10% (13/135), and 4% (9/203)] and percentages of litters with resorptions [12% (3/25), 64% (9/14), 57% (8/14), and 39% (7/18)]. The resorptions were considered secondary to unusually low control values and unrelated to treatment because (1) the data do not follow a dose-response relationship across the three dose levels, and (2) the rates in the high dose group are comparable to historical control values" (p.213).

Endocrine Disruption — Moderate Concern

Maine (2007):

"Van der Ven et al. (2006) studied the effects of a number of PBDE congeners on thyroid hormones, blood biochemistry, and organ weights in adult rats. DecaBDE decreased T3 levels, thymus weight, and brain weight. DecaBDE was less active than other congeners" (p.15).

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"There is suggestive evidence of hypothyroidism in a small group of workers who were occupationally exposed to decaBDE as well as PBBs (Bahn et al. 1980), as summarized in the preceding subsection on endocrine effects of PBBs. In another study, plasma levels of thyroid hormones (T3 and free T4) and eight PBDE congeners (tetra- to heptaBDEs) were monitored for 198–221 days in three electronic dismantling workers (Pettersson et al. 2002). The hormones remained within normal ranges and there were no correlations between levels of hormones and congeners" (p.75).

Neurotoxicity — Moderate Concern

Maine (2007):

"As was discussed in our 2006 report, Swedish investigators documented changes in motor activity in male mice exposed to a single dose of a number of PBDE congeners administered separately during early postnatal development, including PBDE-47, PBDE-99, PBDE-153 or deca BDE. For all congeners, treated mice were less active than controls at the beginning of the one-hour observation period, but did not decrease their activity over time as did controls. This is referred to as failure of habituation, and may result from cognitive or attentional deficits or changes in arousal level.

The Swedish investigators have replicated the effects of decaBDE on activity using rats (Viberg et al., 2006a). Male rats were given a single dose of decaBDE on postnatal day (PND) 3 and tested during early adulthood. The high dose group exhibited lower activity at the beginning of the observation period, and failed to habituate over the one-hour session. The low dose rats, on the other hand, were more active than controls at the beginning of the session, and habituated normally. Such a bi-phasic dose-effect curve (e.g., increase at lower doses and decrease at higher) is commonly observed for motor activity, for drugs as well as environmental chemicals. (Amphetamine is a classic example.) The cholinergic drug nicotine decreased activity in the high-dose group" (p.17).

"Study of endocrine and behavioral effects of deca BDE by USM and the Maine CDC
As described in last year's presentation to the legislature, a study is ongoing at the University

of Southern Maine by Dr. Vincent Markowski in collaboration with Dr. Deborah Rice at the Maine CDC, under contract to Maine CDC. Mice were dosed on PND 2-15 with 6 or 20 mg/kg/day of decaBDE, and locomotor activity and cognitive function were tested during adulthood. As young adults, males in the higher dose group were more active than controls over a two-hour period, but habituated (decreased their activity) over the observation period in the same manner as controls (Rice et al., submitted). There was no effect in the treated females. Treated mice made more errors on a visual discrimination task compared to controls, indicative of cognitive impairment. Blood concentrations of the thyroid hormone T4 were decreased in males at 21 days of age in a dose-dependent manner" (p.18).

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"Neurobehavioral effects of individual PBDE congeners were evaluated in mice that were exposed during perinatal and/or early postnatal periods to 2,2',4,4'-tetraBDE (BDE 47), 2,2',4,4',5-pentaBDE (BDE 99), 2,2',4,4',5,5'-hexaBDE (BDE 153), or 2,2',3,3',4,4',5,5',6,6'-decaBDE (BDE 209). Most of these studies used similar single oral dose experimental designs and evaluated spontaneous motor behavior and swim maze performance at 2–6 months of age. The findings collectively indicate that the nervous system is a target of particular PBDE congeners during a defined critical phase of neonatal brain development, as shown by mild impairments in spontaneous motor behavior and learning and memory in older mice" (p.42).

Acute Toxicity — Low Concern

EU risk assessment (2002):

"DBDPO [decaBDE] exhibits a low acute oral, dermal and inhalation toxicity."

Systemic / Organ Effects — Low Concern

Agency for Toxic Substances and Disease Registry (ATSDR 2004):

"The hepatotoxic potential of lower brominated PBDE mixtures is well-documented in animals by oral exposure. The spectrum of observed hepatic effects includes microsomal enzyme induction, liver enlargement, and degenerative histopathologic alterations that progress to tumors. Repeated dietary exposure to PBDEs typically caused liver enlargement with or without degenerative changes, and effects were generally dose-related in incidence and severity, more frequent and pronounced in males than females, and more severe with octaBDE and pentaBDE than decaBDE. For example, subchronic oral studies in rats showed that commercial pentaBDE mixtures were hepatotoxic at doses ≤10 mg/kg/day. Increased liver weight and hepatocellular enlargement with vacuolation occurred in rats exposed to commercial pentaBDE doses as low as 2–9 mg/kg/day for 4–13 weeks. Increased incidences of degeneration and necrosis of individual hepatocytes were observed 24 weeks following exposure to ≥2 mg/kg/day of commercial pentaBDE for 90 days in rats. In contrast, high purity commercial decaBDE caused no liver pathology in rats and mice at estimated doses as high as 2,000–8,000 and 2,375– 9,500 mg/kg/day, respectively. High purity commercial decaBDE caused liver effects only following lifetime exposure to doses that were still very high. Exposure to 94–97% decaBDE for 103 weeks caused liver thrombosis and degeneration in rats at 2,240 mg/kg/day, and centrilobular hypertrophy and granulomas in mice at ≥3,200 mg/kg/day. No studies are available on hepatic effects of PBDEs in humans. Based on the evidence in animals, lower brominated PBDEs are potentially hepatotoxic in humans" (p.43).

Sensitization — Skin — Low Concern

EU risk assessment (2002):

"Taking into account the negative results from studies in animals on OBDPO and in regard with the two quite large human studies reported on DBDPO, this substance can be considered as a non skin sensitizer" (p.134).

Sensitization — Respiratory — not determined

EU risk assessment (2002):

"No direct information is available from studies in humans or animals on respiratory sensitization" (p.134).

Irritation/Corrosion — Skin — Low Concern

EU risk assessment (2002):

"DBDPO [decaBDE] is not an irritant for skin or eyes" (p.133).

Irritation/Corrosion — Eyes — Low Concern

EU risk assessment (2002):

"DBDPO [decaBDE] is not an irritant for skin or eyes" (p.133).

Immune System Effects — not determined

Ecotoxicity

Acute — Low Concern

EU draft risk assessment (2004):

"The available aquatic toxicity data for decabromodiphenyl ether show no effects at the limit of water solubility of the substance" (p.92).

Chronic — Low Concern

EU draft risk assessment (2004):

"The available aquatic toxicity data for decabromodiphenyl ether show no effects at the limit of water solubility of the substance" (p.92).

Environmental Fate

Persistence — Very High Concern

EU draft risk assessment (2004):

"Although significant photodegradation has been observed in laboratory studies, decabromodiphenyl ether is not readily biodegradable based on a single test. The TGD recommends that in such cases a simulation test for environment degradation should be performed to establish a half-life in marine water and/or sediment. However, no degradation was seen in a 32-week study in anaerobic freshwater sediment. It is therefore not expected to degrade biotically at a significant rate in the environment. Therefore decabromodiphenyl ether is considered to meet the very persistent (vP) criterion" (p.90).

Washington State PBDE Chemical Action Plan (WA 2006):

"Swedish and Dutch scientists measured atmospheric deposition of PBDEs in the Baltic Sea for the first time in research published in January 2004. Measurements were taken from an island in the central basin of the Baltic Sea far from human settlement; deposition of PBDEs

would therefore be the result of long-range transport through the atmosphere. The research compared deposition of PBDEs to the better documented deposition of PCBs. The atmospheric deposition of PBDEs exceeded that of PCBs by a factor of 40, while deposition of PCBs was decreasing. BDE-209 comprised the largest percentage of PBDEs detected, with BDE-47 and BDE-99 representing the next most abundant congeners" (p.29).

"Half-life information for Deca-BDE in water and other media indicate that it is persistent in the environment" (p.52).

Yet, under certain conditions, decaBDE will degrade:

"While further research is needed, Ecology and DOH believe the following conclusions are appropriate:

1. Deca-BDE undergoes degradation. The most common path in laboratory studies is the debromination of deca-BDE to lower PBDE species. Other degradation products have been found in some studies, including brominated dioxins, phenols and dibenzofurans. The negative impact these degradation products have upon human health and the environment is unquantified, but the abundance of studies that document negative impacts makes this a matter of considerable concern.

2. Debromination of deca-BDE occurs through light exposure (both UV radiation and direct sunlight) and biological activity. These pathways lead to a variety of degradation products.

3. The rate of debromination has been determined in laboratory studies. Further work is needed to determine the debromination rate under environmental conditions. Degradation in the environment occurs more slowly. This phenomenon is consistent with what occurs to halogenated compounds with similar chemical structure, and is supported by knowledge of standard chemical processes.

4. Deca-BDE will continue to be a source of lower brominated diphenyl ethers and other degradation products for some time" (WA 2006, p.35).

Bioaccumulation — Moderate Concern

EU draft risk assessment (2004):

"the available data do suggest that uptake by organisms in the environment could occur if the organisms are exposed to decabromodiphenyl ether in a suitable form. The available data also indicate that decabromodiphenyl ether has a relatively short elimination half-life from organisms. This should limit the potential for bioaccumulation of decabromodiphenyl ether, although the fate of metabolites is unclear and the substance can be retained after exposure is stopped, as demonstrated in the study with Grey Seals" (p.38).

But, biomonitoring data indicate that decaBDE is bioaccumulating in the foodweb, as Johnson-Restrepo (2005) found:

"Occurrence of BDE-183, BDE-203, and BDE-209 in addition to other major congeners such as BDE-47, BDE-99, and BDE-100 suggests exposure to all technical PBDE formulations (penta-, octa-, and deca-BDE mixtures) for marine fish. Predominance of BDE-209 relative to otherPBDE congeners in sharks is unique and suggests exposure to deca- BDE mixtures.

Biomagnification of ∑PBDEs and ∑PCBs in the fish-shark-dolphin foodweb indicates the potential for elevated accumulation of these contaminants by apex predators. åPBDE and åPCB concentrations have increased exponentially, with a doubling time of 2-3 years for bull sharks, and 3-4 years for bottlenose dolphin."

APPENDIX 5

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