

# **VCCEP Pilot: Progress on Evaluating Children's Risks and Data Needs**

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## **ABSTRACT**

The Voluntary Children's Chemical Evaluation Program (VCCEP) is designed to provide information to the public on children's potential health risks associated with chemical exposures. The key question of the VCCEP is whether the potential hazards, exposures, and risks to children have been adequately characterized, and, if not, what additional data are necessary. To answer this question, manufacturers or importers of 23 chemicals were asked by the U.S. EPA to sponsor their chemicals in the first tier of a pilot program. These chemicals were selected for evaluation because they have been found as contaminants in human tissue or fluids (adipose tissue, blood, breath, breast milk, or urine); food and water children may eat and drink; or air children may breathe (including residential or school air). Under the VCCEP framework, sponsoring companies agree to prepare Tier 1 hazard, exposure, and risk assessments on the individual chemicals, and identify the need for additional data. These assessment documents are submitted to the U.S. EPA and subsequently undergo review by experts in an independent peer consultation meeting that is open to the public. Following this peer consultation process, the U.S. EPA reviews each submission and makes a data needs determination, which may include requesting further data collection or generation by the sponsor. Sponsoring companies then decide whether to volunteer for the next tier and collect or generate the requested data.

The purpose of this paper is to describe the process and to review and present the key findings from the first set of chemicals that have been fully or partially evaluated under the pilot program (vinylidene chloride, decabromodiphenyl ether, pentabromodiphenyl ether, octabromodiphenyl ether, acetone, methyl ethyl ketone, decane, undecane, and dodecane). Specifically, we provide a brief summary of the sponsors' submissions, the peer consultation panels' discussions, and the U.S. EPA's data needs decisions. Although we do not attempt to conduct independent analyses

of the underlying data, we do identify a number of common themes that have emerged during implementation of the pilot program and discuss several key issues that could become important in the future. The information presented here should be useful for various parties interested in the progress of the VCCEP and the results of the initial (Tier 1) children's assessments.

**KEY WORDS**

VCCEP, children's health, risk assessment, industrial chemicals

## INTRODUCTION

Children's health issues have become an increasingly important topic of scientific research over the last decade. In particular, greater attention has focused on the potential for children's increased (or reduced) susceptibility to chemicals and on children's unique behavior and exposure patterns (ATSDR 1997; Armstrong et al. 2000; Bruckner 2000; Calabrese 2001; Charnley 2001; Charnley and Putzrah 2001; Cohen-Hubal et al. 2000; Dourson et al. 2002; Etzel et al. 1999; Juberg 2002; Scheuplein et al. 2002; Schneider and Freeman 2000; U.S. EPA 2003; Weaver et al. 1998). Approaches for conducting child-specific exposure and risk analyses have also populated the literature in recent years (AIHC 1994; Armstrong et al. 2000; Finley et al. 1994; Cohen-Hubal et al. 2000; U.S. EPA 1989, 1997, 2002b; Resiss et al. 2003; Williams et al. 2003). In response to growing concerns about children's health issues in the United States, several federal laws and a number of nationwide policies and initiatives aimed at studying and protecting children from environmental health hazards have been enacted. These include the Food Quality Protection Act, the Children's Health Act, the U.S. Environmental Protection Agency's (U.S. EPA) Office of Children's Health Protection and other Agency initiatives, and various programs initiated by the Food and Drug Administration and Centers for Disease Control and Prevention (CDC 2001, 2003; CHA 2000; FDA 2001; FQPA 1996; U.S. EPA 2000a, 2002a).

The Voluntary Children's Chemical Evaluation Program (VCCEP), which is part of the U.S. EPA's Chemical-Right-to-Know Initiative, represents one of several child-centered programs started in 2000. This unique pilot program was designed to provide data to the public that would increase their understanding of potential health risks to children from chemical exposures and to encourage the participation of interested stakeholders (U.S. EPA 2000b). The VCCEP is based

on the voluntary participation of chemical manufacturers and importers. The basic structure of the program is that the available hazard and exposure data for a chemical are evaluated and used to characterize risks to children and prospective parents. The identification of additional data needs is informed by the findings of the health risk assessment. This consideration of the available exposure and hazard data to inform the need for analyses or data collection represents a paradigm shift from previous testing programs.

In the VCCEP pilot, the U.S. EPA asked the manufacturers and importers of 23 chemicals to volunteer to sponsor their chemicals for evaluation of risks to children's health. These chemicals were selected by the U.S. EPA because they have been found as contaminants in human tissue or fluids (e.g., adipose tissue, blood breath, breast milk, urine); food and water children may eat and drink; or air children may breathe (including residential or school air). Thirty-five companies and ten consortia volunteered to sponsor 20 of the 23 chemicals (**see Table 1**). Under the VCCEP framework, sponsoring companies agree to prepare Tier 1 hazard, exposure, and risk assessments on the individual chemicals, and identify the need for additional data. The sponsors' assessment documents are submitted to the U.S. EPA and subsequently undergo review by experts in an independent peer consultation meeting that is open to the public. Following this peer consultation process, the U.S. EPA reviews each submission and makes a data needs determination, which may include requesting further data collection or generation by the sponsor. Sponsoring companies then decide whether to volunteer for the next tier and collect or generate the requested data.

Thus far, six chemicals have completed Tier 1 of VCCEP (vinylidene chloride, decabromodiphenyl ether, pentabromodiphenyl ether, octabromodiphenyl ether, acetone, and methyl ethyl ketone). Three additional chemicals have been partially completed under the pilot

program (decane, undecane, and dodecane). In this paper, we provide a brief summary of the highlights of the pilot program, including the industry sponsors' submissions, the peer consultation panels' discussions, and the U.S. EPA's data needs decisions (where applicable). We do not attempt to conduct independent analyses of the underlying data in the assessments, rather we identify a number of common themes that have emerged during implementation of the VCCEP and discuss several key issues that could be important in the future. The information presented here should be useful for various parties interested in the progress of the VCCEP and the results of the initial (Tier 1) children's assessments.

*INSERT TABLE 1 ABOUT HERE*

## **BACKGROUND**

The VCCEP pilot represents a novel approach for determining the need for collection of further toxicity and exposure information for existing chemicals. The intent of the pilot is to gain insight on how best to design and efficiently implement the ultimate program. The VCCEP pilot is structured into three tiers to facilitate decisions on whether more testing or data are needed to adequately characterize the risks to children or prospective parents from selected chemicals. Sponsoring companies or consortia of manufacturers and importers of each chemical volunteer for each tier separately, allowing them to choose whether to participate in subsequent tiers if requested to do so by the U.S. EPA. By volunteering to be sponsors, the companies or consortia agree to collect or develop health effects and exposure information about the chemicals, to integrate this information into a risk assessment that characterizes the risks to children, and to identify potential data needs.

The three tiers of the pilot program increase in scope and sophistication from basic screening level assessments to more refined and robust analyses (see **Figure 1**). The tiered

assessments include four specific components: hazard assessment, exposure assessment, risk assessment, and data needs. For the hazard assessment, the U.S. EPA has identified specific toxicity tests that should be considered for each tier, ranging from acute and genetic toxicity screening tests in Tier 1 to chronic, neurotoxicity, and developmental neurotoxicity studies in Tier 3 (see **Table 2**). The purpose of this tiered approach was to reach a compromise among the various stakeholders and to identify definite points to stop and assess what is known about each chemical before deciding on the need for further testing or data compilation. While a list of toxicity tests was provided for hazard, minimal guidance was provided on how to assess children's exposures. For example, the U.S. EPA (2000b) loosely defines a Tier 1 exposure assessment as representing a "screening level" analysis in which conservative estimates are based on readily available data, and a Tier 2 or 3 exposure assessment as more "advanced" analyses that rely on well-designed monitoring studies or exposure models and include central tendency and high end estimates. A 3-day workshop was held prior to the first VCCEP submission to discuss various approaches for collecting and presenting exposure information under the pilot program, but a standardized approach was not prescribed, allowing sponsors the flexibility to develop their own frameworks (U.S. EPA 2002c). Although the VCCEP is designed in tiers, with increasing complexity of data and analyses, sponsors are expected to use all available data for the Tier 1 assessment.

To provide a wide-ranging scientific review of the sponsor's assessments, each submission must undergo an evaluation and discussion by a peer consultation panel comprised of various independent experts. The peer consultation meetings are open to the public and all interested parties are invited to submit technical comments on the submission for consideration by the sponsors and the peer consultation panel members. The purpose of the peer consultation

is to provide a science-based evaluation of the data needs for each chemical based on the assessment submitted by the sponsor, as well as, the expertise and knowledge of the panel. The results of the peer consultation can assist the sponsor in identifying further evaluation and research, if needed. A non-profit group, Toxicology Excellence for Risk Assessment (*TERA*), has thus far conducted all of the VCCEP pilot peer consultation meetings using a transparent and open process. Specifically, panelist candidates are nominated by various parties (including VCCEP sponsors, the public, and *TERA*), and nominees are screened by *TERA* for potential conflicts of interest and bias. The panel uses a “charge” or list of questions and issues to form the structure for the panel discussions, which is designed to elicit panel members’ opinions about key questions regarding the adequacy of available data and analyses to characterize risks to children and prospective parents. The results of the panel discussions are summarized by *TERA* (2005a) in a meeting report that is made available to the public via the web. Note that a peer consultation does not seek panel consensus; rather, the individual opinions of each panel member are noted in the meeting reports along with areas of agreement and disagreement among panel members. Unlike the traditional peer review process, the peer consultations were designed to elicit more active participation of the various stakeholders.

Following the peer consultation meeting for a chemical, the U.S. EPA reviews the sponsor’s submission and the peer consultation panel’s report and determines whether the information for each chemical is sufficient to adequately characterize the risks to children. If not, additional testing or data are requested and a higher tiered analysis is recommended. This three-step process (sponsor submission, panel review, U.S. EPA evaluation) is repeated for each tier. Note that the sponsors of each chemical volunteer for one tier at a time, so that volunteering for Tier 1 does not obligate them to volunteer for Tier 2 or 3 if data from these subsequent tiers are deemed

necessary. According to the VCCEP framework (2000b), the risk information generated for each chemical will ultimately be disseminated and communicated to the public, and any risks identified as unacceptable will require mitigation.

It is noteworthy that the U.S. EPA conducted a series of stakeholder dialogs during the development of the VCCEP, in which numerous concerns were raised about the structure and implementation of the program. Specifically, individuals and groups representing industry, environmental, public health, and/or animal welfare interests commented on the appropriateness or validity of the chemicals selected, the tiered testing approach, the provision of renewed commitments at each tier, industry's preparation of assessments, and the peer consultation process (U.S. EPA 2005a). The U.S. EPA therefore introduced the VCCEP as a pilot program, so that it could gain insight into how best to design the program and to test the performance of the peer consultation process.

*INSERT FIGURE 1 ABOUT HERE*

*INSERT TABLE 2 ABOUT HERE*

## **CHEMICALS EVALUATED UNDER THE VCCEP**

To date, six chemicals have completed the VCCEP Tier 1 process, while three additional chemicals have been partially completed (i.e., the U.S. EPA has not yet provided a data needs decision for these latter chemicals). The following section provides a brief summary of the current status and findings related to all nine chemicals. This includes the hazard, exposure, risk assessment, and data needs assessments for each chemical as determined by the sponsors, peer consultation panelists, and U.S. EPA. Because our review of each chemical is intended to highlight only the most salient issues from the pilot program (and includes summary data provided directly from the sponsors' documents), it does not include all the findings or opinions

presented or expressed by the sponsors or individual panel members. More details about the VCCEP documents are available from *TERA* (2005a) and the U.S. EPA (2005a).

Note that relatively early in the VCCEP pilot, the peer consultation panels adopted the term “data gaps” in addition to “data needs” to represent two distinct concepts. Specifically, data gaps were defined as areas for which information were not available or where there were significant uncertainties, but which did not necessarily require additional research or data collection in order to adequately characterize children’s health risks. For example, missing data on a particular toxicity endpoint may not have a significant consequence on the results of the risk characterization for a chemical if there is no or very low exposure to the chemical. With a very large estimated margin of exposure, the collection of more data may not change the overall conclusions of the risk assessment, and therefore the missing data on the toxicity endpoint may be identified as a data gap. On the other hand, data needs were defined as data gaps for which additional information would be required before the risks to children could be adequately evaluated.

### ***Vinylidene Chloride***

The vinylidene chloride assessment prepared by the Dow Chemical Company was the first industry submission under the VCCEP pilot (Dow 2002). Vinylidene chloride is used as a chemical intermediate in the production of polymers and other chemicals. It can also be reacted to produce polyvinylidene chloride latex and resin polymers. These production processes consist primarily of closed-system operations in industrial settings. Primary applications include latex for carpet backing, adhesives, and film coatings; flame retardant clothing; food packaging; and water or oil resistant textiles.

The sponsor's submission noted that vinylidene chloride has been extensively studied in a variety of assays and test animals, and multiple studies are available for most Tier 1-3 categories. Several existing hazard benchmarks were identified for this chemical, including the U.S. EPA reference dose (RfD) of 50 µg/kg-day, a benchmark dose limit for liver toxicity (BMDL<sub>10</sub>) of 4600 µg/kg-day, the U.S. EPA reference concentration (RfC) of 200 µg/m<sup>3</sup>, and the California reference exposure level (REL) of 70 µg/m<sup>3</sup>. Four exposure pathways were ultimately considered in the quantitative analysis, including the inhalation of general ambient air, inhalation of indoor air due to residual monomers in carpet backing, ingestion of contaminated water, and ingestion of food from contact with packaging (dermal exposures were considered to be insignificant or irrelevant). During the panel meeting, the sponsor also presented information on potential inhalation of vapors migrating into indoor air of buildings located over contaminated groundwater plumes (this pathway was not presented in the submission document because it is not part of the "chain of commerce" for this chemical). Aggregate exposures based on the four pathways were calculated using "typical" and "high end" estimates, and both a margin of safety (MOS) and margin of exposure (MOE) approach were used to characterize chronic (non-cancer) risks for children and prospective parents (**see Table 3**). The sponsor concluded that vinylidene chloride did not pose a risk to children because exposures were likely to be inconsequential and the hazard data do not suggest any unusual age-related sensitivity. The sponsor also thought the available data were adequate to characterize risks to children.

*INSERT TABLE 3 ABOUT HERE*

A peer consultation panel reviewed the sponsor's Tier 1 submission of vinylidene chloride in January 2003 (*TERA 2003a*). Most panel members concluded that the hazard benchmarks employed in the submission were appropriate, and some panelists thought the

toxicity studies covered essentially all the data sought from the three VCCEP testing tiers. However, some panelists noted that developmental toxicity could not be ruled out because reports of developmental toxicity by Dawson et al. (1990, 1993) indicated cardiac abnormalities in rat pups exposed *in utero*. The results of this work were of unknown significance (and were inconsistent with earlier developmental studies), and some panelists suggested that additional work be considered to resolve these outstanding questions. Some panelists also wanted more information about whether vinylidene chloride and its metabolites cross the placenta and are found in breast milk. Although some panelists questioned whether the life-stages evaluated by the sponsor were sufficient, they acknowledged there did not appear to be specific exposure periods during which children were expected to be especially vulnerable. Additionally, several panelists would have liked more information on the potential for inhalation exposure from contaminated groundwater plumes, but they did not consider it the sponsor's responsibility to generate these data. Despite these data gaps, the panelists were in general agreement that the available data were sufficient to characterize children's risks and none of the panelists identified any data needs for vinylidene chloride.

The U.S. EPA (2005b) issued a data needs decision and data needs assessment document on Dow's VCCEP Tier 1 submission in August of 2005. The U.S. EPA concurred with the sponsor that the existing toxicology database was extensive and covered tier 1 and some studies from tiers 2 and 3. Although the U.S. EPA discussed the Dawson et al. reports and other toxicological data gaps identified by the peer consultation panel in their review, they concluded it was unlikely that additional toxicity data would impact the sponsors' calculations given the relatively large estimated margin of exposure or safety for children. The U.S. EPA did not identify any Tier 2 data needs for this chemical, but did note some issues regarding the

transparency and clarity of Dow's submission document. In particular, the U.S. EPA questioned whether conservative assumptions were made for the carpet exposure scenario and noted that some exposure scenarios and populations of interest were excluded from the analysis without adequate explanation. The U.S. EPA concluded that these concerns were addressed, however, based on supplemental information that was provided by the sponsor after the peer consultation process.

### ***Decabromodiphenyl Ether***

The VCCEP submission for decabromodiphenyl ether was prepared by the American Chemistry Council's Brominated Flame Retardant Industry Panel (ACC 2002).

Decabromodiphenyl ether (also known as decabromodiphenyl oxide) is used as a flame retardant to prevent or delay ignition in flammable materials. The primary applications of this chemical are in electrical and electronic products (television sets, computers, wire and cable) and to a lesser extent in upholstery textiles and fabric. Consumers are expected to have limited direct exposure to decabromodiphenyl ether because it is not sold directly to the public and it is encapsulated in a polymer matrix in all of its applications.

The sponsors' submission indicates that this chemical is poorly absorbed and of minimal toxicity based on extensive mammalian and other testing data. A no observed adverse effect level (NOAEL) of at least 1,000 mg/kg-day was identified for this chemical. Because it was based on more recent data, the sponsors chose to use the oral RfD of 4 mg/kg-day developed by the National Academy of Sciences (NAS) as a hazard benchmark, rather than the U.S. EPA RfD of 0.01 mg/kg-day. The sponsors identified five plausible exposure scenarios that were quantitatively considered in the assessment, including the ingestion of contaminated breast milk from occupationally-exposed mothers (in either chemical manufacturing or electronic

disassembly facilities), the mouthing of electronics or furniture containing decabromodiphenyl ether, and general ambient exposures (including ingestion or inhalation of contaminated air, soil, or food). Aggregate exposures for three scenarios were calculated using “reasonable” and “upper” estimates, and a hazard quotient (HQ) approach was used to evaluate children’s chronic (noncancer) risks (see **Table 4**). The sponsor’s submission did not identify any data needs for decabromodiphenyl ether. Note that a summary of the sponsors’ exposure assessment for decabromodiphenyl ether was recently published by Hays et al. (2003), which was subsequently commented on by Rudel and Newton (2004) in a letter to the editor.

*INSERT TABLE 4 ABOUT HERE*

A peer consultation panel met in April 2003 to review the VCCEP submission on decabromodiphenyl ether (TERA 2003b). In general, the panel members were divided about whether the sponsor’s risk assessment was adequate to characterize children’s health risks, and about half of the panelists identified one or more data needs. In particular, individual panelists noted that there were only a few studies that have evaluated the effects of decabromodiphenyl ether on young animals, and one of these studies found that a single gavage dose given to neonatal mice resulted in behavioral disturbances as the mice matured. Although several panelists did not think additional toxicology studies would change the overall risk characterization in any meaningful way, other panelists did not agree and noted uncertainties in metabolism, the lack of inhalation studies, and possible thyroid toxicity as areas of concern. Most panelists thought the sponsors’ choice of hazard benchmark (the NAS RfD) was appropriate, but some questioned whether this RfD was sufficiently conservative for children because it was based on limited (historical) serum data from adults. During the peer consultation, several new studies on decabromodiphenyl ether in dust and breast milk were also

discussed (these were not available when the sponsor's submission was prepared). Most panelists favored collecting more serum and/or breast milk measurements from the U.S. population to help better assess exposure. Some panelists also thought that decabromodiphenyl ether's persistence in the environment could eventually increase human exposures and decrease safety margins. Some panelists therefore wanted industry emissions to be more thoroughly assessed and more work to be done to identify consumer products that contained decabromodiphenyl ether.

The U.S. EPA (2005c) issued its data needs decision on the VCCEP Tier 1 submission on decabromodiphenyl ether in August of 2005. The U.S. EPA concluded that the Tier 1 assessment was not sufficient to adequately characterize risks to children and requested the sponsors proceed to Tier 2 for this chemical. In particular, the U.S. EPA noted that there were some transparency issues and unaddressed uncertainties in regards to the exposure assessment. Specifically, the U.S. EPA stated that there was a lack of understanding about decabromodiphenyl ether's migration from consumer products and potential to degrade to other substances in the environment. Consequently, the U.S. EPA identified this as a significant exposure data need, and suggested specific test methods and approaches for future fate and transport studies of decabromodiphenyl ether. The U.S. EPA also noted that the polybrominated diphenyl ethers would be included in future National Health and Nutrition Examination Surveys (NHANES), which would provide baseline serum levels for the U.S. population. Although the U.S. EPA did not identify any Tier 2 hazard data needs for decabromodiphenyl ether, they noted that the European Union would be requiring a developmental neurotoxicity assay (which is a Tier 3 study under VCCEP), the results of which may provide further information and fill in the developmental neurotoxicity data gaps for this chemical.

### *Pentabromodiphenyl Ether*

Great Lakes Chemical Company sponsored the VCCEP Tier 1 assessment for pentabromodiphenyl ether (GLCC 2003a). This chemical (also known as pentabromodiphenyl oxide) is another brominated flame retardant that is used almost exclusively as an additive in the manufacture of flexible polyurethane foam for cushions and mattresses. Although the majority of commercial pentabromodiphenyl ether is currently used by the furniture and upholstery industries, a small percentage is used in commercial adhesive products. Pentabromodiphenyl ether was also historically used in a variety of applications, including coatings for specialty textiles, printed circuit board components, hydraulic and oilfield completion fluids, rubber products, automotive and airplane seating cushions, and specialty fire-resistant clothing and carpets.

The sponsor's submission indicated that adequate toxicity data were available for many of the Tier 1, 2, and 3 endpoints for pentabromodiphenyl ether. Three health endpoints were considered of possible relevance for children or prospective parents, and the sponsor identified screening toxicity benchmark values for each endpoint. These included thyroid hormone disruption (0.07 mg/kg-day), thyroid hyperplasia (0.04 mg/kg-day), and liver enzyme induction (0.002 mg/kg-day). Three general sources of exposure were evaluated, including in the workplace, in indoor environments (home, school, office), and the ambient environment (air, soil, foods, human milk). Aggregate exposures were calculated for seven child-specific age groups and adults by modeling the physical characteristics and behaviors of the "reasonably highest exposed individual." A hazard index (HI) approach was used to evaluate chronic (non-cancer) health risks for children and prospective parents (see **Table 5**). The sponsor concluded that estimated exposures were below the benchmark values and that pentabromodiphenyl ether

posed little health risk to children or prospective parents. The sponsor identified several data gaps for pentabromodiphenyl ether, including lack of a chronic bioassay and limited mechanistic studies, but did not believe that filling these data gaps would change the Tier 1 assessment results.

*INSERT TABLE 5 ABOUT HERE*

A peer consultation panel reviewed the VCCEP submission for pentabromodiphenyl ether in June 2003 (*TERA* 2004a). The panelists expressed a wide variety of opinions regarding the adequacy of the available hazard and exposure data for this chemical, and all panel members identified one or more data needs for pentabromodiphenyl ether. While some panel members thought the existing hazard data were adequate for a screening assessment, many members identified areas for which they believed data were insufficient (e.g., metabolism, bioaccumulation, fertility, reproduction, *in vivo* genotoxicity, carcinogenicity, and developmental neurotoxicity). Many panelists also disagreed with the choice of uncertainty factors used to derive the toxicity benchmark values. In the exposure assessment, some members believed that certain population subgroups should have been considered in the overall risk characterization, such as pregnant women and people with iodine deficiency. Several panelists also expressed concern that recent studies in general populations have found blood levels of polybromodiphenyl ether chemicals up to 40 times higher than the high-end exposures estimated in the sponsor's submission. Some panelists believed that environmental levels of pentabromodiphenyl ether were increasing because of increased production and from decomposition and disposal of products containing the chemical. Additionally, a lack of data on half-life and exposure pathways, together with problems differentiating between commercial mixtures and individual

congeners, convinced some panelists that the available information was not sufficient to determine the exposure conditions or the populations of concern.

The U.S.EPA (2005d) issued a data needs decision on the Tier 1 VCCEP assessments for pentabromodiphenyl ether in August of 2005. The U.S. EPA determined that additional data beyond the Tier 1 assessments were needed to characterize the risks to children to this chemical. Specifically, the U.S. EPA raised several data needs for pentabromodiphenyl ether and discussed addressing these within the context of Tiers 2 and 3. For Tier 2, the U.S. EPA recommended that the sponsors undertake a two-generation reproductive toxicity study and include satellite groups to determine body burdens. The U.S. EPA also noted that there is a need to further understand the pathways of human exposure and that there were uncertainties in the sponsor's exposure estimates because of the lack of robust biomonitoring data for the general U.S. population and workers. They suggested using the forthcoming NHANES data with the available body burden data to better understand the pathways of human exposure for pentabromodiphenyl ether. According to the U.S. EPA, the resulting Tier 2 assessment would help determine if other data gaps and questions regarding exposure pathways would need to be addressed in Tier 3.

### ***Octabromodiphenyl Ether***

Great Lakes Chemical Company also sponsored the VCCEP assessment for octabromodiphenyl ether (GLCC 2003b). This chemical (also known as octabromodiphenyl oxide) is another brominated flame retardant that is used almost exclusively as an additive in the manufacture of acrylonitrile butadiene-styrene polymers (which are present in casings for computers, monitors, and other electronic equipment). The majority of commercial octabromodiphenyl ether is used by the electronics and plastic industries, including in flexible polyurethane foam, textile coatings, wire and cable insulation, and electrical and electronic

connectors. A small percentage of octabromodiphenyl ether is also used in other types of polymers.

The sponsors concluded in their Tier 1 submission on octabromodiphenyl ether that adequate toxicity data were available for many of the tiered endpoints for this chemical. The sponsor identified three health endpoints of possible relevance for children or prospective parents: thyroid hormone disruption (0.09 mg/kg-day), reproductive or developmental effects (0.09 mg/kg-day), and liver enzyme induction (0.003 mg/kg-day). The same approaches were used to estimate exposures and non-cancer risks for octabromodiphenyl ether as was done for pentabromodiphenyl ether (**see Table 6**). The sponsors concluded that exposure to octabromodiphenyl ether posed little health risk to children or prospective parents. Although the sponsor identified several data gaps for octabromodiphenyl ether, including the lack of a chronic bioassay and single or multiple generation reproductive toxicity studies, the sponsor did not characterize these as critical or necessarily representing data needs.

*INSERT TABLE 6 ABOUT HERE*

A peer consultation panel reviewed the Tier 1 assessment of octabromodiphenyl ether in June 2003 (*TERA 2004b*). The panel members were divided about whether the sponsors' risk assessment was adequate to characterize children's health risks, and all panel members identified one or more additional data needs for octabromodiphenyl ether. Panel members found the toxicity data for octabromodiphenyl ether to be less than that available for pentabromodiphenyl ether, and they discussed the possibility of using the pentabromodiphenyl ether data to fill some of data gaps on octabromodiphenyl ether. For such data extrapolations to be justified, however, the panel members concluded that the toxicities of the two chemicals must be known to occur via the same mechanism (i.e., thyroid effects). Not all panel members felt that the toxicity

mechanisms of these chemicals were sufficiently understood to support such extrapolations. Many panelists also concluded that the fate of octabromodiphenyl ether was not adequately understood, and like pentabromodiphenyl ether, there was little information available on chemical-specific half-life or exposure pathways. Although some panelists noted that octabromodiphenyl ether was present in the environment at lower levels than pentabromodiphenyl ether (and was less bioaccumulative), other panelists wanted better data on measurements of octabromodiphenyl ether in humans and the environment. Panel members also noted that while octabromodiphenyl ether itself may have a wide margin between estimated exposure and toxicity benchmarks, the toxicities of all the polybrominated diphenyl ethers might be additive. If this is the case, then panelists noted that total exposure to all the polybrominated diphenyl ether chemicals must be better understood before adequate risk characterizations can be done for any one of them.

The U.S.EPA (2005e) issued a data needs decision on the Tier 1 VCCEP assessments for octabromodiphenyl ether during the same time as that of pentabromodiphenyl ether. As was the case for pentabromodiphenyl ether, the U.S. EPA determined that additional data beyond the Tier 1 assessments were needed to characterize the risks to children to this chemical, and recommended that the sponsors undertake a two-generation reproductive toxicity study (including satellite groups to determine body burdens) and use the NHANES data along with the available body burden data to better understand the pathways of human exposure.

### ***Acetone***

The VCCEP assessment on acetone was prepared by the American Chemistry Council Acetone Panel on behalf of six member companies (ACC 2003a). Acetone, which is manufactured primarily as a co-product of phenol production in continuous and enclosed

operations, is a widely used industrial solvent. Industrial applications of acetone include its use in the manufacture of cellulose acetate fibers and as a chemical intermediate in the manufacture of several other chemicals. Acetone is also used in various surface coatings, cleaning fluids, pharmaceutical applications, and adhesives; in the extraction of fats, oils, waxes, and resins from natural products; and as a denaturant for ethyl alcohol. Small quantities of pure acetone are sold directly to consumers. In addition, acetone occurs naturally in a wide variety of foods and is a normal by-product of fatty acid metabolism in humans.

The sponsor's submission reported that all Tier 1, 2, and 3 toxicity studies have been completed for acetone, or its immediate metabolic precursor (isopropanol). Although the U.S. EPA's RfD of 0.9 mg/kg-day for acetone was acknowledged, the sponsors did not rely on this toxicity benchmark because it was below normal daily endogenous production in healthy persons. Instead, the sponsors used toxicity criteria developed by researchers who utilized a physiologically-based pharmacokinetic (PBPK) model to allow for better interspecies and route-to-route extrapolation. This included a lower-bound oral RfD of 8.7 mg/kg-day and an inhalation RfC of 29 ppm. Both endogenous and exogenous exposures to acetone were evaluated by the sponsor. For this latter category, a number of possible exposure pathways were quantified, including inhalation of ambient and indoor air; the consumption of food, water, and human milk; and inhalation and dermal contact with selected consumer products believed to have the greatest potential for exposure. Aggregate exposures were calculated for five age groups (including nursing infants with non-occupationally exposed and occupationally exposed mothers) using "typical" and "upper-bound" estimates for the individual product use scenarios, and a hazard index (HI) approach was used to characterize chronic (non-cancer) risks for children and prospective parents (see **Table 7**). One-day acute and short-term exposures and

risks were also evaluated for dietary exposures (milk) and selected consumer products. Besides noting that endogenously produced acetone is the dominant source of exposure to children, the sponsor concluded that children were not uniquely susceptible to acetone and no significant health risks were associated with children's estimated exposure to this chemical. No additional data needs were identified for acetone by the sponsor.

*INSERT TABLE 7 ABOUT HERE*

A peer consultation panel met in November 2003 to discuss the acetone VCCEP submission (TERA 2004c). A major topic of discussion was the sponsor's recommended PBPK models for acetone and whether isopropyl alcohol could be used to fulfill some of the Tier 2 and 3 data requirements for acetone (most panel members found this latter practice to be acceptable). The panel also discussed the available RfDs as benchmarks and the majority of panel members concluded that using these was questionable because they did not account for endogenous acetone. Although several panelists questioned whether the product-use assumptions used in the exposure assessment were truly worst case, others noted that even if more conservative assumptions had been used, acetone exposures from consumer products would still be below endogenous production. The majority of the panelists concluded that the exposure assessment was sufficient for screening purposes, but a few panelists suggested using the existing exposure data with the PBPK model to estimate exposures in those situations where data do not exist (i.e., *in utero*). No panel members identified any data needs for acetone, but several panelists suggested that the submission would benefit by increased explanation and clarity in some parts.

The U.S. EPA (2005f) issued a data needs decisions for the Tier 1 VCCEP assessment on acetone in August 2005. The U.S. EPA concurred with the sponsor and the peer consultation panel that the available data on acetone were sufficient to characterize the risks to children and

there were no data needs identified for this chemical. The U.S. EPA also agreed with the sponsor that the use of toxicological data on isopropanol and the PBPK models were appropriate in the assessment of acetone. The U.S. EPA did note a few issues related to transparency in the initial Tier 1 assessment, however, but stated that these had been addressed in supplemental materials provided by the Acetone Panel after the peer consultation.

### ***Methyl Ethyl Ketone***

The VCCEP assessment on methyl ethyl ketone was prepared by the American Chemistry Council Ketones Panel on behalf of four member companies (ACC 2003b). Methyl ethyl ketone, which is manufactured in an enclosed continuous process, is a widely used industrial solvent and chemical intermediate. This chemical is also frequently used in the production of various consumer products such as surface coatings, adhesives, printing inks magnetic tapes, and lube oil dewaxing agents. To a lesser extent, methyl ethyl ketone is used in the food industry as an extraction and flavoring agent. In addition, methyl ethyl ketone exists naturally in the environment (from trees, plants, and other organisms), is present in various food groups, and is a naturally occurring human metabolite.

The sponsor concluded that ample toxicity studies have been completed for methyl ethyl ketone or its immediate metabolic precursor (secondary butyl alcohol), which show low acute and repeated dose toxicity. The U.S. EPA's recent oral RfD of 0.6 mg/kg-day and inhalation RfC of 5.0 mg/m<sup>3</sup> were used to evaluate chronic health effects, while an acute NOAEL of 200 ppm developed by NIOSH was used to evaluate potential acute health effects. A number of plausible pathways were evaluated, including the inhalation of ambient and indoor air, ingestion of food and breast milk, and inhalation and dermal exposures from selected consumer products. Potential aggregate exposures were only calculated for chronic and subchronic exposures to

selected consumer products, however. Specifically, exposures were estimated for six age groups actively or passively involved in the chronic or single use of selected consumer products, and both a margin of safety (MOS) and margin of exposure (MOE) approach were used to characterize chronic and acute (non-cancer) risks for children (**see Table 8**). The sponsors noted that the natural presence of methyl ethyl ketone in food is likely to be the greatest source of exposure to methyl ethyl ketone on a daily chronic basis, and concluded that children's exposure from ambient background and consumer product sources posed negligible health risks. No additional data needs for methyl ethyl ketone were identified by the sponsor.

*INSERT TABLE 8 ABOUT HERE*

A peer consultation panel met in February 2004 to review the Tier 1 assessment of methyl ethyl ketone (TERA 2004d). Panelists agreed with using the results from toxicity tests on secondary butyl alcohol to support the dataset on methyl ethyl ketone. Several panelists also thought that the RfD and RfC values used for methyl ethyl ketone were overly conservative. Although many panelists favored the approach that was used in the exposure assessment, some were not satisfied with how the exposure calculations and evaluations were presented for prospective parents or for fetuses. Some panelists noted that potential short-term exposures were not aggregated for all of the target populations. Most panel members also agreed that the exposure assessment could be improved by more clearly presenting the reasons why certain population groups were not individually assessed. In general, panel members concluded that the database was adequate to characterize risks to children for the VCCEP program, and no data needs were identified by any of the panel members for methyl ethyl ketone.

The U.S. EPA (2005g) issued its data needs decision on the Tier 1 methyl ethyl ketone VCCEP assessment in August 2005. The U.S. EPA agreed with the sponsor and the peer

consultation panel that there were sufficient Tier 1 data to characterize the risks to children for methyl ethyl ketone and did not identify any Tier 2 data needs. The U.S. EPA did identify several deficiencies in the initial Tier 1 assessment, however, but stated that these had been addressed in supplemental materials provided by the Ketone Panel after the peer consultation.

### *N-Alkanes (Decane, Undecane, and Dodecane)*

The VCCEP assessment on the n-alkanes was prepared by the American Chemistry Council N-Alkane VCCEP Consortium on behalf of three sponsors (ACC 2004). The three n-alkanes in the VCCEP pilot (decane, undecane, and dodecane) are typically produced as process streams from petroleum distillates in completely closed-systems. These streams generally contain a range of n-alkanes, rather than pure chemicals. The primary use of pure n-alkanes is as a chemical intermediate in the manufacture of linear alkylbenzenes, which are subsequently used in the manufacture of surfactants and detergents. Although a small amount of pure n-alkanes are also used as laboratory reagents, no known consumer products contain pure n-alkanes. The primary applications of the n-alkanes are as constituents in various petroleum products, such as kerosene, jet fuel, home heating oil, and hydrocarbon solvents (e.g., mineral spirits).

The sponsor's submission indicated that complete Tier 1 toxicity data (and much of the Tier 2 and 3 toxicity data) were available for one or more of the individual n-alkanes (i.e., the sponsors treated the three chemicals as a single category given their similarities in chemistry and toxicity). With no existing risk values for the n-alkanes, the sponsor identified an acute NOAEL of 5,000 mg/m<sup>3</sup> and a subchronic NOAEL of 1000 mg/m<sup>3</sup>. The sponsor also relied on a chronic inhalation RfC of 1 mg/m<sup>3</sup> developed by the Total Petroleum Hydrocarbon Criteria Working Group and the proposed occupational exposure limit (OEL) of 1200 mg/m<sup>3</sup> developed by the European Chemical Industry Council. Although several possible exposure routes were

considered, including dermal contact and ingestion of contaminated water or human milk, only the inhalation route was determined to be significant by the sponsor. Three inhalation scenarios were quantitatively considered, including chronic indoor air exposures, short-term exposures from a renovated (painted) home, and occupational exposures during painting or refueling operations at an airport. Exposure estimates for each scenario were calculated based on “representative” and “upper-bound” estimates, and both a margin of safety (MOS) and margin of exposure (MOE) approach were used to characterize chronic and subchronic (non-cancer) risks for children and prospective parents (see **Table 9**). The sponsors concluded that the n-alkanes posed a low risk of harm to infants, children, and prospective parents and there was no suggestion that children are more sensitive to any effects than adults. Although the sponsor recognized that there was a lack of data on infant exposures from occupationally exposed mothers, no additional data needs were identified by the sponsor because of the large estimated margins of safety.

*INSERT TABLE 9 ABOUT HERE*

A panel of experts met for a peer consultation on the n-alkanes VCCEP submission in September 2004 (*TERA* 2005). The panel agreed with the sponsor that it was appropriate to consider decane, undecane, and dodecane as a single category and to use the data from one n-alkane to fill in missing data for another n-alkane. Most panelists also agreed that using the toxicity data from the n-alkanes (alone or in mixtures) was appropriate for assessing chemical hazards, rather than using toxicity data from studies of more complex chemical mixtures (e.g., jet fuel). Many members thought the greatest hazard presented by the n-alkanes was pulmonary aspiration associated with accidental ingestion. Some panelists also noted a lack of data on young animals, while others noted difficulties in understanding some of the exposure or risk

values based on the information presented. A few panelists disagreed with how “upper-bound” exposure was defined and thought that higher levels of exposure should have been considered. Although most panel members did not identify any data needs for the n-alkanes, a few panelists wanted more developmental and neurotoxicity data if further work shows n-alkanes exposures to be greater than has been estimated, and one thought that more information on these chemicals in various consumer products was needed.

Unlike that for the prior six chemicals, the U.S. EPA has not yet issued its data needs decision for the three n-alkanes.

## **DISCUSSION**

The goal of the VCCEP is to ensure that adequate data are available to evaluate the potential health risks of industrial chemicals to children. To date, six chemicals have undergone an initial (Tier 1) assessment by industry sponsors, peer consultation by an independent panel of expert scientists, and data needs decision by the U.S. EPA. Three additional chemicals have undergone a Tier 1 sponsor assessment and peer consultation review, but have not received a data needs decision by the U.S. EPA. As part of the VCCEP, the U.S. EPA (2000b) is expected to evaluate the efficiency and effectiveness of the pilot program and the peer consultation process, but the Agency has not yet begun this process. A number of common themes and issues have emerged during the pilot program’s implementation, however, and the most notable of these are discussed briefly below.

First, as indicated in the various sponsor assessments, extensive toxicity data exist for many of the VCCEP chemicals evaluated to date. Most of the chemicals have toxicity studies that meet the VCCEP Tier 1 requirements, and many chemicals have extensive Tier 2 and 3 testing data. Additionally, nearly all of the initial nine chemicals have existing health benchmarks (such

as RfDs) developed by federal agencies and/or scientific bodies. These benchmarks were used to characterize children's health risks in the sponsors' assessments. Acetone was the only exception; the sponsors developed a new health benchmark for acetone because the existing value was below normal daily endogenous production in humans. Because the first group of chemicals evaluated under the VCCEP pilot has relatively abundant toxicity data, it is not possible to use this experience to determine how the tiered toxicity testing approach will work for data-poor chemicals. This could become a particularly important issue in the future, given the initial (and ongoing) debate about whether or how this type of tiered toxicity testing approach can be used to reliably assess the need for higher tiered studies (ACC 2000, Yokota et al. 2004).

Second, for some chemicals, when information was found to be missing for certain health endpoints, the sponsors identified other appropriate data sets to fill these toxicity data gaps. For example, in the sponsor's evaluation of the n-alkanes, acute oral toxicity data on decane and undecane were used to fill in missing acute toxicity data for dodecane. Other examples include (1) the use of multiple repeated-dose toxicity studies to represent missing immunotoxicity data for vinylidene chloride, (2) the use of toxicity data from a metabolic precursor (isopropanol) to represent missing developmental neurotoxicity data for acetone, and (3) the use developmental toxicity and subchronic toxicity studies to represent missing neurotoxicity data for methyl ethyl ketone (Becker 2004). In these instances, the peer consultation panelists and the U.S. EPA agreed that this was an acceptable approach for filling in data gaps.

Third, it was not surprising to find that the specific exposure pathways and target populations identified for each chemical differed, depending on the chemical's primary uses and applications. However, all of the sponsor assessments included a quantitative or qualitative evaluation of general background or environmental exposures, such as exposures from ambient

air, indoor air, water, soil, food, and/or mothers' milk. Most of the chemical-specific analyses also evaluated potential exposures from specific consumer products considered to be relevant to children and/or prospective parents due to their direct or indirect contact with these products (e.g., paint, nail polish, adhesives, textiles, fabrics, etc.). Because infants and children are key populations of concern under the VCCEP, the potential mouthing of materials such as carpeting, electronics, and furniture, was also considered in several of the sponsors' submissions.

Additionally, some of the chemical assessments examined potential occupational exposures in order to assess the risks to prospective parents or to nursing infants from occupationally exposed mothers. However, this exposure pathway was not included in some chemical risk characterizations if it was deemed insignificant or irrelevant (i.e., vinylidene chloride and methyl ethyl ketone) or if there were insufficient data on the levels in breast milk (i.e., n-alkanes). For the most part, dermal exposures were not quantitatively evaluated in the sponsors' submissions because this was considered to be a negligible exposure route. Of all the exposure pathways considered in the chemical-specific assessments, the inhalation of ambient or indoor air and the ingestion of mother's milk were typically found to account for the greatest contribution to total potential exposure for infants, children, and/or prospective parents (particularly if occupational exposures were identified).

Fourth, although there was some uniformity in the way sponsors identified and screened potentially relevant exposure pathways and receptors, there was a lack of consistency and transparency in the way the exposure assessments were conducted or presented. A variety of approaches were used to calculate childhood exposures, ranging from basic deterministic methods to more sophisticated probabilistic (Monte Carlo) approaches. These varied both within and among the chemical assessments (i.e., different approaches were often used depending on

the exposure pathways). Decisions regarding whether or how to estimate aggregate exposures also differed among the sponsor submissions, with some exposure assessments including all possible pathways and others including only those pathways considered by the sponsors to be significant or relevant. Additionally, a host of qualitative descriptors were applied to the various exposure estimates. For example, measures of central tendency were identified as “average,” “typical,” “reasonable,” or “representative,” while more conservative estimates were identified as “upper,” “upper-bound,” “high end,” or “worst case.” Although these terms were not explicitly defined in many instances, central tendency estimates were typically based on mean or median values, while upper-bound estimates were often based on maximum or 95<sup>th</sup> percentile values (in some instances a combination of “average” and “upper bound” values was used). Regardless of the underlying approach or assumptions, all of the sponsors characterized their exposure estimates as being overly conservative (i.e., likely to over-estimate actual exposure levels). However, for certain chemicals, some panel members strongly disagreed that the exposure assessments were overly conservative. Despite this difference of opinion, the majority of panelists concluded that, for most chemicals, the collection of additional data or analyses would not appreciably affect the outcome of the risk characterization because of the large estimated margins of safety.

Fifth, the sponsors relied on several different approaches or a combination of approaches to estimate children’s non-cancer health risks. These generally included a hazard quotient (HQ) or hazard index (HI) approach, in which estimated exposures were compared to health benchmarks, or a margin of safety (MOS) or margin of exposure (MOE) approach, in which health benchmarks (with or without uncertainty factors) were compared to estimates of exposure. Predicted health risks were expected to be negligible if the estimated HQ or HI was less than

one, or if the MOS or MOE was greater than one or 100, respectively. Although these alternative approaches can sometimes result in different conclusions about risk, this was not an issue in the first set of chemical assessments because estimated exposures were usually found to be well below existing or established health benchmarks. The presentation and discussion of data uncertainties and limitations, and their potential impact on the overall risk characterization, also varied considerably among the sponsor submissions. This lack of consistency in how risks are characterized is typical of many risk assessments that have been conducted over the last 30 years (Williams and Paustenbach 2002).

Sixth, it became clear during the initial peer consultation meetings that a distinction between “data gaps” and “data needs” was necessary. Data gaps were defined as areas for which data were not available or where there were significant uncertainties, but which did not necessarily require additional research or data collection in order to adequately characterize children’s health risks. Not all gaps identified in the hazard or exposure data sets were therefore considered critical or in need of follow-up work. In particular, for those chemicals having large estimated margins of exposure, it was often determined that filling these data gaps was unnecessary because it would have little consequence on the overall conclusions of the risk assessment. On the other hand, data needs were defined as data gaps requiring additional information before the potential risks to children could be adequately characterized, and these were identified within the context of all available information. Although none of the chemical sponsors identified any data needs in their submissions (but there was some discussion of data gaps), some peer consultation panel members identified one or more data needs for the three brominated flame retardants (decabromodiphenyl ether, pentabromodiphenyl ether, and octabromodiphenyl ether). The primary concerns raised by the panelists for these chemicals related to a lack of exposure data for

selected pathways, such as breast milk or consumer products, and limited or questionable data sets regarding toxic endpoints like developmental and reproductive effects. For the remaining six chemicals (vinylidene chloride, acetone, methyl ethyl ketone, decane, undecane, and dodecane), no data needs were identified by either the sponsors or peer consultation panel members.

Seventh, the peer consultation panelists often took a broader view in identifying potential data needs than was originally intended for the VCCEP pilot. Specifically, the panels did not always restrict their assessment of data needs to the specific toxicity testing protocols or types of exposure analyses set forth in the tiered frameworks presented by the U.S. EPA (2000b). For example, panelists often identified higher tiered (Tier 2 or 3) toxicity data in order to evaluate a chemical's hazard. For some chemicals, such as decabromodiphenyl ether, panelists also wanted data on the toxicity of the chemical's metabolite in addition to the chemical itself. The U.S. EPA, however, limited its decisions on data needs to Tier 2 needs only (although they sometimes noted that Tier 3 work may be needed depending upon the results of the Tier 2 work).

Lastly, the chemicals that have been evaluated thus far have not been especially controversial. That is, many of these initial pilot chemicals were found to have a very low hazard potential and the available toxicity data do not indicate that children are uniquely susceptible to any of the chemicals. Additionally, because the primary applications of most of these chemicals are as intermediates in industrial processes, it was determined that there would be limited opportunities for children's exposures to occur. Furthermore, estimated exposure levels for nearly all of the VCCEP chemicals were well below identified health benchmarks, indicating a large margin of safety for children. Therefore, there have not been many instances

in which the sponsors and peer consultation panelists have disagreed substantially regarding the need for additional toxicity or exposure data.

As the VCCEP process continues to evolve, there will be more opportunities to evaluate the usefulness and applicability of the pilot program. For example, upcoming chemicals such as benzene, may elicit more differences of opinion than the first nine chemicals due to greater opportunities for human exposure and/or the presence of cancer endpoints. The VCCEP process also has not yet been tested with chemicals that pose a unique threat to children or that have minimal hazard data. Because the concept of a tiered toxicity approach is not supported by all parties, the use of a tiered approach may become more controversial with subsequent chemical assessments. It is also unknown what impact the pilot program will have on various stakeholders, such as government agencies or industry groups, in terms of data collection and analysis or risk management and communication efforts. Another issue that may require further discussion is whether a more standardized exposure or risk assessment framework should be developed in order to improve the consistency and transparency of future chemical assessments. As indicated, a variety of approaches have been used to conduct and present the chemical-specific assessments in the submissions completed to date, which sometimes makes it difficult to compare the estimates of exposure and risk across the different chemicals.

One of the next steps of the VCCEP process is for the U.S. EPA to evaluate the overall efficiency and effectiveness of the pilot program and the peer consultation process. The pilot introduces a number of concepts that will benefit from an evaluation. In particular, the pilot provides a number of opportunities to evaluate different approaches and concepts to determine the need for further testing and data collection for risk characterization, such as the tiered toxicity testing approach. Sponsors have also relied on various techniques to present exposure and risk

data and lessons can be learned from the approaches that have been used to date. While some might criticize that the incomparable approaches, methods, and findings from the different chemical assessments are detrimental to a better understanding of potential health risks to children, the inability to compare exposure and risk findings is not necessarily a weakness of the VCCEP since one purpose of the pilot was to provide information that better informs decisions regarding data needs. Whether the peer consultation process as designed and implemented is effective and efficient should also be evaluated. Lastly, because the VCCEP pilot is a voluntary program that recruits industry sponsors to prepare risk assessments and identify data needs, there is some concern regarding the ability of industry to prepare objective assessments. These are all factors that will need to be considered and weighed in the U.S. EPA's evaluation of the program. Despite these issues, one of the key promises of the VCCEP pilot is its potential to illustrate how various parties can work together under a voluntary program, and how toxicity and exposure data can be integrated to make decisions regarding the adequacy of risk information for children.

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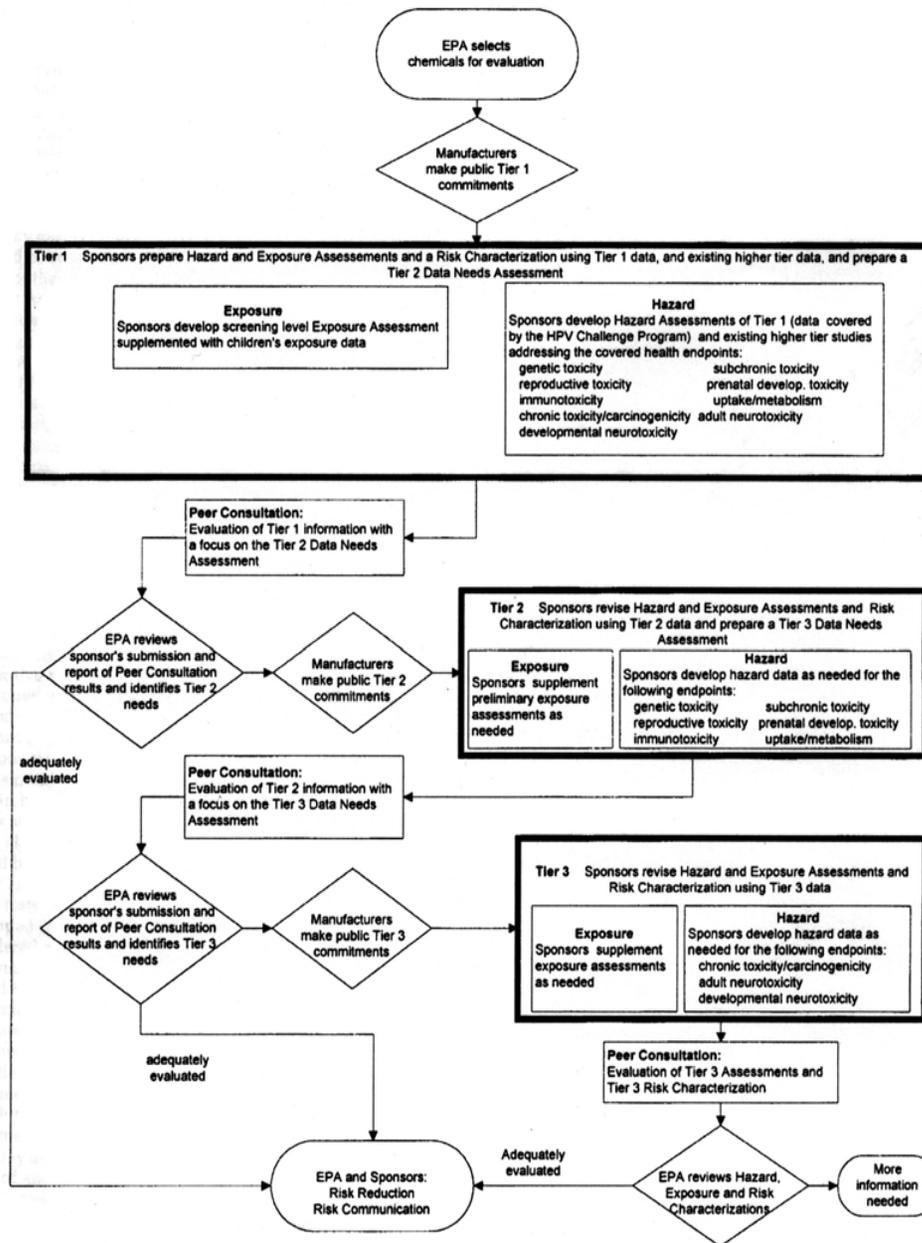
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## Figure Legend

Figure 1. VCCEP Tiered Framework



Source: USEPA 2000b

**Table 1. Status of Sponsored Chemicals in the VCCEP Pilot**

CAS Number	Sponsored VCCEP Chemical	Status of Tier 1 Assessment (Completed)			Sponsor
		Sponsor Submission	Peer Consultation Panel Review	USEPA Data Needs Decisions	
<b><i>First Set of Chemicals Evaluated in Pilot</i></b>					
75-35-4	Vinylidene chloride	X	X	X	Dow Chemical Company ACC Brominated Flame
1163-19-5	Decabromodiphenyl ether	X	X	X	Retardant Industry Panel Great Lakes Chemical
32534-81-9	Pentabromodiphenyl ether	X	X	X	Company Great Lakes Chemical
32536-52-0	Octabromodiphenyl ether	X	X	X	Company
67-64-1	Acetone	X	X	X	ACC Acetone Panel.
78-93-3	Methyl ethyl ketone	X	X	X	ACC Ketones Panel
124-18-5	Decane	X	X		ACC N-Alkane Consortium
112-40-3	<i>n</i> -Dodecane	X	X		ACC N-Alkane Consortium
1120-21-4	Undecane	X	X		ACC N-Alkane Consortium
<b><i>Future Chemicals to be Evaluated in Pilot</i></b>					
71-43-2	Benzene				
106-46-7	<i>p</i> -Dichlorobenzene				
107-06-2	Ethylene dichloride				
108-38-5	<i>m</i> -Xylene				
108-88-3	Toluene				
123-91-1	<i>p</i> -Dioxane				
127-18-4	Tetrachloroethylene				
79-01-6	Trichloroethylene				
80-56-8	<i>a</i> -Pinene				
95-47-5	<i>o</i> -Xylene				
100-41-4	Ethylbenzene				

Source: U.S. EPA 2000b