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State Water Resources Control Board

March 15, 2016

Karl Palmer, Chief
Safer Products and Workplaces Program
Department of Toxic Substances Control
1001 I Street
Sacramento, CA 95814

SUBJECT: REQUEST FOR EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF CHILDREN'S FOAM-PADDED SLEEPING PRODUCTS CONTAINING TRIS (1,3-DICHLORO-2-PROPYL) PHOSPHATE (TDCPP) AND/OR TRIS(2-CHLOROETHYL) PHOSPHATE (TCEP) AS A PRIORITY PRODUCT

Dear Mr. Palmer:

This letter responds to the attached December 10, 2015 request for external scientific peer review for the subject noted above. The review process is described below. All steps were conducted in confidence. Reviewers' identities were not disclosed.

To begin the process for selecting reviewers, I contacted the University of California, Berkeley (University) and requested recommendations for candidates considered qualified to perform the assignment. The University was provided with the December 10, 2015 request letter to me and attachments. No additional material was asked for. This service by the University includes interviews of each promising candidate and is supported through an Interagency Agreement co-signed by Cal/EPA and the University.

Each candidate who was both qualified and available for the review period was asked to complete a Conflict of Interest (COI) Disclosure form and send it to me for review, with Curriculum Vitae. The cover letter for the COI form describes the context for COI concerns that must be taken into consideration when completing the form. "As noted, staff will use this information to evaluate whether a reasonable member of the public would have a serious concern about [the candidate's] ability to provide a neutral and objective review of the work product."

In subsequent letters to candidates approved as reviewers, I provided the attached January 7, 2009 Supplement to the Cal/EPA Peer Review Guidelines, which, in part, serves two purposes: a) it provides guidance to ensure confidentiality through the course of the external review, and b) it notes reviewers are under no objection to discuss their comments with third-parties after reviews have been submitted. We recommend they do not. All outside parties are provided opportunities to address a proposed regulatory action, or potential basis for such, through a well-defined rulemaking process.

Later, I sent each reviewer the material to be reviewed and a detailed cover letter to initiate the review (attached).

Also, attached to the cover letter was the December 10, 2015 request for reviewers to me. Its Attachment 2 was highlighted as the focus for the review. Each reviewer was asked to address each topic, as expertise allows, in the order given. Thirty days were provided for the review. I also asked reviewers to direct enquiring third-parties to me after they have submitted their reviews.

Reviewers' names, affiliations, curriculum vitae, and reviews are being sent to you now with this letter. All attachments can be electronically accessed through the bookmark icon at the left of the screen.

Approved reviewers are as follows:

1. Gary L. Ginsberg, Ph.D.
   Assistant Professor of Community Medicine
   University of Connecticut, M.P.H. Program
   The Exchange
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   Farmington, CT 06032

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2. Heather M. Stapleton, Ph.D.
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   and Sustainable Environmental Management
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3. Lucio G. Costa, PharmD
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If you have any questions, or require clarification from the reviewers, please contact me directly.

Regards,

Gerald W. Bowes, Ph.D.
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State Water Resources Control Board
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Attachments:

(1) December 10, 2015 Request by Karl Palmer for Scientific Peer Review
(2) Letters to Reviewers Initiating the Review
  (a) Gary L. Ginsberg, Ph.D.
  (b) Heather M. Stapleton, Ph.D.
  (c) Lucio G. Costa, PharmD
(3) January 7, 2009 Supplement to Cal/EPA Peer Review Guidelines
(4) Curriculum Vitae
  (a) Gary L. Ginsberg, Ph.D.
  (b) Heather M. Stapleton, Ph.D.
  (c) Lucio G. Costa, PharmD
(5) Reviews
  (a) Gary L. Ginsberg, Ph.D.
  (b) Heather M. Stapleton, Ph.D.
  (c) Lucio G. Costa, PharmD

Attachment 1

Department of Toxic Substances Control

Matthew Rodriquez
Secretary for
Environmental Protection

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Edmund G. Brown Jr.
Governor

TO: Gerald Bowes, Ph.D.
Manager, CalEPA Scientific Peer Review Program
Office of Research, Planning and Performance
State Water Resources Control Board

FROM: Karl Palmer, Chief
Safer Products and Workplaces Program
Department of Toxic Substances Control

DATE: December 10, 2015

SUBJECT: REQUEST FOR EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF CHILDREN'S FOAM-PADDED SLEEPING PRODUCTS CONTAINING TRIS(1,3-DICHLORO-2-PROPYL) PHOSPHATE (TDCPP) AND/OR TRIS(2-CHLOROETHYL) PHOSPHATE (TCEP) AS A PRIORITY PRODUCT

The subject of this review is a proposed regulation to adopt the following product-chemical combination as a Priority Product:

Children's Foam-Padded Sleeping Products Containing Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP).

The California Department of Toxic Substances Control (DTSC) is responding to the Safer Consumer Product regulations[1] that require DTSC to identify product-chemical combinations that pose risks to people or the environment and to adopt them as Priority Products[2] in regulation. Once a Priority Product has been adopted in regulation, manufacturers must take one of the following actions to improve the safety of their products:

- remove or replace the chemical(s) of concern in the product, or
- remove the product from the California marketplace, or

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[1] California Code of Regulations, Title 22, sections 69503 – 69503.7

[2] "Priority Products" are consumer products that a) contain chemicals included in DTSC's Candidate Chemicals List; b) may expose people or the environment to these chemical(s) through normal use; and c) have been adopted in regulation. Candidate Chemicals exhibit hazard traits or environmental or toxicological endpoints and are included on authoritative lists established by government agencies or scientific organizations (www.dtsc.ca.gov/SCP).

- conduct an Alternatives Analyses to determine if safer alternatives exist.

In accordance with Health and Safety Code section 57004, DTSC requests external scientific peer review of the basis for proposing *Children's Foam-Padded Sleeping Products Containing TDCPP and/or TCEP* as a Priority Product. As required by regulation, DTSC reviewed available scientific literature and concluded that this product-chemical combination meets the required regulatory criteria[3] for listing as a Priority Product for the following reasons:

- exposure to the flame retardants, TDCPP and/or TCEP, may contribute to or cause significant or widespread adverse impacts to people, particularly to infants, children, pregnant women, and school and day care workers; and
- people, particularly the sensitive subpopulations noted above, may be exposed to these chemicals through normal use, handling, or disposal of children's foam-padded sleeping products that contain one or both of these chemicals.

For this review, DTSC recommends that reviewers have expertise in the following areas, in order of importance:

- human toxicology associated with flame retardants, and/or
- human exposure assessment.

We estimate that two reviewers will be adequate to cover all needed areas of expertise.

DTSC intends to initiate the formal rulemaking process in January 2016, with a proposed adoption date of August 30, 2016. The documents are ready for review at any time, and the preferred period of review is 60 days. The following attachments are enclosed:

- Attachment 1: Plain English summary of the proposal to Adopt *Children's Foam-Padded Sleeping Products Containing Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP)* as a Priority Product
- Attachment 2: Scientific Conclusions to Be Addressed by Peer Reviewers
- Attachment 3: List of Participants
    - Section A: DTSC Participants
    - Section B: External Participants

Please direct inquiries regarding this request to Lisa Quagliaroli, of my staff, at lisa.quagliaroli@dtsc.ca.gov or 916-445-3077.

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[3] Prior to proposing a product-chemical combination for adoption as a Priority Product, DTSC must ensure that the product-chemical combination meets both of the following criteria: 1) there must be potential public and/or environmental exposure to the chemical(s) in the product; and 2) there must be potential for one or more exposures to contribute to or cause significant or widespread adverse impacts (22CCR section 69503.2(a)).

Attachment 1:

Plain English Summary of the Proposal to Adopt *Children's Foam-Padded Sleeping Products Containing Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP)* as a Priority Product

A. Brief Statement of Conclusions[4]

DTSC identified children's foam-padded sleeping products containing TDCPP and/or TCEP as a Priority Product. This determination was based on a consideration of available, reliable scientific information regarding the potential exposure to TDCPP and/or TCEP in children's foam-padded sleeping products and the potential for these exposures to contribute to or cause significant or widespread adverse human health impacts.

TDCPP and TCEP are semi-volatile compounds used as additive flame retardants that are not chemically bonded to polyurethane foam and are easily released to indoor and outdoor environments. Both TDCPP and TCEP are ubiquitous compounds and have been detected worldwide, including in California, in dust sampled in indoor environments such as homes, offices, and daycare centers. TDCPP and TCEP have been detected in waterways and wastewater treatment influent and effluent in the U.S. and other nations. Further, TDCPP and TCEP have been detected in wildlife such as fish, mussels, and birds.

Both TDCPP and TCEP are known to the State of California to cause cancer, and carcinogenicity has been demonstrated in animal studies for both TDCPP and TCEP. Research studies suggest that TDCPP and TCEP exposure is associated with other hazard traits including reproductive toxicity, neurotoxicity, and kidney and liver toxicity. TDCPP exposure has also been linked to developmental toxicity and endocrine disruption.

Human exposure to TDCPP has been demonstrated by detection in human breast milk, adipose tissue, and seminal plasma, as well as the detection of primary metabolites in urine samples collected from adults, including pregnant women, and children. Human exposure to TCEP has been demonstrated by detection in human breast milk, as well as detection of primary metabolites in adult urine samples. Further, TDCPP has been detected in hand wipe samples from adults and children and TCEP has been detected in hand wipe samples from children, demonstrating an important route for potential exposure to these chemical flame retardants.

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[4] From the "*Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product*". Section X, page 38.

DTSC determined that exposure to TDCPP or TCEP through the normal use of children's foam-padded sleeping products may contribute to or cause significant or widespread adverse health impacts with the greatest risks borne by sensitive subpopulations such as pregnant women, children, infants, and day care center and school employees. This determination is based on the ubiquitous detection of TDCPP and TCEP in indoor and outdoor environments, the hazard traits associated with each compound, and the data showing widespread exposures to both TDCPP and TCEP in adults, children, and wildlife.

B. Overview of the Safer Consumer Products Regulatory Program

The Safer Consumer Products (SCP) program's primary goal is to ensure safer products and healthier lives by reducing and eliminating use of toxic chemicals in consumer products sold in California. DTSC will advance the creation of safer substitutes for hazardous ingredients by asking manufacturers to answer two questions:

- is this chemical necessary?
- is there a safer alternative?

The SCP regulations, implemented on October 1, 2013, specify the process for identifying consumer products that contain hazardous chemicals, evaluating safer alternatives to those chemicals, and eliminating or reducing potential exposures to and adverse impacts from these products.

As required by regulation, DTSC published the initial list of Priority Products on March 13, 2014, and held public workshops throughout California to solicit stakeholder input on the selection of these products. The initial list of Priority Products includes the following product-chemical combinations:

- children's foam-padded sleeping products containing tris(1,3-dichloro-2-propyl) phosphate (TDCPP) and/or tris(2-chloroethyl) phosphate (TCEP),
- paint and varnish strippers containing methylene chloride, and
- spray polyurethane foam systems containing methylene diphenyl diisocyanates.

To be adopted as a Priority Product in regulation, DTSC must show that each product-chemical combination meets the following regulatory criteria:

- the product contains the chemicals of concern to DTSC and is sold in California;
- exposure to these chemicals may cause significant or widespread adverse impacts to people or the environment; and
- exposure to these chemicals may occur through normal use, handling, or disposal of the product.

Once DTSC adopts a Priority Product in regulation, we are authorized to require product manufacturers to take specific actions including:

- removing or replacing the chemical of concern in the product with a safer alternative, or
- removing the product from the California marketplace, or
- conducting an alternatives analyses to determine if safer alternatives exist.

If the product manufacturers do not comply, DTSC is authorized to require importers, assemblers, and/or retailers to stop selling the product in California.

It should be noted that manufacturers are not required to include flame retardants in the products that are the subject of this proposed regulation. Furthermore, flame retardant-free foam is widely available and it offers equivalent performance at a lower cost than foam made with flame retardants. Therefore, DTSC anticipates that manufacturers will choose to remove these chemicals from their products rather than replacing them with other flame retardants, removing their products from the California marketplace, or conducting in-depth alternatives analyses.

C. Overview of the Proposal to Adopt Children's Foam-Padded Sleeping Products as a Priority Product

This is the first Priority Product proposed by DTSC for adoption under the Safer Consumer Products regulatory program and the first proposal of its kind submitted for external scientific peer review. DTSC intends to request external scientific peer review for the two remaining proposed Priority Products noted above by January 2016. Once the Safer Consumer Products Program is fully implemented, DTSC expects to submit new Priority Products for adoption, and for external scientific peer review, on an ongoing basis.

The proposed regulation defines *children's foam-padded sleeping products* as products designed for children, toddlers, babies or infants to nap or sleep on that incorporate polyurethane foam mats, pads, or pillows that contain TDCPP and/or TCEP. The following individual products are included in this definition:

- nap mats,
- soft-sided portable cribs,
- play pens,
- play yards,
- infant travel beds,
- portable infant sleepers,
- bassinets,
- nap cots,

- infant sleep positioners,
- bedside sleepers,
- co-sleepers, and
- baby or toddler foam pillows.

As required by regulation, DTSC considered a number of factors including the hazard traits, toxicological endpoints, and environmental fates associated with TDCPP and TCEP as well as potential adverse impacts to sensitive subpopulations including infants, children and workers from using or handling children's foam-padded sleeping products that contain one or both of these chemicals.

After reviewing the scientific literature and obtaining stakeholder input during several public workshops, DTSC concluded that people, particularly infants and children, are likely to be exposed to TDCPP and/or TCEP from using or handling children's foam-padded sleeping products that contain one or both of these chemicals and these exposures may cause significant or widespread adverse impacts to those exposed due to the following hazard traits and toxicological endpoints:

- For TDCPP: carcinogenicity including liver, kidney, and testicular tumors; genotoxicity including mutations, chromosomal aberrations, and cell transformation; developmental toxicity; reproductive toxicity; endocrine disruption including thyroid abnormalities; neurotoxicity; hepatotoxicity; nephrotoxicity; hematotoxicity; ocular toxicity; dermatotoxicity; and acute toxicity.
- For TCEP: carcinogenicity including kidney and thyroid tumors; genotoxicity including mutations, chromosomal aberrations, and cell transformation; reproductive toxicity; neurotoxicity; hepatotoxicity; and nephrotoxicity;

By concluding that exposures to TDCPP and/or TCEP through the use of children's foam-padded sleeping products could cause harm, DTSC has met the regulatory requirements to adopt this 'product-chemical' combination as Priority Product in regulation. Once this regulation is adopted, DTSC will have the authority to require the manufacturers to determine if there are safer alternatives to these chemicals.

Attachment 2:

Scientific Conclusions to Be Addressed by Peer Reviewers Regarding DTSC's Proposal to Adopt *Children's Foam-Padded Sleeping Products Containing Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP)* as a Priority Product

The statutory mandate for external scientific peer review (Health and Safety Code section 57004) states that the reviewer's responsibility is to determine whether the scientific portion of the proposed regulation is based on sound scientific knowledge, methods, and practices.

DTSC requests that you make this determination for each of the following conclusion statements that constitute the scientific portion of the proposed regulation. An explanatory statement is provided for each conclusion to focus this review.

The subject of this review is a proposed regulation to adopt *Children's Foam-Padded Sleeping Products Containing TDCPP and/or TCEP* as Priority Product under the Safer Consumer Products regulatory framework. This framework requires DTSC to ensure that all product-chemical combinations proposed as Priority Products meet the following criteria:

- the product contains the chemicals of concern to DTSC and is sold in California;
- exposure to these chemicals may cause significant or widespread adverse impacts to people or the environment; and
- exposure to these chemicals may occur through normal use, handling, or disposal of the product.

Following a review of available scientific literature, DTSC concluded that the proposal to adopt *Children's Foam-Padded Sleeping Products Containing TDCPP and/or TCEP* as a Priority Product meets the required regulatory criteria described above and requests that this review focus on the following conclusions:

- exposure to chemical flame retardants, TDCPP and/or TCEP, may contribute to or cause significant or widespread adverse impacts to people, particularly to infants, children, pregnant women, and school and day care workers; and
- people, particularly the sensitive subpopulations noted above, may be exposed to these chemicals through normal use, handling, or disposal of children's foam-padded sleeping products that contain one or both of these chemicals.

The results of DTSC's scientific literature review are presented in the report, "*Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl)*

Phosphate (TCEP) as a Priority Product" completed in June, 2015. **The references listed in the specific sections of this report noted below will be provided on CD(s). DTSC will provide additional references from this report upon request.**

Conclusion #1 -

The hazard information that DTSC relied upon is sufficient to conclude that there is the *potential* for one or more exposures to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these Chemicals of Concern to contribute to or cause significant or widespread adverse impacts to human health.

TDCPP was removed from children's pajamas in the 1970s due to concerns regarding mutagenicity, but it continues to be used in baby and children's products. TDCPP and TCEP are both known to the State of California to cause cancer and exposure to these chemicals is associated with other adverse health effects including kidney toxicity, liver toxicity, neurotoxicity, and reproductive toxicity. In addition, TDCPP has shown evidence of genotoxicity, developmental toxicity, and endocrine toxicity. In biomonitoring studies, TDCPP and TCEP have been found in breast milk and hand wipes from both children and adults while TDCPP and TCEP metabolites have been found in urine from both adults and children. In addition, TDCPP has been found in human fat and seminal fluid and TDCPP metabolites have been found in the urine of pregnant women. These biomonitoring results indicate exposure to both TDCPP and TCEP for sensitive populations including infants, children and pregnant women. TDCPP and TCEP have been detected in dust in homes, offices, daycares, automobiles, hospitals and commercial aircraft, indicating exposure to the chemicals for both the general population and workers. The Consumer Product Safety Commission (CPSC) calculated that adult and children's TDCPP exposures are above the acceptable daily intake for non-cancer health effects. TDCPP and TCEP have both also been measured in surface water, sediments and wildlife.

The sections of the technical report (noted above) that pertain to Conclusion #1 include:

- Section I – Executive Summary, pages 5 – 8,
- Section IV – Hazard Traits, pages 13 – 20,
- Section VI – Potential for TDCPP to Degrade, Form Reaction Products, or Metabolize into Another Candidate Chemical or a Chemical that Exhibits One or More Hazard Traits, pages 22 – 24, and
- Section VII – Adverse Impacts Associated with Structurally/Mechanistically Similar Chemicals, page 25 – 26.

References included in these sections will be provided to the reviewers on CD or DVD as part of this request.

Conclusion #2

The information that DTSC relied upon to evaluate exposures is sufficient to conclude that there is a *potential* for exposure to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these Chemicals of Concern.

TDCPP is a high production volume chemical and is one of the most commonly used flame retardants found in baby products containing polyurethane foam. TCEP is structurally similar to TDCPP and has also been found in baby products containing polyurethane foam. Additive flame retardants are typically added to polyurethane foam at percent levels by weight, are not chemically bonded to polyurethane foam, and have been demonstrated to escape into indoor (and ultimately, outdoor) environments. Exposure to TDCPP and TCEP from polyurethane foam contained in children's foam-padded sleeping products may occur through dermal contact, inhalation, or ingestion (including via hand-to-mouth exposure of contaminated dust that gets onto a child's hands). Due to its ease of release from foam products, TDCPP and TCEP have been detected in dust in homes, offices, automobiles, commercial airplanes, hospitals, and daycare centers worldwide. Human exposure to TDCPP and TCEP through drinking water has also been suggested. TDCPP and TCEP have both also been measured in surface water, sediments and wildlife.

The sections of the technical report (noted above) that pertain to Conclusion #2 include:

- Section I – Executive Summary, pages 5 – 8,
- Section III – Physicochemical Properties, pages 12 – 13,
- Section V – Environmental Fate, pages 21 – 22,
- Section VIII – Exposure Potential of People or Wildlife to TDCPP or TCEP in Children's Foam Padded Sleeping Products, pages 25 – 36, and
- Section IX – Potential Exposure of Sensitive Subpopulations to TDCPP or TCEP, pages 36 – 38.

References included in these sections will be provided to the reviewers on CD or DVD as part of this request.

The Big Picture

Reviewers are not limited to addressing only the specific issues presented above, and are asked to contemplate the following questions.

(a) In reading the staff technical reports and proposed implementation language, are there any additional scientific issues that are part of the scientific basis of the proposed regulation not described above? If so, please comment with respect to the statutory language given above.

(b) Taken as a whole, is the scientific portion of the proposed regulation based upon sound scientific knowledge, methods, and practices?

Reviewers should also note that some proposed regulatory actions may rely significantly on professional judgment where available scientific data are not as extensive as desired to support the statutory requirement for absolute scientific rigor. In these situations, the proposed course of action is favored over no action.

The preceding guidance will ensure that reviewers have an opportunity to comment on all aspects of the scientific basis of the proposed regulation. At the same time, reviewers also should recognize that DTSC has a legal obligation to consider and respond to all feedback on the scientific portions of the proposed regulation. Because of this obligation, reviewers are encouraged to focus feedback on the scientific issues that are relevant to the central regulatory elements being proposed.

Reviewers should also note that DTSC is required to review and revise, as appropriate, the Priority Products List every three years and intends to accept and review additional data as it becomes available for individual Priority Products. The technical report that is the basis for the proposed regulation is therefore seen as providing the best currently-available information for program implementation at this time.

Attachment 3: List of Participants

Section A. California Department of Toxic Substances Control Personnel

Name	Title	Program	Location
André Algazi	Senior Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Tracy Behrsing*	Staff Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Rob Brushia	Research Scientist III	Safer Products and Workplaces Program	Sacramento, CA
Anne Cooper Doherty	Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Lynn Goldman	Attorney	Office of Legal Affairs	Sacramento, CA
Stephanie Hammel*	DTSC Intern	Safer Products and Workplaces Program	Sacramento, CA
Dennis Guo	Research Scientist III	Safer Products and Workplaces Program	Sacramento, CA
Patrick Kerzic	Staff Toxicologist	Human and Ecological Risk Office	Chatsworth, CA
Daphne Molin	Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Lynn Nakayama Wong	Associate Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Karl Palmer	Environmental Program Manager I	Safer Products and Workplaces Program	Sacramento, CA
Christine Papagni	Senior Environmental Scientist	Safer Products and Workplaces Program	Chatsworth, CA
Frank Parr	Senior Industrial Hygienist	Safer Products and Workplaces Program	Chatsworth, CA
Lisa Quagliaroli	Senior Environmental Scientist	Safer Products and Workplaces Program	Sacramento, CA
Eric Sciullo	Staff Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Michael Wade	Senior Toxicologist	Human and Ecological Risk Office	Sacramento, CA
Meredith Williams	Deputy Director	Safer Products and Workplaces Program	Sacramento, CA

* No longer works for DTSC

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Section B. External Participants.

Name	Title	Department / Program	Location
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David Harrington*	Health Educator Consultant III	California Department of Public Health, Occupational Health Branch	Richmond, CA
Sara Hoover	Research Scientist III	Scientific Affairs Division, Office of Environmental Health Hazard Assessment	Sacramento, CA
Gail Krowech	Staff Toxicologist	Scientific Affairs Division, Office of Environmental Health Hazard Assessment	Sacramento, CA
Melanie Marty	Deputy Director	Scientific Affairs Division, Office of Environmental Health Hazard Assessment	Sacramento, CA
Jennifer McNary	Research Scientist	California Department of Public Health, Occupational Health Branch	Richmond, CA
Claudia Polsky	Deputy Attorney General	California Department of Justice	Oakland, CA
Martha Sandy	Supervising Toxicologist	Scientific Affairs Division, Office of Environmental Health Hazard Assessment	Sacramento, CA
Eileen Sheehan	Senior Policy Advisor - Green Chemistry	U.S. Environmental Protection Agency, Region 9	San Francisco, CA
Gina Solomon	Deputy Secretary for Science and Health	California Environmental Protection Agency	Sacramento, CA
Dennis Shusterman	Professor	University of California - San Francisco, School of Medicine	San Francisco, CA

* No longer works for the listed department

Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product

July 2015

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Safer Consumer Products Program

Department of Toxic Substances Control

California Environmental Protection Agency

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Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product

June 2015

I. Executive Summary

The purpose of this document is to illustrate how DTSC identified and prioritized Children's Foam-Padded Sleeping Products with Tris(1,3 dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) for listing as a Priority Product. DTSC conducted an extensive literature review on the associated hazard traits and exposure potential of TDCPP and TCEP and the potential for these chemical flame retardants in children's foam-padded sleeping products to contribute to or cause significant or widespread adverse impacts. This report summarizes the technical information evaluated and presents the conclusions of this evaluation.

A. Summary of Technical Information for TDCPP

TDCPP is a high production volume chemical that is commonly used as an additive flame retardant. TDCPP is a replacement for pentabromodiphenyl ether (pentaBDE) flame retardants in polyurethane foam. The pentaBDE mixture was banned in California in 2006 (California Health and Safety Code section 108922) (OEHHA 2011b). Additive flame retardants are not chemically bonded to polyurethane foam and can migrate into indoor and outdoor environments (Marklund et al. 2003). TDCPP was removed from children's pajamas in the 1970s due to concerns regarding mutagenicity, but it is still used in baby and children's products containing polyurethane foam (Stapleton et al. 2011). Following the national phase-out of pentaBDE flame retardants and California's ban of pentaBDEs in 2006, the use of TDCPP grew significantly in flexible polyurethane foam. TDCPP is currently one of the most commonly used flame retardants found in baby products containing polyurethane foam (Stapleton et al. 2011). Exposure to TDCPP from polyurethane foam contained in consumer products may occur through dermal contact, inhalation, or ingestion of TDCPP-laden dust. Infant and toddler hand-to-mouth behavior plays a significant role in exposure to flame retardants in dust (ATSDR 2012; Stapleton et al. 2014).

TDCPP is known to the State of California to cause cancer (OEHHA 2011a). Evidence of carcinogenicity includes increased incidence of liver and kidney tumors in male and female rats and testicular tumors in male rats (ATSDR 2012; Bio/dynamics 1980; Freudenthal and Henrich 2000; OEHHA 2011b; OEHHA 2012; WHO 1998). TDCPP is metabolized in the body to several compounds that are also known to the State of California to cause cancer (OEHHA 2011b). TDCPP is associated with other adverse health effects including kidney, liver, and testicular abnormalities (ATSDR 2012; OEHHA 2011b). Research has also shown evidence of genotoxicity, developmental toxicity, reproductive toxicity, endocrine toxicity, and neurotoxicity related to TDCPP exposure (see Section IV. Hazard Traits).

In biomonitoring studies, TDCPP has been found in human fat, breast milk and seminal fluid, and metabolites of TDCPP have been detected in urine (Butt et al. 2014; Hoffman et al. 2014; Hudec et al. 1981; LeBel and Williams 1983; LeBel and Williams 1986; LeBel et al. 1989; Sundkvist et al. 2010). TDCPP has also been detected in hand wipe samples taken from children and adults (Hoffman et al. 2015; Stapleton et al. 2014).

TDCPP has been detected in dust in homes, offices, automobiles, commercial airplanes, hospitals, and day care centers in California and other locations around the world (see Section VIII. Exposure Potential). In an air and dust monitoring study of California early childhood education (ECE) facilities[1], TDCPP was detected at higher concentrations in ECE facilities with foam-filled nap mats than those without (Bradman et al. 2014). The U.S. Environmental Protection Agency (U.S. EPA) estimates that children ages one to five years old ingest on average approximately 100-200 mg dust/day. This is as much as five to ten times greater than adults, who on average ingest approximately 20-50 mg dust/day (Stapleton et al. 2009). Further, children have a smaller body mass relative to adults, so their dosage in terms of mg dust/kg of body mass will be even greater compared to adults.

In a Consumer Product Safety Commission (CPSC) staff preliminary risk assessment report, it was calculated that adult and children's TDCPP exposures are above the acceptable daily intake (ADI) of 0.005 mg/kg/day for non-cancer health effects. It was estimated that TDCPP in furniture foam alone exposes adults to twice the ADI, and exposes children to five times the ADI. Further, the cancer risk for a lifetime of exposure to TDCPP-treated foam-filled furniture was estimated to be 300

[1] Bradman's studies use the term ECE facilities which can include home-based child care providers, private for-profit or non-profit preschools, and programs run by government agencies (e.g., preschools in school districts or Head Start) or religious institutions. For the purposes of this document, the term ECE is used when referring to Bradman's studies while the term "day care center" is used for all other study citations.

per million; a substance may be considered hazardous if the lifetime individual cancer risk exceeds one per million. In children, the estimated cancer risk from exposure to upholstered furniture during the first two years of life was 20 per million (Babich 2006).

TDCPP contamination exists in surface water, sediment, and wastewater. TDCPP has been detected in San Francisco Bay waters and sediment (Klosterhaus et al. 2012; SFEI 2013). TDCPP was detected in surface water in more than half of 139 freshwater streams tested across the U.S. including in California (Kolpin et al. 2002). TDCPP was measured in influents, effluents, and sludge of Swedish sewage facilities (Marklund et al. 2005b). TDCPP has also been detected in U.S. laundry wastewater samples from homes, as well as in the influents and effluents from the wastewater treatment plants associated with those homes, thus indicating the release of TDCPP to waterways from wastewater effluent (Schreder and La Guardia 2014).

TDCPP has been detected in samples of fish, mussels, birds, and bird eggs (Evenset et al. 2009; Green et al. 2008; Leonards et al. 2011; Sundkvist et al. 2010; Takahashi et al. 2013).

Based on these factors, DTSC has determined that the potential exposure to TDCPP in children's foam-padded sleeping products may contribute to or cause significant and widespread adverse impacts to human health and the environment within California.

B. Summary of Technical Information for TCEP

TCEP is an organophosphate chemical that is used as an additive flame retardant. TCEP is structurally similar to TDCPP (OEHHA 2011b). Like TDCPP, TCEP can migrate from foam products to indoor and outdoor environments (Marklund et al. 2003). Exposure to TCEP in consumer products containing polyurethane foam may occur through dermal absorption, inhalation, or ingestion of TDCPP-laden dust. Infant and toddler hand-to-mouth behavior plays a significant role in exposure to flame retardants in dust (EC 2009; Stapleton et al. 2014). TCEP has been detected in polyurethane foam in several children's foam-padded products (Stapleton et al. 2011).

TCEP is a carcinogen and reproductive toxicant and is also associated with other potential adverse health effects. TCEP is known to the State of California to cause cancer and is classified by the European Commission as a reproductive toxicant

(ECHA 2012; OEHHA 2011a). Evidence of carcinogenicity includes increased incidence of kidney tumors in male and female rats, while follicular thyroid cancer was increased in rats but not clearly related to chemical exposure (Matthews et al. 1993; NTP 1991). TCEP is classified by the European Commission as a reproductive toxicant (ECHA 2012) Evidence of reproductive toxicity in mice includes decreased number of pups per litter and number of litters per breeding pair, as well as decreased sperm parameters in exposed male mice (Gulati et al. 1991). Research has also shown evidence of kidney toxicity, liver toxicity, and neurotoxicity related to TCEP exposure (EC 2009; Gulati et al. 1991; Matthews et al. 1990; Matthews et al. 1993; NTP 1991).

In biomonitoring studies, TCEP has been detected in human breast milk (Kim et al. 2014; Sundkvist et al. 2010) and metabolites have been found in human urine samples (Hoffman et al. 2014; Schindler et al. 2009). TCEP has also been detected in baby products containing polyurethane foam (Stapleton et al. 2011) and in hand wipe samples taken from children (Stapleton et al. 2014). TCEP has been detected in dust in various indoor environments including homes, offices, and day care centers worldwide (see Section VIII. Exposure Potential).

TCEP contamination in the environment has been documented in multiple studies. TCEP has been detected worldwide in rivers and streams, wildlife, sediment, and Antarctic ice. In California, TCEP has been detected in both drinking and surface waters (see Section VIII. Exposure Potential).

TCEP has been detected in samples of fish, mussels, crabs, birds, and bird eggs (Green et al. 2008; Leonards et al. 2011; Sundkvist et al. 2010).

Based on consideration of these factors, DTSC has determined that there is potential exposure to TCEP from children's foam-padded sleeping products that may contribute to or cause significant or widespread adverse impacts to human health and the environment within California.

II. Identification of the Priority Product and the Chemicals of Concern

DTSC has identified as a Priority Product children's foam-padded sleeping products containing the following Candidate Chemicals: tris(1,3-dichloro-2-propyl) phosphate (TDCPP) and/or tris(2-chloroethyl) phosphate (TCEP).

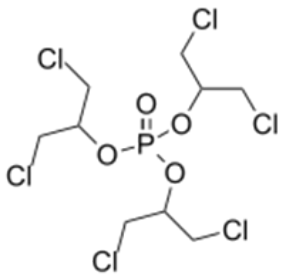
This Priority Product includes the following sleeping products containing polyurethane foam and the additive flame retardants TDCPP and/or TCEP:

- Nap mat
- Soft-sided portable cribs
- Play pen
- Play yard (or playard)
- Infant travel bed
- Portable infant sleeper
- Bassinet
- Nap cot
- Infant sleep positioner
- Bedside sleeper
- Co-sleeper
- Baby or toddler foam pillow

This Priority Product listing does not include: (1) mattresses (as defined and covered by the requirements of CPSC 1632/1633) or products containing mattresses;
(2) upholstered furniture covered by the requirements of California Technical Bulletin 117-2013; and (3) add-on child restraint systems for use in motor vehicles and aircraft that are required to meet federal flammability standards.

A. Tris(1,3-dichloro-2-propyl) phosphate (TDCPP)

- Chemical Abstract Service (CAS) Registry Number: 13674-87-8
- Molecular formula: $C_9H_{15}Cl_6O_4P$
- Chemical structure:



- IUPAC and common names (ATSDR 2012; ChemSpider 2013; ECHA 2014; NRC 2000)

  Chlorinated Tris
  Chloroalkyl phosphate
  1,3-dichloro-2-propanol phosphate (3:1)

Phosphoric acid tris(1,3-dichloro-2-propyl) ester
2-propanol, 1,3-dichloro-, phosphate
Tris(β, β'-dichloroisopropyl) phosphate
Tris(1-chloromethyl-2-chloroethyl) phosphate
Tris(1,3-dichloroisopropyl) phosphate
Tris(1,3-dichloropropan-2-yl) phosphate
Tris(1,3-dichloro-2-propanyl) phosphate
Tris(1,3-dichloro-2-propyl) phosphate
Tris(2-chloro-1-(chloromethyl)ethyl) phosphate
Tris(2,2′-dichloroisopropyl) phosphate
TCCP
TDCP
TDCPP
TDClPP

- Trade names (ATSDR 2012; ChemSpider 2013; ECHA 2014; NRC 2000)

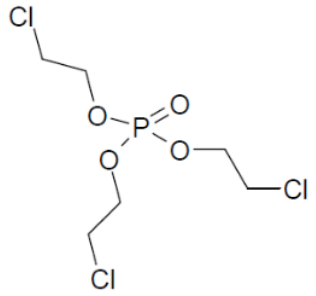
  Amgard
  Amgard TDCP
  Antiblaze 195
  Apex Flame Proof Emulsion 197 or 212
  CRP
  Emulsion 212
  Firemaster T33P
  Foforan Troj-(1,3-dwuchloroizopropylowy) [Polish]
  FR2
  Fyrol FR2
  Fyrol FR-2
  MDL number MFCD00083121
  PF 38
  PF 38/3
  Tolgard TDCP
  Tolgard TDCP MK1

TDCPP meets the conditions specified in California Code of Regulations, Title 22, section 69503.6(a) in that it appears on one or more of the authoritative lists in California Code of Regulations, Title 22, section 69502.2(a)(1) and is a chemical listed in California Code of Regulations, Title 22, section 69502.2(a)(2):

- TDCPP is listed as known to the State of California to cause cancer under Proposition 65 (Safe Drinking Water and Toxic Enforcement Act of 1986) (OEHHA 2011a).
- TDCPP is listed as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014).

B. Tris(2-chloroethyl) phosphate (TCEP)

- Chemical Abstract Service (CAS) Registry Number: 115-96-8
- Molecular formula: $C_6H_{12}Cl_3O_4P$
- Chemical structure:



- IUPAC and common names (ATSDR 2012; EC 2009)

  Ethanol, 2-chloro-, phosphate (3:1)
  Phosphoric acid tris-(2-chlorethyl) ester
  Tri(2-chloroethyl) phosphate
  Trichloroethyl phosphate
  Tris(β-chloroethyl) phosphate
  Tris(beta-2-chloroethyl) phosphate
  Tris(2-chloroethyl) orthophosphate
  Tris(2-chlorethyl) phosphat
  Tris(2-chloroethyl) phosphate
  TRCP
  TCEP

- Trade Names (ATSDR 2012; EC 2009; Stapleton et al. 2011)

  Antiblaze 100
  Celluflex CEF

Disflamoll TCA
Fyrol CEF
Genomoll P
Hostaflam UP810
Levagard EP
Niax 3CF
NIAX flame retardant
Tolgard TCEP
V6 (contains approx. 4.5 – 7.5 % TCEP as an impurity)
Antiblaze V6 (contains approx. 10% TCEP as an impurity)

TCEP meets the conditions specified in California Code of Regulations, Title 22, section 69503.6(a) in that it appears on one or more of the authoritative lists in California Code of Regulations, Title 22, section 69502.2(a)(1) and is a chemical listed in California Code of Regulations, Title 22, section 69502.2(a)(2):

- TCEP is listed as known to the State of California to cause cancer under Proposition 65 (Safe Drinking Water and Toxic Enforcement Act of 1986) (OEHHA 1992).
- TCEP is classified by the European Commission as a reproductive toxicant (ECHA 2012).
- TCEP is listed as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014).

III. Physicochemical Properties

A. Physicochemical Properties of TDCPP

- Physical description: Viscous, clear liquid (HSDB 2015)
- Molecular weight: 430.90 g/mol (ChemSpider 2013; HSDB 2015)
- Density: 1.48 kg/L at 25 °C (HSDB 2015)
- Boiling point: Between 236 and 237 °C at 5 mmHg (HSDB 2015)
- Melting point: 27 °C (OEHHA 2011b)
- Flashpoint: 252 °C (HSDB 2015)
- Octanol/water partition coefficient: log K_{ow} = 3.65 (HSDB 2015)
- Soil organic carbon/water partition coefficient: K_{oc} of 1,100 (estimate) (HSDB 2015)
- Water Solubility: 7 mg/L at 24 °C (HSDB 2015)
- Solubility: Soluble in most organic solvents (HSDB 2015)
- Vapor Pressure: 2.86 x 1^{0-7} mmHg at 25 °C (estimate) (HSDB 2015)

- Henry's Law constant = $2.61X10^{-9}$ atm-m^3/mol at 25 °C (estimate) (HSDB 2015)

B. Physicochemical Properties of TCEP

- Physical description: Clear, transparent low viscosity liquid (ATSDR 2012; HSDB 2014)
- Molecular weight: 285.49 g/mol (HSDB 2015)
- Density: 1.425 g/cm^3 at 20°C (ATSDR 2012)
- Boiling point: 330 °C at 1 atm (ATSDR 2012; HSDB 2014)
- Melting point: -55 °C (ATSDR 2012; HSDB 2014)
- Flash point: 216 °C (ATSDR 2012; HSDB 2015)
- Octanol/water partition coefficient: log K_{ow} = 1.44 (ATSDR 2012)
- Soil organic carbon/water partition coefficient: K_{oc} = 390 (estimate) (HSDB 2014)
- Water Solubility: 7.82 g/L at 20 °C (HSDB 2015)
- Solubility: Insoluble in benzene. Soluble in most organic solvents (HSDB 2015)
- Vapor pressure: 6.125 x 10^{-2} mmHg at 25 °C (ATSDR 2012)
- Henry's Law Constant: 3.3 x 10^{-6} atm-m^3/mol at 25 °C (estimate) (HSDB 2015)

IV. Hazard Traits

A. Hazard Traits of TDCPP

TDCPP exposure has been shown to cause a number of hazard traits including carcinogenicity, genotoxicity, developmental toxicity, reproductive toxicity, neurotoxicity, endocrine toxicity, and hematotoxicity. These are summarized below.

1. Carcinogenicity

a. TDCPP is known to the State of California to cause cancer under California's Proposition 65 law (Safe Drinking Water and Toxic Enforcement Act of 1986) (OEHHA 2011a). Exposure to TDCPP above 5.4 µg/day exceeds the Office of Environmental Health Hazard Assessment's (OEHHA) No Significant Risk Level (NSRL) for TDCPP. The NSRL is the estimated intake per day over a 70-year lifetime that results in a risk of one excess cancer in a population of 100,000 people and for TDCPP is based on liver, kidney, and testicular tumor incidence data in experimental animals (OEHHA 2012).
b. TDCPP is classified as a Category 2 Carcinogen (H351 - Suspected of causing cancer) by the European Chemical Agency (ECHA) Committee for Risk Assessment under Regulation (EC) No 1272/2008 (ECHA 2010; ECHA 2014).

c. A U.S. Consumer Product Safety Commission (CPSC) 2006 staff preliminary risk assessment report on flame retardants concluded that TDCPP is a probable human carcinogen based on evidence in animal studies (Babich 2006).
d. Two-year studies in male and female rats showed statistically significant increases in the incidence of tumors at multiple sites including liver, kidneys, testes, and adrenal gland (ATSDR 2012; Bio/dynamics 1980; Freudenthal and Henrich 2000; OEHHA 2011b; WHO 1998).

2. Genotoxicity

TDCPP has tested positive for genotoxicity in both *in vitro* and *in vivo* assay systems (OEHHA 2011b). Evidence of genotoxicity includes findings of induction of mutations, chromosomal aberrations, and DNA binding in animal assays. Selected genotoxicity studies are summarized below.

a. TDCPP readily bound to DNA and proteins in liver, kidney, and muscle in mice treated intravenously with TDCPP (Morales and Matthews 1980; OEHHA 2011b).
b. Studies in Salmonella strains (TA 97, TA 98, TA1537, and TA 1538) indicate that TDCPP induces frameshift mutations (i.e., a genetic mutation caused by a deletion or insertion in a DNA sequence that shifts the way the sequence is read), with or without metabolic activation (Gold et al. 1978; OEHHA 2011b)
c. Treatment of Salmonella strains TA 100 and TA 1535 (sensitive to base pair substitution mutations) with TDCPP resulted in mutations (Gold et al. 1978; OEHHA 2011b)
d. TDCPP caused an increase in chromosomal aberrations (i.e., any irregularity or abnormality of chromosome distribution, number, structure, or arrangement) *in vitro* in mouse lymphoma and Chinese hamster fibroblast cells, but not in Chinese hamster ovary cells (Brusick et al. 1979; Covance 2004; Ishidate 1983; OEHHA 2011b).
e. In one study, TDCPP weakly induced sister chromatid exchanges (i.e., genetic damage demonstrated by the exchange of genetic material between sister chromatids during mitosis) in mouse lymphoma cells; another study did not reveal such changes (Brusick et al. 1979; OEHHA 2011b; Stauffer 1977).
f. In an *in vitro* rat hepatocyte DNA repair synthesis (UDS) assay TDCPP induced a weakly positive response in the absence of, but not in the presence of, phenobarbital induction (OEHHA 2011b).
g. Studies of TDCPP in *in vitro* mammalian cell assays for gene mutation gave both positive and negative results (ATSDR 2012; Brusick et al. 1979; Inveresk 1985; OEHHA 2011b; Soderlund et al. 1985).

h. TDCPP did not induce mutations in *Saccharomyces cerevisiae* (OEHHA 2011b).

3. Developmental Toxicity

Several recent studies on the effects of TDCPP exposure on embryonic development are summarized below.

a. *In Vitro*
   - An *in vitro* study in PC12[2] cells indicated that TDCPP has the potential to cause developmental neurotoxicity, as evidenced by inhibited DNA synthesis, decreased cell number, and altered neurodifferentiation. (Dishaw et al. 2011).

b. Studies in Zebrafish
   - Exposure of zebrafish embryos to various concentrations of TDCPP resulted in dose-dependent developmental toxicity, including decreased body weight, reduced hatching, reduced survival and heartbeat rates, and increased malformation (e.g., spinal curvature) (Wang et al. 2013).
   - TDCPP exposure resulted in significantly smaller rates of hatching and survival in a dose- and time-dependent manner (Liu et al. 2013a).
   - TDCPP exposure post-fertilization negatively affected zebrafish embryo development and formation. This was demonstrated by increased mortality, inhibited cell rearrangement, delay in epiboly[3], and abnormal fetal development (e.g., short tail, reduced body size, trunk curvature, tail malformations, craniofacial malformations, decreased body length) (Fu et al. 2013; McGee et al. 2012).

c. Studies in Chickens
   - TDCPP exposure in chicken eggs was associated with decreases in head-plus-bill length, embryo mass, and gall bladder size in chicken embryos (Farhat et al. 2013).

[2] PC 12 cells are a clonal cell line derived from a pheochromocytoma of the rat adrenal medulla.
[3] Epiboly is a cell movement that occurs in the early embryo. It is one of many coordinated movements in early embryonic development that allows for dramatic physical restructuring. The movement is generally characterized as being a thinning and spreading of cell layers.

d. Studies in Rats
   - Two studies found that when pregnant rats were exposed to high doses of TDCPP, there were high mortality rates in the pregnant dams, decreased live births, and an increased incidence of fetal death (EC 2008; Kawashima et al. 1983). Maternal toxicity was also demonstrated by decreased body weight and decreased food consumption (EC 2008; Kawashima et al. 1983).
   - One study in rats exposed to TDCPP during pregnancy showed no developmental effects in the offspring at dose levels that significantly reduced weight gain in the dams. However, fetal viability was significantly decreased in high dose rats. Maternal toxicity was noted as increased mortality at the high dose and decreased body weight and decreased food consumption at the mid- and high doses (ATSDR 2012; Stauffer 1981b).

4. Reproductive Toxicity

Some studies suggest that TDCPP exposure may be associated with male reproductive toxicity. Below are summaries of findings from studies that are relevant to male reproductive toxicity; both positive and negative studies are discussed.

a. A 2010 study reported evidence that TDCPP concentrations in house dust may be associated with decreased sperm concentration in men recruited from an infertility clinic (Meeker and Stapleton 2010).
b. A two-year study found a higher incidence of small seminal vesicles and testicular enlargement in male rats treated with TDCPP at the mid- and high-dose as compared to control males (EC 2008; Freudenthal and Henrich 2000; OEHHA 2011b; Stauffer 1981a).
c. Fertility was not affected and significant alterations of sperm were not observed in male rabbits dosed with TDCPP and then mated with untreated female rabbits (Anonymous 1977; ATSDR 2012).
d. No changes in mating behavior, fertility, or sperm quality or quantity were noted in rabbits exposed to TDCPP via oral gavage (Babich 2006; Brandwene 2001; Wilczynski et al. 1983).
e. A 2008 risk assessment by the European Union concluded that there is no concern for male fertility due to TDCPP exposure based on a weight of evidence approach. The report further stated that there is a lack of data regarding female reproductive toxicity related to TDCPP exposure (EC 2008).

5. Endocrine Toxicity

Recent studies using human cells and zebrafish have indicated that TDCPP has the potential to disrupt normal endocrine function, including thyroid abnormalities and alterations in steroid hormone metabolism.

a. TDCPP could potentially disrupt endocrine function through multiple mechanisms, including effects on steroidogenesis or estrogen metabolism, as suggested by studies in human cell lines and zebrafish (Liu et al. 2012; Liu et al. 2013b).
b. Exposure to various concentrations of TDCPP resulted in altered thyroid hormone levels in zebrafish embryos (Wang et al. 2013).
c. Chicken embryos exposed to TDCPP had lower thyroid hormone levels compared to controls (Farhat et al. 2013).
d. Endocrine disruption potential of TDCPP via human nuclear receptors was reported in an *in vitro* study, showing activity against the pregnane X receptor, androgen receptor, and glucocorticoid receptor (Kojima et al. 2013).
e. TDCPP has the potential to induce estrogenic effects as demonstrated in a combination of *in vitro* assays, such as the E-screen and luciferase reporter gene assays in XX cells (Zhang et al. 2014).
f. Concentrations of TDCPP in house dust correlated with decreased concentrations of circulating thyroid hormone in men recruited from an infertility clinic (Meeker and Stapleton 2010).

6. Neurotoxicity

Most studies that assessed neurotoxicity as an endpoint report TDCPP-induced neurotoxicity. Located studies are summarized below.

a. In an *in vitro* study in PC12 cells, TDCPP displayed concentration-dependent neurotoxicity as indicated by inhibited DNA synthesis, decreased cell number, and altered neurodifferentiation. In this study, TDCPP was a more potent neurotoxicant than chlorpyrifos, an insecticide whose use has been restricted since 2001. (Dishaw et al. 2011).
b. Long-term exposure to TDCPP in zebrafish led to reductions of dopamine and serotonin levels in female brains, and downregulation of genes involved in nervous system development[4] in male and female brain tissues (Wang et al. 2015).

[4] Downregulation of nervous system development is any process that stops, prevents, or reduces the frequency, rate or extent of nervous system development, the origin and formation of nervous tissue.

c. Acute exposure to high doses of TDCPP in rats led to clinical signs suggestive of neurotoxicity, such as hyperactivity and convulsions (Babich 2006; Stauffer 1981b).
d. In a two-year dietary study in rats TDCPP did not induce clinical signs or morphological alterations in the brain or spinal cord. In the same study, changes in measured red blood cell cholinesterase levels were inconsistent (ATSDR 2012; Stauffer 1981b).

7. Other Hazard Traits

a. Acute Toxicity - TDCPP also induces non-cancer chronic health effects in animals and is classified as “acutely toxic” under the Federal Hazardous Substances Act (FHSA) regulations. This includes acute oral and dermal toxicity as well as eye irritation (Babich 2006).
b. Hepatotoxicity - An increased incidence of altered hepatocellular foci (i.e., altered liver cells) in high-dose female rats was reported following 24 months of dosing (Bio/dynamics 1980; Freudenthal and Henrich 2000; OEHHA 2011b).
c. Nephrotoxicity - An increased incidence of hyperplasia[5] of the convoluted tubules of the kidney was reported in male and female rats in a two-year study (Bio/dynamics 1980; Freudenthal and Henrich 2000; OEHHA 2011b).
d. Hematotoxicity - Decreases in hemoglobin, hematocrit, and total erythrocyte counts were reported following high dose treatment of TDCPP in male and female rats in a two-year study (Bio/dynamics 1980; Freudenthal and Henrich 2000; OEHHA 2011b).
e. Ocular toxicity - An increased number of sacculations (i.e., pouches) along the course of the retinal arterioles were observed (ATSDR 2012; Stauffer 1981a).
f. Dermatotoxicity - A higher prevalence of dermatitis was reported for TDCPP-exposed workers compared to non-exposed workers in a study submitted to U.S. EPA (ATSDR 2012; EC 2009; Stauffer 1983).

[5] Hyperplasia is the enlargement of an organ or tissue caused by an increase in the reproduction rate of its cells, often as an initial stage in the development of cancer.

B. Hazard Traits of TCEP

TCEP exposure has been shown to cause carcinogenicity, reproductive toxicity, hepatotoxicity, nephrotoxicity, and neurotoxicity. These are summarized below.

1. Carcinogenicity

a. TCEP is known to the State of California to cause cancer under Proposition 65 (Safe Drinking Water and Toxic Enforcement Act of 1986) (OEHHA 1992).
b. The National Toxicology Program (NTP) has concluded that there is clear evidence of carcinogenic activity of TCEP in F344/N rats administered TCEP by gavage (NTP 1991).
c. The International Agency for Research on Cancer (IARC) found that there is limited evidence for carcinogenic activity of TCEP in experimental animals and concluded that TCEP is not classifiable as to its carcinogenicity to humans (IARC 1999a).
d. In a two-year study of rodents administered TCEP by oral gavage, renal tubule adenomas[6] in the kidneys were significantly increased in male rats. Female rats appeared to be relatively more resistant to this effect than males. Cancers that may have been related to TCEP exposure include thyroid follicular cell cancers and mononuclear cell leukemia in rats. Findings in mice were equivocal (Matthews et al. 1993).

2. Reproductive Toxicity

Reproductive toxicity resulting from TCEP exposure has been demonstrated in laboratory animals.

a. TCEP is classified by the European Commission as a reproductive toxicant (ECHA 2012).
b. NTP reported that TCEP treatment in mice adversely affected both the number of pups per litter and number of litters per breeding pair in a continuous breeding protocol. The study found that a number of sperm parameters were decreased in exposed male mice. Adverse impacts on the reproductive capacity of mice were also seen at low doses (Gulati et al. 1991).

[6] An adenoma is a benign tumor of epithelial tissue with glandular origin, glandular characteristics, or both; they have the potential to become adenocarcinomas which are malignant or cancerous.

3. Hepatotoxicity

TCEP exposure resulted in liver toxicity in animal studies.

a. The European Union concluded that liver weight was significantly increased following short and long term oral exposure to TCEP (EC 2009).
b. Liver toxicity was seen in F344/N rats and B6C3F1 mice administered TCEP by gavage. In 14-day exposure studies, increases in female rat liver weights were seen following 16-week exposures, increased liver weights in both sexes of rats and mice were seen (Matthews et al. 1990; NTP 1991).

4. Nephrotoxicity

TCEP exposure resulted in kidney toxicity in animal studies.

a. Significant kidney weight increase was observed in rats following both short- (16 day) and long-term (16-18 weeks) oral exposure to TCEP (EC 2009; NTP 1991).
b. In a two-year study of oral TCEP administration, karyomegaly (i.e., a condition of having an enlarged cell nucleus) was recorded in kidney cells in both sexes of B6C3F1 mice. Rats displayed renal tissue damage in both sexes following repeat exposure (NTP 1991).

5. Neurotoxicity

TCEP-induced neurotoxicity has been shown in animal studies.

a. Neuronal necrosis was seen in rats after both short- and long-term TCEP exposures. The neuronal damage was both dose and sex dependent, with female rats appearing more susceptible than male rats. In some rats, hemorrhages and other neuronal tissue damage were seen (Matthews et al. 1990; Matthews et al. 1993).
b. Brain lesions were identified following both 2 year, 66 week, and 16 week oral TCEP exposure in rats (EC 2009; NTP 1991).

V. Environmental Fate

A. Environmental Fate of TDCPP

TDCPP production and use as an additive flame retardant for polyurethane foams may result in its release to the environment.

1. Air

Based on an estimated vapor pressure of 2.9 x 10^{-7} mmHg at 25 °C and as a function of TDCPP's physical properties, TDCPP volatilizes into the ambient atmosphere, and can adsorb onto dust particles (HSDB 2015). Vapor-phase TDCPP is degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals with an estimated half-life of 21.3 hours. Particulate-phase TDCPP is removed from the atmosphere by wet and dry deposition (HSDB 2015).

2. Soil

In soil, TDCPP is expected to have slight mobility based upon an estimated K_{oc} of 1,100. Volatilization from moist soil surfaces is not expected to be an important pathway for removal of TDCPP based upon an estimated Henry's Law constant of 2.61 x 10^{-9} atm-m^3/mole. Biodegradation is not expected to be an important environmental fate process in soil based upon a 0-4% biological oxygen demand as determined using the Japanese MITI test (HSDB 2015).

3. Water/Sediment

In water, TDCPP is expected to adsorb to suspended solids and sediment based upon its estimated log K_{ow} of 3.6. Volatilization from water surfaces is not expected to be an important environmental fate process based upon TDCPP's estimated Henry's Law constant of 2.6 x 10^{-9} atm-m^3/mole at 25 °C. Limited data suggests that TDCPP will be resistant to hydrolysis in most environmental waters such as ground water, surface water, and drinking water. Bioconcentration factors (BCFs) ranging from 0.3 to 113 suggest that the potential for bioconcentration in aquatic organisms is low to moderate (HSDB 2015).

B. Environmental Fate of TCEP

TCEP production and use as an additive flame retardant for polyurethane foam may result in its release to the environment.

1. Air

Based on a vapor pressure of 6.13 x 10^{-2} mmHg at 25 °C and as a function of TCEP's physical properties, TCEP will volatilize into the ambient atmosphere, and can adsorb onto dust particles. Vapor-phase TCEP will degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an estimated half-life of 16 hrs. TCEP is not expected to be susceptible to direct photolysis by sunlight (HSDB 2015).

2. Soil

In soil, TCEP is expected to have moderate mobility based upon an estimated K_{oc} of 390. Volatilization from moist soil surfaces is not expected to be an important pathway for removal of TCEP based upon an estimated Henry's Law constant of 3.3 x 10^{-6} atm-m^3/mole. Based on results from the Japanese MITI test, biodegradation in soil is not considered an important environmental fate process (HSDB 2015).

3. Water/Sediment

In water, TCEP is expected to adsorb to suspended solids and sediment based upon the estimated K_{oc} of 390. Volatilization from water surfaces is expected to be an important environmental fate process based upon this compound's estimated Henry's Law constant of 3.3 x 10^{-6} atm-m^3/mole. Estimated volatilization half-lives for a model river and model lake are 19 and 140 days, respectively. BCFs ranging from 0.6 to 5.1 suggest bioconcentration in aquatic organisms is low. TCEP may undergo hydrolysis in the environment based on an estimated hydrolysis half-life of 20 days at pH 5 to 9 (HSDB 2015).

VI. Potential for TDCPP to Degrade, Form Reaction Products, or Metabolize into Another Candidate Chemical or a Chemical that Exhibits One or More Hazard Traits

A number of metabolites and putative metabolites of TDCPP have been reported to be carcinogenic or exhibit other hazard traits. The carcinogenic and mutagenic metabolites of TDCPP include 1,3-dichloro-2- propanol, 3-chloro-1,2-propanediol (3-MCPD), 1,3-dichloro-2-propanone, dichloroacetone, epichlorohydrin, and glycidol.

1. Metabolites of TDCPP

a. Diester, bis(1,3-dicholoro-2-propyl) phosphate (BDCPP) (Lynn et al. 1981; Nomeir et al. 1981; OEHHA 2011b; Sasaki et al. 1984).
b. Monoester, 1,3-dichloro-2-propyl phosphate (MDCPP) (Lynn et al. 1981; OEHHA 2011b).
c. 1,3-Dichloro-2- propanol (Lynn et al. 1981; Nomeir et al. 1981; OEHHA 2011b; Ulsamer et al. 1980).
   - Mutagenic (Gold et al. 1978; Lynn et al. 1981; OEHHA 2010a; OEHHA 2011b).
   - Listed as known to the State of California to cause cancer under Proposition 65 (OEHHA 2011a; OEHHA 2011b).
   - Identified as a Group 2B carcinogen (i.e., possibly carcinogenic to humans) by the International Agency for Research on Cancer (IARC) (IARC 2012a).
   - On the DTSC Candidate Chemicals list (DTSC 2014).
     - Hazard trait: Carcinogenicity
d. 3-MCPD (ATSDR 2012; Nomeir et al. 1981; OEHHA 2011b).
   - Mutagenic (OEHHA 2010b; OEHHA 2011b).
   - Listed as known to the State of California to cause cancer under Proposition 65 (OEHHA 2011a; OEHHA 2011b).
   - Identified as a Group 2B carcinogen (i.e., possibly carcinogenic to humans) by IARC (IARC 2012b).
   - On the DTSC Candidate Chemicals list (DTSC 2014).
     - Hazard trait: Carcinogenicity

2. Proposed metabolite of TDCPP

a. 1,3-Dichloroacetone (aka 1,3-dichloro-2-propanone) (Gold et al. 1978; Nomeir et al. 1981; OEHHA 2011b).
   - Strong, direct-acting mutagen (Gold et al. 1978; OEHHA 2011b).

3. Metabolites of 1,3-dichloro-2- propanol

a. 1,3-Dichloroacetone (OEHHA 2010a; OEHHA 2011b).
   - Mutagen and tumor initiator (OEHHA 2010a; OEHHA 2011b).
b. Epichlorohydrin (OEHHA 2010a; OEHHA 2011b).
   - Listed as known to the State of California to cause cancer under Proposition 65 (OEHHA 2011a; OEHHA 2011b).
   - Identified as a Group 2A carcinogen (i.e., probably carcinogenic to humans) by IARC (IARC 1999b).

- On the DTSC Candidate Chemicals list (DTSC 2014).
  - Hazard traits: Carcinogenicity, ocular toxicity, reproductive toxicity, respiratory toxicity

4. Metabolites of 3-MCPD

a. Glycidol (OEHHA 2010b; OEHHA 2011b).
   - Listed as known to the State of California to cause cancer under Proposition 65 (OEHHA 2011a; OEHHA 2011b).
   - Identified as a Group 2A carcinogen (i.e., probably carcinogenic to humans) by IARC (IARC 2000).
   - On the DTSC Candidate Chemicals list (DTSC 2014).
     - Hazard traits: Carcinogenicity, reproductive toxicity

b. β-Chlorolactaldehyde (OEHHA 2011b).

VII. Adverse Impacts Associated with Structurally/Mechanistically Similar Chemicals

DTSC may also evaluate and consider the adverse impacts associated with structurally or mechanistically similar chemicals for which there is a known toxicity profile. The compounds listed below have been identified as structurally similar to TDCPP and TCEP (OEHHA 2011). Each of these compounds can be used as a flame retardant. Research studies have demonstrated similar hazard traits and exposure potential for TDCPP, TCEP, and tris(2,3-dibromopropyl) phosphate (TDBPP aka Tris). While long term carcinogenicity studies have not been conducted on tris(1-chloro-2-propyl) phosphate (TCPP), it is structurally similar to TDCPP and TCEP, has demonstrated genotoxicity in *in vitro* studies, and is listed on DTSC's Candidate Chemicals list.

1. Tris(2,3-dibromopropyl) phosphate (TDBPP; Tris) - a brominated analogue of TDCPP

a. Carcinogenic in rats and mice (Gold et al. 1978; IARC 1999b; OEHHA 2011b).
b. Listed as known to the State of California to cause cancer under Proposition 65 (DTSC 2014; OEHHA 2011a).
c. Identified as a 2A Carcinogen by IARC (DTSC 2014; IARC 2015).
d. Listed as *reasonably anticipated to be a human carcinogen* in the National Toxicology Program's 12th Report on Carcinogens (DTSC 2014; NTP 2010).
e. Identified as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014; DTSC 2014).

f. Genotoxic *in vitro* and *in vivo* (Blum and Ames 1977; Gold et al. 1978; IARC 1999b; OEHHA 2011b).
g. On the Candidate Chemicals list (DTSC 2014).
h. Causes sterility in animals (Blum et al. 1978; Gold et al. 1978).
i. Absorbed through human skin (Gold et al. 1978).

2. Tris(1-chloro-2-propyl) phosphate (TCPP) – a chlorinated phosphate triester

a. Genotoxic in *in vitro* but not *in vivo* assays (EC 2008; OEHHA 2011b).
b. Has not been tested in long-term studies for carcinogenicity (OEHHA 2011b).
c. On the Candidate Chemicals list (DTSC 2014).
d. Identified as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014; DTSC 2014).

VIII. Exposure Potential of People or Wildlife to TDCPP or TCEP in Children's Foam-Padded Sleeping Products

Pursuant to the SCP Regulations, DTSC may draw from a large number of information sources to evaluate exposure including, but not limited to, biomonitoring data, market share data, data on the volume of a chemical or product in commerce, the physicochemical properties of the chemical under evaluation, data indicating a chemical's presence in household dust, on interior surfaces, indoor air, drinking water, surface waters or sediments, or data showing a chemical to be present in (or released from) products present in homes, schools, or places of employment. In evaluating the potential for exposure to TDCPP or TCEP in children's foam-padded sleeping products, DTSC considered the factors below.

A. Exposure Potential to TDCPP in Children's Foam-Padded Sleeping Products

1. Routes of Exposure

a. Routes of exposure include inhalation, ingestion, and dermal absorption (ATSDR 2012).
b. Children's overall exposure to flame retardants may be influenced by their hand-to-mouth behavior (Stapleton et al. 2014).
c. Both inhalation and dust ingestion have been identified as important routes of exposure (Babich 2006; Stapleton et al. 2014).
d. TDCPP is readily absorbed through skin and the gastrointestinal tract in laboratory animals (Nomeir et al. 1981).

e. Occupational exposure to TDCPP may occur through dermal contact and inhalation at workplaces where TDCPP is produced or used (HSDB 2015).
f. Monitoring data indicate that the general population may be exposed to TDCPP via ingestion of drinking water (HSDB 2015).
g. Adult exposures to TDCPP have been confirmed by detection of TDCPP in breast milk (Kim et al. 2014; Sundkvist et al. 2010) and hand wipe samples (Hoffman et al. 2015), and the detection of urinary metabolites (Butt et al. 2014; Hoffman et al. 2014).
h. Children's exposures to TDCPP have been confirmed by hand wipe samples (Stapleton et al. 2014) and detection of urinary metabolites (Butt et al. 2014).
i. Infant exposure has been confirmed through by detection of TDCPP in breast milk (Kim et al. 2014; Sundkvist et al. 2010).
j. Presence of TDCPP contamination in surface water and wildlife has been confirmed in California and in several countries (Evenset et al. 2009; Kim et al. 2007; Klosterhaus et al. 2012; Kolpin et al. 2002; SFEI 2013; Sundkvist et al. 2010).

2. Market Presence

a. TDCPP is a high production volume chemical (OEHHA 2011b; U.S. EPA 2006). Approximately 10 to 50 million pounds/year of TDCPP is produced in the U.S. (U.S. EPA 2013).
b. TDCPP is one of the most widely used flame retardants in polyurethane foam (Markets and Markets 2012).
c. Chlorinated flame retardants such as TDCPP are widely used in infant products (Markets and Markets 2012).
d. The global market for chlorinated flame retardants was estimated at approximately 360 million pounds in 2011 and is expected to reach approximately 440 million pounds by 2017 (Markets and Markets 2012).
e. Several manufacturers in China list TDCPP on their websites as one of multiple flame retardant chemicals available for purchase.
f. In a survey of 63 U.S. companies that manufacture or import and distribute infant products, approximately 1.8 million play yards and greater than 2 million play yards were sold in 2011 and 2012 in the U.S., respectively. Approximately 500,000 and 570,000 cradles and bassinets were sold in the U.S. in 2011 and 2012, respectively (JMPA 2013).

3. Studies on the Presence of TDCPP in Foam-Padded Products

a. TDCPP was the most common flame retardant detected in a study which analyzed 101 polyurethane foam samples from commonly used baby

products in the U.S. including sleep positioners, portable mattresses, nursing pillows, baby carriers, high chairs, car seats, changing table pads, and baby walkers (Stapleton et al. 2011).

b. The Center for Environmental Health (CEH) had foam samples from 24 children's nap mats analyzed for flame retardants. TDCPP was detected in 9 of the 24 nap mats (Cox 2013).

4. Containment of the Chemical of Concern within the Product

a. TDCPP in polyurethane foam is not chemically bonded to the foam and can migrate into air and dust throughout the lifetime of the product. Losses to the environment may occur through volatilization, leaching, or abrasion (Marklund et al. 2003). TDCPP can also migrate to the surface of the product where people can be dermally exposed

5. Studies on the Presence of TDCPP in Indoor Dust and Air

a. Flame retardant concentrations were measured in air and dust from 40 California ECE facilities. Detected concentrations of TDCPP in dust were higher in ECE facilities where foam nap mats were used compared to ECE facilities where foam nap mats were not used. Levels of TDCPP were higher indoors compared to outdoors. Child TDCPP exposure estimates in this study exceeded the age-adjusted NSRL for carcinogenicity in 51% of the facilities for children less than six years old (Bradman et al. 2014; Bradman et al. 2012).
b. TDCPP has been detected in indoor dust samples from multiple locations in the United States and abroad including homes, offices, hotels, retail spaces, automobiles, and commercial airplanes (Abdallah and Covaci 2014; Ali et al. 2012a; Ali et al. 2012b; Allen et al. 2013; Bergh et al. 2011; Brandsma et al. 2014; Brommer et al. 2012; Cao et al. 2014; Carignan et al. 2013; Dirtu et al. 2012; Dodson et al. 2012; Hoffman et al. 2015; Marklund et al. 2003; Marklund et al. 2005a; Meeker and Stapleton 2010; OEHHA 2011b; Schreder and La Guardia 2014; Staaf and Ostman 2005; Stapleton et al. 2009; Takigami et al. 2009; Van den Eede et al. 2011).
c. In a study of 30 homes in North Carolina in which children ages 2-5 lived, TDCPP was detected in 100% of house dust samples (Stapleton et al. 2014).
d. In a study of dust collected from 16 homes in California in 2006 and 2011, TDCPP was detected at concentrations higher than previously reported in the U.S. (Dodson et al. 2012).
e. TDCPP was detected in the dust from 96% of the homes included in a study of 50 homes in Boston, MA (Stapleton et al. 2009).

f. In a study conducted in Sweden, TDCPP was detected in dust and air samples taken from homes, day care centers, hospitals, and offices (Marklund et al. 2003).
g. TDCPP was detected in air and dust samples taken from day care centers, workplaces, and homes in Sweden. The air concentrations of TDCPP were approximately 2-8 times higher in day care centers and workplaces than in homes (Bergh et al. 2011).

6. Studies on the Presence of TDCPP in Hand Wipe Samples

a. In a study of 30 North Carolina homes, hand wipe samples were taken from 43 children ages 2-5 years old and 96% contained TDCPP. Further, higher levels of flame retardants detected in house dust were consistently associated with higher hand wipe levels (Stapleton et al. 2014).
b. In a study of indoor exposure to TDCPP in North Carolina homes, TDCPP was detected in 90.6% of hand wipe samples taken from 53 adults (Hoffman et al. 2015).

7. Biomonitoring

a. TDCPP is listed as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014).
b. TDCPP collects in adipose (fat) tissue (CECBP 2008). TDCPP has been detected in adipose tissue (LeBel and Williams 1983; LeBel and Williams 1986; LeBel et al. 1989) and in human seminal plasma (Hudec et al. 1981).
c. TDCPP has been detected in the lipids of human breast milk in Sweden (Sundkvist et al. 2010).
d. TDCPP was detected in human breast milk in Japan (Kim et al. 2014).
e. The primary metabolite of TDCPP, BDCPP, was detected in 38 out of 39 urine samples from a cohort of pregnant women in North Carolina (Hoffman et al. 2014).
f. BDCPP was detected in 100% of urine samples taken from 21 mother-toddler pairs (Butt et al. 2014). Further, BDCPP urinary levels in children were 4.9 times those of the mothers (Butt et al. 2014), suggesting that children had greater exposure to TDCPP, or a greater dose due to their smaller body mass.
g. BDCPP was detected in 94% of urine samples taken from 16 adults living in northern California homes (Dodson et al. 2014).
h. BDCPP was detected in urine samples taken from 7 men in the U.S. over the course of 3 months. TDCPP in house dust was measured in the same study and a correlation between urinary BDCPP and TDCPP concentrations in

house dust was noted. This study concluded that house dust may be an important source of exposure to TDCPP (Meeker et al. 2013).

8. Human Exposure Estimates

a. The U.S. EPA estimates that children ages 1-5 ingest an approximate average of 100-200 mg dust/day, whereas adults ingest an approximate average of 20-50 mg dust/day (U.S. EPA 2002).
b. The calculated cumulative average exposure to flame retardants from dust is 1.6 µg/day for children and 0.325 µg/day for adults (Stapleton et al. 2009).
a. An analysis of potential dust exposures to several flame retardants, including TDCPP, suggests that an adult consumer may be exposed to a median concentration of 0.05 ng TDCPP/kg bw/day and a toddler may be exposed to a median concentration of 0.73 ng TDCPP/kg bw/day using mean dust ingestion assumptions Infant exposure has been confirmed through by detection of TDCPP in breast milk (Kim et al. 2014; Sundkvist et al. 2010).
c. (Ali et al. 2012a). Thus, children may be receiving much higher exposures to TDCPP than adults due to ingestion of dust.
d. Stapleton et al. have predicted that infants may receive greater exposure to TDCPP from products containing polyurethane foam than the average child or adult receives from upholstered furniture. Infants have smaller body mass than adults, and spend a greater portion of their time in intimate contact with foam-padded sleeping products (Stapleton et al. 2011).
e. It has been estimated that children's exposure to TDCPP from treated furniture foam is five times higher than the ADI for non-cancer endpoints (Babich 2006). Scrap foam from furniture is sometimes used in children's foam-padded sleeping products.
f. It has been estimated that the cancer risk for a lifetime of exposure to TDCPP-treated upholstered furniture is 300 per million. In children, the estimated cancer risk from exposure to upholstered furniture during the first two years of life is 20 per million (Babich 2006). Consumer Product Safety Commission (CPSC) staff considers cancer risks greater than one in a million relevant for regulatory consideration (Babich 2006).

9. Potential for the Chemical of Concern to be Released into Environmental Media

Published reports indicate that TDCPP has been found in wastewater treatment plant influent and effluent, laundry waste water, surface water, drinking water, sediment, and wildlife.

a. TDCPP in Water

- TDCPP has been detected in San Francisco Bay waters and sediment. Further, TDCPP is relatively abundant in San Francisco Bay sediment, with concentrations comparable to those of polybrominated biphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in the same samples (Klosterhaus et al. 2012; SFEI 2013). PBDEs and PCBs have been banned or phased out of production due to their environmental persistence and high concentration levels previously detected in the environment.
- TDCPP has been detected in surface water in over half of 139 freshwater streams studied across the U.S., including streams in California, suggesting significant releases of TDCPP to the environment (Kolpin et al. 2002; OEHHA 2011b).
- Samples from Lake Mead, NV have been found to contain TDCPP and other organophosphorus compounds. There was evidence to suggest that the water infiltrated into the sediment had a different chemical composition than the rest of the water column and could be a potential exposure risk to bottom-dwelling aquatic organisms (Alvarez et al. 2012).
- TDCPP has been detected in river water, drinking water, treated wastewater, and influents, effluents, and sludge of sewage treatment facilities (Andresen et al. 2004; Green et al. 2008; Marklund et al. 2005b; Martinez-Carballo et al. 2007; OEHHA 2011b; Rodil et al. 2012; Stackelberg et al. 2004).
- TDCPP was detected in 100% of household laundry wastewater samples taken from 20 Washington state homes, as well as in influents and effluents of two wastewater treatment plants associated with those homes (Schreder and La Guardia 2014), indicating the release of TDCPP to waterways from effluent.
- Precipitation and in storm water runoff samples in Germany were found to contain TDCPP; however, the concentrations of TDCPP were below the analytical limit of detection in several precipitation samples (Regnery and Puttmann 2010).
- TDCPP has been detected in groundwater and surface water sources used for drinking water at very low concentration levels, typically below the analytical reporting limit (Barnes et al. 2008; Focazio et al. 2008; Schaider et al. 2014).
- In a 2006 study in Germany, TDCPP was detected in surface water used for drinking; however, after the water went through the purification process, it was detected at very low concentrations (Andresen and Bester 2006).

b. TDCPP in Sediment
   - TDCPP was found in sediments from Taihu Lake, one of the largest freshwater lakes in China (Cao et al. 2012).
   - Bottom sediment in Lake Mead, NV contained TDCPP (Alvarez et al. 2012).

c. TDCPP in Leachate
   - Leachate from a solid waste disposal site near Osaka, Japan was found to contain TDCPP (Kawagoshi et al. 2002).

d. TDCPP in Wildlife
   - TDCPP has been detected in fishes, mussels (Evenset et al. 2009; Green et al. 2008; Takahashi et al. 2013) and bird blood/plasma and eggs in Norway (Leonards et al. 2011; Takahashi et al. 2013).
   - In Sweden, TDCPP has been detected in freshwater fishes from lakes close to emission sources (Sundkvist et al. 2010; Takahashi et al. 2013).

B. Exposure Potential of TCEP in Children's Foam-Padded Sleeping Products

1. Routes of Exposure

b. Occupational exposure to TCEP may occur through inhalation and dermal contact with this compound at workplaces where TCEP is produced or used (HSDB 2015).
c. A 2009 risk assessment identified inhalation, ingestion, and dermal absorption as potential routes of occupational and consumer exposure to TCEP (EC 2009).
d. Monitoring data indicate that the general population may be exposed to TCEP via inhalation of ambient air, ingestion of contaminated food and drinking water, and dermal contact with consumer products containing TCEP (HSDB 2015).
e. Children's overall exposure to flame retardants may be influenced by their hand-to-mouth behavior (Stapleton et al. 2014).
f. The presence of TCEP in surface water and wildlife has been confirmed in several countries (van der Veen and de Boer 2012).
g. Adult exposures have been confirmed by detection of TCEP in human breast milk (Kim et al. 2014; Sundkvist et al. 2010) and the detection of urinary metabolites (Dodson et al. 2014; Schindler et al. 2009).

h. Children's exposures to TCEP have been confirmed by hand wipe samples (Stapleton et al. 2014).
i. Infant exposure has been confirmed through by detection of TCEP in breast milk (Kim et al. 2014; Sundkvist et al. 2010).

2. Market Presence

a. Production volume for TCEP of 500,000-1,000,000 lbs. was reported to the US EPA in 2006 under the Inventory Update Rule (TOXNET 2014).
b. Global production appears to have peaked with 1.8 million pounds produced in 1989 and declining amounts in subsequent years (WHO 1998).
c. TCEP is no longer produced within the European Union, as of 2009 (EC 2009).
d. Chlorinated flame retardants such as TCEP are widely used in infant products (Markets and Markets 2012).
e. The global market for chlorinated flame retardants was estimated at approximately 360 million pounds in 2011 and is expected to reach approximately 440 million pounds by 2017 (Markets and Markets 2012).
f. Several manufacturers in China list TCEP as one of multiple flame retardant chemicals available for purchase on their websites.
g. In a survey of 63 U.S. companies that manufacture or import and distribute infant products, approximately 1.8 million play yards and greater than 2 million play yards were sold in 2011 and 2012 in the U.S., respectively. Approximately 500,000 and 570,000 cradles and bassinets were sold in the U.S. in 2011 and 2012, respectively (JMPA 2013).

3. Studies on the Presence of TCEP in Foam-Padded Products

a. Analysis of multiple consumer products has identified TCEP in sleep positioners, portable mattresses, nursing pillows, baby carriers, children's car seats, changing table pads, and infant bath mats (Stapleton et al. 2011).

4. Containment of the Chemical of Concern within the Product

a. TCEP in polyurethane foam is not chemically bonded to the foam and can migrate into air and dust throughout the lifetime of the product. Factors such as volatilization, leaching, or abrasion may contribute to this (Marklund et al. 2003). TCEP can also migrate to the surface of the product where people can be dermally exposed.

5. Studies on the Presence of TCEP in Indoor Dust and Air

a. Flame retardant concentrations were measured in air and dust from 40 California ECE facilities. Detected concentrations of TCEP in dust were higher in ECE facilities where foam nap mats were used compared to ECE facilities where foam nap mats were not used. Levels of TCEP were higher indoors compared to outdoors (Bradman et al. 2014).
b. Multiple indoor locations were sampled in the Stockholm area of Sweden, and TCEP was detected in home, work, and day care environments. Samples taken from day care centers had the highest TCEP concentrations among the indoor environments (Bergh et al. 2011).
c. In a study exploring associations of flame retardants in children's hand wipes to house dust, TCEP was found in both dust and hand wipe samples (Stapleton et al. 2014).
d. TCEP has been detected in indoor dust samples from multiple locations in the United States and abroad including homes, hotels, offices, retail spaces, and automobiles (Abdallah and Covaci 2014; Ali et al. 2012a; Ali et al. 2012b; Bradman et al. 2014; Brandsma et al. 2014; Brommer et al. 2012; Cao et al. 2014; Dirtu et al. 2012; Dodson et al. 2012; Ingerowski et al. 2001; Marklund et al. 2003; Schreder and La Guardia 2014; Stapleton et al. 2014; Takigami et al. 2009; Van den Eede et al. 2011).
e. TCEP is present as an impurity, at about 5-10%, in the flame retardant V6. Production and use of V6 could lead to environmental releases of TCEP (EC 2009). In one study, TCEP was found as an impurity in a V6 commercial mixture at levels of 14% by weight. In the same study, TCEP was found in house and automobile dust samples, a significant correlation between the concentrations of TCEP and the flame retardant V6 was observed in the dust samples, suggesting that the use of V6 is a significant source of TCEP in indoor environments (Fang et al. 2013).
f. Indoor air environments sampled around the world have also been found to be contaminated with TCEP including theaters, offices, retail establishments, and homes (Bergh et al. 2011; Bradman et al. 2014; Hartmann et al. 2004; Ingerowski et al. 2001; Makinen et al. 2009; Marklund et al. 2003; Marklund et al. 2005a; Staaf and Ostman 2005).

6. Studies on the Presence of TCEP in Children's Hand Wipe Samples

a. In a recent study, 43 children from 30 families were sampled for the presence of multiple flame retardants including TCEP on hand wipes and in house dust. TCEP was found on 47% of hand wipe samples and in 100% of house dust samples (Stapleton et al. 2014).

7. Biomonitoring

a. TCEP is listed as a priority chemical by the California Environmental Contaminant Biomonitoring Program (CECBP 2014).
b. Samples of human breast milk in women from 4 urban areas in Sweden contained TCEP as well as other flame retardants (Sundkvist et al. 2010).
c. TCEP has been detected in human breast milk in Japan, Vietnam and the Philippines (Kim et al. 2014).
d. The urinary metabolite of TCEP, bis(2-chloroethyl) phosphate (BCEP), was detected in 75% of urine samples taken from 16 adults living in northern California homes and TCEP was detected in 13% of the same samples (Dodson et al. 2014).
e. The urinary metabolite BCEP was detected in 50% of urine samples taken in Germany from persons ranging in age from 11 to 68 years (Schindler et al. 2009).

8. Human Exposure Estimates

a. The U.S. EPA estimates that children ages 1-5 ingest an approximate average of 100-200 mg dust/day, whereas, adults ingest an approximate average of 20-50 mg dust/day (U.S. EPA 2002).
b. The calculated cumulative average exposure to flame retardants from dust is 1.6 µg/day for children and 0.325 µg/day for adults (Stapleton et al. 2009).
c. An analysis of potential dust exposures to several flame retardants, including TCEP, suggests that an adult consumer may be exposed to a median concentration of 0.02 ng TCEP/kg bw/day and a toddler may be exposed to a median concentration of 0.34 ng TCEP/kg bw/day using mean dust ingestion assumptions (Ali et al. 2012a). Thus, children may be receiving much higher exposures to TCEP than adults due to ingestion of dust.
d. Dietary intake estimates of TCEP have been calculated to be 4.9 ng/kg and 6.5 ng/kg for children aged 6-11 months and 2 years old, respectively. Estimates for adults range from 1.3 - 3.1 ng/kg (ATSDR 2012; Gunderson 1995). Thus, children may be receiving much higher exposures to TCEP than adults due to ingestion from food sources.

9. Potential for the Chemical of Concern to be Released into Environmental Media

Published reports indicate that TCEP can be found in wastewater treatment plant effluents, surface water, finished drinking water, wildlife, sediments, and Antarctic ice.

a. TCEP in Water
   - Samples from urban river systems and lakes have been found to contain TCEP and other organophosphorus compounds within California and Nevada (Alvarez et al. 2012; Sengupta et al. 2014). In one study, there was evidence to suggest that the water infiltrated into the sediment had a different chemical composition than the rest of the water column and could be a potential exposure risk to bottom-dwelling aquatic organisms (Alvarez et al. 2012).
   - Streams, drinking water, ground water, wastewater and laundry effluent were found to contain TCEP in several US states (Barnes et al. 2008; Kolpin et al. 2002; Schreder and La Guardia 2014; Stackelberg et al. 2004).
   - Outside of the US, TCEP has been found in river water, rain water, storm water runoff, aquifers, drinking water, treated waste water, and influents, effluents, and sludge of sewage treatment facilities (Andresen and Bester 2006; Andresen et al. 2004; Bacaloni et al. 2007; Dsikowitzky et al. 2004; Fries and Puttmann 2001; Green et al. 2008; Kim et al. 2007; Marklund et al. 2005b; Martinez-Carballo et al. 2007; Matamoros et al. 2012; Meyer and Bester 2004; Regnery and Puttmann 2010; Rodil et al. 2012; Rodriguez et al. 2006).
   - TCEP was detected in 100% of household laundry wastewater samples taken from 20 Washington state homes, as well as in influents and effluents of two wastewater treatment plants associated with those homes (Schreder and La Guardia 2014), indicating the release of TCEP to waterways from effluent.

b. TCEP in Sediment
   - In Austria, TCEP was detected in river sediment within the Schwechat River (Martinez-Carballo et al. 2007).
   - Sediment samples from four locations in Norway contained TCEP as well as other contaminants (Leonards et al. 2011).
   - TCEP was found in sediments from Taihu Lake, one of the largest freshwater lakes in China (Cao et al. 2012).

c. TCEP in Antarctic Ice

- Analysis of the East Antarctic Ice Sheet identified TCEP as one of several contaminants found in fresh snow samples (Cheng et al. 2013).

d. TCEP in Leachate

- Leachate from a solid waste disposal site near Osaka, Japan was found to contain TCEP (Kawagoshi et al. 2002).

e. TCEP in Wildlife

- A study in Sweden found TCEP in herring, perch, mussels, and salmon (Sundkvist et al. 2010).
- A separate analysis in Sweden also found TCEP in mussels, crab, fish, and eagles (Leonards et al. 2011).

IX. Potential Exposure of Sensitive Subpopulations to TDCPP or TCEP

1. Infants and children

a. Infants are exposed to TDCPP and TCEP through breast milk, as evidenced by studies detecting TDCPP and TCEP in human breast milk (Kim et al. 2014; Sundkvist et al. 2010).
b. Children's exposures to TDCPP and TCEP have been confirmed by hand wipe samples (Stapleton et al. 2014) and detection of urinary metabolites (Butt et al. 2014).
c. The primary urinary metabolite of TDCPP (BDCPP) has been detected in urine samples taken from toddlers (Butt et al. 2014). Further, BDCPP urinary levels in children were 4.9 times those of the mothers tested in the same study (Butt et al. 2014), suggesting that either children were exposed to a greater amount of TDCPP or had higher metabolite levels due to their smaller body mass.
d. Children's overall exposure to flame retardants may be influenced by their hand-to-mouth behavior (Stapleton et al. 2014).
e. TDCPP and TCEP have been detected in numerous foam-filled children's products (Stapleton et al. 2011).
f. TDCPP has been detected in dust samples in homes where children ages 2-5 lived (Stapleton et al. 2014).
g. The U.S. Environmental Protection Agency (U.S. EPA) estimates that children ages 1-5 ingest on average approximately 100-200 mg dust/day; this is significantly more than adults, who on average ingest approximately 20-50 mg dust/day (U.S. EPA 2002). As a result, children may have a greater

exposure to TDCPP in dust than adults. Further, due to children's smaller body mass relative to adults, the dosage received by children in mg/kg of body mass is substantially greater than this 4-5 fold dust ingestion rate difference with adults might suggest.

h. One study calculated a cumulative average exposure to flame retardants from dust of 1.6 µg/day for children and 0.325 µg/day for adults (Stapleton et al. 2009).
i. Based on human exposure estimates (Ali et al. 2012a; ATSDR 2012; Gunderson 1995), children may be receiving much higher exposures to TDCPP and TCEP than adults due to ingestion of dust and food sources. Thus, children's exposure to TDCPP and TCEP is of concern due to their greater dust ingestion rate and greater exposure on a mg/kg of body weight basis due to their smaller body mass as compared to adults.
j. Flame retardant concentrations were measured in air and dust from 40 California ECE facilities. Detected concentrations of TDCPP and TCEP in dust were higher in ECE facilities where foam nap mats were used compared to ECE facilities where foam nap mats were not used. Levels of TDCPP and TCEP were higher in indoor air as compared to outdoor air. Child TDCPP exposure estimates in this study exceeded the age-adjusted NSRL for carcinogenicity in 51% of the facilities for children less than six years old (Bradman et al. 2014; Bradman et al. 2012).
k. In children, the estimated cancer risk from exposure to upholstered furniture during the first two years of life is 20 per million (Babich 2006).

2. Pregnant women

a. The primary metabolite of TDCPP, BDCPP, was detected in 38 out of 39 urine samples from a cohort of pregnant women (Hoffman et al. 2014).

3. Workers

a. Occupational exposure to TDCPP may occur through dermal contact with and inhalation of this compound at workplaces where TDCPP is produced or used (HSDB 2015).
b. TDCPP and TCEP have been detected in dust and air in California day care centers (Bradman et al. 2014; Bradman et al. 2012).
c. TDCPP and TCEP have been detected in offices, retail spaces, automobiles, hospitals, commercial airplanes, day care facilities, and other public spaces (Ali et al. 2012a; Ali et al. 2012b; Allen et al. 2013; Bergh et al. 2011; Brommer et al. 2012; Cao et al. 2014; Carignan et al. 2013; Dirtu et al. 2012; Dodson et al. 2012; Hartmann et al. 2004; Hoffman et al. 2015; Makinen et al.

2009; Marklund et al. 2003; Marklund et al. 2005a; Meeker and Stapleton 2010; OEHHA 2011b; Schreder and La Guardia 2014; Staaf and Ostman 2005; Stapleton et al. 2009; Takigami et al. 2009; Van den Eede et al. 2011).

X. Conclusions

DTSC identified children's foam-padded sleeping products containing TDCPP and/or TCEP as a Priority Product. This determination was based on a consideration of available, reliable scientific information regarding the potential exposure to TDCPP and/or TCEP in children's foam-padded sleeping products and the potential for these exposures to contribute to or cause significant or widespread adverse human health impacts.

TDCPP and TCEP are semi-volatile compounds used as additive flame retardants that are not chemically bonded to polyurethane foam and are easily released to indoor and outdoor environments. Both TDCPP and TCEP are ubiquitous compounds and have been detected worldwide, including in California, in dust sampled in indoor environments such as homes, offices, and daycare centers. TDCPP and TCEP have been detected in waterways and wastewater treatment influent and effluent in the U.S. and other nations. Further, TDCPP and TCEP have been detected in wildlife such as fish, mussels, and birds.

Both TDCPP and TCEP are known to the State of California to cause cancer, and carcinogenicity has been demonstrated in animal studies for both TDCPP and TCEP. Research studies suggest that TDCPP and TCEP exposure is associated with other hazard traits including reproductive toxicity, neurotoxicity, and kidney and liver toxicity. TDCPP exposure has also been linked to developmental toxicity and endocrine disruption.

Human exposure to TDCPP has been demonstrated by detection in human breast milk, adipose tissue, and seminal plasma, as well as the detection of primary metabolites in urine samples collected from adults, including pregnant women, and children. Human exposure to TCEP has been demonstrated by detection in human breast milk, as well as detection of primary metabolites in adult urine samples. Further, TDCPP has been detected in hand wipe samples from adults and children and TCEP has been detected in hand wipe samples from children, demonstrating an important route for potential exposure to these chemical flame retardants.

DTSC determined that exposure to TDCPP or TCEP through the normal use of children's foam- padded sleeping products may contribute to or cause significant or widespread adverse health impacts with the greatest risks borne by sensitive subpopulations such as pregnant women, children, infants, and day care center and school employees. This determination is based on the ubiquitous detection of TDCPP and TCEP in indoor and outdoor environments, the hazard traits associated with each

compound, and the data showing widespread exposures to both TDCPP and TCEP in adults, children, and wildlife.

XI. References

Abdallah MA, Covaci A (2014) Organophosphate flame retardants in indoor dust from Egypt: implications for human exposure. Environmental science & technology 48(9):4782-9 doi:10.1021/es501078s

Ali N, Dirtu AC, Van den Eede N, et al. (2012a) Occurrence of alternative flame retardants in indoor dust from New Zealand: indoor sources and human exposure assessment. Chemosphere 88(11):1276-82 doi:10.1016/j.chemosphere.2012.03.100

Ali N, Van den Eede N, Dirtu AC, Neels H, Covaci A (2012b) Assessment of human exposure to indoor organic contaminants via dust ingestion in Pakistan. Indoor air 22(3):200-211

Allen JG, Stapleton HM, Vallarino J, et al. (2013) Exposure to flame retardant chemicals on commercial airplanes. Environmental health : a global access science source 12:17 doi:10.1186/1476-069X-12-17

Alvarez DA, Rosen MR, Perkins SD, Cranor WL, Schroeder VL, Jones-Lepp TL (2012) Bottom sediment as a source of organic contaminants in Lake Mead, Nevada, USA. Chemosphere 88(5):605-11 doi:10.1016/j.chemosphere.2012.03.040

Andresen J, Bester K (2006) Elimination of organophosphate ester flame retardants and plasticizers in drinking water purification. Water research 40(3):621-9 doi:10.1016/j.watres.2005.11.022

Andresen JA, Grundmann A, Bester K (2004) Organophosphorus flame retardants and plasticisers in surface waters. The Science of the total environment 332(1-3):155-66 doi:10.1016/j.scitotenv.2004.04.021

Anonymous (1977) Health and safety data for 4 chemicals with cover letter dated 021089 (sanitized). Submitted to the U.S. Environmental Protection Agency under TSCA Section 8D. EPA86-8900001189. OTS0516689, p 1-Slide 10-14; p 4-Slide 214, 222, 223; p 5-Slide 271; p 13; Slide814-815 p 15; Slide 954-984 p 20; Slide 1227, 1253, 1278; p 25. [As described by ATSDR 2012].

ATSDR (2012) Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Phosphate Ester Flame Retardants. Atlanta, GA

Babich MA (2006) CPSC Staff Preliminary Risk Assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam. Bethesda, MD, pp. 1-129.

Bacaloni A, Cavaliere C, Foglia P, Nazzari M, Samperi R, Lagana A (2007) Liquid chromatography/tandem mass spectrometry determination of organophosphorus flame retardants and plasticizers in drinking and surface waters. Rapid communications in mass spectrometry : RCM 21(7):1123-30 doi:10.1002/rcm.2937

Barnes KK, Kolpin DW, Furlong ET, Zaugg SD, Meyer MT, Barber LB (2008) A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States--I) groundwater. The Science of the total environment 402(2-3):192-200 doi:10.1016/j.scitotenv.2008.04.028

Bergh C, Torgrip R, Emenius G, Ostman C (2011) Organophosphate and phthalate esters in air and settled dust - a multi-location indoor study. Indoor air 21(1):67-76 doi:10.1111/j.1600-0668.2010.00684.x

Bio/dynamics (1980) Bio/dynamics, Inc. A Two Year Oral Toxicity/Carcinogenicity Study on Fyrol FR-2 in Rats (Final Report). Volume V. Submitted to Stauffer Chemical Co. by Bio/dynamics, Inc. Project No. 77- 2016. Sept. 21, 1981. [As described by OEHHA 2011].

Blum A, Ames BN (1977) Flame-retardant additives as possible cancer hazards. Science 195(4273):17-23

Blum A, Gold MD, Ames BN, et al. (1978) Children absorb tris-BP flame retardant from sleepwear: urine contains the mutagenic metabolite, 2,3-dibromopropanol. Science 201(4360):1020-3

Bradman A, Castorina R, Gaspar F, et al. (2014) Flame retardant exposures in California early childhood education environments. Chemosphere 116:61-6 doi:10.1016/j.chemosphere.2014.02.072

Bradman A, Gaspar F, Castorina R, Tong-Lin E, McKone T, Maddelena R (2012) Environmental Exposures in Early Childhood Education Environments, Final Draft Report. Berkeley, CA, pp. 1-143.

Brandsma SH, de Boer J, van Velzen MJ, Leonards PE (2014) Organophosphorus flame retardants (PFRs) and plasticizers in house and car dust and the influence of electronic equipment. Chemosphere doi:10.1016/j.chemosphere.2014.02.036

Brandwene D (2001) High Production Volume (HPV) Challenge Program test plan and robust summary for tris(l,3-dichloro-2-propy1) phosphate. Akzo Nobel Functional Chemicals LLC, Dobbs Ferry, NY. March 2001. [As described by Babich 2006].

Brommer S, Harrad S, Van den Eede N, Covaci A (2012) Concentrations of organophosphate esters and brominated flame retardants in German indoor dust samples. Journal of environmental monitoring : JEM 14(9):2482-7 doi:10.1039/c2em30303e

Brusick D, Matheson D, Jagannath DR, et al. (1979) A comparison of the genotoxic properties of tris(2,3-dibromopropyl)phosphate and tris(1,3-dichloro-2-propyl)phosphate in a battery of short-term bioassays. Journal of environmental pathology and toxicology 3(1-2):207-26

Butt CM, Congleton J, Hoffman K, Fang M, Stapleton HM (2014) Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environmental science & technology 48(17):10432-8 doi:10.1021/es5025299

Cao S, Zeng X, Song H, et al. (2012) Levels and distributions of organophosphate flame retardants and plasticizers in sediment from Taihu Lake, China. Environmental toxicology and chemistry / SETAC 31(7):1478-84 doi:10.1002/etc.1872

Cao Z, Xu F, Covaci A, et al. (2014) Differences in the seasonal variation of brominated and phosphorus flame retardants in office dust. Environment international 65:100-6 doi:10.1016/j.envint.2013.12.011

Carignan CC, McClean MD, Cooper EM, et al. (2013) Predictors of tris(1,3-dichloro-2-propyl) phosphate metabolite in the urine of office workers. Environment international 55:56-61 doi:10.1016/j.envint.2013.02.004

CECBP (2008) Brominated and chlorinated organic chemical compounds used as flame retardants. Materials for the December 4-5, 2008 Meeting of the California Environmental Contaminant Biomonitoring Program (CECBP) Scientific Guidance Panel (SGP). Agenda Item: "Consideration of Potential Designated Chemicals" In. http://www.biomonitoring.ca.gov/sites/default/files/downloads/120408flamedoc.pdf Accessed November 2013

CECBP (2014) California Environmental Contaminant Biomonitoring Program (CECBP). Biomonitoring California Priority Chemicals June 2014. In. http://biomonitoring.ca.gov/sites/default/files/downloads/PriorityChemicalsList_June2014.pdf

ChemSpider (2013) ChemSpider, Royal Society of Chemistry. Tris(1,3-dichloro-2-propyl)phosphate. In. http://www.chemspider.com/ Accessed October 8 2013

Cheng W, Sun L, Huang W, et al. (2013) Detection and distribution of Tris(2-chloroethyl) phosphate on the East Antarctic ice sheet. Chemosphere 92(8):1017-21 doi:10.1016/j.chemosphere.2013.03.038

Covance (2004) Covance Laboratories Inc. Chromosomal aberrations in Chinese hamster ovary (CHO) cells (Unpublished report). [As described by European Commission 2009 and OEHHA 2011].

Cox C (2013) Naptime nightmares? Toxic flame retardants in child care nap maps. Center for Environmental Health Report. Oakland, CA, pp. 1-18.

Dirtu AC, Ali N, Van den Eede N, Neels H, Covaci A (2012) Country specific comparison for profile of chlorinated, brominated and phosphate organic contaminants in indoor dust. Case study for Eastern Romania, 2010. Environment international 49:1-8 doi:10.1016/j.envint.2012.08.002

Dishaw LV, Powers CM, Ryde IT, et al. (2011) Is the PentaBDE replacement, tris (1,3-dichloro-2-propyl) phosphate (TDCPP), a developmental neurotoxicant? Studies in PC12 cells. Toxicology and applied pharmacology 256(3):281-9 doi:10.1016/j.taap.2011.01.005

Dodson RE, Perovich LJ, Covaci A, et al. (2012) After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environmental science & technology 46(24):13056-66 doi:10.1021/es303879n

Dodson RE, Van den Eede N, Covaci A, Perovich LJ, Brody JG, Rudel RA (2014) Urinary biomonitoring of phosphate flame retardants: levels in California adults and recommendations for future studies. Environmental science & technology 48(23):13625-33 doi:10.1021/es503445c

Dsikowitzky L, Schwarzbauer J, Kronimus A, Littke R (2004) The anthropogenic contribution to the organic load of the Lippe River (Germany). Part I: Qualitative characterisation of low-molecular weight organic compounds. Chemosphere 57(10):1275-88 doi:10.1016/j.chemosphere.2004.08.052

DTSC (2014) Department of Toxic Substances Control (DTSC), State of California. Candidate Chemical Database. In. http://cit.dtsc.ca.gov/scp/chemicalsearch/ChemicalSearch.aspx Accessed October 16 2013

EC (2008) European Commission (EC). Tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP). European Union Risk Assessment Report. Prepared by Rapporteur Member States Ireland and United Kingdom. Final Report.

EC (2009) European Commission (EC) Risk assessment report: tris (2-chloroethyl) phosphate. Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Dortmund

ECHA (2010) European Chemicals Agency (ECHA). Committee for Risk Assessment (RAC) opinion proposing harmonized classification and labelling at community level of TDCP (Tris[2-chloro-1-chloromethyl)ethyl]. ECHA/RAC/Doc. No. CLH-0-0000000953-71-03/F. Adopted 3 September 2010.

ECHA (2012) CMR substances from Annex VI of the CLP Regulation registered under REACH and notified under CLP – a first screening. Helsinki, Finland

ECHA (2014) European Chemicals Agency (ECHA). Tris[2-chloro-1-(chloromethyl)ethyl] phosphate. In. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb07130-1b0d-1644-e044-00144f67d031/DISS-9eb07130-1b0d-1644-e044-00144f67d031_DISS-9eb07130-1b0d-1644-e044-00144f67d031.html Accessed January 2014

Evenset A, Leknes H, Christensen G, Warner N, Remberger M, Gabrielsen G (2009) Norwegian Pollution Control Authority (SFT). Screening of new contaminants in samples from the norwegian arctic. Silver, Platinum, Sucralose, Bisphenol A, Tetrabrombisphenol A, Siloxanes, Phtalates (DEHP) and Phosphororganic flame retardants.

Fang M, Webster TF, Gooden D, et al. (2013) Investigating a novel flame retardant known as V6: measurements in baby products, house dust, and car dust. Environmental science & technology 47(9):4449-54 doi:10.1021/es400032v

Farhat A, Crump D, Chiu S, et al. (2013) In Ovo effects of two organophosphate flame retardants--TCPP and TDCPP--on pipping success, development, mRNA expression, and thyroid hormone levels in chicken embryos. Toxicological sciences : an official journal of the Society of Toxicology 134(1):92-102 doi:10.1093/toxsci/kft100

Focazio MJ, Kolpin DW, Barnes KK, et al. (2008) A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States--II) untreated drinking water sources. The Science of the total environment 402(2-3):201-16 doi:10.1016/j.scitotenv.2008.02.021

Freudenthal RI, Henrich RT (2000) Chronic toxicity and carcinogenic potential of tris-(1,3-dichloro- 2-propyl) phosphate in Sprague-Dawley rat. International Journal of Toxicology 19(2):119-125

Fries E, Puttmann W (2001) Occurrence of organophosphate esters in surface water and ground water in Germany. Journal of environmental monitoring : JEM 3(6):621-6

Fu J, Han J, Zhou B, et al. (2013) Toxicogenomic responses of zebrafish embryos/larvae to tris(1,3-dichloro-2-propyl) phosphate (TDCPP) reveal possible molecular mechanisms of developmental toxicity. Environmental science & technology 47(18):10574-82 doi:10.1021/es401265q

Gold MD, Blum A, Ames BN (1978) Another flame retardant, tris-(1,3-dichloro-2-propyl)-phosphate, and its expected metabolites are mutagens. Science 200(4343):785-7

Green N, Schlabach M, Bakke T, et al. (2008) Norwegian Pollution Control Authority (SFT). Screening of selected metals and new organic contaminants 2007.

Gulati D, Hommel-Barnes L, Chapin R, Heindel J (1991) Reproductive Toxicity of Tris(2-chloroethyl)phosphate (CAS No. 115-96-8) in CD-1 Swiss Mice. NTP Report # RACB92040. NTP

Gunderson EL (1995) Dietary intakes of pesticides, selected elements, and other chemicals: FDA Total Diet Study, June 1984-April 1986. Journal of AOAC International 78(4):910-21

Hartmann PC, Burgi D, Giger W (2004) Organophosphate flame retardants and plasticizers in indoor air. Chemosphere 57(8):781-7 doi:10.1016/j.chemosphere.2004.08.051

Hoffman K, Daniels JL, Stapleton HM (2014) Urinary metabolites of organophosphate flame retardants and their variability in pregnant women. Environment international 63:169-72 doi:10.1016/j.envint.2013.11.013

Hoffman K, Garantziotis S, Birnbaum LS, Stapleton HM (2015) Monitoring indoor exposure to organophosphate flame retardants: hand wipes and house dust. Environmental health perspectives 123(2):160-5 doi:10.1289/ehp.1408669

HSDB (2015) Hazardous Substances Data Bank, National Library of Medicine (HSDB). In. http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm Accessed May 2015

Hudec T, Thean J, Kuehl D, Dougherty RC (1981) Tris(dichloropropyl)phosphate, a mutagenic flame retardant: frequent occurrence in human seminal plasma. Science 211(4485):951-2

IARC (1999a) International Agency for Research on Cancer (IARC). IARC monographs on the evaluation of carcinogenic risks to humans vol. 71. Tris(2-chloroethyl) phosphate.

IARC (1999b) International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 71. Re-Evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Summary of Data Reported and Evaluation. Epichlorohydrin. In. http://monographs.iarc.fr/ENG/Monographs/vol71/index.php Accessed December 4 2013

IARC (2000) International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 77. Some Industrial Chemicals. Summary of Data Reported and Evaluation. Glycidol. In. http://monographs.iarc.fr/ENG/Monographs/vol77/index.php Accessed December 4 2013

IARC (2012a) International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 101. 1,3-dichloro-2-propanol (1,3-DCP). In. http://monographs.iarc.fr/ENG/Monographs/vol101/mono101-011.pdf Accessed December 4 2013

IARC (2012b) International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 101. 3-monochloropropane-1,2-diol (3-MCPD) In. http://monographs.iarc.fr/ENG/Monographs/vol101/mono101-010.pdf Accessed December 4 2013

IARC (2015) Agents Classified by the IARC Monographs, Volumes 1–112. In. http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf Accessed May 2015

Ingerowski G, Friedle A, Thumulla J (2001) Chlorinated ethyl and isopropyl phosphoric acid triesters in the indoor environment--an inter-laboratory exposure study. Indoor air 11(3):145-9

Inveresk (1985) Inveresk Research International. TDCP LV: Mouse lymphoma mutation assay (unpublished report). [As described by OEHHA 2011].

Ishidate M (1983) Application of chromosomal aberration tests *in vitro* to the primary screening for chemicals with carcinogenic and/or genetic hazards. In: Garattini (Ed) S (ed) Tests courts de cancérogénèse: Quo vadis? , Montpellier: Centre de Recherches Clin Midy, p 58-79. [As described by European Commission 2009 and OEHHA 2011]

JMPA (2013) Juvenile Product Manufacturers Association (JMPA). Juvenile Product Manufacturers Association 2013 Annual Industry Study – Final Report. Part 1 of 3: Manufacturer Data Summary. Manufacturer's Shipment and Sales Data from 2011 & 2012.

Kawagoshi Y, Nakamura S, Fukunaga I (2002) Degradation of organophosphoric esters in leachate from a sea-based solid waste disposal site. Chemosphere 48(2):219-25

Kawashima K, Tanaka S, Nakaura S, et al. (1983) Effect of phosphoric acid tri-esters flame retardants on the prenatal and postnatal developments of rats. The Journal of toxicological sciences 8(1):339 [As described by NRC 2000]

Kim JW, Isobe T, Muto M, et al. (2014) Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. Chemosphere doi:10.1016/j.chemosphere.2014.02.033

Kim SD, Cho J, Kim IS, Vanderford BJ, Snyder SA (2007) Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. Water research 41(5):1013-21 doi:10.1016/j.watres.2006.06.034

Klosterhaus S, Yee D, Sedlak M, Wong A, Sutton R (2012) Contaminants of emerging concern in San Francisco Bay: a summary of occurrence data and identification of data gaps. RMP Contribution 698. San Francisco Estuary Institute, Richmond, CA, p. 24-30.

Kojima H, Takeuchi S, Itoh T, Iida M, Kobayashi S, Yoshida T (2013) In vitro endocrine disruption potential of organophosphate flame retardants via human nuclear receptors. Toxicology 314(1):76-83 doi:10.1016/j.tox.2013.09.004

Kolpin DW, Furlong ET, Meyer MT, et al. (2002) Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999-2000: a national reconnaissance. Environmental science & technology 36(6):1202-11

LeBel GL, Williams DT (1983) Determination of organic phosphate triesters in human adipose tissue. Journal - Association of Official Analytical Chemists 66(3):691-9

LeBel GL, Williams DT (1986) Levels of triaryl/alkyl phosphates in human adipose tissue from Eastern Ontario. Bulletin of environmental contamination and toxicology 37(1):41-6

LeBel GL, Williams DT, Berard D (1989) Triaryl/alkyl phosphate residues in human adipose autopsy samples from six Ontario municipalities. Bulletin of environmental contamination and toxicology 43(2):225-30

Leonards P, Steindal EH, van der Veen I, Berg V, Bustnes JO, van Leeuwen S (2011) Norwegian Climate and Pollution Agency (KLIF). Screening of organophosphor flame retardants 2010.

Liu C, Wang Q, Liang K, et al. (2013a) Effects of tris(1,3-dichloro-2-propyl) phosphate and triphenyl phosphate on receptor-associated mRNA expression in zebrafish embryos/larvae. Aquatic toxicology 128-129:147-57 doi:10.1016/j.aquatox.2012.12.010

Liu X, Ji K, Choi K (2012) Endocrine disruption potentials of organophosphate flame retardants and related mechanisms in H295R and MVLN cell lines and in zebrafish. Aquatic toxicology 114-115:173-81 doi:10.1016/j.aquatox.2012.02.019

Liu X, Ji K, Jo A, Moon HB, Choi K (2013b) Effects of TDCPP or TPP on gene transcriptions and hormones of HPG axis, and their consequences on reproduction in adult zebrafish (Danio rerio). Aquatic toxicology 134-135:104-11 doi:10.1016/j.aquatox.2013.03.013

Lynn RK, Wong K, Garvie-Gould C, Kennish JM (1981) Disposition of the flame retardant, tris(1,3-dichloro-2-propyl) phosphate, in the rat. Drug metabolism and disposition: the biological fate of chemicals 9(5):434-41

Makinen MS, Makinen MR, Koistinen JT, et al. (2009) Respiratory and dermal exposure to organophosphorus flame retardants and tetrabromobisphenol A at five work environments. Environmental science & technology 43(3):941-7

Markets and Markets (2012) Flame Retardant Chemicals Market By Type, Application & Geography – Market Estimates Up To 2017.

Marklund A, Andersson B, Haglund P (2003) Screening of organophosphorus compounds and their distribution in various indoor environments. Chemosphere 53(9):1137-46 doi:10.1016/S0045-6535(03)00666-0

Marklund A, Andersson B, Haglund P (2005a) Organophosphorus flame retardants and plasticizers in air from various indoor environments. Journal of environmental monitoring : JEM 7(8):814-9 doi:10.1039/b505587c

Marklund A, Andersson B, Haglund P (2005b) Organophosphorus flame retardants and plasticizers in Swedish sewage treatment plants. Environmental science & technology 39(19):7423-9

Martinez-Carballo E, Gonzalez-Barreiro C, Sitka A, Scharf S, Gans O (2007) Determination of selected organophosphate esters in the aquatic environment of Austria. The Science of the total environment 388(1-3):290-9 doi:10.1016/j.scitotenv.2007.08.005

Matamoros V, Arias CA, Nguyen LX, Salvado V, Brix H (2012) Occurrence and behavior of emerging contaminants in surface water and a restored wetland. Chemosphere 88(9):1083-9 doi:10.1016/j.chemosphere.2012.04.048

Matthews HB, Dixon D, Herr DW, Tilson H (1990) Subchronic toxicity studies indicate that tris(2-chloroethyl)phosphate administration results in lesions in the rat hippocampus. Toxicology and industrial health 6(1):1-15

Matthews HB, Eustis SL, Haseman J (1993) Toxicity and carcinogenicity of chronic exposure to tris(2-chloroethyl)phosphate. Fundamental and applied toxicology : official journal of the Society of Toxicology 20(4):477-85

McGee SP, Cooper EM, Stapleton HM, Volz DC (2012) Early zebrafish embryogenesis is susceptible to developmental TDCPP exposure. Environmental health perspectives 120(11):1585-91 doi:10.1289/ehp.1205316

Meeker JD, Cooper EM, Stapleton HM, Hauser R (2013) Urinary metabolites of organophosphate flame retardants: temporal variability and correlations with house dust concentrations. Environmental health perspectives 121(5):580-5 doi:10.1289/ehp.1205907

Meeker JD, Stapleton HM (2010) House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters. Environmental health perspectives 118(3):318-23 doi:10.1289/ehp.0901332

Meyer J, Bester K (2004) Organophosphate flame retardants and plasticisers in wastewater treatment plants. Journal of environmental monitoring : JEM 6(7):599-605 doi:10.1039/b403206c

Morales NM, Matthews HB (1980) In vivo binding of the flame retardants tris(2,3-dibromopropyl) phosphate and tris(1,3-dichloro-2-propyl) phosphate to macromolecules of mouse liver, kidney and muscle. Bulletin of environmental contamination and toxicology 25(1):34-8

Nomeir AA, Kato S, Matthews HB (1981) The metabolism and disposition of tris(1,3-dichloro-2-propyl) phosphate (Fyrol FR-2) in the rat. Toxicology and applied pharmacology 57(3):401-13

NRC (2000) National Research Council (NRC). Subcommittee on Flame-Retardant Chemicals Committee on Toxicology Board on Environmental Studies and Toxicology Commission on Life Sciences. Toxicological Risks of Selected Flame-Retardant Chemicals, Ch. 16 Tris (1,3-dichloropropyl-2)

Phosphate, pages 358-386. In: National Academy Press. http://www.nap.edu/openbook.php?record_id=9841&page=358 Accessed October 2013

NTP (1991) Technical Report no. 391: Toxicology and carcinogenesis studies of tris (2-chloroethyl) phosphate in F344/N rats and B6C3F1 mice. Research Triangle Park, NC

NTP (2010) National Toxicology Program's 12th Report on Carcinogens

OEHHA (1992) Office of Environmental Health Hazard Assessment (OEHAA), California Environmental Protection Agency (Cal/EPA). Chemicals Known to the State to Cause Cancer or Reproductive Toxicity

OEHHA (2010a) Office of Enviromental Health Hazard Assessment (OEHHA). Evidence on the Carcinogenicity of 1,3-Dichloro-2-propanol (1,3-DCP; α,γ-Dichlorohydrin). Update. September 2010.

OEHHA (2010b) Office of Environmental Health Hazard Assessment (OEHHA). Evidence on the Carcinogenicity of 3-Monochloropropane-1,2-diol (3-MCPD; α-Chlorohydrin). Update. September 2010.

OEHHA (2011a) Office of Environmental Health Hazard Assessment (OEHAA), California Environmental Protection Agency (Cal/EPA). Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. In. http://oehha.ca.gov/prop65/prop65_list/files/P65single061915.pdf

OEHHA (2011b) Office of Environmental Health Hazard Assessment (OEHHA), California Environmental Protection Agency (Cal/EPA). Evidence on the carcinogenicity of Tris(1,3-dichloro-2-propyl)phosphate. July 2011.

OEHHA (2012) Office of Environmental Health Hazard Assessment (OEHAA), California Environmental Protection Agency (Cal/EPA). Initial Statement of Reasons Title 27, California Code of Regulations. Proposed Amendment To: Section 25705(B) Specific Regulatory Levels Posing No Significant Risk. Tris(1,3-Dichloro-2-Propyl) Phosphate (TDCPP).

Regnery J, Puttmann W (2010) Seasonal fluctuations of organophosphate concentrations in precipitation and storm water runoff. Chemosphere 78(8):958-64 doi:10.1016/j.chemosphere.2009.12.027

Rodil R, Quintana JB, Concha-Grana E, Lopez-Mahia P, Muniategui-Lorenzo S, Prada-Rodriguez D (2012) Emerging pollutants in sewage, surface and drinking water in Galicia (NW Spain). Chemosphere 86(10):1040-9 doi:10.1016/j.chemosphere.2011.11.053

Rodriguez I, Calvo F, Quintana JB, Rubi E, Rodil R, Cela R (2006) Suitability of solid-phase microextraction for the determination of organophosphate flame retardants and plasticizers in water samples. Journal of chromatography A 1108(2):158-65 doi:10.1016/j.chroma.2006.01.008

Sasaki K, Suzuki T, Takeda M, Uchiyama M (1984) Metabolism of phosphate acid triesters by rat liver homogenate. Bull Environ Contam Toxicol 33:281-288

Schaider LA, Rudel RA, Ackerman JM, Dunagan SC, Brody JG (2014) Pharmaceuticals, perfluorosurfactants, and other organic wastewater compounds in public drinking water wells in a shallow sand and gravel aquifer. The Science of the total environment 468-469:384-93 doi:10.1016/j.scitotenv.2013.08.067

Schindler BK, Forster K, Angerer J (2009) Determination of human urinary organophosphate flame retardant metabolites by solid-phase extraction and gas chromatography-tandem mass spectrometry. Journal of chromatography B, Analytical technologies in the biomedical and life sciences 877(4):375-81 doi:10.1016/j.jchromb.2008.12.030

Schreder ED, La Guardia MJ (2014) Flame retardant transfers from U.S. households (dust and laundry wastewater) to the aquatic environment. Environmental science & technology 48(19):11575-83 doi:10.1021/es502227h

Sengupta A, Lyons JM, Smith DJ, et al. (2014) The occurrence and fate of chemicals of emerging concern in coastal urban rivers receiving discharge of treated municipal wastewater effluent. Environmental toxicology and chemistry / SETAC 33(2):350-8 doi:10.1002/etc.2457

SFEI (2013) San Francisco Estuary Institute (SFEI). The Pulse of the Bay: Contaminants of Emerging Concern. SFEI Contribution 701. San Francisco Estuary Institute, Richmond, CA, p 68-69.

Soderlund EJ, Dybing E, Holme JA, et al. (1985) Comparative genotoxicity and nephrotoxicity studies of the two halogenated flame retardants tris(1,3-dichloro-2-propyl)phosphate and tris(2,3-dibromopropyl)phosphate. Acta pharmacologica et toxicologica 56(1):20-9

Staaf T, Ostman C (2005) Organophosphate triesters in indoor environments. Journal of environmental monitoring : JEM 7(9):883-7 doi:10.1039/b506631j

Stackelberg PE, Furlong ET, Meyer MT, Zaugg SD, Henderson AK, Reissman DB (2004) Persistence of pharmaceutical compounds and other organic wastewater contaminants in a conventional drinking-water-treatment plant. The Science of the total environment 329(1-3):99-113 doi:10.1016/j.scitotenv.2004.03.015

Stapleton HM, Klosterhaus S, Eagle S, et al. (2009) Detection of organophosphate flame retardants in furniture foam and U.S. house dust. Environmental science & technology 43(19):7490-5

Stapleton HM, Klosterhaus S, Keller A, et al. (2011) Identification of flame retardants in polyurethane foam collected from baby products. Environmental science & technology 45(12):5323-31 doi:10.1021/es2007462

Stapleton HM, Misenheimer J, Hoffman K, Webster TF (2014) Flame retardant associations between children's handwipes and house dust. Chemosphere doi:10.1016/j.chemosphere.2013.12.100

Stauffer (1977) Stauffer Chemical Company. Mutagenicity evaluation of FR-2. (Unpublished report). [As described by European Commission 2008 and OEHHA 2011].

Stauffer (1981a) Stauffer Chemical Company. A two year study of Fyrol-2 in rats. In: A two-year oral toxicity/ carcinogenicity study of Fyrol FR-2 in rats (Volume I-IV) (final reports) with attachments, cover sheets, and letter dated 093081. Submitted to the U.S. Environmental Protection Agency under TSCA Section 8E. EPA88-8100282. OTS0204911. [As described by ATSDR 2012].

Stauffer (1981b) Stauffer Chemical Company. Toxicity reports on Fyrol FR-2 (Volume I-II) with attachments and cover letters dated 020381. Submitted to the U.S. Environmental Protection Agency under TSCA Section 8E. EPA88-8100271. OTS0204911. [As described by ATSDR 2012 and Babich 2006].

Stauffer (1983) Stauffer Chemical Company. A mortality survey of workers employed at a Fyrol FR-2 manufacturing plant. (Unpublished report). Submitted to the U.S. Environmental Protection Agency under TSCA Section E. OTS0204911. [As described by ATSDR 2012 and European Commission 2009].

Sundkvist AM, Olofsson U, Haglund P (2010) Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. Journal of environmental monitoring : JEM 12(4):943-51 doi:10.1039/b921910b

Takahashi S, Katsumasa A, Kera Y (2013) Chapter 5. Microbial Degradation of Persistent Organophosphorus Flame Retardants. In: Marian Petre (ed.) (ed) Environmental Biotechnology - New Approaches and Prospective Applications. p 91-122

Takigami H, Suzuki G, Hirai Y, Ishikawa Y, Sunami M, Sakai S (2009) Flame retardants in indoor dust and air of a hotel in Japan. Environment international 35(4):688-93 doi:10.1016/j.envint.2008.12.007

TOXNET (2014) US National Library of Medicine Toxicology Data Network. In. http://toxnet.nlm.nih.gov/

U.S. EPA (2002) U.S. Environmental Protection Agency (U.S. EPA). Child-Specific Exposure Factors Handbook. National Center for Environmental Assessment. EPA-600-P-00-002B.

U.S. EPA (2006) U.S. Environmental Protection Agency (U.S. EPA). U.S. Environmental Protection Agency Inventory Update for 2-propanol, 1,3-dichloro-, phosphate (3:1). [As described in OEHHA 2011].

U.S. EPA (2013) U.S. Environmental Protection Agency (U.S. EPA). U.S. EPA ChemView. U.S. EPA's High Production Volume Information System (HPVIS). In. http://java.epa.gov/chemview Accessed October 23 2013

Ulsamer AG, Osterberg RE, McLaughlin J, Jr. (1980) Flame-retardant chemicals in textiles. Clinical toxicology 17(1):101-31 doi:10.3109/15563658008985072

Van den Eede N, Dirtu AC, Neels H, Covaci A (2011) Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. Environment international 37(2):454-61 doi:10.1016/j.envint.2010.11.010

van der Veen I, de Boer J (2012) Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere 88(10):1119-53 doi:10.1016/j.chemosphere.2012.03.067

Wang Q, Lam JC, Man YC, et al. (2015) Bioconcentration, metabolism and neurotoxicity of the organophorous flame retardant 1,3-dichloro 2-propyl phosphate (TDCPP) to zebrafish. Aquatic toxicology 158:108-15 doi:10.1016/j.aquatox.2014.11.001

Wang Q, Liang K, Liu J, et al. (2013) Exposure of zebrafish embryos/larvae to TDCPP alters concentrations of thyroid hormones and transcriptions of genes involved in the hypothalamic-pituitary-thyroid axis. Aquatic toxicology 126:207-13 doi:10.1016/j.aquatox.2012.11.009

WHO (1998) World Health Organization (WHO). Environmental Health Criteria 209. Flame retardants: Tris(chloropropyl) phosphate and tris(2-chloroethyl) phosphate.

Wilczynski SL, Killinger JM, Zwicker GM, Freudenthal RI (1983) Fyrol FR-2 fertility study in male rabbits. The Toxicologist 3(22 (Abstract only.) [As described in Babich 2006.])

Zhang Q, Lu M, Dong X, et al. (2014) Potential estrogenic effects of phosphorus-containing flame retardants. Environmental science & technology 48(12):6995-7001 doi:10.1021/es5007862

Attachment 2

CALIFORNIA
Water Boards

EDMUND G. BROWN JR.
GOVERNOR

MATTHEW RODRIQUEZ
SECRETARY FOR
ENVIRONMENTAL PROTECTION

State Water Resources Control Board

February 11, 2016 **VIA FEDERAL EXPRESS**

Gary L. Ginsberg, Ph.D.
Assistant Professor of Community Medicine
University of Connecticut, M.P.H. Program
The Exchange
270 Farmington Avenue
Farmington, CT 06032

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF CHILDREN'S FOAM-PADDED SLEEPING PRODUCTS CONTAINING TRIS (1,3-DICHLORO-2-PROPYL) PHOSPHATE (TDCPP) AND/OR TRIS(2-CHLOROETHYL) PHOSPHATE (TCEP) AS A PRIORITY PRODUCT

Dear Professor Ginsberg,

My letter today is intended to initiate the external review.

Included with this letter are the following:

1. December 10, 2015 memorandum from Karl Palmer, Chief of the Department of Toxic Substances Control (DTSC), to me, "Request for an External Peer Review for the Proposed Adoption of Children's Foam-Padded Sleeping Products Containing Tris (1,3-Dichloro-2-Propyl) Phospate (TDCPP) and/or Tris (2-chloroethyl) Phosphate (TCEP) as a Priority Product."

2. Subject of Review: "Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product."

3. CD of all references listed in foregoing document.

4. January 7, 2009 Supplement to the Cal/EPA Peer Review Guidelines.

<u>Comments on the Foregoing</u>

1. You have been sent a copy of the December 10, 2015 request memorandum during the solicitation process for reviewer candidates conducted by the University of California, Berkeley Institute of the Environment.

2. <u>Attachment 2 to the request memorandum provides focus for the review</u>. I ask that you <u>address all topics, as expertise allows, in the order listed</u>.

3. The January 7, 2009 Supplement – you received this earlier when I approved you as a reviewer. I am sending it again to make certain that you have it. In part, it provides guidance to ensure the review is kept confidential through its course. The Supplement notes reviewers are under no obligation to discuss their comments with third-parties after reviews have been submitted. We recommend they do not. All outside parties are provided opportunities to address a proposed regulatory action through a well-defined regulatory process. Please direct third parties to me.

Questions about the review, or material, should be for clarification, in writing – email is fine, and addressed to me. My responses will be in writing also. DTSC should not be contacted.

Please send your reviews to me on March 14, 2016, not before. I will subsequently forward all reviews together to DTSC with reviewers' Curriculum Vitae. All this information will be posted at the appropriate DTSC program website.

Your acceptance of this review assignment is most appreciated.

Sincerely,

Gerald W. Bowes

Gerald W. Bowes, Ph.D.
Manager, Cal/EPA Scientific Peer Review Program
Office of Research, Planning and Performance
State Water Resources Control Board
1001 "I" Street, 16th Floor
Sacramento, California 95814

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CALIFORNIA
Water Boards

EDMUND G. BROWN JR.
GOVERNOR

MATTHEW RODRIQUEZ
SECRETARY FOR
ENVIRONMENTAL PROTECTION

State Water Resources Control Board

February 11, 2016 **VIA FEDERAL EXPRESS**

Heather M. Stapleton, Ph.D.
Dan and Bunny Gabel Associate Professor of Environmental Ethics
and Sustainable Environmental Management
Nicholas School of the Environment, Duke University
450 Research Drive, LSRC Room A220
Durham, NC 27519

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF CHILDREN'S FOAM-PADDED SLEEPING PRODUCTS CONTAINING TRIS (1,3-DICHLORO-2-PROPYL) PHOSPHATE (TDCPP) AND/OR TRIS(2-CHLOROETHYL) PHOSPHATE (TCEP) AS A PRIORITY PRODUCT

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CALIFORNIA
Water Boards

EDMUND G. BROWN JR.
GOVERNOR

MATTHEW RODRIQUEZ
SECRETARY FOR
ENVIRONMENTAL PROTECTION

State Water Resources Control Board

February 16, 2016 **VIA FEDERAL EXPRESS**

Lucio G. Costa, PharmD
Professor, Env. & Occ. Health Sciences
School of Public Health, University of Washington
4225 Roosevelt, Suite 100
Seattle, WA 98195

SUBJECT: EXTERNAL PEER REVIEW FOR THE PROPOSED ADOPTION OF CHILDREN'S FOAM-PADDED SLEEPING PRODUCTS CONTAINING TRIS (1,3-DICHLORO-2-PROPYL) PHOSPHATE (TDCPP) AND/OR TRIS(2-CHLOROETHYL) PHOSPHATE (TCEP) AS A PRIORITY PRODUCT

Dear Professor Costa,

My letter today is intended to initiate the external review.

Included with this letter are the following:

1. December 10, 2015 memorandum from Karl Palmer, Chief of the Department of Toxic Substances Control (DTSC), to me, "Request for an External Peer Review for the Proposed Adoption of Children's Foam-Padded Sleeping Products Containing Tris (1,3-Dichloro-2-Propyl) Phospate (TDCPP) and/or Tris (2-chloroethyl) Phosphate (TCEP) as a Priority Product."

2. Subject of Review: "Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris(1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product."

3. CD of all references listed in foregoing document.

4. January 7, 2009 Supplement to the Cal/EPA Peer Review Guidelines.

<u>Comments on the Foregoing</u>

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Questions about the review, or material, should be for clarification, in writing – email is fine, and addressed to me. My responses will be in writing also. DTSC should not be contacted.

Please send your review to me on March 14, 2016, not before. Place your name, affiliation and date on top of first page.

I will subsequently forward all reviews together to DTSC with reviewers' Curriculum Vitae. All this information will be posted at the appropriate DTSC program website.

Your acceptance of this review assignment is most appreciated.

Sincerely,

Gerald W. Bowes

Gerald W. Bowes, Ph.D.
Manager, Cal/EPA Scientific Peer Review Program
Office of Research, Planning and Performance
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1001 "I" Street, 16th Floor
Sacramento, California 95814

Telephone: (916) 341-5567
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Attachment 3

January 7, 2009

Supplement to Cal/EPA External Scientific Peer Review Guidelines – "Exhibit F" in Cal/EPA Interagency Agreement with University of California Gerald W. Bowes, Ph.D.

Guidance to Staff:

1. Revisions. If you have revised any part of the initial request, please stamp "Revised" on each page where a change has been made, and the date of the change. Clearly describe the revision in the cover letter to reviewers, which transmits the material to be reviewed. The approved reviewers have seen your original request letter and attachments during the solicitation process, and must be made aware of changes.

2. Documents requiring review. All important scientific underpinnings of a proposed science-based rule must be submitted for external peer review. The underpinnings would include all publications (including conference proceedings), reports, and raw data upon which the proposal is based. If there is a question about the value of a particular document, or parts of a document, I should be contacted.

3. Documents not requiring review. The Cal/EPA External Peer Review Guidelines note that there are circumstances where external peer review of supporting scientific documents is not required. An example would be "A particular work product that has been peer reviewed with a known record by a recognized expert or expert body." I would treat this allowance with caution. If you have any doubt about the quality of such external review, or of the reviewers' independence and objectivity, that work product – which could be a component of the proposal - should be provided to the reviewers.

4. Implementation review. Publications which have a solid peer review record, such as a US EPA Criteria document, do not always include an implementation strategy. The Cal/EPA Guidelines require that the implementation of the scientific components of a proposal, or other initiative, must be submitted for external review.

5. Identity of external reviewers. External reviewers should not be informed about the identity of other external reviewers. Our goal has always been to solicit truly independent comments from each reviewer. Allowing the reviewers to know the identity of others sets up the potential for discussions between them that could devalue the independence of the reviews.

6. Panel Formation. Formation of reviewer panels is not appropriate. Panels can take on the appearance of scientific advisory committees and the external reviewers identified through the Cal/EPA process are not to be used as scientific advisors.

7. Conference calls with reviewers. Conference calls with one or more reviewers can be interpreted as seeking collaborative scientific input instead of critical review. Conference calls with reviewers are not allowed.

Guidance to Reviewers from Staff:

1. Discussion of review.

   Reviewers are not allowed to discuss the proposal with individuals who participated in development of the proposal. These individuals are listed in Attachment 3 of the review request.

   Discussions between staff and reviewers are not permitted. Reviewers may request clarification of certain aspects of the review process or the documents sent to them.

   Clarification questions and responses must be in writing. Clarification questions about reviewers' comments by staff and others affiliated with the organization requesting the review, and the responses to them, also must be in writing. These communications will become part of the administrative record.

   The organization requesting independent review should be careful that organization-reviewer communications do not become collaboration, or are perceived by others to have become so. The reviewers are not technical advisors. As such, they would be considered participants in the development of the proposal, and would not be considered by the University of California as external reviewers for future revisions of this or related proposals. The statute requiring external review of science-based rules proposed by Cal/EPA organizations prohibits participants serving as peer reviewers..

2. Disclosure of reviewer Identity and release of review comments.

   Confidentiality begins at the point a potential candidate is contacted by the University of California. Candidates who agree to complete the conflict of interest disclosure form should keep this matter confidential, and should not inform others about their possible role as reviewer.

   Reviewer identity may be kept confidential until review comments are received by the organization that requested the review. After the comments are received, reviewer identity and comments must be made available to anyone requesting them.

   Reviewers are under no obligation to disclose their identity to anyone enquiring. It is recommended reviewers keep their role confidential until after their reviews have been submitted.

3. Requests to reviewers by third parties to discuss comments.

   After they have submitted their reviews, reviewers may be approached by third parties representing special interests, the press, or by colleagues. Reviewers are under no obligation to discuss their comments with them, and we recommend that they do not.

   All outside parties are provided an opportunity to address a proposed regulatory action during the public comment period and at the Cal/EPA organization meeting where the proposal is considered for adoption. Discussions outside these provided avenues for comment could seriously impede the orderly process for vetting the proposal under consideration.

4. Reviewer contact information.

The reviewer's name and professional affiliation should accompany each review. Home address and other personal contact information are considered confidential and should not be part of the comment submittal.

Attachment 4

CURRICULUM VITAE

GARY L. GINSBERG, Ph.D.

Current Address

University of Connecticut Health Center
MPH Program
The Exchange, 270 Farmington Ave. Farmington CT 06032
Phone: (860) 509-7750 gary.ginsberg@ct.gov

Education

B.S. (Pharmacy): State University of N.Y. at Buffalo, 1977
Ph.D. (Toxicology): University of Connecticut, 1986

Current Position

Connecticut Department of Public Health, Toxicologist, since 1994
University of Connecticut, Assistant Professor of Community Medicine, since 1999

Professional Activities

Member, National Academy of Sciences Panel on Inorganic Arsenic (2012-2013 & 2015-2017)
Member, USEPA's Scientific Advisory Board (2008-2015)
Member, National Academy of Sciences Panel on Biomonitoring (2004-2006)
Member, National Academy of Sciences Panel on USEPA Risk Methods (Science & Decisions) (2006-2008)
Member, Children's Health Protection Advisory Committee: Federal Advisory Committee overseeing USEPA activities with respect to children's health (2004-2009)
External Reviewer, IRIS Peer Review Panels (methyl mercury, 2000; kepone, 2008; carbon tetrachloride, 2008; mutagenic mode of action 2008, ETBE 2010, trimethylbenzenes 2014; ethylene oxide 2014, volatile PCBs 2015)
External Reviewer, OSHA Silica Standard (2009 and 2014)
External Reviewer, CPSC Cadmium in Jewelry (2011)
Principle investigator for USEPA NCEA funded research: Inter-individual Variability Due to Genetic Polymorphisms in Xenobiotic Metabolizing Enzymes (2005-2010)
Co-investigator on USEPA STAR grant: Use of Biomonitoring Data to Help Set a Developmental RfD for Chlorpyrifos (Hattis, Clark Univ, PI; 2007-2010).
External Reviewer for New Jersey Dept of Environmental Protection: Carcinogenic Potency of Chromium VI. (October 2008 to January 2009)
External Reviewer for Massachusetts Dept of Environmental Protection: Perchlorate MCL (2006 to 2008)
External Reviewer for Massachusetts Dept of Environmental Protection: Perchloroethylene Cancer Potency (2007-2011)
External Reviewer for California OEHHA Occupational Lead Model (2011-2012)

Professional Affiliations

ORISE Fellow for educational exchange with USEPA NCEA, 2009-2012
Member, Society of Toxicology since 1986

Communication/Educational Activities

Lecturer, Royal Melbourne Institute of Technology, Bundoora Australia, 2012
Adjunct Faculty: Yale University, School of Public Health, 1993-2015
Assistant Clinical Professor, Univ. of Connecticut School of Community Medicine, 1999-2015
Co-Author of "What's Toxic What's Not" Berkley Books, 2006

Awards

Society of Toxicology, Best Risk Assessment Paper of 2009 (Ginsberg, Asgharian et al. 2008)
Society of Toxicology, Public Communications Award, to be awarded at National Meeting New Orleans, March 2016

Recent Publications

Ginsberg G and Balk, S (2016) Consumer products as sources of chemical exposure to children: case study with triclosan. Curr Opinion Peds (in press).

Ginsberg G, Toal B and McCann P (2015) Updated risk/benefit analysis of fish consumption effects on neurodevelopment: implications for setting advisories. Human and Ecological Risk Assessment 21: 1810–1839.

Segal D, *Ginsberg G*, Lin YS, Sonawane B (2015) A conceptual framework for evaluating the interaction of a chemical and nonchemical stressor in human health risk assessments: a case study for lead and psychosocial stress. Human and Ecol Risk Assess 21: 1840-1868.

Ginsberg GL, Dietert RR, and Sonawane, BR (2014) Susceptibility based upon chemical interaction with disease processes: potential implications for risk assessment. Current Environmental Health Reports 1: 314-324.

Ginsberg G., Sonawane B, Nath, R. and Lewandowski P. (2014) Methylmercury-Induced Inhibition of Paraoxonase-1 (PON1)-Implications for Cardiovascular Risk. J Toxicol. Environ. Health Part A 77(17):1004-23.

Lin YS, *Ginsberg G*, Lin JW, Sonawane B. (2014) Mercury exposure and O-3 fatty acid intake in relation to renal function in the US population. Int J Hyg Env Health. 217: 465-72.

Lin YS, *Ginsberg G*, Caffrey JL, Xue J, Vulimiri SV, Nath RG, Sonawane B. (2014) Association of body burden of mercury with liver function test status in the U.S. population. Env Int 70: 88-94.

Ginsberg G. (2012) Cadmium risk assessment in relation to background risk of chronic kidney disease. J. Toxicol. Environ. Health Part A 75: 374-390.

Ginsberg G., Toal B, Simcox, N, Bracker, A, Golembiewski B, Kurland, T and Hedman, C (2011) Human health risk assessment of synthetic turf fields based upon investigation of five fields in Connecticut. J Toxicol Environ Health 74: 1150-1174.

Ginsberg G., Toal, B. and Kurland, T. (2011) Benzothiazole toxicity assessment in support of synthetic turf field human health risk assessment. J Toxicol Environ Health 74: 1175-1183.

Chui W.A. and *Ginsberg G.L. (2011)* Development and evaluation of a harmonized physiologically based pharmacokinetic (PBPK) model for perchloroethylene toxicokinetics in mice, rats, and humans. Toxicol Appl Pharmacol 253: 203-234.

Ginsberg, G.L., Guyton, K.Z., Angle, K. and Sonawane B. (2011) Polymorphism in the DNA Repair Enzyme XRCC1: Utility of Current Database and Implications for Human Health Risk Assessment. Mutation Research Reviews – in press.

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EDUCATION:

Southampton College	Biology and Chemistry	B.S.	1997
University of Maryland	Environmental Chemistry	M.S.	2000
University of Maryland	Environmental Chemistry	Ph.D.	2003
NIST	Analytical Chemistry Division	Postdoc	2003-2005

APPOINTMENTS:

Associate Professor, Nicholas School of the Environment 07/12-present
Assistant Professor, Nicholas School of the Environment 09/05 – 07/12
Duke University, Durham, NC

- Faculty Member, Integrated Toxicology Program 05/06- present
- Secondary Appointment, Civil & Environ Engineering 04/09- present

National Research Council Postdoctoral Fellow 09/03 – 08/05
National Institute of Standards and Technology, Gaithersburg, MD

AWARDS AND RECOGNITIONS:

- Testified at US Senate Hearing on Flame Retardants (July 2012)
- Recipient of the Best Science Paper of 2011: *Environmental Science and Technology*
- Environmental Health News Communication Fellow (2010)
- Recipient of a 2008 NIEHS "Outstanding New Environmental Scientist" (ONES) award ($2.2 million for 5 years)
- First Runner-Up for the Top Environmental Science Paper Award of 2005: *Environmental Science and Technology.*
- National Research Council (NRC) Postdoctoral Research Fellowship (Sept. 2003 – Aug. 2005)
- Otto Hutzinger Award for the best student presentation at the 2003 International Symposium on Halogenated Organic Compounds in the Environment (Dioxin).
- Awarded a 3-year fellowship from the E.P.A.'s Science To Achieve Results (STAR) program. (September 1999). Fellowship number U-915564-01-0

PUBLICATIONS (select examples from a total list of >70)**:**

Hoffman, K., Butt, C.M., Chen, A., Limkakeng, A.T., **Stapleton, H.M.** 2015. High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. *Environ. Sci. Technol.*, DOI: 10.1021/acs.est.5b03577.

Mendelsohn,E., Hagopian, A., Hoffman, K., Butt, C.M., Lorenzo, A., Congleton, J., Webster, T.F. **Stapleton, H.M**. 2015. Nail Polish as a Source of Exposure to Triphenyl Phosphate. *Environ. International,* Accepted.

Macaulay, L.J., Chen, A., Rock, K., Dishaw, L., Dong, W., Hinton, D.E., **Stapleton, H.M.** 2015. Developmental toxicity of the PBDE Metabolite 6-OH-BDE-47 in Zebrafish and the Potential Role of Thyroid Receptor β. *Aquatic Toxicol*., Accepted.

Miranda, M.L., Anthopolos, R., Wolkin, A., **Stapleton, H.M.** 2015. Associations of Birth Outcomes with Maternal Polybrominated Diphenyl Ethers and Thyroid Hormones During Pregnancy. *Environ. International:* 85: 244-253.

Fang, M., Webster, T.F., **Stapleton, H.M.** 2015. Effect-Directed Analysis of Human Peroxisome Proliferator-Activated Nuclear Receptors (PPARγ1) Ligands in Indoor Dust. *Environ. Sci. Technol*. **DOI:** 10.1021/acs.est.5b01524

ACTIVE MEMBERSHIPS IN PROFESSIONAL SOCIETIES:
American Chemical Society
Society of Environmental Toxicology and Chemistry
Association of Environmental Engineering and Science Professors

SERVICE ACTIVITIES:
2014: Invited guest at the United Nations Persistent Organic Pollutants Review Committee (POPRC10) (October, Rome, Italy)
2012: Senate testimony provided for the Environmental & Public Works committee (July, Washington DC)
Organized the 7th annual North American Workshop on Brominated Flame Retardants, held June 13-15, 2005 at NIST in Gaithersburg, MD (165 participants)
Proposal Reviewer: NIEHS, NOAA, Environment Canada, Health Canada
Ad hoc Journal Reviewer: *Environmental Science & Technology*, *Chemosphere*, *Marine Pollution Bulletin, Environment International, Analytical and Bioanalytical Chemistry, Environmental Health Perspectives, Talanta, Toxicological Sciences, Environmental Toxicology & Chemistry*
Journal Editorial Board: *Environment International*
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Dr. Julie Daniels, University of North Carolina, Chapel Hill
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Dr. Russ Hauser, Harvard University
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Dr. Robert J. Letcher, Carleton University, Ottawa, Canada
Dr. John Meeker, University of Michigan School of Public Health
Dr. Marie Lynn Miranda, University of Michigan
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Dr. David Volz, University of South Carolina
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PostDoc Advisor: Dr. Michele Schantz, National Institute of Standards and Technology

Lucio G. COSTA Brief CV

Education

1977 Doctorate in Pharmacy (Pharmacology), University of Milano, Italy

Positions and Employment

1980-1983 Research Scientist, Division of Toxicology, Department of Pharmacology, University of Texas Medical School at Houston, Texas.

1983-present Faculty, Department of Environmental Health, University of Washington, Seattle, Washington (Asst. Prof, 1983-1986; Assoc. Prof., 1987-1991; Professor, 1992-present).

1991-2000 Director, Toxicology Program, Dept. of Environmental Health, UW

1985-present Core faculty, Environmental Pathology/Toxicology Training Program, UW

1995-present Director, Neurotoxicology Research Core, NIEHS Center for Ecogenetics and Environmental Health, UW

2007-present Research Affiliate, Center on Human Development and Disability, University of Washington

Other Experience and Professional Memberships (Selected)

1989- Associate Editor, NeuroToxicology

1997- Editor, Current Protocols in Toxicology

2011- Associate Editor, Toxicological Sciences

2011- Member, Editorial Board, Neurotoxicology and Teratology

2012- Editor, BMC Pharmacology and Toxicology

2010-16 Member, ECVAM's Scientific Advisory Committee, JRC Ispra

2013-15 Member, FEEDAP Panel, European Food Safety Authority, Parma

2010 Member, FAO/WHO Expert group on Risk and Benefit of Fish, Rome

2009 Member, HENVINET Expert Panel on "Chlorpyrifos", Dresden

2009 Member, WHO Expert Panel on "Brominated Flame Retardants", Copenhagen

2008 Chair, Review panel on EPA IRIS on "Toxicological review of thallium and compounds"

2006-07 Member, Review Panel on EPA IRIS on "Toxicological Review of Polybrominated Diphenyl Ethers"

Honors and Awards

1994 Fellow, American Association for the Advancement of Sciences

1995 Achievement Award, Society of Toxicology

1997 Zeneca Travel Lectureship Award, Society of Toxicology

1993- Fellow, Academy of Toxicological Sciences (2010-2013 Board of Directors)

2006- European Certified Toxicologist

Full Bibliography

301 Peer reviewed papers

117 Book Chapters

18 Books

16 Miscellanea articles

260 Abstracts

Research Interests and selected publications

Mechanisms of toxicity of insecticides

a. Costa LG, Murphy SD. [3H]-Nicotine binding in rat brain: alteration after chronic acetylcholinesterase inhibition. J. Pharmacol. Exp. Ther. 1983; 226:392-397.
b. Costa LG, Olibet G, Murphy SD. Alpha2-adrenoceptors as a target for formamidine pesticides: in vitro and in vivo studies in mice. Toxicol. Appl. Pharmacol. 1988; 93:319-328.

Developmental neurotoxicity of ethanol

a. Guizzetti M, Costa LG. Effect of ethanol on protein kinase C zeta and p70S6 kinase activation by carbachol: a possible mechanism for ethanol-induced inhibition of glial cell proliferation. J. Neurochem. 2002; 82: 38-46.
b. Guizzetti M, Moore NH, Giordano G, VanDeMark KL, Costa LG. Ethanol inhibits neuritogenesis induced by astrocyte muscarinic receptors. Glia 2010; 58: 1395-1406.

Biomarkers of acrylamide toxicity

a. Calleman CJ, Bergmark E, Costa LG. Acrylamide is metabolized to glycidamide in the rat: evidence from hemoglobin adduct formation. Chem. Res. Toxicol. 1990; 3:406-412.
b. Calleman CJ, Wu Y, He F, Tian G, Bergmark E, Zhang S, Deng H, Wang Y, Crofton KM, Fennell T, Costa LG. Relationship between biomarkers of exposure and neurological effects in a group of workers exposed to acrylamide. Toxicol. Appl. Pharmacol. 1994; 126:361-371.

Gene-environment interactions: paraoxonase 1 (PON1)

a. Shih DM, Gu L, Xia YR, Navab M, Li WF, Hama S, Castellani LW, Furlong CE, Costa LG, Fogelman AM, Lusis AJ. Mice lacking serum paraoxonase are susceptible to organophosphate toxicity and atherosclerosis. Nature 1998; 394: 284-287.
b. Li WF, Costa LG, Richter RJ, Hagen T, Shih DM, Tward A, Lusis AJ, Furlong CE. Catalytic efficiency determines the in vivo efficacy of PON1 for detoxifying organophosphates. Pharmacogenetics 2000; 10: 767-779.

Oxidative stress and neuroinflammation as mechanisms of neurotoxicity: glutathione and paraoxonase 2

a. Giordano G, White CC, McConnachie LA, Fernandez C, Kavanagh TJ, Costa LG. Neurotoxicity of domoic acid in cerebellar granule neurons in a genetic model of glutathione deficiency. Mol. Pharmacol. 2006; 70: 2116-2126.
b. Giordano G, Tait L, Furlong CE, Cole TB, Kavanagh TJ, Costa LG. Gender differences in brain susceptibility to oxidative stress are mediated by levels of paraoxonase-2 (PON2) expression. Free Rad. Biol. Med. 2013; 58: 98-108.

Selected publications on flame retardants

a. Branchi I, Capone F, Alleva E, Costa LG. Polybrominated diphenyl ethers: neurobehavioral effects following developmental exposure. Neurotoxicology 2003; 24: 449-462.
b. Evandri MG, Costa LG, Bolle P. In vitro assessment of mutagenicity and clastogenicity of BDE-99, a pentabrominated diphenyl ether flame retardant. Environ. Mol. Mutagen. 2003; 42: 85-90.
c. Costa LG, Giordano G. Developmental neurotoxicity of polybrominated diphenyl ether (PBDE) flame retardants. Neurotoxicology 2007; 28: 1047-1067.
d. Giordano G, Kavanagh TJ, Costa LG. Neurotoxicity of a polybrominated diphenyl ether mixture (DE-71) in mouse neurons and astrocytes is modulated by intracellular glutathione levels. Toxicol. Appl. Pharmacol. 2008; 232: 161-168.

Attachment 5

Review Comments of Gary Ginsberg, Ph.D., Toxicologist, Assistant Professor of Community Medicine, University of Connecticut Health Center, MPH Program

on the

Proposed Adoption of Children's Foam-Padded Sleeping Products Containing Tris (1,3-Dichloro-2-Propyl)Phosphate (TDCPP) and/or TRIS (2-Chloroethyl)Phosphate (TCEP) as a Priority Product

Submitted to Dr. Gerald Bowes, Manager Cal/EPA

Scientific Peer Review Program

March 11, 2016

Proposed Conclusion 1: The hazard information that DTSC relied upon is sufficient to conclude that there is the potential for one or more exposures to TDCPP and or TCEP related to the use of children's foam-padded sleeping products containing these chemicals of concern to contribute to or cause significant or widespread adverse impacts to human health.

Comments on TDCPP's Proposed Conclusion 1: The DTSC has identified hazard information for TDCPP that has clear implications for adverse health outcomes in children who become exposed via foam-padded sleeping products. The database is strong with respect to evidence for cancer in animals with the dose response for renal and testicular tumors in rats showing the clearest compound-related effect. Other tumor sites were also elevated. While the mechanism for these tumors has not been elucidated, the evidence of genotoxic effect in multiple studies suggests a genotoxic action. There are no negative (free of effect) cancer studies or coherent mechanistic information that would suggest that TDCPP would not produce a cancer risk at low dose in exposed children. While early life cancer vulnerabilities have not been explored, the positive genotoxicity response suggests that the series of age-dependent adjustment factors applied to mutagenic carcinogens may be appropriate for TDCPP. The National Academy of Sciences report on flame retardants derived a cancer slope factor and risk estimates for a variety of TDCPP exposure scenarios (NAP 2000). Thus, the cancer endpoints identified by DTSC are strongly supported and represent a major concern to children who may receive exposure via foam padded products. Other endpoints described by DTSC have merit as potentially adding to TDCPP's human health impact although in each case (developmental toxicity, reproductive toxicity, endocrine toxicity, neurotoxicity, acute toxicity) suggestive findings for certain endpoints could use additional research to explore the implications for low dose exposures in early life stage human receptors.

Supporting Information: the evidence that TCDPP can degrade via metabolism to other toxic chemicals adds to the weight of evidence of adversity for this flame retardant. The list of mutagenic and

carcinogenic degredates is substantial. However, the document provides no insight into the percent production of these degradates and metabolites in environmental media or biological samples. For example, formation of the bis-metabolite (BDCPP) is mentioned in passing – examination of one of the references- Sasaki et al. 1984 – indicates that the glutathione conjugate (detoxification) can be more rapidly and efficiently produced from TCDPP than the oxidative metabolite (allegedly activation step). Thus this section should focus on the most quantitatively important degredates and better describe the levels which have been detected, the systems and enzymes responsible, the stability (half-life) of the degredates, and their potential contribution to the hazard profile of TDCPP.

Comments on TCEP's Proposed Conclusion 1: The DTSC has identified hazard information for TCEP that indicates adversity of effect in animals with clear implications for adverse health outcomes in children who become exposed via foam-padded sleeping products. In cancer studies TCEP caused a clear dose response for kidney tumors in male rats (renal tubule adenomas) with a trend for this effect also occurring in female rats. Given the lack of genotoxicity evidence, this kidney cancer effect may not have arisen from an effect on the integrity of the DNA template. However, the cancer mechanism has not been explored and so remains an uncertainty. Another adverse effect seen in TCEP testing is fetotoxicity with poor pup survival in a multi-generation design in mice. ATSDR considered the fetotoxic effect in generation F2 pups a serious reproductive effect. A NOAEL for this effect was not identified as the lowest dose was associated with poorer survival. TCEP has shown evidence of a severe neurotoxic effect in adult rats dosed by gavage for 16 weeks. The effect in female rats was particularly noteworthy in which there was a high incidence of necrosis in hippocampal neurons along a dose response which showed evidence of a no effect at the lowest dose tested. These three serious adverse effects clearly caused by TCEP in animal testing, renal cancer, necrosis of brain neurons, and fetotoxicity, show that TCEP can be a carcinogen, developmental toxicant and neurotoxicant. These effects produce a concern for human health in general and children's health in particular in relation to their potential exposures from foam-padded sleeping products.

Supporting Information: I note that DTSC did not provide information on environmental or metabolic products that may contribute to the overall hazard profile of TCEP. Therefore it is assumed that none such products or structural analogues exist.

Proposed Conclusion #2: The information that DTSC relied upon to evaluate exposures is sufficient to conclude that there is a potential for exposure to TDCPP and or TCEP related to the use of children's foam-padded sleeping products containing these chemicals of concern.

Comments on TDCPP's Proposed Conclusion 2: This exposure conclusion is worded in a vague manner that does not necessarily confer a health concern even if a finding of sufficiency of evidence is made. The conclusion is with respect to whether there is a potential for exposure. This does not ask whether there is a low vs high potential for exposure, or whether exposure may be frequent and consistent vs sporadic or even rare, and whether exposure may only last a short duration or is likely to continue for a substantial window of early life development. The manner in which the exposure evidence is laid out by DTSC is as a loosely connected string of facts rather than as coherent documentation of exposure from a specific type of consumer product. For example the environmental fate properties of TDCPP described

on Page 21 state that TDCPP can volatilize into ambient air. Is TDCPP considered a volatile or semi-volatile organic compound? Will its release rate from products be sufficient to support indoor air concentrations? If it is present in foam that is underneath a layer of covering plastic, will molecules find their way through the covering layer? Does this covering layer need to be ripped for TDCPP to reach indoor air? Are there any models which describe TDCPP release from such products with formation of indoor air concentrations and sorption onto dust particles? On Pages 25-29 an array of facts from cited sources are listed: that TDCPP is found in a variety of house dust studies, that it has been found on children's hand wipes and in breast milk and that TDCPP may be inhaled or absorbed across the skin or via dust ingestion. This evidence is useful to show TDCPP is mobile in the indoor environment and has an exposure potential; however, most of this evidence is not specific to foam-padded products. There were only a few entries that were specific to the exposure question at hand: evidence that TCDPP is in children's products (Cox 2013, Stapleton et al. 2011 – but how much released from these products was not tested). Perhaps the most compelling exposure evidence implicating children's sleep mats was that indoor dust concentrations were higher in day care centers where foam nap mats were in use (Bradman et al. 2012/2014). This constitutes reasonably strong evidence that children's foam padded products can make a substantial contribution to a child's exposure to TDCPP. Calculations by Stapleton et al. 2011 and Babich 2006 that TDCPP from treated foam can lead to greater exposure than from other sources and can exceed a non-cancer ADI is additional supporting evidence. It would appear that the concepts and evidence from these three groups (Bradman et al. 2012, 2014; Stapleton et al. 2011; Babich 2006) could be used to build a narrative concerning the release of TDCPP from children's foam sleep products that would better highlight the exposure potential and justify the listing of this type of product as a priority. That narrative could include the fact that TDCPP is frequently found in children's foam products, the types of activities and amounts of time young children spend around such products, estimates of the offgas rates from foam into indoor air and house dust, and a summary of the pathways (inhalation, dermal, ingestion) and frequencies of these pathways which lead to substantiative childhood contact; this type of review and analysis would better document the exposure potential and support the nomination of foam padded sleeping products as being of high priority. .

Comments on TCEP's Proposed Conclusion #2: My comments are similar for TCEP as for TDCPP. TCEP has also been shown to be higher in day care settings where children's sleeping mats are in use thus implicating children's foam padded products as a substantiative source. TCEP has a vapor pressure that is orders of magnitude greater than TDCPP – however, the implications of this physical feature on the potential for children's exposure is not described. It does not appear that CPSC (Babich 2006) analyzed TCEP and so the type of exposure analysis conducted for TDCPP from foam products does not appear to be available for TCEP.

Overall, I agree that the evidence is supportive for substantiative exposure to children to both TDCPP and TCEP from foam padded products but the DTSC report could have done a better job documenting this exposure by highlighting the key studies (e.g. Bradman et al. 2014), exploring the utility of fate and exposure modeling, exploring the uncertainties in the statements made, and by better definition of the exposure scenario involving children and their contact with the foam padded products.

The Big Picture – Additional Scientific Issues, The Use of Sound Science

A key issue is with respect to the question of whether a risk assessment is needed to further document the hazard associated with foam padded sleep mats to children. Risk assessments are complex and involve a number of key assumptions about exposure rates, pro-rating of exposures to match the time frame of the health outcome, identification of well accepted toxic potency values (e.g., RfDs, Cancer Potency Factors), and extrapolations across species and from high to low dose. Thus, risk assessments involve a degree of uncertainty and bounding assumptions which can affect their utility for risk management decision-making. While the document provides an array of exposure estimates, these are generally without context as we cannot tell whether the exposure estimate is: 1) close to a level of exposure that is a health concern; and 2) what portion of that exposure is coming from the products in question (foam padded products for children). Risk assessment values were mentioned when describing the Bradman et al. 2012/2014 results in that the TDCPP results are described as surpassing the age-adjusted No Significant Risk Level (NSRL) for carcinogenicity for 51% of the child care facilities. However, from this we don't know if this risk was driven by the presence of foam padded sleep mats, whether the TCEP data were also associated with elevated health risk, and whether any other approaches or data may be available to confirm an elevated health risk from TDCPP or TCEP in the nominated products. On the one hand, I don't believe a formal risk assessment is needed to justify an elevated concern as these flame retardants are carcinogens with a variety of other actions and foam padded mats are a fairly obvious source of children's exposure. However, going through a risk assessment one learns where the key data can be found and where there are important data gaps which create uncertainty in exposure and risk. Organizing the analysis around a comparative exposure assessment (what are the most important sources of these flame retardants in a child's environment) or a risk assessment would help place the data into a larger context and potentially be an aid to risk management.

NICHOLAS SCHOOL OF THE ENVIRONMENT
DUKE UNIVERSITY

March 14, 2016

Gerald W. Bowes, PhD
Manager, CA/EPA Scientific Peer Review Program
Office of Research, Planning and Performance
State Water Resources Control Board
1001 "I" Street, 16th Floor
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Dear. Dr. Bowes,

I have reviewed the "Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris (1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product". Please find attached my comments and conclusions regarding the scientific knowledge, methods and practices used in preparing the document.

If you have any further questions or requests of me, please do not hesitate to ask.

Sincerely,

Heather Stapleton

Heather Stapleton, PhD

Associate Professor of Environmental Chemistry
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External Peer Review Comments

After a thorough review of the published scientific literature up through 2015, the Department of Toxic Substances Control (DTSC) within the California Environmental Protection Agency drafted a technical summary describing research related to the use of Tris (1,3-dichloro-2-propyl) Phosphate (TDCPP) and Tris(2-chloroethyl) Phosphate (TCEP) in consumer products, potential human exposure to TDCPP and TCEP and reported health effects, both in animal studies and human epidemiological studies. This report was titled "Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products with Tris (1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris(2-chloroethyl) Phosphate (TCEP) as a Priority Product". Two conclusions were reached based on the information presented in the technical report. These two conclusions were as follows:

1. The hazard information that DTSC relied upon is sufficient to conclude that there is the *potential* for one or more exposures to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these Chemicals of Concern to contribute to or cause significant or widespread adverse impacts on human health.

2. The information that DTSC relied upon to evaluate exposures is sufficient to conclude that there is a *potential* for exposure to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these Chemicals of Concern.

In the following I will comment on the scientific data presented and conclusions drawn. I would like to begin with comments related to Conclusion #2 above.

Based on the scientific data provided in the technical document is is quite clear that exposure to both TDCPP and TCEP is ubiquitous among the US population. Higher levels of the urinary metabolites of TDCPP and TCEP have been detected at rates typically greater than 94% in several studies, and levels are significantly higher in young children relative to adults. Furthermore, *potential* exposure to TDCPP and/or TCEP from children's foam-padded sleeping products is very feasible given the applications of these chemicals to these products. One study in particular demonstrated that TDCPP was the most common flame retardant used in infant products containing polyurethane foam, which included changing table pads, sleep positioners and portable mattresses. Given that off-gassing is hypothesized to be a primary route by which these chemicals migrate out of the products over time, exposure to these chemicals is very likely. As further support to this testament, a recently published study (Hoffman et al. 2015), which was not included in the technical report, found that the levels of the urinary metabolite of TDCPP (BDCIPP) measured in infant's urine were significantly associated with the number of foam-containing infant products the parents reported owning in the home. This suggested that the foam-containing children's products were a source of exposure to the infants. Furthermore, the average level of BDCIPP measured in infant's urine was higher than the average level measured in toddler's urine (Butt et al. 2014), and significantly higher than levels measured in adults. Therefore, I do believe the conclusions reached in Conclusion #2 are based on sound scientific knowledge and methods.

Secondly, I will comment on the data presented to support Conclusion #1, related to the potential for exposure to TDCPP and/or TCEP to contribute to or cause significant or widespread adverse impacts on human health. The key words that need to be examined in this statement are "significant/widespread" and "adverse impacts on human health". Both of these terms/phrases can be somewhat subjective and therefore one must rely upon scientific judgment. Below are several specific comments on statements made in the technical summary that should be considered further in evaluating this conclusion.

1. On page 6, it states that "The U.S. Environmental Protection Agency (U.S. EPA) estimates that children ages one to five years old ingest on average approximately 100-200 mg dust/day." I do

not believe that this estimate is accurate, and it is unclear as to where this ingestion rate was taken from in the literature. The U.S. EPA updates the Exposure Factors Handbook (EFH) every few years, and the 2011 version of the EFH states that children ages 1 to <21 years are estimated to ingest approximately 60 mg of dust/day. I believe the ingestion rates cited in the DTSC technical document were either taken from significantly older versions of the EFH, or from scientific literature that did not cite the most recent EFH. Therefore, I think this needs to be updated with the more recent and accurate ingestion rates as this will alter the potential exposure estimates.

2. On page 13, it states that "Exposure to TDCPP above 5.4 micrograms/day exceeds the Office of Environmental Health Hazard Assessment (OEHHA) No Significant Risk Level (NSRL) for TDCPP." This threshold level should be re-checked with OEHHA as I was under the impression that the NSRL was 5.4 micrograms/kg body weight/day. The latter estimate would also be more in line with the Acceptable Daily Dose (ADD) defined by the Consumer Product Safety Commission as outlined in the report by Babich, 2006 related to increased risk for cancer.

3. Pages 13-20 describe a number of studies reporting on adverse effects observed in animal studies conducted in laboratories following exposure to either TDCPP or TCEP. However, in each description, no exposure levels are provided. This makes it very challenging to evaluate the potential for "significant adverse impacts" among the human population. The technical report could be significantly improved by creating a table in the report that summarizes all the animal studies based on: species/strain, doses tested, route of exposure, developmental period tested, duration of exposure, and outcomes observed. To evaluate this risk for adverse impacts in a human population, one must weigh the exposure levels eliciting specific adverse impacts in animal studies relative to the exposure levels occurring in the human population, with inclusion of a safety factor for inter-species comparisons (U.S. EPA, Integrated Risk Information System). It does seem quite clear that a variety of potential adverse effects (e.g. carcinogenicity, neurotoxicity) can occur, but what is not clear is the internal dose levels at which these effects occur, and how that relates to exposure levels measured in the US population. There are two ways in which this could be addressed.
    a. The DTSC could use the dust ingestion rates reported in the EFH (60 mg/day) and estimate children's exposure to TDCPP and TCEP based on measured levels in house dust and then compare the estimated exposure to an effects threshold. Only one study referenced in the technical report used this approach (Bradman et al. 2012). They estimated that 51% of 40 ECE facilities (i.e. childcare centers) tested in California had TDCPP exposure levels that exceeded the No Significant Risk Level (NSRL) for carcinogenicity. This study provides a sound scientific rationale to support Conclusion #1; however, further analyses should be conducted to determine how frequently exposure levels in most homes across the US exceed the NSRL for carcinogenicity. Again this can be accomplished by taking measured levels reported in the literature and using the dust ingestion rates reported in the EFH. On page 29, the DTSC report references two studies (Kim et al. 2014 and Sundkvist et al. 2010 that did use a dust ingestion rate to estimate median exposure to TDCPP. The median exposure estimates ranged from 0.05 to 0.73 ng/kg/day for adults and toddlers, respectively. However, these estimates were made in populations outside the US (where exposure levels are likely lower) and they did not take into account the non-normal distribution of TDCPP levels in home environments. Studies demonstrate that TDCPP and TCEP levels in house dust are not normally distributed, indicating that some homes have very high levels and some homes have very low levels. Exposure estimates should be calculated taking these very high exposure levels (e.g. 95th percentile TDCPP levels in house dust) into consideration.

b. A second approach that could be used to estimate exposure levels in the US population would be to estimate exposure using urinary metabolite levels (see Lorber and Calafat, 2012).

4. In order to compare effects observed in animals with levels measured in human tissues it would also be beneficial for the DTSC to create a table listing the range and median levels of TDCPP and TCEP measured and categorized by tissue type (e.g. breast milk, adipose, urine), and by country. The latter category is particularly important as studies have demonstrated that exposure to TDCPP in particular varies substantially depending on the population/country (likely a reflection of different chemical use patterns among countries). Thus levels measured in European countries/populations may be quite different, and thus have different risks, compared to levels in the US. As reported in the technical information on pages 26-29, it is impossible to tell what country and populations these measurements were made from.

5. One page 19 under carcinogenicity of TCEP, it states that the International Agency for Research on Cancer (IARC) found that there was limited evidence for carcinogenic activity of TCEP in experimental animals and concluded that TCEP is not classifiable as to its carcinogenicity to humans. This statements appears to contradict the previous statement in which the National Toxicology Program (NTP) did conclude that there was clear evidence of carcinogenic activity of TCEP in rats. It would be helpful if the DTSC could summarize the rationale used by the IARC in not declaring TCEP as a carcinogen given the findings of the NTP study.

6. On page 19, please define and describe the "adverse impacts on the reproductive capacity of mice seen at low doses" and define the dose and pathway tested. I cannot locate a copy of this reference provided to support this statement (Gulati et al. 1991).

Based on the information provided in the technical summary, and my own scientific judgment, I do think there is *some evidence* to suggest that exposure to TDCPP/TCEP may cause adverse effects on human health. In my opinion, the data provided by Babich 2006 and Bradman et al. 2012 are the best scientific evidence to support this statement. Babich (2006) in particular estimated that exposure to TDCPP from treated upholstered furniture was higher than the Acceptable Daily Dose (ADD) for an increased risk of cancer. His estimate was 300 per million, which is higher than the CPSC's suggested threshold of one per million. However, it should be noted that this estimate is based solely on exposure from treated upholstery. Infants may have higher exposure to TDCPP through greater contact times with foam-treated baby products such as car seats, mattresses, and sleep positioners (as suggested by Hoffman et al. 2015), thus increasing the cancer risk.

Lastly, it would be beneficial to more clearly estimate exposure levels among the US population, using approaches described in Comment #3 above, and comparing those exposure levels with the NSRL as further support. Unfortunately, there is no systematic biomonitoring program that estimates exposure among the US population based on age and demographics (similar to the program available for other hazardous chemicals such as DDT and PCBs through the National Health and Nutrition Examination Survey (NHANES)). Therefore, it is critical that an estimation of the likely range of exposures, particularly for sensitive populations such as infants, be characterized. While there are numerous reports of effects in animals following exposure to TDCPP or TCEP, the lack of information provided on exposure levels and pathways that elicit these effects prevent me from adequately assessing their likelihood to lead to significant adverse effects in the human population.

External peer review of the proposed adoption of document "Children's Foam-Padded Sleeping Products Containing Tris (1,3-dichloro-2-propyl) Phosphate (TDCPP) and/or Tris (2-chloroethyl) Phosphate (TCEP) as a Priority Product"

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The purpose of this review is to critically evaluate the document entitled "Summary of Technical Information and Scientific Conclusions for Designating Children's Foam-Padded Sleeping Products Containing Tris (1,3-dichloro-2 propyl) Phosphate (TDCPP) and/or Tris (2-chloroethyl) Phosphate (TCEP) as a Priority Products" (Safety Consumer Product Program, Department of Toxic Substances Control, California Environmental Protection Agency, July 2015, pp. 47).

Introduction

The document was developed with the of intent of illustrating the rationale of DTSC (California Department of Toxic Substances Control) in identifying and prioritizing children's foam-padded sleeping products containing the flame retardants TDCPP and/or TCEP for listing as a Priority Product. In order to adopt Children's Foam-Padded Sleeping Products Containing TDCPP and/or TCEP as Priority Product under the Safer Consumer Products regulatory framework, DTSC is required to ensure that the following conditions are met: (1) The products contains the chemicals of concern and is sold in California; (2) Exposure to these chemicals may cause significant or widespread adverse impacts to people or the environment; and (3) Exposure to these chemicals may occur through normal use, handling, or disposal of the products.

The main focus of this review thus relates to (1) whether the hazard information that DTSC relied upon is sufficient to conclude that one or more exposures to these chemicals can cause or contribute to adverse health effects on human health; and (2) whether the information is sufficient to conclude that there is the potential for exposure to these chemicals related to the use of children's padded sleeping products. In simplified terms, the overall question to address is: Could humans be exposed to these chemicals, and if so, is there the possibility of adverse health effects, particularly in sensitive subpopulations?

The document by DTCS concludes that the proposal to adopt Children's Foam-Padded Sleeping Products Containing TDCPP and/or TCEP as Priority Product under the Safer Consumer Products regulatory framework meets the required regulatory criteria, and presents the following conclusions: (1) Exposure to the flame retardants TDCPP and/or TCEP may contribute to or cause significant or widespread adverse impacts to people, particularly to infants, children, pregnant women, and school and day care workers; and (2) people, particularly the sensitive subpopulations noted above, may be exposed to

these chemicals through normal use, handling, or disposal of children's foam-padded sleeping products that contain one or both of these chemicals.

My review of the document is articulated in three parts. In the first two parts I will address the two conclusions, commenting on the assumptions, the findings, and the supporting evidence. In the third part I will provide general and specific suggestions and/or queries related to the document.

Comments on Conclusion No. 1

Conclusion No. 1 states that "*The hazard information that DTCS relied upon is sufficient to conclude that there is the potential for one or more exposures to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these chemicals of concern to contribute to or cause significant or widespread adverse impacts to human health*". To reach this conclusion, the literature on the toxicology of TDCCP and TCEP was carefully and extensively reviewed, considering in vitro and animal studies, and human epidemiological studies when available. A further literature analysis did not reveal additional significant information, with the exception of a few supporting and/or clarifying references which are listed at the end of this review. The supporting evidence for the conclusion is thus solid and the conclusion itself is based on a discussion of the adverse effects of these compounds discussed, separately for each compound, in section IV (Hazard Traits). TDCPP is the compound for which more information is available; indeed it had been removed from children's pajamas in the 1970s because of toxicological concerns related particularly to its mutagenicity/carcinogenicity. These important end-points of toxicity are highly significant, and TDCPP is classified as a Category 2 compound (Suspected of causing Cancer) by the European Chemical Agency (ECHA), and is listed as a carcinogen in the State of California under Proposition 65. Supporting evidence for this is based on positive animal carcinogenesis bioassays, and on the positive genotoxicity results observed with TDCPP in vitro and in vivo. Several other end-points of toxicological relevance for TDCPP are discussed in the document, and provide supportive evidence for the conclusion that this chemical can cause adverse health effects. In particular, TDCPP is an endocrine disruptor, as indicated by several studies in various animal species which show interference with estrogens and with thyroid hormones. Evidence for other adverse effects (e.g. neurotoxicity, hepatotoxicity, reproductive toxicity) is less strong, as both positive and negative effects have been reported; in addition, the data base of toxicological information is not as complete as one would wish.

In addition to the adverse effects associated with exposure to TDCPP, the document also evaluated the possible effects of its metabolites (Section VI). Of much relevance is the finding that two TCDPP metabolites (1,3-dichloro-2-propanol and 3-MCPD) are mutagenic and carcinogenic. Indeed both are listed as carcinogens under Proposition 65 and are listed as 2B carcinogens (possible human carcinogens) by the International Agency for Research on Cancer (IARC). These findings add support and strength to the conclusion. A compound structurally very similar to TCDPP, i.e. TBDPP [Tris (1,3-dibromopropyl) phosphate], also used as a flame retardant, is also carcinogenic in rats and mice, and is classified as a 2A carcinogen (probable human carcinogen) by IARC. This adds indirect support to the overall toxicological evaluation of TCDPP.

Less toxicological information is available for TCEP. TCEP was found to be clearly carcinogenic in a study in rats done by the National Toxicology Program, and possibly carcinogenic in another study in mice, and for this reason is listed as a carcinogen under Proposition 65. However, IARC concluded that TECP is not classifiable as to its carcinogenicity to humans because of limited evidence. Surprisingly, no information on the genotoxicity of TCEP is available, which would have provided further important evidence. A chemical which is structurally similar to TCEP [TCPP; Tris (1-chloro-2-propyl) phosphate] has been shown to be genotoxic in vitro but not in vivo. The main adverse effect caused by TCEP appears to be reproductive toxicity, as this compound has been found to be a male and female reproductive toxicant, and is classified as a reproductive toxicant by ECHA. Additional toxic effects of TCEP include hepatotoxicity, nephrotoxicity, and neurotoxicity. I also found recent evidence that TCEP may exert endocrine toxicity (see reference at the end of this review).

In summary, there is ample evidence that exposure to TDCPP and to some of its metabolites can cause severe adverse health effects; for TCEP the evidence is less strong, partly because the data-base is not as extensive as desired to support the statutory requirement for absolute scientific rigor. However, in such situations the proposed course of action is favored over no action. Thus overall, the DTSC succeeds in showing that exposure to TDCPP and/or TCEP may cause adverse effects on human health.

Comments on Conclusion No. 2

Conclusion No. 2 states that "*The information that DTSC relied upon to evaluate exposures is sufficient to conclude that there is a potential for exposure to TDCPP and/or TCEP related to the use of children's foam-padded sleeping products containing these chemicals of concern*". Both TDCPP and TCEP are "additive" flame retardants, i.e. they are not chemically bound to the polymer of the product (polyurethane foam in this case). As such, like other similar flame retardants (e.g. the polybrominated diphenyl ethers) they tend to leach from the product to the environment. The physicochemical properties of the two chemicals are briefly summarized in the document, and show in particular the lipophilicity of TDCPP. As is the case with several other compounds with similar characteristics, TDCPP and TCEP would tend to accumulate in a variety of biota including dust, soil, and sediments. The presence of TDCPP and TCEP in dust and air is most relevant with regard to human exposure, and of the two chemicals TDCPP is of higher concern, because of the toxicological characteristics discussed in conclusion No. 1, its production volume which is two orders of magnitude higher than that of TCEP, and the results of biomonitoring studies, which reveal its presence in almost all media and biota analyzed. The document clearly and effectively shows how TDCPP has been detected in dust samples from multiple locations, in air, and in hand-wipe samples. As exposure would occur through the oral, dermal and inhalation routes, exposure to TDCPP would thus certainly be expected. This is confirmed by the findings of biomonitoring investigations in which TDCPP was detected in human adipose tissue, urine, and breast milk. With regard to TCEP, the compound was detected in indoor dust samples, in hand-wipe samples, and in indoor air. Biomonitoring studies have indicated the presence of TCEP and/or its metabolite DCEP [bis (2-chloroethyl) phosphate] in human urine and breast milk.

A main issue of conclusion No. 2 relates to the potential exposure to TDCPP and TCEP of sensitive subpopulations. Infants and toddlers are the most significant of these subpopulations, not only because of their intrinsic higher susceptibility to toxic insults (due for example to an incomplete development of xenobiotic metabolizing enzymes), but also because of a higher exposure compared to adults give that these chemicals are used in children's foam-padded sleeping products. Thus, high levels of TDCPP and TCEP in indoor dust and air in environments such as ECE (Early Childhood Education) facilities would lead to significant oral (through hand to mouth behavior) and inhalation exposures of toddlers. In addition, the presence of TDCPP and TCEP in breast milk would inevitably lead to exposure of infants to these chemicals. Human exposure estimates indicate a higher exposure to TDCPP than to TCEP (by about two-fold), which is understandable given their relative usage. However, the most significant and alarming parameter is the estimated relative exposure of adults and toddlers, based on exposure through indoor dust, which indicates a >15-fold higher exposure of the latter (data are in ng/kg bw/day):

	TDCPP	TCEP
Adults	0.05	0.02
Toddlers	0.73	0.34

Limited biomonitoring data confirm this scenario. For example, levels of the primary urinary metabolite of TDCPP, i.e. BDCPP [bis (1,3-dichloro-2-propyl) phosphate], were found in one study to be 4.9-fold higher in children than in their mothers. In addition, as said, exposure through breast milk of infants may also occur.

In summary, there is documented evidence that, because of their nature as additive flame retardants, TDCPP and TCEP are released in the environment; their presence in various media (dust, air) leads to human exposure, as confirmed by biological monitoring findings. In addition, data show that potentially more sensitive sub-populations, such as infants and toddlers, are exposed to significantly higher levels than adults, through dust, air, and breast milk.

General and specific comments on the document

As indicated in the preceding paragraphs, the conclusions are supported by reasonable assumptions, evidence and findings, which are endorsed by this reviewer. However, the document itself may benefit of a number of changes and possible improvements. In this section I will indicate some general aspects that may be considered in a revision of the document, as well as specific comments for each section of the document.

A general comment, which I will reiterate later, is that there is a lack of "quantitative indicators" throughout the document. Indeed the first numbers seem to be presented only on p. 29. With regard to toxicology, it would be useful if at least some statements are completed by indications of the dose and the duration of exposure. Indeed, the review of the toxicity data (Section IV) only points to a series of observed effects without any consideration on doses or concentrations, which would be of relevance,

allowing placing the various toxic effects in perspective. With regard to exposure, similar considerations would apply, as there is only indication that TDCPP, TCEP and/or their metabolites were detected in various media and biota, without any indication of the levels. Nevertheless, the data summarized in the report clearly support the notion that these compounds are capable to cause adverse effects in animals and presumably in humans, and that human exposure is common and well documented.

It would be very useful to add a list of abbreviations and acronyms at the beginning or at the end of the document to facilitate the reader.

Specific comments on each section are as follows:

Section I. Executive Summary
This section is generally good. I would recommend deleting duplicate sentences on the classification of TCEP as a reproductive toxicant (p. 7, last line and p. 8 line 4).

Section II. Identification of the priority product and the chemicals of concern
I have no comments on this section.

Section III. Physicochemical properties
Perhaps a sentence for each compound would be useful explaining what the major characteristics are and its consequences for human exposure and body burden and with regard to environmental bioaccumulation.

Section IV. Hazard traits
As indicated earlier, quantitative aspects are lacking in this section.
Overall, the section presents a comprehensive summary of adverse health effects, with indications of both positive and negative studies.
p. 13: is there any IARC classification of TDCPP?
p. 17: in the section on endocrine toxicity, a reference by Dishaw et al. (2014) may be added.
p. 18: In the list of various toxic effects, no indications of dose levels are reported making it difficult to ascertain their significance and their relative importance.
p. 19: Is the any information on TCEP genotoxicity?
p. 19: Could more details be added regarding TCEP carcinogenicity?
p. 19: Could the statement on TCEP classification as a reproductive toxicant be expanded?
p. 20: A reference (Chen et al. 2015) on TCEP endocrine toxicity in mice may be added

Section V. Environmental fate
No further comments.

Section VI. Potential for TDCPP to degrade, form reaction products, or metabolize into another candidate chemical that exhibits one or more hazard traits

p. 23: Have the compounds listed as metabolites of TDCPP been identified in vivo in animals and/or humans?
p. 23: the main metabolite of TDCPP appears to be BDCPP (see also p. 28). Does it have any toxicity? Is its detection only useful to indicate exposure to TDCPP?
p. 23: Proposed metabolites of TDCPP. Has this metabolite ever been detected (in vitro/ in vivo)? Is it only a compound presumed to be formed in vivo? More details are needed.

Section VII. Adverse impacts associated with structurally/mechanistically similar chemicals
The significance of this section needs to be better explained in the introductory paragraph, as there are significant toxicological differences between the two compounds described in this section (TDBPP and TCPP) and those that are the focus of the report.

Section VIII. Exposure potential of people of wildlife to TDCPP or TCEP in children's foam-padded sleeping products
The lack of quantitative information does not allow an understanding of the significance of exposure with regard to body burden. The simple detection of unspecified, presumably low levels of TDCPP or TCEP or their metabolites is not a direct indication of hazard.
p. 25: A recent study (Schreder et al. 2016) suggests that inhalation is a relevant route of exposure to TDCPP in children.
p. 27: Give ranges of TDCPP levels in indoor house dust.
p. 28: It should be specified that detection of BDCPP only indicates possible exposure to TDCPP and is not associated with specific toxicity.
p. 28- 29: a recent paper by Hoffman et al. (2015) also reports on body burden.
p. 29: A paragraph begins with a reference (8c).
p. 29: In sub-section 8e some quantitative information seems necessary.
p. 32: It may be noted that production of TCEP is two orders of magnitude less than that of TDCPP.
p. 32: TCEP is reported to have been found in children's car seats though these had been stated earlier not be covered by this report.
p. 33: TCEP levels found in dust should be indicated (at least a range).
p. 33: The chemical name of V6 [tetrekis (2-chloroetheyl) dichloroisopentyldiphosphate] should be indicated.

Section IX. Potential exposure of sensitive subpopulations to TDCPP or TCEP
p. 36 (1a): Detection of TDCPP and TCEP in breast milk does not necessarily imply exposure. First sentence may be modified from " Infants are exposed to …" to "Infants may be exposed to…".

Section X. Conclusions
This section summarizes well the main issues at hand.

Section XI. References
The list of references is very comprehensive.

The following newer references (cited above) may be added:

Chen G, Jin Y, Wu Y, Liu L, Fu Z (2015) Exposure of male mice to two kinds of organophosphate flame retardants (OPFRs) induce oxidative stress and endocrine disruption. Environmental Toxicology & Pharmacology 40: 310-8.

Dishaw LV, Macaulay LJ, Roberts SC, Stapleton HM (2014) Exposures, mechanisms, and impacts of endocrine-active flame retardants. Current Opinion in Pharmacology 19: 125-33.

Hoffman K, Butt CM, Chen A, Limkakeng AT, Stapleton HM (2015) High exposure to organophosphate flame retardants in infants: associations with baby products. Environmental Science & Technology 49: 14554-9.

Schreder ED, Uding N, LA Guardia MJ (2016) Inhalation a significant exposure route for chlorinated organophosphate flame retardants. Chemosphere (in press).