U.S. Consumer Product Safety Commission
LOG OF MEETING

SUBJECT: National Academy of Sciences Subcommittee on Flame Retardant Chemicals in Upholstered Furniture (Public Session)

DATE OF MEETING: September 22, 1999

LOG ENTRY SOURCE: Michael A. Babich, HS MAB

DATE OF LOG ENTRY: September 28, 1999

LOCATION: National Academy of Sciences Arnold and Mabel Beckman Center, University of California, 100 Academy Drive, Conference Room 2D, Irvine, California

CPSC ATTENDEE(S): Michael A. Babich, HS; Patricia M. Bittner, HS

NON-CPSC ATTENDEE(S):
Members of the National Academy of Sciences (NAS) Subcommittee: Donald Gardner, Chair, David Gaylor, Sidney Green, Sam Kacew, Robert Snyder, Robert Tardiff, and Mary Vore. (See attachment. Not all Subcommittee members were present).

NAS staff: Kulbir Bakshi, Project Director, Michelle Catlin, and Evelyn Simeon.

NAS Contractors: Representatives from TERA, Syracuse Research Associates, and Oak Ridge National Laboratory.

American Furniture Manufacturers Association (AFMA): Judith MacGregor, Russ Batson

SUMMARY OF MEETING: The National Academy of Sciences is under contract to CPSC to perform a study of the toxicological risk associated with 16 flame retardant (FR) chemicals or chemical classes. This is the second meeting of the subcommittee. The afternoon session (9/22) is the only portion of the 2-day meeting (9/22-23) that was open to the public. Donald Gardner introduced the subcommittee members and reviewed the purpose of the meeting and the statement of task. Michael Babich provided an overview of the upholstered furniture project, the Federal Hazardous Substances Act, and the CPSC risk assessment process for FR chemicals. Patricia Bittner summarized the CPSC staff toxicity reviews of the second set of 7 FR chemicals or chemical classes: tetrakis hydroxymethylphosphonium salts precondensate with urea, organic phosphonates and cyclic phosphonate esters, ammonium polyphosphates and blends, antimony pentoxide and sodium antimonate, chlorinated paraffins, zinc

borate, and calcium and zinc molybdates. (The first 7 were discussed at the July 29 meeting. The remaining 2--tris (chloropropyl) phosphate and aromatic phosphates--will be discussed at the next meeting.) Mr. Babich and Ms. Bittner responded to questions.

ATTACHMENTS:
Agenda
Subcommittee Roster
Statement on the purpose of the meeting
Statement of Task
Statement of Michael Babich
Statement of Patricia Bittner

THE NATIONAL ACADEMIES
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SUBCOMMITTEE ON FLAME-RETARDANT CHEMICALS
Committee on Toxicology
Board on Environmental Studies and Toxicology
Commission on Life Sciences
National Research Council

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September 22, 1999

AGENDA
(Revised)

Wednesday, September 22, 1999

12:45 p.m.	**Welcome and Introduction of Subcommittee Members and Guests**	**Donald Gardner** *Subcommittee Chair*
1:00 p.m.	**Summary of CPSC Toxicology Reviews on Flame-Retardant Chemicals**	**Patricia Bittner,** ***Toxicologist*** **Michael Babich,** ***Chemist*** **CPSC**
2:30 p.m.	**ADJOURN**	

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Board on Environmental Studies and Toxicology
Committee on Toxicology

Subcommittee on Risk Assessment of Flame-Retardant Chemicals

All Member Terms end March 1, 2000

ROSTER

Donald E. Gardner, Ph.D., *Chair*
President, Inhalation Toxicology Associates, Inc.
Raleigh, NC

Joseph Borzelleca, Ph.D.
Emeritus Professor
Virginia Commonwealth University
Richmond, VA

David W. Gaylor, Ph.D.
U.S. Food and Drug Administration
National Center for Toxicological Research
Jefferson, AR

Sidney Green, Ph.D.
Department of Pharmacology
Howard University
Washington, DC

Richard Horrocks, Ph.D.
Bolton Institute
Bolton, U.K.

Michael A. Jayjock, Ph.D.
Rohm and Haas Company
Research Laboratories
SpringHouse, PA

Sam Kacew, Ph.D.
Faculty of Medicine
University of Ottawa
Ottawa, Ontario, Canada

James N. McDougal, Ph.D.
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Wright Patterson AFB, OH

Richard K. Miller, Ph.D.
School of Medicine and Dentistry
University of Rochester
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Robert Snyder, Ph.D.
Department of Pharmacology and Toxicology
Rutgers University College of Pharmacy, and
Piscataway, NJ

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Robert G. Tardiff, Ph.D., ATS
The Sapphire Group, Inc.
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Committee on Toxicology

This meeting is being held to gather information to help the committee conduct its study. This committee will examine the information and material obtained during this, and other public meetings, in an effort to inform its work. Although opinions may be stated and lively discussion may ensue, no conclusions are being drawn at this time; no recommendations will be made. In fact, the committee will deliberate thoroughly before writing its draft report. Moreover, once the draft report is written, it must go through a rigorous review by experts who are anonymous to the committee, and the committee then must respond to this review with appropriate revisions that adequately satisfy the Academy's Report Review committee and the chair of the NRC before it is considered an NRC report. Therefore, observers who draw conclusions about the committee's work based on today's discussions will be doing so prematurely.

Furthermore, individual committee members often engage in discussion and questioning for the specific purpose of probing an issue and sharpening an argument. The comments of any given committee member may not necessarily reflect the position he or she may actually hold on the subject under discussion, to say nothing of that person's future position as it may evolve in the course of the project Any inference about an individuals's position regarding findings or recommendations in the final report are therefore also premature.

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Statement of Task

Major Unit: CLS
Division, Office or Board: Board on Environmental Studies and Toxicology
Sub-Unit: Toxicology and Risk Assessment Program
Subject Committee: Flame-Retardant Chemicals
Staff Officer Name: Kulbir Bakshi

STATEMENT OF TASK

This project will review the toxicology, epidemiology, bioavailability, and available exposure data (including, but not limited to information provided by CPSC) on approximately 15 FR chemicals that are used or considered likely to be used to treat fabrics used in residential upholstered furniture to reduce the risk of death, injury, and property damage from small-open-flame ignited upholstered furniture fires. Based on available toxicity data and potential human exposure levels, the toxicological risks associated with these chemicals will be assessed. The assessments will include considerations of oral, dermal, and inhalation exposures. The uncertainties associated with the toxicological risk assessments will also be identified both quantitatively and qualitatively. Deficiencies in the database on the FR chemicals will be identified, and where appropriate recommendations for future research will be made.

Sponsor(s): Consumer Product Safety Commission

Date of Statement: 07/19/99
Date of Previous Statement: 02/22/99

RISK ASSESSMENT OF FLAME RETARDANT CHEMICALS IN UPHOLSTERED FURNITURE*

Michael A. Babich, Ph.D.
Directorate for Health Sciences
U.S. Consumer Product Safety Commission

September 22, 1999

Slide 1. Good afternoon, Mr. Chairman, and members of the subcommittee. Today I will present an update of the U.S. Consumer Product Safety Commission (CPSC) staff's risk assessment of flame retardant (FR) chemicals in upholstered furniture. This will include a discussion of CPSC's risk assessment process, laboratory studies on exposure and bioavailability, and related activities at other agencies. The views expressed in this presentation are those of the Commission's Directorate for Health Sciences and have not been reviewed or approved by the Commission.

Slide 2. As we discussed at the July subcommittee meeting, the Commission initiated a regulatory proceeding in 1994 to address the hazard of small open flame ignitions of upholstered furniture.[1] Small open flame sources include cigarette lighters, matches, and candles. Such ignitions of upholstered furniture are associated with an estimated 90 deaths, 420 injuries, and $40 million in property damage per year in the U.S.[2] The CPSC staff has developed a draft performance standard to address this hazard.[3] Furniture manufacturers would be free to choose the means of complying with the standard. However, manufacturers have reported that they would generally use FR-treated fabrics to meet the draft standard. In addressing the hazard associated with the small open flame ignition of upholstered furniture, the CPSC staff is working to develop a performance standard to reduce furniture ignitions without creating other hazards to consumers. Thus, the CPSC staff is assessing the potential risks from exposure to FR chemicals.

Slide 3. CPSC addresses chemical hazards under the Federal Hazardous Substances Act, or FHSA. The FHSA is risk-based. To be considered a "hazardous substance" under the FHSA, a substance or product must satisfy a two-part definition.[4] First, it must be toxic under the FHSA, or present one of the other hazards enumerated in the statute. Second, it must have the potential to cause "substantial" illness or injury during or as a result of "reasonably foreseeable handling or use."

Slide 4. Therefore, exposure and risk must be considered in addition to toxicity when assessing potential hazards under the FHSA.[5] The FHSA includes both acute and chronic hazards. It does not require manufacturers to perform any specific battery of toxicological tests to assess the potential for chronic hazards. Thus, risk assessments are based on all the available data. The FHSA does not provide for pre-market registration or approval. This places the responsibility on manufacturers to ensure either that their products are not hazardous substances under the FHSA or, if they are, that they are labeled as required by the FHSA.

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* Presented before the National Academy of Sciences, Subcommittee on Flame Retardant Chemicals in Upholstered Furniture. Irvine, CA. September 22, 1999.

Slide 5. The first step in determining whether a substance may be hazardous under the FHSA is to determine whether it is toxic. Acute toxicity is defined by LD_{50} values in regulations issued under the FHSA.[6] However, reliable human experience data take precedence over animal data.[7] In 1992, the Commission issued guidelines for assessing chronic hazards under the FHSA, including carcinogenicity, neurotoxicity, reproductive/developmental toxicity, exposure, bioavailability, risk assessment, and acceptable risk.[8, 9]

Slide 6. A substance is considered "toxic" under the FHSA due to chronic toxicity, if it is either known to be or probably toxic in humans.[10] Under the FHSA, a substance or mixture is classified as "known to be toxic" in humans only if there is sufficient evidence in humans. It is considered "probably toxic" if there is either limited evidence in humans or sufficient evidence in animals. If it is concluded that a substance is toxic under the FHSA due to chronic toxicity, then a quantitative assessment of exposure and risk is performed.

Slide 7. As part of the risk assessment process for FR chemicals, the Commission held a public hearing in May 1998. In its testimony, the Fire Retardant Chemicals Association (FRCA) provided a list of 16 chemicals or classes that its members "would market" for use in upholstered furniture if the draft standard were adopted.[11] The CPSC staff recently completed toxicity reviews on these 16 chemicals. We reported on the first 7 of the 16 toxicity reviews at the July 29 meeting of this subcommittee. The next 7 chemicals will be discussed later today. The remaining two will be addressed at the next subcommittee meeting.

FR chemicals may be applied to textiles by a variety of methods, and the method of application may affect the potential for exposure.[12, 13, 14, 15] Little information relating to exposure is available at this time. Information on FR chemical loading rates, that is, the amount of FR chemical per unit of fabric, would help to define the maximum amount of chemical available for exposure. For a given FR chemical, the loading that would be needed to meet the draft standard depends on the properties of the fabric and, therefore, must be determined on a case-by-case basis. Nonetheless, some data on the loading rates used in typical textile applications are available.

Slide 8. The United Kingdom (UK) has a furniture flammability standard in place. Included in the UK standard is a requirement called the "match test," which is essentially similar to the CPSC's draft standard. FR backcoating is the most common method of treating upholstered furniture for the UK market.[16, 17, 18] FR chemicals are mixed with an emulsion polymer such as an acrylic latex that is applied to the back of the fabric. Backcoatings typically contain antimony trioxide in combination with a brominated FR such as decabromodiphenyl oxide or hexabromocyclododecane. However, other FR's can be applied in backcoatings as well. Backcoatings are most often used with synthetic fabrics such as polyester and polyolefins, although they are also used with cellulosic fabrics. Backcoating may reduce the potential for exposure, because the FR chemicals are encapsulated in the polymer and the polymer is applied to the back of the fabric.

Slide 9. Upholstery fabrics generally range in weight from 4 to 22 ounces per square yard.[19] The application of an FR-backcoating increases the weight by an additional 10 to 50 percent. Antimony is generally present at levels between 1 and 4 percent of the total weight of the fabric.[20, 21, 22, 23] Brominated FR's are likely to be used at levels of roughly 5 to 20 percent of the total weight.[24]

Slide 10. Another method of applying antimony trioxide and decabromodiphenyl oxide is to mix them with an acrylic latex binder and apply the mixture to both surfaces of the fabric.[25] The binder is heat cured and then the fabric is washed. A typical formulation contains 37.5 percent bromine and 18.8 percent antimony in the binder. The binder-FR mixture may be applied at up to 35 percent of the weight of the untreated fabric.[26] This method was developed for use with cotton-polyester blends and is used in some upholstered furniture sold in the UK.

Slide 11. Cotton and rayon fabrics may be treated with reactive FR chemicals. Phosphonate ester FR's, such as Pyrovatex®, are typically applied in a solution that contains a durable press resin such as trimethylol melamine, phosphoric acid, and ethyleneurea.[27, 28] The fabric is then dried, heat-cured, and washed. The N-methylol group of the phosphonate ester forms a covalent bond with the hydroxyl groups in the cellulose fibers and with the melamine resin. This method is used to treat cellulosic fabrics in furniture sold in the UK.[29] Treated fabrics generally contain from 1 to 2 percent phosphorus by weight.[30]

Slide 12. Tetrakis (hydroxymethyl) phosphonium salts, or THPX, such as Proban®, were developed to treat cotton. These compounds react to form an insoluble polymer which is physically trapped within the fibers.[31, 32]

Slide 13. In one process, the chloride salt, THPC, is first reacted with urea to form THPC-urea. The fabric is treated with a solution containing THPC-urea, THPC, and sodium hydroxide. After the fabric is dried, it is exposed to anhydrous ammonia, which leads to the formation of the polymer. Then, the polymer is oxidized with hydrogen peroxide, which changes the phosphorus to a more stable pentavalent form. Finally, unreacted compounds are removed by washing.

The use of reactive FR's such as THPX and phosphonate esters is expected to reduce exposure to FR chemicals, because they are chemically or physically bound to the fibers. However, exposure to unreacted starting materials, reaction by-products, or decomposition products is possible. Loewengart and Van Duuren reported that small amounts of phosphorus, nitrogen, and formaldehyde were extracted with aqueous solvents from fabrics treated with THPX.[33] The chemical forms of the phosphorus and nitrogen were not identified.

Slide 14. Cyclic phosphonate esters, or CPE's, such as Antiblaze® N and Antiblaze® NT, are non-reactive FR compounds developed for use with polyester fabrics.[34, 35] The two commercial formulations are mixtures of two compounds referred to as the monomer and dimer in different proportions.

Slide 15. Fabrics are treated by immersion in a CPE solution. The treated fabric is then baked to soften the fibers, allowing from 25 to 50 percent of the CPE to become trapped within the fibers. The portion of CPE remaining on the fiber surface can be washed off before the fabric is used, although this step is sometimes omitted. Treated and washed fabrics generally contain from 1 to 2 percent phosphorus by weight.

Slide 16. Maibach studied the percutaneous absorption of ^{14}C-labeled CPE and treated fabric in monkeys.[36] When pure CPE was applied to the abdominal skin of monkeys, 10 percent of the applied dose was absorbed within 9 days. Monkeys were also exposed to treated, unwashed fabric for 24 hours. The fabric was saturated with urine to enhance the transfer of unbound CPE to the skin. In this case, 0.1 percent of the applied dose was absorbed within 9 days.

Slide 17. Tris (2,3-dibromopropyl) phosphate, or TRIS, is no longer manufactured and is not a candidate for use in upholstered furniture.[37, 38] However, it may serve as a useful model for assessing exposure and bioavailability of other FR chemicals. Most of the TRIS in treated fabrics was bound within the fibers and could not be extracted with a 1:3 mixture of benzene and hexane.[39] The portion of TRIS that was on the fiber surface, however, was not tightly bound.

Slide 18. When pure ^{14}C-labeled TRIS was applied to the skin of rabbits, approximately 15 percent of the applied dose was absorbed in 96 hours.[40] Ulsamer et al. prepared fabric containing ^{14}C-labeled surface TRIS, and placed it in contact with rabbit skin.[41] With dry TRIS-treated fabric, 4.3 percent of the applied dose of surface TRIS was absorbed in 96 hours. When the fabric was saturated with urine, the amount absorbed increased to 17 percent.

Slide 19. Migration studies with FR-treated fabrics are underway at the CPSC chemistry laboratory. Fabrics will be exposed to aqueous and non-aqueous solvents and detergent solutions to simulate a variety of potential exposures. These studies are limited to the range of FR-treated fabrics that are available for study. Fabric samples available for study at this time include fabrics treated with FR backcoatings, phosphonate ester, and tetrakis (hydroxymethyl) phosphonium salts.

Slide 20. *In vitro* percutaneous absorption studies with radiolabeled FR chemicals will be performed at the EPA National Health and Environmental Effects Research Laboratory, NHEERL. Candidate chemicals for testing include decabromodiphenyl oxide, hexabromocyclododecane, and tris (1,3-dichloro-2-propyl) phosphate. The percentage of the applied dose that is absorbed in 24 hours will be determined.

Slide 21. In addition to the risk assessment for consumer exposure, the CPSC staff is cooperating with the U.S. EPA to develop a significant new use rule (SNUR) for the use of FR chemicals in upholstered furniture. The SNUR process addresses potential risks to consumers, workers, and the environment. The SNUR could be used to obtain additional toxicity or exposure data where needed. The CPSC staff is also cooperating with NIOSH to review the potential occupational exposures and health effects associated with the use of FR chemicals in textile and upholstered furniture manufacturing. As part of CPSC's FY99 appropriations, Congress provided funds for an independent study by the NAS of the "toxic risk" associated with

the use of flame retardant chemicals in upholstered furniture, which is the work of this subcommittee.

Slide 22. To summarize, the CPSC staff is in the process of assessing the potential risk to consumers from exposure to FR chemicals in upholstered furniture. Toxicity reviews of 16 chemicals likely to be used for this purpose have been completed. Limited data on the potential for exposure to FR chemicals are available. Laboratory studies on the migration of FR chemicals from treated fabrics are underway. *In vitro* percutaneous absorption studies are planned. When completed, these studies will contribute to the staff's risk assessment. The staff is also working with NIOSH to address worker exposure, and with EPA to develop a significant new use rule.

Slide 23. All the available toxicity data on the first 7 of 16 FR chemicals were reviewed at the July 29 subcommittee meeting. At this time, Patricia Bittner will discuss the toxicity of the next 7 FR chemicals.

References

[1] U.S. Consumer Product Safety Commission (CPSC) (1994) Upholstered furniture; advance notice of proposed rulemaking; request for comments and information. Federal Register, 59: 30735-30738. June 15, 1994.

[2] Medford, R.L. (1999) Opening statement of Ronald L. Medford, Assistant Executive Director for Hazard Identification and Reduction, U.S. Consumer Product Safety Commission, to the National Academy of Sciences Subcommittee on Flame Retardant Chemicals in Upholstered Furniture. Washington, DC. July 29, 1999.

[3] Briefing Package on Upholstered Furniture Flammability: Regulatory Options for Small Open Flame and Smoking Material Ignited Fires. U.S. Consumer Product Safety Commission, Bethesda, MD 20814. October 1997.

[4] 15 USC 1261 (f)(1)(A).

[5] U.S. Consumer Product Safety Commission (CPSC) (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register, 57: 46626-46674.

[6] 16 CFR 1500.3 (c) (2) (i).

[7] 16 CFR 1500.4.

[8] U.S. Consumer Product Safety Commission (CPSC) (1992)

[9] The guidelines are summarized at 16 CFR 1500.135.

[10] 16 CFR 1500.3 (c)(2)(ii).

[11] Parkes, D. (1998) Testimony presented before the U.S. Consumer Product Safety Commission. May 5, 1998.

[12] Sanders, H.J. (1978) Flame retardants. Chemical and Engineering News. Pages 22-36, April 24, 1978.

[13] Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980) Flame-retardant chemicals in textiles. Clinical Toxicology, 17: 101-131.

[14] Powell, C., and R. Rose (1998) Testimony presented before the U.S. Consumer Product Safety Commission. May 5, 1998.

[15] Fire Retardant Chemicals Association (1998) Letter from Russell C. Kidder, Fire Retardant Chemicals Association, Lancaster, PA to the Office of the Secretary, U.S. Consumer Product Safety Commission, with attachments. August 3, 1998.

[16] Powell, C., and R. Rose (1998)

[17] Fire Retardant Chemicals Association (1998)

[18] Wilkinson, C.L. (1998) Testimony presented before the U.S. Consumer Product Safety Commission. May 6, 1998.

[19] Fansler, L.S., and S.-B Chen (1997) FR backcoated and non-FR backcoated upholstery fabrics. September 19, 1997. In, Briefing package on upholstered furniture flammability: regulatory options for small open flame and smoking material ignited fires. U.S. Consumer Product Safety Commission, Bethesda, MD 20814. October 1997.

[20] Chen, S.-B. (1997) Migration of flame retardant in fabrics of upholstered furniture. April 28, 1997. In, briefing package on upholstered furniture flammability: regulatory options for small open flame and smoking material ignited fires. U.S. Consumer Product Safety Commission, Bethesda, MD 20814. October 1997.

[21] Fansler, L.S., and S.-B Chen (1997)

[22] Compare also, Wilkinson, C.L. (1998)

[23] Compare also, International Association for Research on Cancer (IARC) (1989) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 47: 291-305.

[24] Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980)

[25] Mischutin, V. (1975) A new FR system for synthetic/cellulosic blends. Textile Chemist and Colorist, Volume 7. March 1975.

[26] Keys, R. (1975) Processing polyester/cotton with P-44. Textile Chemist and Colorist, Volume 7. March 1975.

[27] Sanders, H.J. (1978)

[28] D'Ruiz, C. (1998a) Testimony presented before the U.S. Consumer Product Safety Commission. May 6, 1998.

[29] Fire Retardant Chemicals Association (1998) Letter from Russell C. Kidder, Fire Retardant Chemicals Association, Lancaster, PA to the Office of the Secretary, U.S. Consumer Product Safety Commission, with attachments. August 3, 1998.

[30] D'Ruiz, C. (1998b) Letter from Carl D'Ruiz, Ciba Specialty Chemicals Corporation, High Point, NC to Dale Ray, U.S. Consumer Product Safety Commission. March 4, 1998.

[31] Sanders, H.J. (1978)

[32] Albright & Wilson (1998), Letter from Celia Powell, Albright & Wilson, Glen Allen, VA to Dale Ray, U.S. Consumer Product Safety Commission, with attachments. July 17, 1998.

[33] Loewengart, G., and B.L. Van Duuren (1977) Evaluation of chemical flame retardants for carcinogenic potential. J. Toxicol. Environ. Health, 2: S39-46. As cited in, Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980).

[34] Albright & Wilson (1998)

[35] Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980)

[36] Maibach, H.I. (1979) Percutaneous absorption studies in the Rhesus monkey using ^{14}C AB-19T. University of California, Department of Dermatology, San Franciso, CA. Prepared for Mobil Chemical Company, Edison, NJ. March 1979.

[37] Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980)

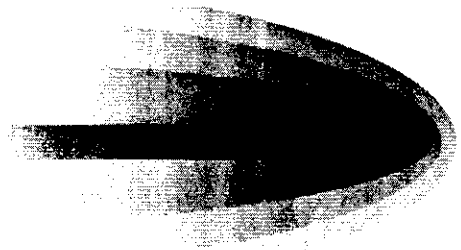
[38] U.S. Consumer Product Safety Commission (CPSC) (19977) Children's wearing apparel containing TRIS; interpretation as a banned hazardous substance. Federal Register, 42: 18850-18854. April 8, 1977. [Later withdrawn following judicial proceedings.]

[39] Ulsamer, A.G., R.E. Osterburg, and J. McLaughlin, Jr. (1980)

[40] Ibid.

[41] Ulsamer, A.G., W.K. Porter, and R.E. Osterberg (1978) Percutaneous absorption of radiolabeled TRIS from flame-retarded fabric. Journal of Environmental Pathology and Toxicology, 1: 543-549.

Risk Assessment of Flame Retardant Chemicals in Upholstered Furniture



Michael A. Babich, Ph.D.

U.S.Consumer Product Safety Commission

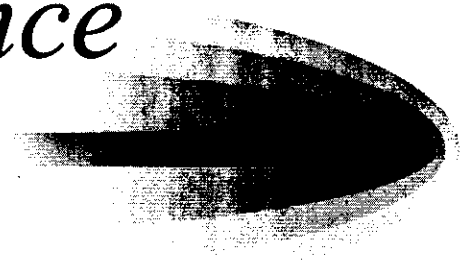
September 22, 1999

Small open flame ignitions

Annually in the U.S.

- 90 Fatalities
- 420 Injuries
- $40 Million in property damage

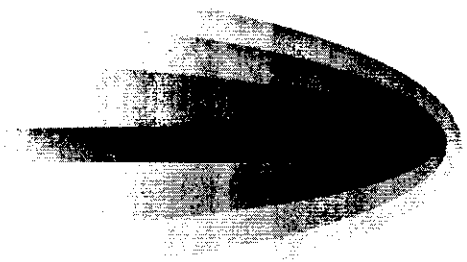
Hazardous Substance



Two-Part definition of hazardous substance:

- "Toxic" under the FHSA
- Cause "substantial" illness or injury from "reasonably foreseeable handling or use"

The FHSA ...



- Considers exposure and risk
- Includes acute and chronic effects
- Does not require testing for chronic hazards
- Does not provide for pre-market approval
- Requires manufacturers to ensure that their products are not hazardous or are properly labeled

FHSA Definition of "Toxic"

- Acute toxicity
  - Based on LD_{50} as defined in FHSA regulations
- Chronic toxicity
  - Based on CPSC chronic hazard guidelines
  - Carcinogenicity, neurotoxicity, reproductive/developmental toxicity, exposure, bioavailability, risk assessment, and acceptable risk

FHSA Definition of Chronic Toxicity

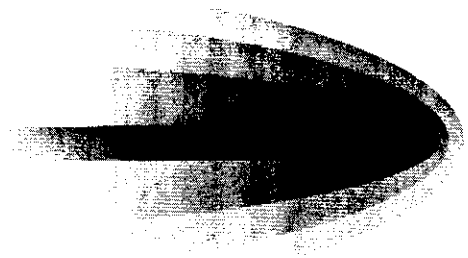
	Human	Animal
Sufficient	Known*	Probable*
Limited	Probable*	Possible
Inadequate	Possible	-----

* Considered "toxic" under the FHSA.

FR Chemicals Association

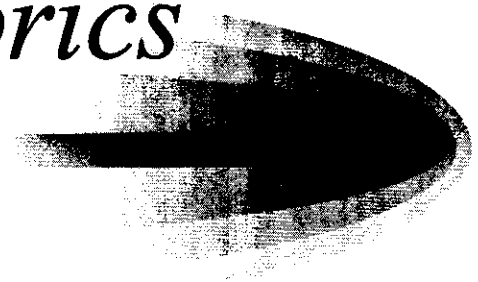
- 16 FR chemicals that FRCA members would market for use in upholstered furniture (May 1988)
- CPSC reviewed toxicity data on these 16

FR Backcoating



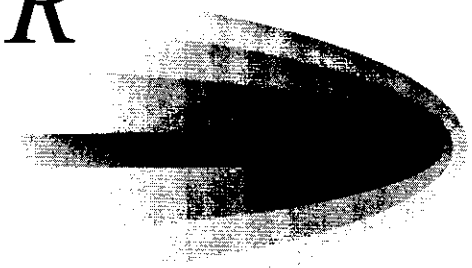
- Used in UK Furniture
- Acrylic or vinyl latex:
  - Antimony trioxide and
  - Decabromodiphenyl oxide or
  - Hexabromocyclododecane
- Applied to the back of the fabric
- Used primarily with synthetic fabrics

FR-Backcoated Fabrics



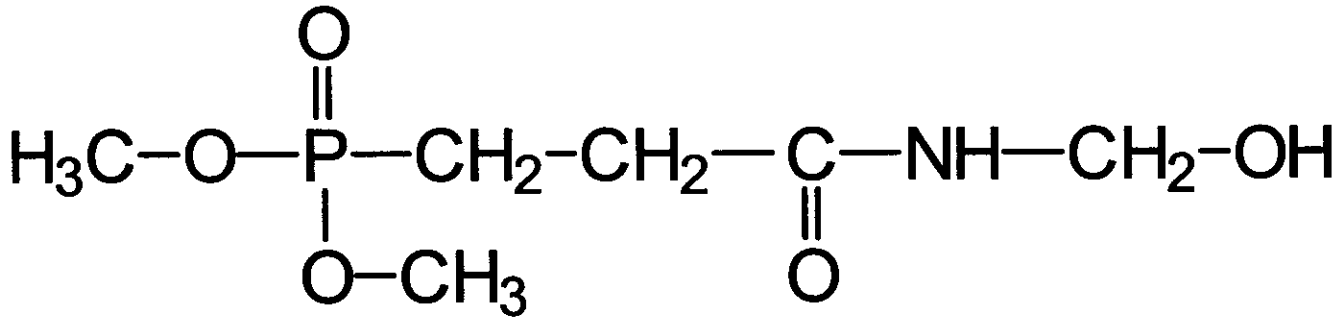
- Untreated fabrics generally weigh from 4 to 22 oz/yd ^{2}
- Backcoating adds 10 to 50 %
- Antimony -- 1 to 4 % of total weight
- Brominated FR -- 5 to 20 % of total weight

Adhesive-Based FR



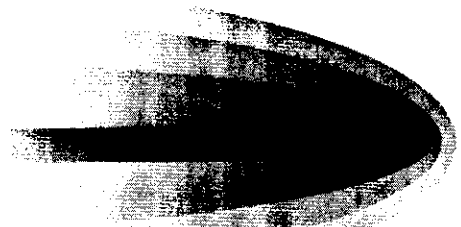
- Acrylic latex binder with:
  - Antimony trioxide and
  - Decabromodiphenyl oxide
- Applied to both surfaces
  - Heat cured
- Used with cotton-polyester blends
- Used in UK Furniture

Phosphonate Ester (Pyrovatex®)



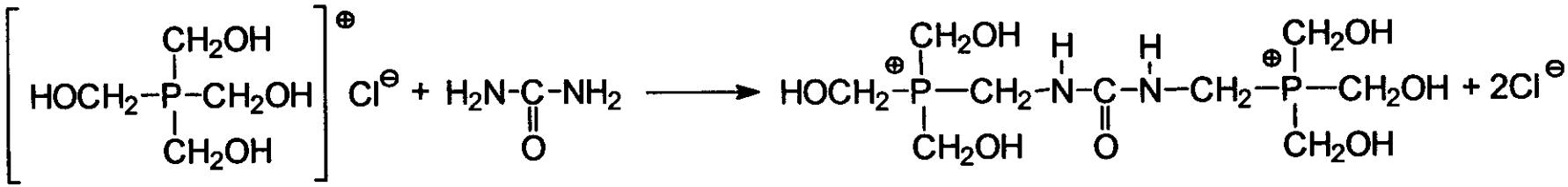
- Forms covalent bonds with cellulose fibers
- Used with cotton and rayon
- Used in UK furniture
- Treated fabric contains 1 to 2 % phosphorus

THPX

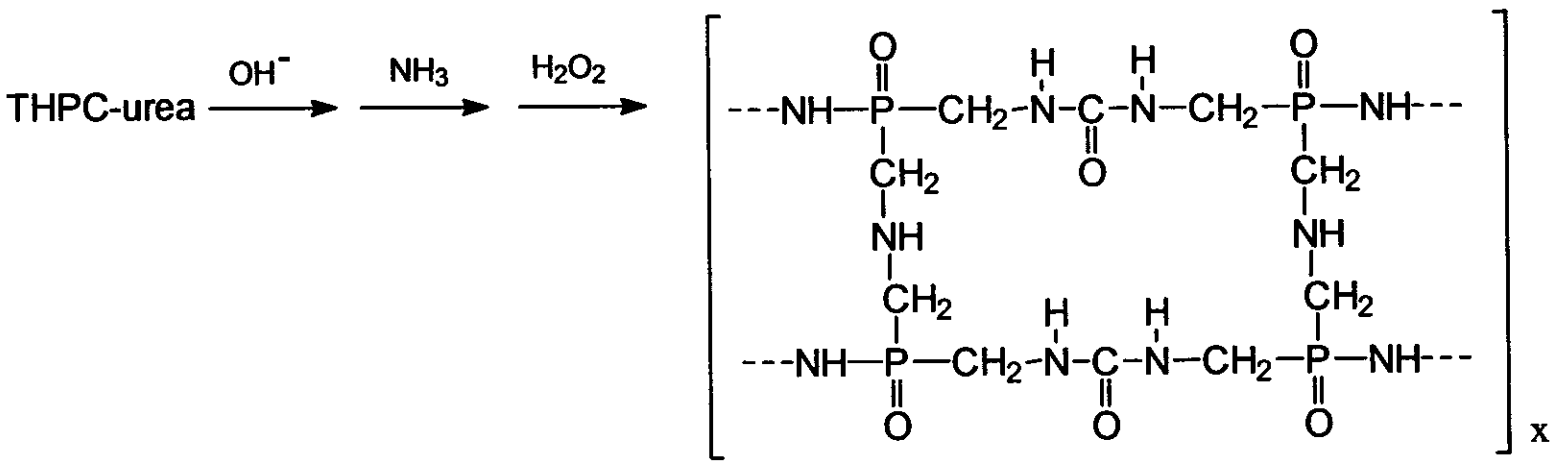


- Tetrakis (hydroxymethyl) phosphonium salt precondensate with urea
  - Proban®
- Used with cellulosic fabrics
- Forms an insoluble polymer

Application of THPC-Urea



THPC Urea THPC-urea

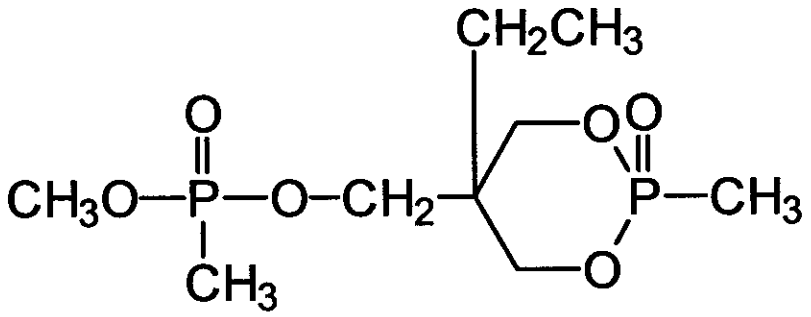


THPC-urea polymer

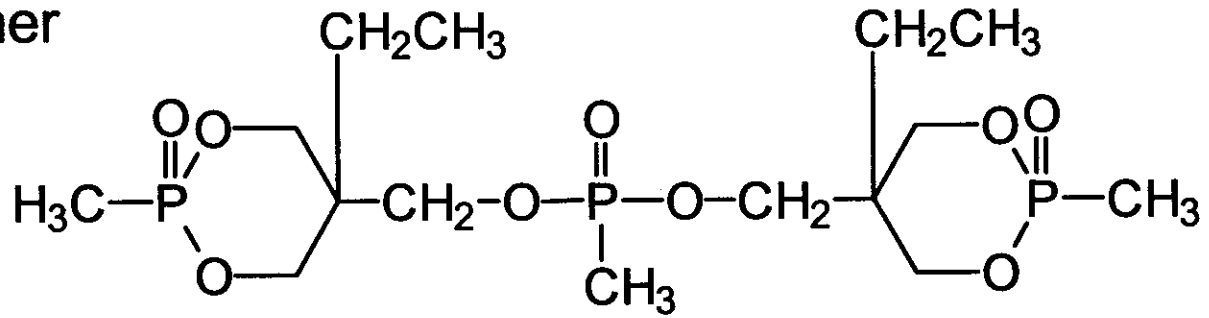
Cyclic Phosphonate Esters

Antiblaze® N/NT

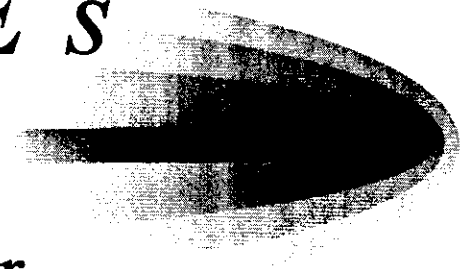
Monomer



Dimer



Application of CPE's

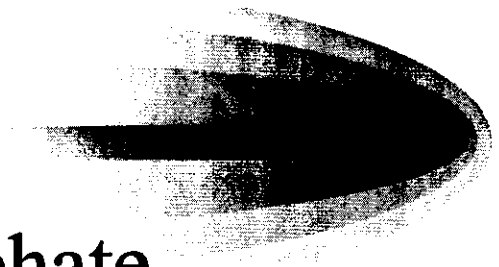


- CPE 1 -- 65 % monomer, 19% dimer
- CPE 2 -- 60 % monomer, 18 % dimer
- Treat fabrics by immersion
  - Heat to soften the fiber
  - 25 to 50 % of CPE trapped within the fibers
  - Wash off surface compounds
- Treated fabrics contain 1 to 2 % phosphorus

Dermal Biovailability of CPE's

- Percutaneous absorption studied in monkeys (Maibach, 1979)
- Pure CPE
  - 10% of ^{14}C-CPE absorbed over 9 days
- Treated unwashed fabric
  - Saturated with urine
  - 0.1 % of ^{14}C-CPE absorbed over 9 days

TRIS

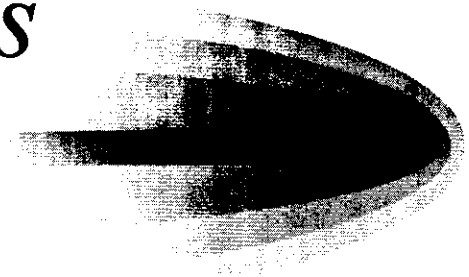


- Tris (2,3-dibromopropyl) phosphate
- No longer manufactured
- TRIS was added before the fibers were spun
- Most TRIS was bound within the fibers
  - Not extractable with benzene-hexane (1:3)
- Surface TRIS
  - Extractable and bioavailable

Bioavailability of Surface TRIS

- Percutaneous absorption studied in rabbits (Ulsamer et al., 1980)
  - Prepared fabric with ^{14}C-labeled surface TRIS
- % of Applied dose absorbed in 96 hours:
  - Pure TRIS 15 %
  - Dry fabric 4.3 %
  - Urine saturated fabric 17 %

Migration Studies

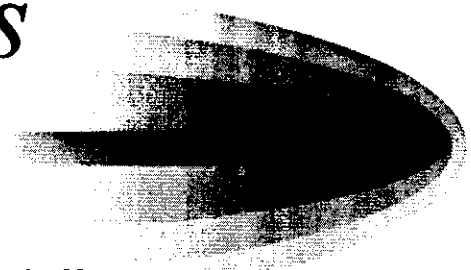


- CPSC Chemistry Laboratory
- Solvents: water, saline, 0.1 N HCl, detergent, organic solvents
- Fabrics treated with:
  - FR-backcoatings
  - Phosphonate ester
  - THPX

Percutaneous Absorption Studies

- *In vitro* studies with animal skin
- Cooperative study with EPA / NHEERL
- 3 Chemicals:
  - Decabromodiphenyl oxide
  - Tris (1,3-dichloro-2-propyl) phosphate
  - Hexabromocyclododecane.

Related Activities

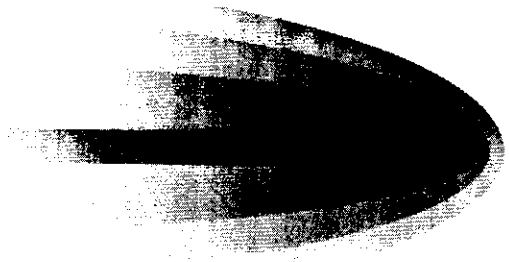


- EPA / OPPTS developing a Significant New Use Rule (SNUR)
- NIOSH to review potential occupational exposures and health effects
- NAS to study the "toxic risk" to consumers associated with FR chemicals in upholstered furniture.

Risk Assessment of FR Chemicals

- Toxicity reviews of 16 chemicals
  - CPSC staff (completed)
- Migration studies with FR-treated fabrics
  - CPSC laboratory (in progress)
- Percutaneous absorption study
  - EPA / NHEERL (planned)
- Risk assessment for consumer exposure
  - CPSC staff (in progress)

Risk Assessment of Flame Retardant Chemicals in Upholstered Furniture



Michael A. Babich, Ph.D.
U.S.Consumer Product Safety Commission
September 22, 1999

TOXICITY ASSESSMENT OF SEVEN FLAME RETARDANT CHEMICALS OR CHEMICAL CLASSES UNDER THE FHSA

Patricia M. Bittner, M.S.
Directorate for Health Sciences
U.S. Consumer Product Safety Commission

September 22, 1999

Slide 1.

Good morning Mr. Chairman and members of the subcommittee. As sponsor of the NAS Study on the Toxicological Risk of Flame Retardant Chemicals, the U.S. Consumer Product Safety Commission staff is pleased to once again have the opportunity to present to you summaries of the toxicity reviews of seven FR chemicals, assessed using the criteria found in the Federal Hazardous Substances Act or FHSA. Of the 16 FR chemicals or chemical classes to be considered by this subcommittee, summaries on the toxicity of 7 will be presented today, 7 were presented at your initial meeting, and 2 will be discussed at your final meeting. As you may recall, the Fire Retardant Chemicals Association (FRCA) provided the initial list of the 16 chemicals or chemical classes likely to be used in residential upholstered furniture.

Slide 2.

The seven chemicals or chemical classes to be presented today are tetrakis hydroxymethylphosphonium salts precondensate with urea, organic phosphonates and cyclic phosphonate esters, ammonium polyphosphates and blends, antimony pentoxide and sodium antimonate, chlorinated paraffins, zinc borate, and calcium and zinc molybdates.

In addition to summarizing the toxicity of these chemicals, I will discuss the key studies or factors that led to these determinations. For some of these chemical classes, several chemicals from each class were chosen for review. I will highlight the findings on each of these chemicals. The chemicals chosen for review in each of the classes either were suggested as candidates for use by the FRCA, are currently in use, are produced in high volume, are of suspected toxicological concern, or have significant toxicity data available compared to others in the class.

The toxicity reviews being discussed today were performed by Drs. Jacque Ferrante, Kris Hatlelid, and me. Dr. Michael Babich, also of the CPSC Health Sciences staff, and I will address any questions that you may have after this presentation. The views expressed in this presentation are those of the Commission's Directorate for Health Sciences and have not been reviewed or approved by the Commission.

It is important to remember that the CPSC staff evaluated the toxicity of these chemicals using the criteria in the relevant statute administered by our agency, that is, the FHSA, and its implementing regulations. The FHSA defines a "hazardous substance" as a substance that satisfies a two-part test. To be a hazardous substance, a product must first present one or more of the hazards enumerated in the statute; that is, it must be toxic, corrosive, flammable, an irritant, or a strong sensitizer, or generate pressure through decomposition, heat, or other means. Second, the product must have the potential to cause substantial personal injury or substantial illness during or as a result of any customary or reasonably foreseeable

Slide 4.

THPS is acutely toxic by the oral route of exposure under the FHSA. THPS is a dermal irritant in animals. No data are available regarding the potential for THPS to cause dermal sensitization.

Ingestion of THPS caused hepatocytic vacuolar degeneration in rats and mice in 13-week studies. THPS is probably toxic to humans, based on sufficient evidence of liver toxicity in rats and mice exposed to THPS in the 13-week study. Therefore, THPS may be considered toxic under the FHSA, due to chronic toxicity.

THPS caused neurological effects, including tremors and paralysis, in rats and mice after oral administration in subchronic studies, but no lesions of the nervous system were reported. Therefore, THPS may be regarded as a "possible neurological toxin" in humans, based on limited evidence of neurological toxicity in animals. The conclusion that THPS is possibly neurotoxic in humans does not, in itself, meet the FHSA definition of toxic.

There was no evidence of carcinogenicity in well-conducted studies in rats and mice treated orally with THPS. Insufficient data are available to fully evaluate whether there are reproductive or developmental effects of exposure to THPS.

Slide 5.

An acceptable daily intake value of 0.05 mg/kg-day was derived for THPS, based on a NOEL of 5 mg/kg/d for liver effects in a 13-week study.

Slide 6.

THPS is an acute and chronic toxicant under the FHSA. If THPS is present in consumer products, a quantitative assessment of exposure and risk would need to be performed to determine whether THPS may present a hazard to consumers. Products that contain THPS would be considered "hazardous" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake.

Slide 7.

THPC is acutely toxic by the oral, but not the dermal, route of exposure under the FHSA. THPC caused dermal irritation in animals. THPC meets the criteria for a dermal irritant under the FHSA, based on results in rats and rabbits. No data are available regarding the potential for these substances to cause dermal sensitization.

Although THPC was mutagenic in mammalian cell cultures, it was not mutagenic in *Salmonella* assays. THPC has not been shown to be carcinogenic in rodents after oral administration in well-conducted studies using two animal species. THPC does not appear to be carcinogenic by the dermal route of exposure, but there are few data.

Ingestion of THPC in subchronic or chronic studies caused hepatocytic vacuolar degeneration in rats and mice and decreased survival in rats. Therefore, THPC may be regarded as probably toxic in humans, based on sufficient evidence of toxicity in animals. Furthermore, THPC may be considered toxic under the FHSA due to chronic toxicity.

THPC also caused neurological effects, including tremors and axonal degeneration, in well-conducted oral studies in rats and mice. Therefore,

handling or use, including reasonably foreseeable ingestion by children. It is important to keep in mind that even though a FR chemical might cause effects under certain conditions, those conditions may not occur when the chemical is used in upholstered furniture. Any consumer exposures to FR chemicals used on upholstered furniture would most likely occur through the dermal and oral routes, if they were to occur at all.

In evaluating the potential hazards presented by flame retardant chemicals, the Commission staff has appropriately followed the definitions for toxicity (both acute and chronic), irritancy, and sensitization in the FHSA and its implementing regulations, 16 CFR 1500. At this time, there is insufficient information for the staff to conduct the second part of the analysis to determine what, if any, hazards these products would present if used as flame retardants in upholstered furniture. Such an analysis would include an assessment of oral and dermal exposure, and the bioavailability and dose response associated with these routes of exposure. CPSC staff continues to develop information on exposure, bioavailability, and dose response.

Slide 3.

The most important FR chemical to be reviewed today for possible use in upholstered furniture is tetrakis. Although there are numerous tetrakis(hydroxymethyl)phosphonium salts that are used as flame retardants, the most widely studied are the chloride, sulfate, and acetate/phosphate salts. During the fabric application process, THPS and THPC are reacted to form a cross-linked polymer or to produce an insoluble polymer, THPOH/NH_3 (Ulsamer et al. 1980). Proban® CC is a commercial formulation composed of THPC with urea (65% wt), THPC (20% wt), and formaldehyde (0.4% wt) (Albright and Wilson 1998b). Information on the chemical process that the manufacturer provided on the application method for treating fabric with Proban® CC has been supplied to the NAS. In this review, THPS, THPC, THPC with urea, and Proban® CC are discussed. THPA/P has never been a major commercial product (IARC 1990) and thus the data on this chemical will not be presented.

Although conclusions are drawn on specific precursors, the chemical manufacturer has stated that the finished fabric should contain the THPOH/NH_3 reaction product, i.e., insoluble polymer. Study results obtained using treated cloth rather than the chemical itself are more appropriate for use in risk assessment whenever possible, since it would more accurately represent actual exposure media and levels.

The tetrakis(hydroxymethyl)phosphonium salts have been produced for commercial use since the 1950s. They are used to produce crease-resistant flame-retardant finishes on cotton textiles and other predominantly cellulosic fiber fabrics (IARC 1990), chiefly for work clothing and mattress tickings.

THPS, THPC, THPOH/NH_3, and Proban® CC can all be absorbed orally, and both THPS and THPC are absorbed dermally (Afsansa'eva and Evseenko 1971; Aoyama 1975; Connor et al. 1980; Hazleton UK 1990a, 1990b, 1991, 1992; Ishizu 1975; NTP 1987). The polymer THPOH/NH_3 is not expected to penetrate the skin in appreciable amounts due to its size and lack of solubility (Ulsamer et al. 1980). Certain formulations such as Proban® CC, however, are acidic and can cause dermal corrosion (Albright and Wilson 1994b), which might allow direct systemic absorption.

THPC may be regarded as a "probable neurological toxin" in humans, based on sufficient evidence of neurological toxicity in animals. In addition, THPC may be considered "toxic" under the FHSA. The lowest NOEL for these effects was 7.5 mg/kg/d.

THPC exhibited evidence of developmental toxicity in animals, causing increased postimplantation loss, and decreased fetal weight and fetal eye and limb malformations in rabbit fetuses after oral treatment of does during pregnancy. Although these effects were observed at maternally toxic doses, they do not appear to be secondary to maternal effects. THPC was a developmental toxicant at the highest dose level in one animal study. Therefore, it may be regarded as a "possible developmental toxicant in humans", based on limited evidence in animals. The conclusion that THPC is a possible developmental toxicant does not, in itself, satisfy the FHSA definition of toxic.

Slide 8.

An ADI of 0.00375 mg/kg-d was calculated for THPC, based on a LOEL of 3.75 mg/kg/day for liver effects in rats in a chronic study (NTP 1987). An ADI of 0.075 mg/kg-d was derived for neurotoxic effects. Thus, the ADI of 0.00375 mg/kg-day calculated for chronic organ toxicity is lower than the ADI calculated for neurotoxic effects.

Slide 9.

THPC is acutely toxic and is a dermal irritant under the FHSA. Furthermore, THPC may be considered toxic under the FHSA due to chronic toxicity, organ toxicity and neurotoxicity. If THPC is present in consumer products, a quantitative assessment of exposure and risk must be performed to determine whether THPC may present a hazard to consumers. Products that contain THPC would be considered "hazardous" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake of 0.00375 mg/kg-day.

Slide 10.

THPOH/NH_3 is not acutely toxic by either the oral or dermal routes of exposure under the FHSA. Insufficient data exist to determine whether THPOH/NH_3 is a dermal irritant. It caused slight eye irritation in animals in one study. Insufficient data are available to determine the possible target organs after subchronic and chronic exposures or the carcinogenic potential of this compound after oral or dermal exposure. No data are available on the reproductive/developmental or neurotoxic potential of THPOH/NH_3.

Slide 11.

Therefore, THPOH/NH_3 cannot be considered "toxic" under the FHSA. However, this conclusion is based on limited data. It does not mean that this chemical is "safe," only that there are not sufficient data to demonstrate whether it meets the regulatory definition of toxic.

Slide 12.

Proban® CC is acutely toxic by the oral, but not the dermal, route of exposure under the FHSA. Equivocal evidence exists for the mutagenicity of Proban® CC in mammalian systems. Insufficient data are available to determine the possible target organs after subchronic and chronic exposures or the carcinogenic potential of this compound after oral or dermal exposure.

Because there are limited data available, it does not mean that this chemical is "safe," only that there are not sufficient data to demonstrate whether it meets the regulatory definition of toxic.

Proban® CC is corrosive under the FHSA because of results obtained using animals. Proban® CC-treated cloth, however, is not irritating to human or guinea pig skin. Humans do not appear to be sensitized to Proban® CC, although guinea pigs were sensitized. Guinea pigs were not sensitized, however, to Proban® CC-treated cloth.

No neurological effects were observed after low doses of Proban® CC were given orally over subacute durations, but single high gavage doses of either 100% or 50% Proban® CC caused tremors and increased salivation. Proban® CC was neurotoxic in acute-duration animal studies. Therefore, Proban® CC may be regarded as "possibly neurotoxic in humans," based on limited evidence in animals. The conclusion that Proban® CC is possibly neurotoxic does not, in itself, demonstrate that it meets the FHSA definition of toxic.

Proban® CC caused developmental effects in rabbits at maternally toxic doses in a range-finding and main developmental study after oral administration. However, the effects observed, which included postimplantation loss and eye and limb malformations similar to those observed after administration of THPC, do not appear to be secondary to the maternal effects. The NOEL for these effects was 50 mg/kg-d. Thus, the ADI is 0.5 mg/kg-d. Because Proban® CC induced fetal malformations in two well-conducted studies in animals, it may be regarded as a "probable developmental toxicant" in humans, based on sufficient evidence of developmental toxicity in animals.

Slide 13.

Proban® CC is acutely toxic under the FHSA. It is corrosive, although Proban® CC-treated fabric is not. Furthermore, Proban® CC may be considered "toxic" under the FHSA, due to developmental effects. If Proban® CC is present in consumer products, a quantitative assessment of exposure and risk must be performed to determine whether Proban® CC may present a hazard to consumers. Products that contain Proban® CC would be considered "hazardous" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake. Proban® CC contains 20% THPC, which was toxic to the liver and other organs in animals. The ADI for these effects is 0.00375 mg/kg-day. This THPC exposure should be considered in assessing the risk from Proban® CC exposure.

In considering the toxicity of the tetrakis compounds, however, it is expected that most, if not all, of the chemical that remains on the finished fabric will be present as insoluble polymer. Therefore, although THPS, THPC or other compounds may be present in the commercial formulation that is used for fabric finishing, these chemicals may not be present in the finished fabric. Evaluation of the potential risk to consumers from these chemicals should reflect on those actually present and bioavailable in the finished fabric.

Slide 14.

The next two chemical classes to be discussed are the organic phosphonates, which are part of a large and important group of phosphorus-containing flame retardant chemicals, and the cyclic phosphonate esters. I'd like to first present the review of the organic phosphonates.

Slide 15.

Toxicological information is not readily available for most of the chemicals in this class, but two phosphonates with wide-ranging industrial applications have been extensively studied. These are dimethyl phosphonate (DMHP) and dimethyl methylphosphonate (DMMP).

DMHP is used in lubricants and adhesives, as a chemical intermediate, and as a flame retardant in textiles. DMMP has many uses, including as a viscosity depressant in polyester and epoxy resins, a textile conditioner, a gasoline additive, a plasticizer and stabilizer, a flame retardant, and an intermediate in the manufacture of other flame retardant chemicals. DMMP is primarily used in rigid polyurethane foams, polyester resins, and latex formulations.

No information was found concerning the absorption, distribution, metabolism, or excretion of either DMHP or DMMP in animals or humans. DMHP has been shown to cause death in rabbits after dermal application, indicating considerable bioavailability from the dermal route (Keller 1961). The mechanisms of toxicity for either DMHP or DMMP are not known.

Slide 16.

DMHP is acutely toxic by the oral, inhalation, and dermal routes of administration after a single exposure, based upon the criteria in the FHSA. DMMP is not acutely toxic by any route of exposure.

In addition, both DMHP and DMMP meet the FHSA definition of toxic based on chronic toxicity. Repeated-dose subchronic and chronic oral administration of these two compounds caused multiple organ toxicity in rats and mice. Histopathological effects were observed in the lungs, forestomach, eye, brain, heart, liver, kidney, bladder, and testes. DMHP was more toxic than DMMP for both sexes of both species. Therefore, DMHP and DMMP may be regarded as "probably toxic" in humans, based on sufficient evidence of toxicity in animals.

There is inadequate evidence of reproductive toxicity of DMHP in males; no studies were located on reproductive or developmental toxicity of DMHP in females.

There is no evidence of reproductive or teratogenic effects after administration of DMMP to female rats or mice. But DMMP caused morphologic and functional defects in the male reproductive systems in studies in male rats. Sertoli cell and prostate lesions, functional defects in spermatozoa, and reduced spermatogenesis were observed. Therefore, DMMP may be regarded as a "probable reproductive toxicant" in humans, based on sufficient evidence of reproductive toxicity in animals.

Dominant lethal effects were observed after male rats and mice were treated with DMMP. DMHP and DMMP exhibited some evidence of carcinogenicity in gavage studies conducted in mice and rats. Each of these compounds induced a neoplastic response in one sex of one species. Significant increases in lung and forestomach neoplasms were observed in male rats after oral administration of DMHP in a 2-year bioassay. Administration of DMMP caused renal tubular cell adenocarcinomas, renal transitional cell papillomas, and mononuclear cell leukemias in male rats. Therefore, DMHP and DMMP may be regarded as "possible human carcinogens," based on limited evidence of carcinogenicity in animals.

There is inadequate evidence of neurotoxicity in animals. Symptoms of neurological effects from both compounds were generally associated with high doses and were accompanied by serious systemic toxicity and deaths. Thus, the neurotoxicity may be secondary to the severe systemic toxicity.

In addition to systemic effects, DMHP is a probable eye irritant in humans based on sufficient animal evidence. Similarly, DMMP is a probable human skin and eye irritant. No evidence for sensitization was observed in humans or animals.

Slide 17.

Based on the animal studies, the acceptable daily intake can be estimated for the oral route of exposure for both DMHP and DMMP. The oral ADI for DMHP is 0.5 mg/kg-day, based on a NOEL for multiple organ effects in subchronic study in rats. The oral ADI for DMMP is 0.25 mg/kg-day, based on a LOEL for nephrosis and hypospermatogenesis in rats in a 90-day study.

Slide 18.

DMHP is acutely toxic, based upon the criteria in the FHSA by the inhalation, oral, and dermal routes of exposure. DMMP is not acutely toxic by any route of exposure, but both of these compounds meet the FHSA definition for toxic based on chronic toxicity. Subchronic and chronic oral administration of DMMP caused multiple organ toxicity in animals. It is a "probable reproductive toxicant" in humans. It is a probable human skin and eye irritant. A quantitative assessment of exposure and risk must be performed to determine whether DMHP or DMMP may present a hazard to consumers. Products that contain DMHP or DMMP would be considered "hazardous substances" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake.

Slide 19.

The second group that will be discussed along with the organic phosphonates are the cyclic phosphonate esters.

The cyclic phosphonate esters are part of a large and important group of phosphorus-containing flame retardant chemicals. Two commercially available chemicals containing two cyclic phosphonate esters are used in the U.S. as flame retardants in commercial furniture (as either fabric surface treatments or backcoatings), children's sleepwear, work clothing, automotive and aircraft fabrics, mattress tickings, draperies, and wall coverings (Albright and Wilson, 1998).

Cyclic phosphonate ester commercial product 1 (CPE1) and cyclic phosphonate ester commercial product 2 (CPE2) consist of the same two chemical compounds in slightly different ratios. The two compounds are the monomer and dimer. The balance of each product consists of higher molecular weight oligomers and water. A moderate amount of toxicity research has been conducted on these two chemical mixtures, but no studies on the effects of the individual chemicals were found.

Slide 20.

No clinical effects or deaths were observed from acute administration of CPE1; the LD_{50} is greater than 5 g/kg (Gordon, 1981). Thus, under the criteria in the FHSA, the cyclic phosphonate ester products are not acutely toxic by the oral or dermal routes of administration. They do, however, meet the FHSA definition for toxic based on chronic toxicity. Repeated-dose

subchronic oral administration caused some signs of toxicity at relatively high doses in non-gravid animals. Decreased food intake and body weight and increased organ weights were noted in a 90-day oral study in rats; the NOEL for these effects was 1.5 g/kg/day (Terrell 1976). However, more serious maternal toxicity and deaths were observed when dosing during gestation.

Although CPE1 caused dermal irritation in animal studies, repeated dermal applications of an unspecified CPE compound did not cause dermal irritation or sensitization in humans (Chmiel 1975).

There is no evidence of reproductive or teratogenic effects of CPEs in rat studies at doses of 1,000 mg/kg or more, but CPEs induced fetotoxicity, manifested as reduced ossification and rib defects, in a rabbit study (Beliles 1979) at doses that were much lower than the rat studies. Such minor developmental delays or variations generally are not considered sufficient evidence of developmental toxicity in animals. Therefore, CPEs may be regarded as "possible developmental toxicants" in humans, based on limited evidence of developmental toxicity in animals. The conclusion that CPEs are possible developmental toxicants does not, in itself, demonstrate whether they meet the FHSA definition of chronic toxicity.

Although several mutagenicity studies were negative, one *in vitro* cell transformation study was positive. However, there are no studies on carcinogenicity in animals, and thus the cyclic phosphonate esters are not classifiable as to carcinogenicity in humans.

There is no evidence of neurotoxicity in animals, based on observations of treated experimental animals and a single *in vitro* test.

Slide 21.

An ADI of 0.3 mg/kg/day was calculated for CPEs, based on a LOEL of 300 mg/kg/day for developmental effects in rabbits.

Slide 22.

In summary, these cyclic phosphonate esters are not acutely toxic by the dermal, oral or inhalation routes of exposure under the FHSA. They do, however, meet the definition for chronic toxicity under the FHSA based on evidence of systemic toxicity in animals. In addition, CPEs are possible developmental toxicants in humans, based on limited data in animals. No studies specifically considered carcinogenic effects.

A quantitative assessment of exposure and risk must be performed to determine whether CPE1 or CPE2 may present a hazard to consumers. Products that contain CPE1 or CPE2 would be considered "hazardous substances" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake.

Slide 23.

There is limited toxicity information for the ammonium polyphosphates and blends. Albright and Wilson manufactures three ammonium polyphosphates used in and outside the U.S. as flame retardants in upholstery fabrics, automotive interiors, and draperies. Non-FR applications include livestock feed supplements, water treatments, cements, and fertilizers. These flame retardants were marketed as AMGARD® LR2, AMGARD® LR3, and AMGARD® LR4 before March 31, 1998, but are now called ANTIBLAZE® LR2, ANTIBLAZE® LR3, and ANTIBLAZE® LR4, respectively. According to Albright and Wilson, LR2 is

applied directly to cellulose fabrics or cellulose-rich blends, whereas LR3 and LR4 are used in backcoating systems.

Slide 24.

Toxicity data submitted by Albright and Wilson are primarily acute studies involving LR2 and LR4. None was included for LR3. No major effects were observed in any of the acute studies. Studies in rats suggest that LR2 and LR4 have low acute oral toxicity. The acute oral LD_{50} values for LR2 and LR4 were > 5000 mg/kg and > 2000 mg/kg, respectively. None of the treated animals died or showed clinical signs of toxicity.

An acute LC_{50} of > 5.09 mg/l in rats after inhalation exposure is listed in the company's product summary. The acute dermal LD_{50} in rats for both LR2 and LR4 was > 2000 mg/kg. Other dermal studies in several animal species showed that LR2 and LR4 are not irritants or sensitizers. A patch study in humans using 10% LR2 resulted in a slight reaction a few subjects, but a few had a similar reaction to the negative control. LR2 and LR4 were not ocular irritants in rabbits. One *in vitro* study showed that LR2 was not mutagenic. There are no carcinogenicity data available. There are no available data on subchronic or chronic exposures, pharmacokinetics, or reproductive/developmental effects. Data are insufficient to calculate an ADI for this compound.

Slide 25.

Based on the few data that are available, these compounds cannot be considered toxic under the FHSA. However, this does not mean that these chemicals are "safe," only that there are not sufficient data to demonstrate whether they meet the regulatory definition of toxic.

Slide 26.

The next 2 chemicals will be discussed together. They are sodium pentoxide and sodium antimonate. As a component of flame retardant mixtures, antimony pentoxide is used primarily in plastics, including TV and computer cabinets and wires and cable insulation. It also has potential for use in fibers and fabrics because of its relatively small particle size and its translucence. Sodium antimonate is used in formulations requiring deep tone colors or where antimony trioxide is unsuitable (IPCS, 1997).

Antimony pentoxide and sodium antimonate are relatively insoluble and not readily bioavailable. No quantitative data are available, but based on studies of organic and other inorganic antimony compounds, the International Commission on Radiological Protection (1981) assumes 1% as a reference value for gastrointestinal absorption of antimony compounds such as antimony pentoxide and sodium antimonate.

Based on limited data, antimony pentoxide and sodium antimonate are less toxic than antimony trioxide and the least toxic of common antimony compounds. Other antimony compounds, especially the organic forms, cause a wide range of serious effects at low doses. However, the low water solubility and bioavailability of antimony pentoxide and sodium antimonate may contribute to the low relative toxicity.

Slide 27.

Antimony pentoxide and sodium antimonate are probably not acutely toxic by the oral route under the FHSA criteria. Although the experimental animal studies did not test the compounds up to the 5 g/kg definition for acute

toxicity under FHSA, no significant treatment-related effects were observed following oral doses of 4.1 g antimony pentoxide/kg and 3.3 g sodium antimonate/kg, equivalent to 3.1 and 2.1 g antimony/kg, respectively. No data were available for other routes of exposure, but there is no reason to suspect that these compounds are more toxic than antimony trioxide. Since antimony trioxide is not toxic by the dermal route, antimony pentoxide and sodium antimonate are probably not acutely toxic by this route.

There are no chronic studies in animals or humans, and no data are available to draw conclusions about reproductive and developmental toxicity or neurotoxicity. Likewise, there are no data on carcinogenicity, although *in vitro* genotoxicity tests were all negative for antimony pentoxide. The available data are insufficient to estimate the acceptable daily intake levels for either antimony pentoxide or sodium antimonate. There are no animal or human data on skin or eye effects and there are no data concerning other toxic effects, such as sensitization.

Slide 28.

Therefore, based on limited data, antimony pentoxide and sodium antimonate do not meet the definition of toxic under the FHSA. However, this does not mean that these chemicals are "safe," only that there are not sufficient data to demonstrate whether they meet the regulatory definition of toxic.

Slide 29.

Another large group of compounds proposed for use as flame retardant chemicals in upholstered furniture is the chlorinated paraffins. Chlorinated paraffins, or CPs, are a large group of chemicals consisting of chlorinated alkanes with 10-30 carbon chain lengths and 40-70% chlorine by weight. CPs with approximately 70% chlorine are used in flame retardant applications, but the chain length used depends on the substrate for which it is used. CPs are primarily used as plasticizers and flame retardants in plastics, mostly appliance and electronics cabinets and wire and cable insulation.

In general, disposition studies have shown that CPs are not absorbed through intact skin but are bioavailable after oral administration. The half-life in fat may be several weeks, but the compounds are cleared from other tissues within days.

No human or animal studies were located for inhalation exposure, but since these compounds are not volatile or easily aerosolized and are not produced or supplied as dusts, inhalation is not a likely route of exposure. No studies were located on the systemic toxicity of dermally applied CPs.

Slide 30.

Under the FHSA criteria, chlorinated paraffins are not acutely toxic by the oral route of administration after a single exposure, but are acutely toxic after multiple doses. In addition, CPs meet the FHSA definition of toxic, based on chronic toxicity. Repeated-dose acute, subchronic, and chronic oral administration of several CPs caused multiple organ toxicity in mice, rats, rabbits, and dogs. The effects included diarrhea, weight loss, increased liver and kidney weights, histopathological changes in the liver and thyroid, and decreased survival. The short- and medium-chain, heavily chlorinated CPs were generally more toxic than the long-chain CPs. The degree of toxicity was dependent on carbon-chain length and, to a lesser extent, degree of chlorination.

In addition to systemic effects, chlorinated paraffins are probable skin and eye irritants in humans based on sufficient animal evidence. Mild skin irritation was observed in rats treated with short- and medium-chain CPs; the heavily chlorinated short-chain products were somewhat more irritating than the other short-chain CPs tested. No dermal effects were observed with the long-chain CPs. Ocular tests showed mild irritancy from the short-chain CPs.

One short-chained CP product (C_{12},60%Cl) was carcinogenic in two-year gavage studies in mice and rats (Bucher et al. 1987). Clear evidence of hepatocellular tumors was found in both sexes of rats and mice and increases in thyroid follicular cell adenomas and carcinomas were found in female rats and mice. Therefore, C_{12},60%Cl may be regarded as a "probable human carcinogen," based on sufficient evidence of carcinogenicity in animals. A probable human carcinogen may be further regarded as "toxic" under the FHSA. A quantitative assessment of exposure and risk must be performed to determine whether C_{12},60%Cl may present a hazard to consumers. Products that contain C_{12},60%Cl would be considered "hazardous substances" under the FHSA only if the lifetime cancer risk associated with exposure to C_{12},60%Cl during "reasonably foreseeable handling and use" were to exceed one in a million.

The long-chain CP product (C_{23},43%Cl) showed clear evidence of malignant lymphoma in male mice, but no clear evidence of carcinogenicity was observed in male rats or females of either species, although equivocal evidence of hepatocellular carcinoma was found in female mice and of renal medullary pheochromocytomas in female rats. Thus, C_{23},43%Cl may be regarded as a "possible human carcinogen," based on limited evidence of carcinogenicity in animals. Possible human carcinogens are not considered "toxic" under the FHSA. However, these conclusions are based on limited data. This does not mean that this chemical is "safe," only that there are not sufficient data to determine whether it meets the regulatory definition of toxic.

There was no evidence of neurotoxicity in any of the studies performed. However, no studies were conducted that specifically examined neurological endpoints. There was no evidence of reproductive toxicity based on a reproductive study in rats using a medium chain product (Serrone et al. 1987). This was the only reproductive study performed using any of the CPs. There is inadequate evidence of developmental toxicity in animals. Several studies were performed in both rats and rabbits in which no developmental toxicity was observed either in the presence or absence of maternal toxicity. Other studies in rats and rabbits demonstrated developmental effects in the presence and absence of maternal effects, depending upon the compound chain length and degree of chlorination. A developmental study on the medium-chain product showed no effects in the parents, but the pups showed serious toxicity and decreased survival.

Slide 31.

The subchronic oral ADI has been estimated to be 0.1 mg/kg/day, based on a NOEL of 10 mg/kg/day in a subchronic study in dogs.

Slide 32.

Under the FHSA criteria, CPs are toxic, based on chronic toxicity. A short-chain CP (C_{12}60% Cl) is a probable human carcinogen.

Slide 33.

The next compound to be reviewed is zinc borate. Zinc borate is the zinc salt of boric acid. The typical composition is 45% zinc oxide (ZnO) and

34% boric anhydride (B_2O_3) with 20% water of hydration. Because of the lack of toxicological information on zinc borate, it is appropriate to consider the larger body of knowledge concerning zinc oxide and boric anhydride. Further, since boric acid (H_3BO_3) is formed by the reaction of boric anhydride with water, it is included in this review as well.

Zinc borate is primarily used in flame retardant mixtures for plastics and rubber products. It works synergistically with chlorine-based FRs and may be used in cellulosic fabric backcoatings. Zinc borate is also used in medicine and ceramics and as a fungistat and mildew inhibitor in polymer, paper, and textile products. Zinc oxide is used in a variety of industrial applications and products, including cosmetics, ointments, glass, ceramics, rubber, colorants, electronics, and dietary supplements. Boric acid has many uses, including wood treatment, printing and dyeing, leather, carpets, cements, crockery, cosmetics, and personal care products. Boric anhydride is used in glass, electronics, and herbicides (HSDB, 1998).

Slide 34.

Zinc oxide preparations are currently available for use on minor skin irritations and diaper rash. About 20-30% of zinc that is ingested by humans is absorbed by the gastrointestinal tract. Once absorbed, zinc is widely distributed in the body. Data on absorption following inhalation exposure are limited.

Although ultrafine particles (0.2-1 μm) of zinc oxide or freshly generated zinc oxide fumes are associated with metal-fume fever, zinc oxide dust is generally considered a nuisance dust. No studies were found on the effects of zinc oxide dust.

Zinc oxide has minimal effects when applied to the skin of animals, and in humans, only heavy dust exposures were associated with dermal effects. No reports of eye injuries in humans or animals were found.

Under the FHSA criteria, zinc oxide is acutely toxic by the oral route of exposure, based on death in ferrets. No data were available to make a determination about acute toxicity by inhalation or dermal administration. No data were found on the effects of ingestion of zinc oxide in humans, but subchronic studies in ferrets resulted in systemic toxicity, including anemia and nephrosis.

Zinc oxide caused reduced fetal weight and increased fetal resorptions in a developmental study in rats. Therefore, zinc oxide may be regarded as a possible developmental toxicant in humans, based on limited evidence of developmental toxicity in animals. Possible human toxicants are not considered "toxic" under the FHSA. However, these conclusions are based on limited data. This does not mean that this chemical is "safe," only that there are not sufficient data to demonstrate whether it meets the regulatory definition of toxic.

Inhalation of zinc oxide was associated with chromosomal aberrations in the bone marrow cells of one animal species, but two epidemiological studies failed to show an association between zinc exposure and excess cancer mortality. *In vitro* mutagenicity tests have not been conducted on zinc oxide. No carcinogenicity bioassays were conducted in animals. Therefore, there is inadequate evidence for the carcinogenicity of zinc oxide.

Zinc oxide was neurotoxic at a high dose level in one animal study, but no studies specifically considered neurological effects. Therefore, zinc oxide may be regarded as a possible neurotoxicant in humans, based on limited evidence in animals.

Slide 35.

Zinc oxide is an acute toxicant by the oral route of exposure under the FHSA. Although it is a possible developmental, systemic, and neurotoxicant, it does not meet the definition for chronic toxicity under the FHSA. Therefore, an acceptable daily intake was not calculated. These conclusions are based on limited data in experimental animals; *i.e.*, the available subchronic or chronic studies were limited in scope and inadequate for the assessment of chronic toxicity.

Slide 36.

Boric acid is readily absorbed from the gastrointestinal tract, serous cavities, and abraded or inflamed skin. It is not absorbed through intact skin. Boric acid and boric anhydride are bioavailable via these exposure routes. Since no study has demonstrated systemic effects following inhalation exposure, absorption from this route is unknown.

The toxicity related to oral administration of boric anhydride is not well studied. Inhalation of boric anhydride dust or a mixture of boric anhydride and boric acid does not appear to cause serious toxicity. Experimental animal studies and observation of humans suggest that inhalation is not an important route of exposure for boric anhydride or boric acid, although increased eye and upper respiratory irritation have been observed in exposed workers.

Both boron compounds are irritating to the skin and eyes, and systemic toxicity may occur from contact with inflamed or damaged skin, although exposure via intact skin does not lead to systemic effects.

Since only one study was located on oral administration of boric anhydride, the evaluation of boron oxide toxicity from ingestion is based on studies of boric acid. Under the FHSA, boric acid and boric anhydride are acutely toxic by the oral route of exposure. In humans, effects of acute exposure to boric acid range from vomiting and diarrhea to serious organ toxicity and death.

There are no studies in humans or animals on neurological effects of boric acid or boric anhydride. Based on a 2-year bioassay in mice and numerous *in vitro* studies, there is no evidence for boric acid carcinogenicity.

Boric acid induced reproductive effects in both males and females and developmental effects, including reduced fetal weight, skeletal effects, and increased resorptions, in several studies in animals. Therefore, boric acid may be regarded as a "probable developmental toxicant" and a "probable reproductive toxicant" in humans, based on sufficient evidence of developmental and reproductive toxicity in animals. In addition, boric acid may be considered "toxic" under the FHSA. A quantitative assessment of exposure and risk must be performed to determine whether boric acid may present a hazard to consumers. Products that contain boric acid would be considered "hazardous substances" under the FHSA if the exposure during "reasonably foreseeable handling and use" were to exceed the acceptable daily intake.

Slide 37.

The ADI for oral exposure is 0.088 mg/kg/day, based on a NOEL of 8.8 mg/kg/day in dogs.

Slide 38.

Under the FHSA criteria, both boric acid and boric anhydride are acutely toxic by the oral route of exposure. Boric acid meets the definition for chronic toxicity as a "probable developmental toxicant" and a "probable reproductive toxicant" in humans. Both compounds are probable human skin and eye irritants.

Slide 39.

The final category to be presented is the calcium and zinc molybdates. Molybdenum compounds are used as paint and coating corrosion inhibitors, and as flame retardants in transportation textiles, draperies and carpets, usually in combination with antimony and brominated FRs. Compounds have been absorbed after inhalation of the dust and after oral exposure (Fairall et al. 1945).

Slide 40.

Given the paucity of relevant, quantitative data, few conclusions may be made about the toxicity of these molybdenum compounds. Studies cited by secondary sources assert that calcium molybdate and zinc molybdate are "practically nontoxic", that is, they have a lethal dose greater than 15 g/kg. They are, therefore, not acutely toxic as defined by the FHSA by the inhalation, oral, or dermal routes of exposure. However, the data supporting this conclusion were not readily available. No irritation was evident after dermal or ocular exposures (Stokinger 1981 review). Repeated dosing studies in animals provide limited evidence that calcium molybdate may be toxic following chronic oral and inhalation exposure. Effects such as weight loss and death were noted in 2 species. Studies of human occupational exposures to airborne molybdenum dusts provide some evidence that molybdenum compounds are toxic with heavy exposures, but the data are limited and not specific to calcium or zinc molybdates.

Calcium and zinc molybdates may be regarded as "possibly toxic" in humans based on limited evidence in animals and inadequate evidence in humans. Possible human toxicants are not considered "toxic" under the FHSA. However, these conclusions are based on limited data. This does not mean that these chemicals are "safe," only that there are not sufficient data to demonstrate whether they meet the regulatory definition of toxic. No studies on dermal or ocular effects, reproductive or developmental effects, neurological effects, or carcinogenicity of molybdenum compounds were found. The available data are insufficient to estimate the ADI levels for either calcium or zinc molybdates.

Slide 41.

Calcium and zinc molybdates have not been shown to be toxic under the FHSA, but the available data are limited.

Slide 42.

In summary, of the 7 chemicals or chemical classes that I have just reviewed today, the following do not meet the definition of toxic under the FHSA, based on limited data: the tetrakis compound $THPOH/NH_3$, ammonium polyphosphates, antimony pentoxide and sodium antimonate, and calcium and zinc molybdates.

Slide 43.

Based on sufficient evidence in animals, the following chemicals are considered "toxic" under the FHSA: the tetrakis compounds THPC, THPS, Proban® CC; the organic phosphonates DMHP and DMMP; the cyclic phosphonate esters; chlorinated paraffins; zinc oxide, boric acid and boric anhydride. Of these, zinc oxide and boric anhydride are acute toxicants under the FHSA.

Under the FHSA, THPC and THPS are considered toxic, based on acute toxicity, and on chronic toxicity evidenced by hepatic and neurological effects in animals. Proban® CC is toxic, based on acute toxicity, corrosivity, and developmental effects in animals. The organic phosphonates DMHP and DMMP are toxic, based on multiple organ effects in animals. Cyclic phosphonate esters are toxic, based on systemic effects in animals. Chlorinated paraffins are toxic, based on multiple organ effects in animals. Zinc oxide is an acute toxicant, based on death in ferrets. Boric acid is toxic, based on acute toxicity in humans and animals and reproductive and developmental effects in animals. Boric anhydride, is an acute toxicant based on effects in animals.

Slide 44.

As I mentioned at the beginning of this presentation, it is important to remember that any toxicity associated with these chemicals satisfies only one of the two conditions that must be met for a substance to be considered hazardous under the FHSA when used as an FR treatment for upholstered furniture.

The CPSC staff has not fully evaluated the second condition, that is, the potential for causing substantial personal injury or illness during reasonably forseeable handling and use, which must be met in order for a substance to be considered hazardous under the Act. At this time, there is insufficient information for the CPSC staff to conduct the second part of the analysis to determine what hazards these chemicals might be present if used as flame retardants on upholstered furniture. Such an analysis would include an assessment of exposure, bioavailability, and dose response.

Further details on the data that were considered in evaluating the toxicity of these chemicals can be found in the CPSC toxicity reviews. Dr. Babich and I will be happy to take any questions from the subcommittee.

Toxicity Assessment of Seven Flame Retardant Chemicals Under the FHSA

Patricia Bittner, M.S.

Jacque Ferrante, Ph.D.

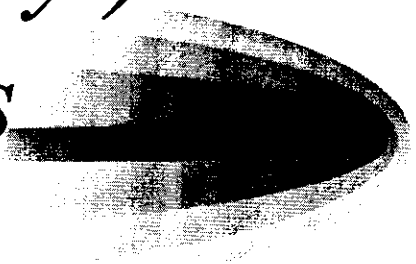
Kris Hatlelid, Ph.D., M.P.H.

September 22, 1999

Some FR Chemicals Under Consideration by NAS

- Tetrakis(hydroxymethyl)phosphonium salts, precondensate with urea
- Organic Phosphonates and Cyclic Phosphonate Esters
- Ammonium Polyphosphates and blends
- Antimony Pentoxide and Sodium Antimonate
- Chlorinated Paraffins
- Zinc Borate
- Calcium and Zinc Molybdates

Tetrakis(hydroxymethyl) phosphonium salts

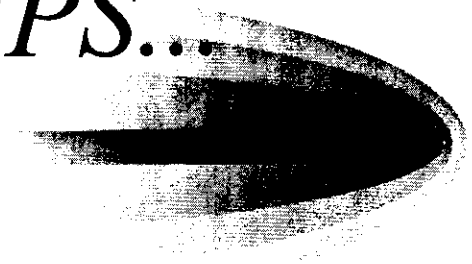


THPS (CAS 55566-30-8)
THPC (CAS 124-64-1)
$THPOH/NH_3$
Proban® CC

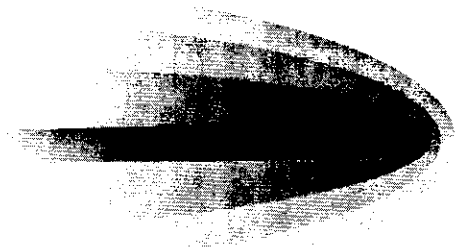
Under the FHSA, THPS is...

- Acutely toxic by the oral route
- Dermal irritant in animals
- Probably toxic (sufficient animal evidence)
- Possible neurotoxicant (limited animal evidence)
- No evidence of carcinogenicity
- Insufficient reproductive and developmental data

Under the FHSA, THPS...



- ADI of 0.05 mg/kg/day, based on a NOEL of 5 mg/kg/day for liver toxicity in rats in a subchronic study

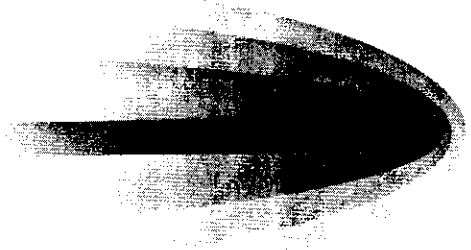


THPS is "toxic" under the FHSA, based on sufficient evidence of acute and chronic (liver) toxicity in animals

Under the FHSA, THPC is…

- Acute toxicant (oral, not dermal)
- Dermal irritant
- Data insufficient to evaluate sensitization potential
- Probable chronic toxicant (liver effects in animals)
- Probable neurotoxicant
- Possible developmental toxicant (limited animal evidence)

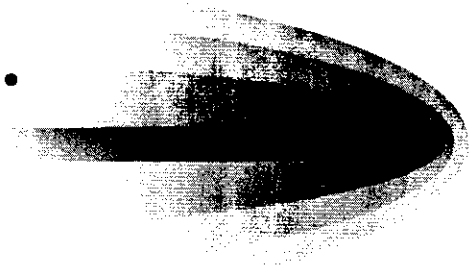
Under the FHSA, THPC...



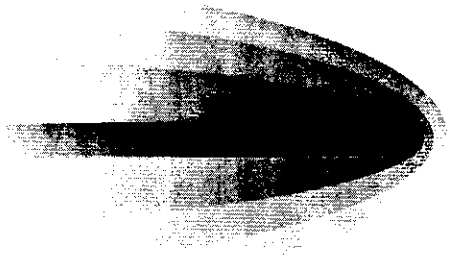
ADI of 0.00375 mg/kg/day, based on a LOEL of 3.75 mg/kg/day for liver effects in rats in a chronic study

THPC is "toxic" under the FHSA, based on sufficient evidence of acute and chronic toxicity and neurotoxicity in animals

Under the FHSA, THPOH/NH_3 is...

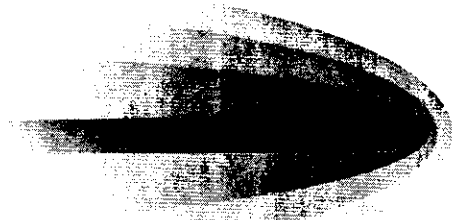


- Not acutely toxic by the oral or dermal routes
- Insufficient data to evaluate dermal irritancy, chronic toxicity, reproductive/developmental toxicity, neurotoxicity, or carcinogenicity

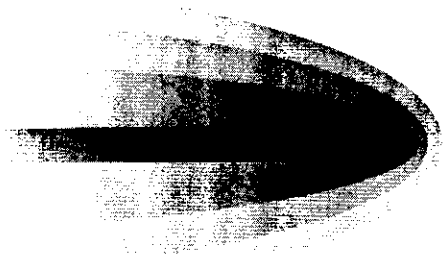


THPOH/NH_3 is <u>not</u> "toxic" under the FHSA, based on limited data

Under the FHSA, Proban® CC is...



- Acutely toxic (oral, not dermal) route
- Data insufficient to evaluate subchronic/chronic toxicity and carcinogenicity
- Corrosive
- Sensitizes guinea pigs, but not humans
- Possible neurotoxicant
- Probable developmental toxicant
- ADI is 0.5 mg/kg-day, based on NOEL for developmental effects



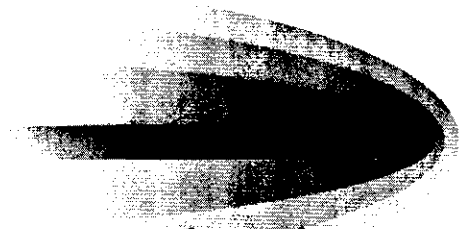
Proban® CC is "toxic" under the FHSA, based on sufficient evidence of acute toxicity, corrosivity, and developmental toxicity in animals

Organic Phosphonates and Cyclic Phosphonate Esters

Organic phosphonates

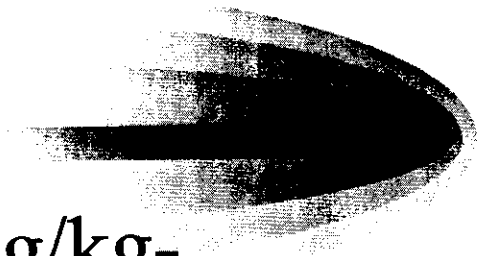
- Dimethyl phosphonate (DMHP) (CAS # 868-85-9)
- Dimethyl methylphosphonate (DMMP) (CAS # 756-79-6)

Under the FHSA, DMHP and DMMP are...



- Acutely toxic (inhalation, oral, dermal) (DMHP)
- Chronic toxicants in animals (multiple organs)
- Inadequate reproductive or developmental data (DMHP)
- Probable reproductive toxicant (DMMP)
- Possible human carcinogens
- Inadequate evidence of neurotoxicity
- Probable eye irritants
- Probable skin irritant (DMMP)

Under the FHSA, DMHP and DMMP...



- Oral ADI for DMHP is 0.5 mg/kg-day, based on a subchronic NOEL of 50 mg/kg/day in rats.
- Oral ADI for DMMP is 0.25 mg/kg-day, based on a subchronic LOEL of 250 mg/kg/day in rats.

DMHP and DMMP are "toxic" under the FHSA, based on sufficient evidence of acute toxicity (DMHP) and chronic toxicity (multiple organs) in animals

Cyclic Phosphonate Esters

Commercial product 1 (CPE1)

65% Monomer (CAS 41203-81-0)

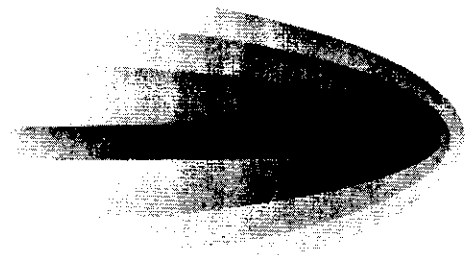
19% Dimer (CAS 42595-45-9)

Commercial Product 2 (CPE2)

60% Monomer (CAS 41203-81-0)

18% Dimer (CAS 42595-45-9)

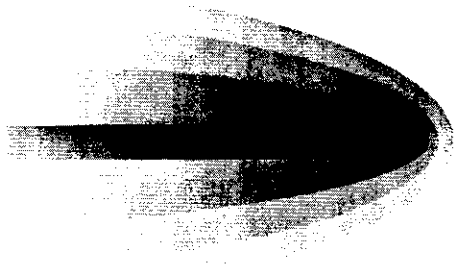
Under the FHSA, CPE1 and CPE2 are...



- Not acute toxicants
- Chronic toxicants (sufficient animal evidence)
- Dermal irritant in animals (CPE1)
- Not a dermal irritant in humans (unspecified)
- Possible developmental toxicant (limited animal evidence)
- No data available to evaluate carcinogenicity

Under the FHSA, Cyclic Phosphonate Esters...

ADI of 0.3 mg/kg-day, based on a LOEL of 300 mg/kg/day for developmental effects in rabbits



Cyclic phosphonate esters are "toxic" under the FHSA, based on sufficient evidence of systemic toxicity in animals

Ammonium Polyphosphates and Blends

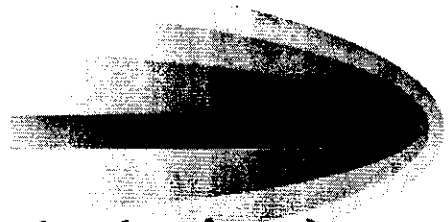
(CAS # 68333-79-9)

Antiblaze® LR2

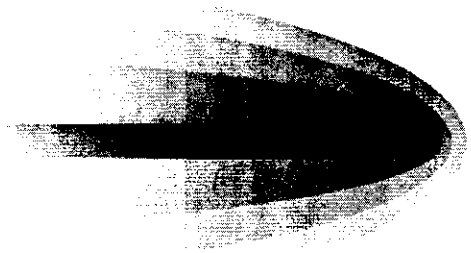
Antiblaze® LR3

Antiblaze® LR4

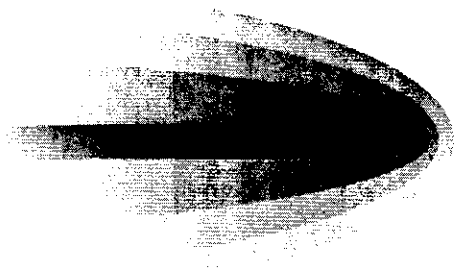
Under the FHSA, LR2 and LR4 are...



- Not acutely toxic (oral, dermal, inhalation)
- Not dermal irritants or sensitizers in animals
- Not human irritants (LR2--1 study)
- Not ocular irritants in animals
- No available data on carcinogenicity, subchronic/chronic exposures, pharmacokinetics, reproductive, and developmental endpoints

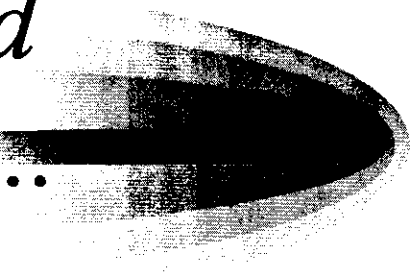


Ammonium polyphosphates are <u>not</u> "toxic" under the FHSA, based on limited data

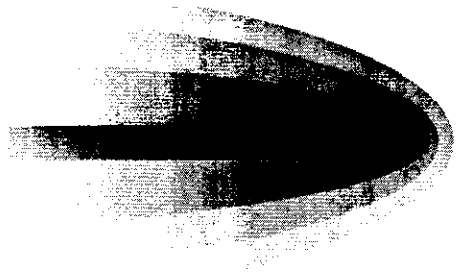


Antimony Pentoxide (CAS # 1314-60-9) and Sodium Antimonate (CAS # 15432-85-6)

Under the FHSA, Antimony Pentoxide and Sodium Antimonate are...



- Probably not acutely toxic (oral)
- No chronic, reproductive, developmental, or neurological data available
- No dermal, ocular, or sensitization data available



Antimony Pentoxide and Sodium Antimonate are <u>not</u> "toxic" under the FHSA, based on limited data

Chlorinated Paraffins (CPs)
(CAS # 63449-39-8 and others)

Categorized by chain length:

(Short--C_{10-13}; Medium--C_{14-17}; Long--C_{20-30})

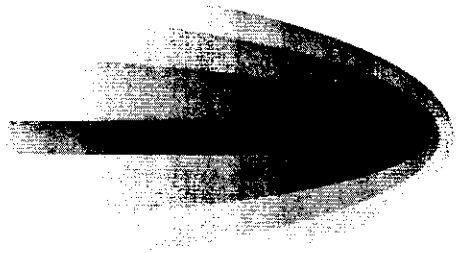
Categorized by chlorine content (% by wt):

40-50%; 51-60%; 61-70%

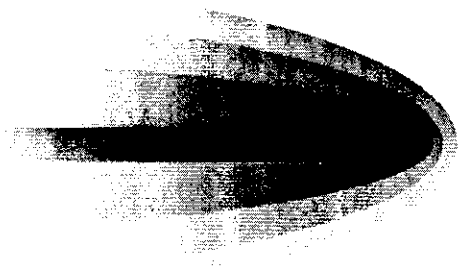
Under the FHSA, Chlorinated Paraffins are...

- Acutely toxic after multiple (not single) oral doses
- Chronic toxicants (multiple organ toxicity)
- Probable eye and skin irritants (sufficient evidence in animals)
- Probable human carcinogen (C_{12}, 60% Cl)
- Possible human carcinogen (C_{23}, 43% Cl)
- No evidence of neurotoxicity or reproductive toxicity; inadequate evidence of developmental toxicity

Under the FHSA, Chlorinated Paraffins...



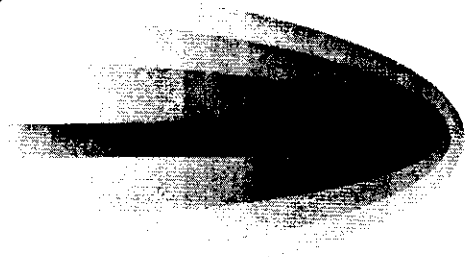
ADI of 0.1 mg/kg-day, based on a NOEL in a subchronic oral study in dogs



Chlorinated Paraffins are "toxic" under the FHSA, based on sufficient evidence of chronic toxicity in animals

Zinc Borate

(CAS # 1332-07-6)



Zinc Oxide

(CAS # 1314-13-2)

Boric Anhydride

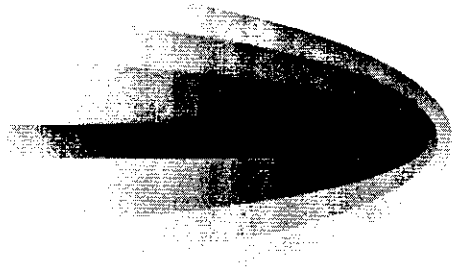
(CAS # 1303-86-2)

Boric Acid

(CAS # 10043-35-3)

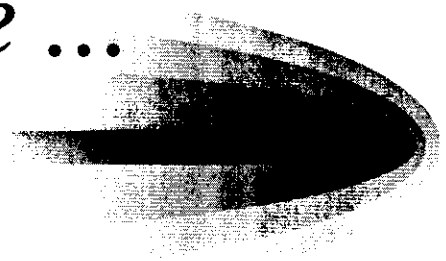
Under the FHSA, Zinc Oxide is...

- Acute oral toxicant
- Possible systemic toxicant
- Possible developmental toxicant
- Inadequate carcinogenicity data
- Possible neurotoxicant



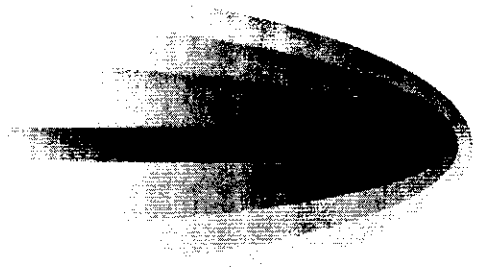
Zinc oxide is "toxic" under the FHSA, based on sufficient evidence of acute toxicity in animals

Under the FHSA, Boric Acid and Boric Anhydride are ...

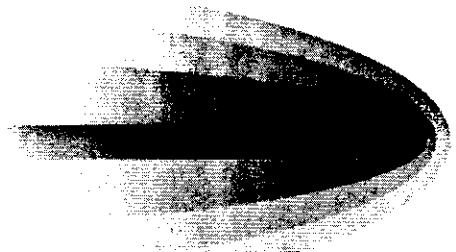


- Dermal and ocular irritants
- Acute oral toxicants
- No data on neurotoxicity
- No evidence of carcinogenicity in bioassay (boric acid)
- Probable developmental toxicant
- Probable reproductive toxicant

Under the FHSA, Boric Acid and Boric Anhydride...



ADI is 0.088 mg/kg-day, based on a NOEL of 8.8 mg/kg/day in dogs in an oral study



Boric Acid and Boric Anhydride are "toxic" under the FHSA, based on sufficient evidence of acute toxicity (both) and chronic toxicity (boric acid) in animals.

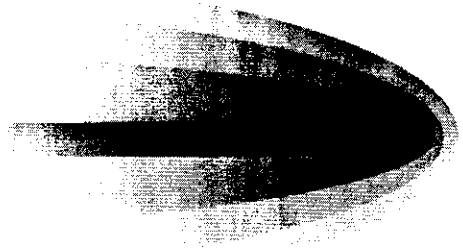
Calcium Molybdate and Zinc Molybdate

CAS # 7789-82-4 ($CaMO_4$)

CAS # 61583-60-6 ($ZnMO_4$)

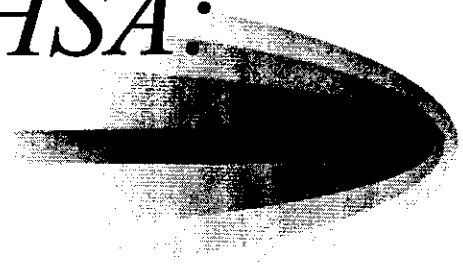
Under the FHSA, Calcium Molybdate and Zinc Molybdate are...

- Not acute toxicants
- Possible chronic toxicants in humans (limited evidence in animals and inadequate evidence in humans)
- Insufficient data to calculate ADI



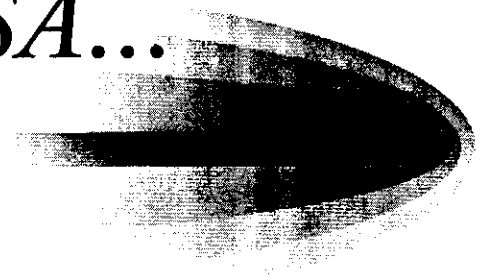
Calcium Molybdate and Zinc Molybdate are <u>not</u> "toxic" under the FHSA, based on limited data

<u>Not</u> "toxic" under FHSA:



- Tetrakis -- $THPOH/NH_3$
- Ammonium Polyphosphates
- Antimony Pentoxide/Sodium Antimonate
- Calcium and Zinc Molybdates

"Toxic" under FHSA...



- Tetrakis compounds: THPC, THPS, Proban® CC
- Organic Phosphonates: DMHP, DMMP
- Cyclic Phosphonate Esters: CPE1, CPE2
- Chlorinated Paraffins
- Zinc Borate: Zinc Oxide, Boric Acid, Boric Anhydride

Summary

Chemicals considered toxic under the FHSA must be evaluated for their potential to cause substantial personal injury or illness during reasonably forseeable handling and use, in order to be considered "hazardous".