Behl gives Duke seminar on NTP flame retardant toxicity screening

By Ernie Hood

Toxicologist Mamta Behl, Ph.D., of the National Toxicology Program (NTP), discussed the novel screening approach developed by NTP to assess the toxicity of classes of compounds in a Jan. 16 talk at Duke University. Her presentation, "Screening Compounds with Developmental and Neurotoxic Potential: Flame Retardants, a Case Example," was part of the Integrated Toxicology and Environmental Health Program seminar series *(http://sites.nicholas.duke.edu/envhealth/events/spring-2015-seminars/)* at the Nicholas School of the Environment. Early results indicate that some newer compounds may present just as much cause for concern as the older flame retardants they are meant to replace.

Behl explained use of the novel screening battery to compare older phased-out flame retardants with newer substitutes. "We want to know the relative toxicity," she said. (Photo courtesy of Steve McCaw)

Before delving into the details of the screening battery, Behl addressed the need to efficiently characterize classes of compounds of environmental or occupational concern. "It's important to be able to look at them in a timely manner," she told her Duke audience. "If you're looking at one chemical at a time, it takes years to get any sort of information, so this is an attempt to come up with a screening approach that allows us to get some information in a timely manner."

Among flame retardants, the major brominated diphenyl ether (BDE), BDE-47, has been phased out of the marketplace. However, there are growing concerns about the effects of exposures to the new class of flame retardants, which are called aromatic phosphates and are now marketed as substitutes for some BDEs. Primary concerns include reproductive or developmental toxicity from long-term exposure, as well as neurological and systemic effects. As part of a larger flame-retardant effort, NTP is studying six of the aromatic phosphates, following their nomination by the Consumer Product Safety Commission.

Screening battery concept

ITEHP seminars draw a large crowd to Field Auditorium, the high-tech classroom in Duke's Environment Hall. (Photo courtesy of Steve McCaw)

The screening battery is conducted in three phases, in increasing levels of biological complexity. The assays were designed to provide comparative toxicity information about four of the BDEs and six of the APs (see text box).

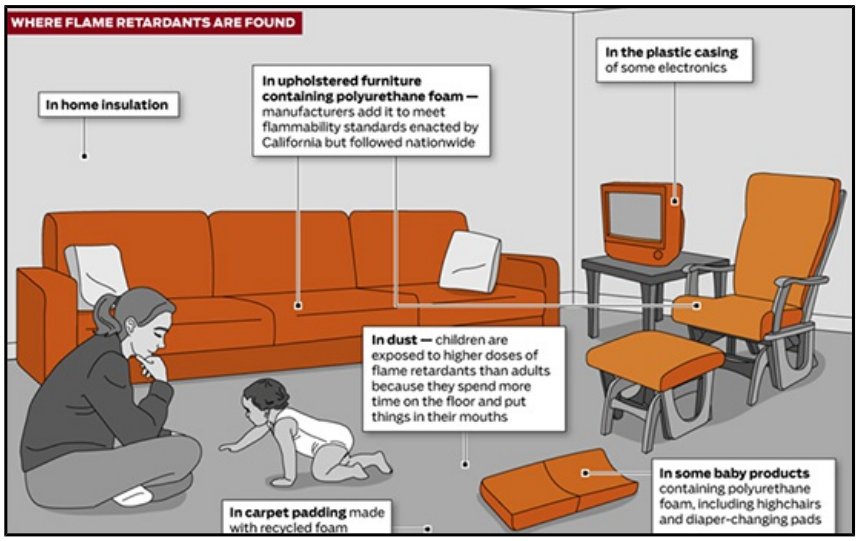
- **High-throughput screening using human cell lines** — Results showed a variety of toxicity levels among both classes. Mitochondrial toxicity appeared to be the most sensitive assay.
- **High content screens** — Neurotoxicological endpoints, such as neurite proliferation and outgrowth, neuronal firing, neuronal crest migration, genomics, and metabolomics, are measured. Again, results suggested that the substitute compounds might be as toxic to neural processes as the compounds they are intended to replace.
- **Screening in complementary animal models** — Exposure effects on feeding, growth, and reproduction were noted in the roundworm *Caenorhabditis elegans*. Studies in zebrafish are ongoing.

"The take-home message is that the alternative flame retardants may have cause for concern," Behl said. "Their use as replacements for BDEs doesn't necessarily mean they're safe, so they should be tested in depth for further hazard characterization."

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

Nicholas School of the Environment faculty member Heather Stapleton, Ph.D. (http://nicholas.duke.edu/people/faculty/stapleton) , an NIEHS grantee who studies flame retardants, naturally had a keen interest in Behl's talk and asked several questions following the presentation. (Photo courtesy of Steve McCaw)

Edward Levin, Ph.D., is a professor of psychiatry and behavioral sciences, organizer of the ITEHP seminar series, and a researcher with the NIEHS-funded Superfund Research Center at Duke. He introduced Behl and moderated the question and answer session. (Photo courtesy of Steve McCaw)



With this slide, Behl set the stage for her discussion of the novel screening battery NTP is using to assess the relative neurotoxicity and developmental toxicity of flame retardants. (Graphic from EPA and Chicago Tribune (http://media.apps.chicagotribune.com/flames/flame-retardants-hard-to-avoid.html) reporting)

Tested flame retardants

BDEs and other aliphatics

- Polybrominated diphenyl ether (BDE-47) (phased out)
- Tris(2-chloroethyl) phosphate (TCEP)
- Tetrabromobisphenol A (TBBPA)
- Tri-o-cresyl phosphate (TOCP)

Replacements (aromatic phosphates)

- Triphenyl phosphate (TPP)
- Tert-butylphenyl diphenyl phosphate (BPDP)
- Tricresyl phosphate (TCP)
- 2-ethylhexyl diphenyl phosphate (EHDP)
- Isodecyl diphenyl phosphate (IDDP)
- Isopropylated phenyl phosphate (IPP)

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