

## **Birnbaum lab premieres publication on flame retardant additive**

By *Sheila Yong*

About a year and a half after the start of its operation, the Laboratory of Toxicology and Toxicokinetics (LTT), headed by NIEHS and NTP Director Linda Birnbaum, Ph.D., showcased its first publication on hexabromocyclododecane (HBCD), an additive flame retardant primarily used in polystyrene foam building materials (see [story](#)). The commercial mix of HBCD consists of three stereoisomers - alpha, beta, and gamma, with gamma making up 70-80 percent of the mixture.

The [study](#),

(<http://www.ncbi.nlm.nih.gov/pubmed/23733921>)

published in the August issue of Toxicological Sciences, focuses on beta-HBCD and its effects on female laboratory mice. LTT is a small team, guided by Mike Sanders, Ph.D., lead author of the study.

Prior to establishing LTT, Birnbaum, a board-certified toxicologist, spent several years researching the toxic effects of flame retardants. <"I'm especially interested in the brominated flame retardants (BFRs),>" said Birnbaum. <"They are the most widely used, because they are cheap and extremely effective in reducing fire-related injury and property damage.>"

Birnbaum said that these chemicals have come under intense scrutiny over the years, because of their potentially harmful effects to the environment and human health. That's why LTT made the study of BFRs its primary focus when it was first founded.

### **Unraveling the beta isomer mystery**

HBCD is a type of BFR that is mixed with the product matrix, rather than being chemically bound. As a result, it escapes easily into the environment. A survey conducted by Birnbaum and colleagues in 2012 found detectable levels of HBCD in 42 percent of food samples from supermarkets in Dallas, Texas. *In vitro* studies have also shown HBCD to be an anti-androgen and aromatase inhibitor, specifically binding to several steroid hormone receptors.

### **Linked Audio**

[Listen to Birnbaum discuss her findings with host Steve Curwood in public radio's 'Living on Earth' \(05:20\).](#)

While extensive toxicokinetic studies have been done on the alpha and gamma isomers of HBCD, toxicology data for the beta isomer is lacking and the implications of exposure are unknown. Therefore, the aim of this study is to obtain comparative kinetics data for the beta isomer, which can be used to support toxicological evaluations and risk assessment of HBCD isomeric mixtures.

The study utilized the same mouse line used in previous studies on the alpha and gamma isomers, to enable an accurate comparison of the exposure effects for all three isomers. The researchers found that, while most of the beta-HBCD given to the mice was excreted within a four-day period, there were still measurable amounts of the chemical accumulated in these animals, particularly in the liver and fat tissues. Higher treatment doses resulted in higher tissue accumulation, especially in the fat tissue, which showed about three-fold higher accumulation for treatment doses of 30 and 100 milligrams per kilogram, compared to 3 milligrams per kilogram. Logically, repeat-dose treatment also led to higher tissue accumulation compared to single-dose treatment.

### **Comparison among the alpha, beta, and gamma isomers**

The study concluded that, like gamma-HBCD, beta-HBCD is extensively metabolized and is less likely to accumulate in the tissues compared to the alpha isomer. This finding may explain why alpha-HBCD is the most prevalent isomer found in the biota, including plants, animals, and even blood and breast milk, among populations living in areas exposed to high levels of HBCD.

Unfortunately, beta-HBCD is far from being safe. The current study reports that a measurable portion of the beta-HBCD was



*Sanders is a former researcher with NTP and a longtime colleague of Birnbaum. (Photo courtesy of Steve McCaw)*



*Birnbaum is the first toxicologist to serve as director of NIEHS and NTP. (Photo courtesy of Steve McCaw)*

converted to the gamma isomer in the treated mice. Previous research by Birnbaum and colleagues has shown that the gamma-HBCD also undergoes rapid stereoisomerization to the alpha and beta isomers. Since both the beta and gamma isomers can potentially be converted to alpha-HBCD, the ultimate outcome could be an even higher alpha-HBCD accumulation in organisms exposed to the chemical.

The LTT is located at NIEHS, but is funded by the National Cancer Institute.

*Citation:* [Sanders JM](#), [Knudsen GA](#), [Birnbaum LS](#).

(<http://www.ncbi.nlm.nih.gov/pubmed/23733921>)

2013. The fate of beta-hexabromocyclododecane in female C57BL/6 mice. *Toxicol Sci* 134(2):251-257.

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

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([bruskec@niehs.nih.gov](mailto:bruskec@niehs.nih.gov))

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