

Written Testimony of Dr. Frederick vom Saal before the Connecticut General Assembly Environment Committee, March 2nd, 2009, Testimony in Support of:
HB 6572 An Act Banning Bisphenol-A in Children's Products and Food Products and Prohibiting Certain Alternative Substances.

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There is now a consensus within the scientific community that at current levels of exposure to BPA due to the use of products directed at infants, there is concern that BPA is causing a wide range of harm. Specifically, three government science advisory panels have recently issued reports: these include the US National Toxicology Program, the science advisory agency to the US FDA on issues of health effects of chemicals, a panel of 38 internationally recognized scientists invited to a NIH sponsored conference on BPA, as well as the Canadian Ministry of Health. This concern is based on evidence from over 160 published studies with experimental animals that report adverse effects,

100% the studies of the over 200 experimental animal studies that report harm due to exposure to low doses of BPA were published by academic and government scientists with no connection to chemical corporations.

100% of studies funded by chemical corporations conclude that low doses of BPA are "safe".
[References and abstracts for all of these studies are online at:
<http://rcp.missouri.edu/endocrinedisruptors/vomsaal/vomsaal.html>].

Why focus on protecting infants?

We are most concerned about exposure to BPA during early life because BPA causes permanent adverse effects due to exposure at very low levels occurs during what are called "critical periods" in development, which includes fetal life through the first 2 years after birth.

An infant's entire intake of food could be contaminated with BPA: due to leaching from the BPA resin lining of infant formula cans (that are heated to high temperatures to sterilize the formula after it is placed into the can, causing BPA to leach out of the resin lining the can), due to leaching from the BPA based polycarbonate baby bottle that is often put into the microwave, which greatly increases the leaching of BPA due to breaking down of the polycarbonate, and due to leaching from the polycarbonate containers that baby food is sold in. The small size of the baby means that the amount of BPA relative to body weight is going to be high compared to adults (Vandenberg et al. 2007).

The maxim in pediatric medicine is that babies are not little adults.

It has been known for decades that at birth, the liver of a baby is not able to rapidly metabolize BPA or any other chemical or drug. In both animals and humans the enzyme that metabolizes BPA is the same enzyme that metabolizes the now banned estrogenic drug DES, which is very similar to BPA in both structure and function and is a known human carcinogen as well as an estrogen. Research has shown that the activity of this liver enzyme is very low at birth in animals and humans.

Statements that “exposure of the general population to BPA is not a concern” is based on exposure of adults, not infants. No regulatory agency anywhere in the world has addressed the unique sensitivity of infants in setting “safe” exposure levels for BPA and the potential for harm due to exposure to very low doses of BPA just during infancy.

Health Effects in Animals at Levels of Current Human Exposure to BPA

Regarding the specific health effects of BPA, anyone with a child knows that while brain development begins during fetal life, it continues throughout infancy. The greatest concern to the NTP in its 2008 final report on BPA was damage to the developing brain, including neurochemical abnormalities identified in numerous animal studies, such as a decrease in the neurotransmitter dopamine, which is associated with ADHD in children. A number of studies have reported that animals exposed during infancy to BPA subsequently become hyperactive and show learning deficits. The NTP also emphasized the disturbing finding that in laboratory animals, very low levels of BPA had the effect of eliminating gender differences in many behaviors, such as play and other social behaviors (Rubin et al. 2006). The disruption of normal gender development was thus a major concern identified by the NTP in its recent report on BPA:
<http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.pdf>

Another concern of the NTP was that very low doses of BPA cause prostate cancer in laboratory animals, and the cancer in animals is similar to that in men in both structure and genetic changes in cancer cells. Also, if human prostate cancer cells are exposed to BPA at 10 times lower amounts of biologically active BPA than are in the blood of the average adult, the prostate cancer cells will begin proliferating, defeating the drug therapy that is designed to block the cancer from spreading (Wetherill et al. 2002).

The scientific community has stated with a high level of confidence that the extensive evidence of harm in animals is relevant to human diseases (vom Saal et al. 2007), because the molecular mechanisms that mediate the harm in animals are virtually identical to the mechanisms that exist in human cells. Hundreds of studies using cultured human and animal cells were recently reviewed in a NIH-sponsored report published in the journal *Reproductive Toxicology* (Wetherill et al. 2007).

All of the studies showing harm at low doses of BPA in infants have been conducted during the last 10 years, but the current FDA/EPA estimated safe daily intake level for BPA was set 20 years ago based a few traditional toxicological studies that only examined very high doses of BPA (IRIS 1988), as opposed to the current studies that are examining doses that are within the range of human exposure (Richter et al. 2007).

The public health community and the general public are now aware that all of the diseases caused by BPA exposure during early life in animals are already occurring in people at increasing rates: These include:

Prostate and breast cancer

(Ho et al. 2006; Durando et al. 2007; Murray et al. 2007)

Obesity and diabetes

(Alonso-Magdalena et al. 2006; Dolinoy et al. 2007)

Early puberty

(Howdeshell et al. 1999; Honma et al. 2002)

Ovarian cysts and uterine fibroids

(Newbold et al. 2007)

Reduced fertility and Miscarriage

(Hunt et al. 2003; Al-Hiyasat et al. 2004)

Neurochemical and behavioral abnormalities such as ADHD

(Ishido et al. 2004; Masuo et al. 2004; Rubin et al. 2006; Ishido et al. 2007).

BPA is also an environmental hazard when thrown away

The Canadian Ministry of the Environment has declared BPA an environmental toxin that is already harming aquatic wildlife http://www.ec.gc.ca/substances/esc/eng/challengec/batch2/batch2_80-05-7.cfm.

We have detected BPA in streams and rivers, as have the Canadians, Japanese and others. While the immediate concern is with removing BPA from infant products, a long-term concern is how to dispose of BPA-containing products so that they do not become an unmanageable threat as billions of pounds of BPA-containing products accumulate in the environment and BPA gradually leaches from them (approximately 8 billion pounds of BPA are expected to be produced in 2009). BPA is found in the sediment in streams and rivers. Here, in the absence of oxygen, BPA becomes a persistent organic pollutant with a virtually zero rate of degradation (these studies are reviewed in detail in the Canadian BPA risk assessment document).

Why has the FDA not acted to regulate BPA?

The FDA recent affirmed that the “safe” daily human exposure level established in the 1980s was still valid.

The US FDA stated in a letter (February 25, 2008) to the US House Energy and Commerce Committee <http://energycommerce.house.gov>:

FDA believes that this level of exposure to adults and infants is safe as defined in 21 CFR §170.3(i). This conclusion is based on our most recently completed reviews of two pivotal multigenerational oral studies performed under applicable regulatory guidelines. The studies that were used by the FDA to make this determination have been criticized as invalid based on the insensitivity of the experiments, as revealed by the finding that very high doses of natural estrogen and the estrogenic drug in birth control pills (ethinylestradiol) were required to elicit responses in each of these experiments.

For example, one of the studies relied on by the FDA (Tyl et al. 2008) reported using as a “positive control” 100 µg/kg/day of estradiol to elicit “estrogenic” responses. Since it is accepted that BPA is not as potent as estradiol, it is unreasonable to expect that a “low dose” of BPA in the range of exposure of human infants (about 1-10 µg/kg/day) would be found to cause any effect in this experiment. However, it is exactly this dose range that many animal studies show cause permanent harm to the brain and reproductive system, as well as cancer.

This was pointed out in the recent NTP report on BPA. A prior NTP panel (NTP 2001) strongly criticized the second study used by the FDA (Tyl et al. 2002), since in this experiment the animal used (the CD-SD rat) was known to be extremely insensitive to any estrogen. This panel stated in their executive summary:

“Because of clear species and strain differences in sensitivity, animal model selection should be based on responsiveness to endocrine active agents of concern (i.e. responsive to positive controls), not on convenience and familiarity.”

The FDA Science Advisory Board called the FDA risk assessment “flawed” and stated that the FDA had without adequate explanation ignored numerous findings from non GLP studies that the NTP had determined to be of “high utility” for assessing the hazards of exposure to low doses of BPA. The FDA then simply stated it would conduct more research, but this is NOT what the Science Advisory Board indicated was needed prior to making a determination as to whether the FDA should continue to assure the public that BPA is completely safe. Instead, the FDA Science Board indicated that the FDA needed to pay attention to the extensive science that was already available, not to wait years while more information was generated. Also, the neurotoxicological study designed by the FDA will use the CD-SD rat that all research has shown to be unresponsive to any estrogen and is thus an inappropriate animal model to use for examining the effects of BPA. This FDA research thus appears to have as its primary objective delaying regulatory action, and not determining whether BPA has adverse effects on the brain using this inappropriate rat model.

The use of “Good Laboratory Practices (GLP) does not mean the study was conducted properly.

Both of the Tyl et al. (2002; 2008) studies selected for use by the FDA, while ALL other studies were not considered in determining the “safe” human exposure level for BPA were conducted using “Good Laboratory Practices”. GLP is conducted in contract laboratories that conduct all types of research, but do not have specific expertise in any area of research. GLP is misrepresented as indicating that these studies are somehow superior to studies conducted by academic and government scientists who are recognized as the world’s leading experts in specific areas of research. This is discussed in detail in a peer-reviewed article co-authored by 36 internationally recognized experts on BPA (Myers et al., *Environ Health Perspectives* 117:309-315, 2009).

Failure to replicate prostate findings in 2 industry funded GLP studies

Two chemical industry trade organization-funded studies were quickly conducted and published (Ashby et al. 1999; Cagen et al. 1999) after initial findings by the vom Saal lab were published in 1997 (Nagel et al. 1997). Both of these studies were conducted using Good Laboratory Practices. The conclusion from both of these studies was that there was no effect of low doses of either BPA or DES (the positive control used in both studies) on prostate development. The chemical industry has used these “negative” findings to create doubt about the validity and reliability of findings published by independent scientists.

Not one person associated with either the Ashby or the Cagen studies had every published a study relating to the male reproductive system. Both of these groups asked vom Saal to train them to conduct the research. Both of these studies were rejected as unusable by 2008 NTP panel due to the failure to find any effects of the positive control drug DES. The NTP rejected both of these industry-funded GLP studies for consideration of the health hazards of BPA stating: “This paper is inadequate for the evaluation process due to absence of response of the positive control group”. GLP does not mean that the study was conducted properly or by competent highly trained scientists.

The EU Food Safety Authority only used “traditional toxicological studies” in reaching its decision that BPA was safe at low doses, while rejecting all studies conducted by independent academic scientists. While the academic studies were acknowledged as existing they were not used in reaching

the conclusions about safety. The EU will hold a meeting on March 30-31, 2009 to reassess the health hazards of BPA due to intense criticism of its BPA risk assessment.

The federal regulatory agencies are using 50-year old scientific approaches to reach decisions while ignoring all research conducted by the worlds leading experts using the most advanced techniques to determine the safety of low doses of BPA.

There is no use of BPA in infant products for which there is not already a safer alternative on the market in the USA. This is also true in Japan, where practically all BPA based products containing food or beverages were rejected by the public 10 years ago (Matsumoto et al. 2003), and most recently in Canada, where the Canadians have simply stopped buying baby products that contain BPA.

I urge the legislature to pass this legislation, since there are alternatives already on the market for all products directed at babies in the USA.

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