Testimony
Before the Subcommittee on Commerce, Trade, and Consumer Protection
Committee on Energy and Commerce
United States House of Representatives

National Toxicology Program Determinations on the Health Effects of Bisphenol A and Phthalates

Statement of
John R. Bucher, Ph.D.
Associate Director
National Toxicology Program
National Institute of Environmental Health Sciences
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 AM
Tuesday, June 10, 2008

Thank you, Mr. Chairman, and good morning. I am Dr. John Bucher, Associate Director of the National Toxicology Program (NTP). The NTP is an interagency program, funded and managed by the National Institute of Environment Health Sciences (NIEHS). NIEHS and NTP are part of the National Institutes of Health, an agency of the Department of Health and Human Services.

The NTP carries out toxicology research and testing on substances of concern to the federal government and the public. We also perform literature review and analysis activities and since 1980 have produced the Report on Carcinogens. In 1998, we established the Center for the Evaluation of Risks to Human Reproduction (CERHR), which carries out literature evaluations on substances that may affect human reproduction and development.

The NTP has extensively researched phthalates for cancer and reproductive effects in animals, and through the CERHR, has reviewed the world's literature on seven phthalates for potential effects on human reproductive health. We have studied bisphenol A (BPA) less extensively in animals, although recently we conducted a lengthy evaluation of the very large literature on the potential for BPA to affect reproduction and development. This evaluation culminates tomorrow with a public peer review of the Draft NTP Brief on Bisphenol A before our NTP Board of Scientific Counselors, a federally -chartered committee of external advisors that provides scientific review for our programs. This draft brief represents our opinion of the science on BPA and is based on our evaluation to date of the literature, informed by the findings of an expert panel and with consideration of public comments solicited on five separate occasions.

BPA is a high-production industrial chemical used to manufacture polycarbonate plastics and epoxy linings of tin cans. It has been known since 1938 to mimic estrogen when given in large amounts to experimental animals. More recently, it has also been studied for its ability at very much lower doses to affect hormonal processes involved in development, when an animal is exposed as a fetus or during infancy. BPA leaches in small amounts from plastic items such as polycarbonate baby bottles and can be measured in infant formula coming from epoxy-lined cans. The 2003-2004 National Health and Nutrition Examination Survey (NHANES III) conducted by the Centers for Disease Control and Prevention (CDC) found detectable levels of bisphenol A in 93% of 2517 urine samples from people six years and older. The CDC NHANES data are considered representative of exposures in the United States.

The scientific evidence that supports a conclusion of "some concern" for exposures in fetuses, infants, and children comes from a number of laboratory animal studies reporting that "low" level exposure to bisphenol A during development can cause changes in behavior and the brain, prostate gland, mammary gland, and the age at which females attain puberty. These studies only provide limited evidence for adverse effects on development, and more research is needed to better understand their implications for human health. However, because these effects in animals occur at bisphenol A exposure levels similar to those experienced by humans, the possibility that bisphenol A may alter human development cannot be dismissed.

Taking this information into account, the NTP reached several preliminary conclusions in our draft brief. We express "some concern" that current estimated exposures of BPA to fetuses, infants, and children could cause neural and behavioral effects, effects on the prostate and mammary gland, and an earlier age at which females attain puberty. We express "negligible

concern" or "minimal concern" that current exposures to BPA could cause adverse health effects in other segments of the population. "Some concern" is the midpoint of a 5 level scale; the levels are negligible concern, minimal concern, some concern, concern, and serious concern.

Although we agreed with our expert panel in expressing "some concern" for current exposures to BPA to produce neural and behavioral effects to fetuses, infants and children, we expressed an elevated level of concern ("some concern") over the conclusions reached by our Expert Panel ("minimal concern") for changes to the prostate as well as earlier puberty in females. The Expert Panel did not specify a level of concern for the mammary gland. These elevated concerns were based on: 1) new literature; 2) clarifications provided in public comments to studies considered of low utility by our Expert Panel; and 3) scientific justification for using data from studies utilizing non oral routes of exposure to neonatal animals.

There are a number of uncertainties in the scientific information on BPA. The literature from experimental animal studies is large, but with many conflicting findings. Moreover, there are insufficient data from studies in humans to determine directly whether BPA is affecting human reproductive health.

The studies on which we base "some concern" have limitations. They are not the traditional safety assessment studies done according to regulatory guidelines. Rather, they are smaller studies carried out in academic labs. These have often examined subtle developmental endpoints in experimental animals that are more difficult to interpret with regard to how they contribute to the weight–of–evidence for human health risks. Despite the limitations of these studies, the NTP determined that because the subtle effects in animals occur at BPA exposure levels similar to those experienced by humans, the possibility that BPA may alter human

development cannot be dismissed. As I mentioned earlier, the NTP Board of Scientific Counselors will review the draft brief at its meeting tomorrow. We will take their recommendations into consideration, and the final brief will be published later this year.

Turning to phthalates, chemicals used to make certain plastics flexible, the NTP has conducted 13 cancer bioassays and 45 studies on reproductive or developmental toxicity with various phthalate esters. The fact that specific phthalates can adversely affect reproduction has been known for more than 25 years, and it is now known is that fetal animals are more sensitive than newborn animals, which in turn are more sensitive than older animals. Since the late 1990s it has been known that certain phthalates specifically affect development of the male reproductive system.

Not all phthalates produce adverse reproductive effects in animal studies. The phthalates that produce adverse reproductive effects are called "active" phthalates. All "active" phthalates cause similar toxicity to the developing rat fetus when exposure occurs during a critical window of sexual differentiation during pregnancy. These agents induce malformations in the male reproductive tract by affecting development that is mediated through androgens (e.g. testosterone). The most severe malformations occur with higher doses. In addition, some phthalates, when administered to the developing fetus, can also induce subsequent testicular tumors in the adult animal after being exposed only during the short window of pregnancy.

In humans, a few small studies have linked maternal exposure to specific phthalates with adverse outcomes in their children, including decreased testosterone levels in boys. However, concerns remain about the assessment of confounding and contamination by breast pump use. Thus, additional research is needed to confirm these findings.

Failure of normal development of the testis has been proposed to explain increases in human male reproductive problems. However, thus far, no cause and effect relationship has been established between any environmental agent and these human outcomes.

As mentioned earlier, the NTP CERHR has reviewed the literature on phthalates. We recently updated the review for one phthalate, di(2-ethylhexyl)phthalate (DEHP). DEHP is used as a plasticizer of polyvinyl chloride in the manufacture of a variety of consumer products and medical devices.

The NTP expressed "serious concern" for male infants for whom exposure to DEHP during certain medical treatments could adversely affect development of the reproductive tract. We expressed "concern" for male offspring of women undergoing certain medical treatments during pregnancy or breastfeeding, and for infants less than one year old exposed to DEHP from diet or mouthing of DEHP-containing objects, or undergoing certain medical treatments. We expressed "some concern" for male children who may be exposed to levels of DEHP higher than those to the general population.

In summary, the NTP has conducted extensive experimental studies on phthalates and has conducted CERHR evaluations of phthalates and BPA. NTP maintains an objective, science-based approach in dealing with critical issues in toxicology and provides sound scientific information on substances of concern to regulatory agencies and the public, contributing to the public health discussions surrounding these important chemicals.

Thank you for this opportunity to appear before you today to provide this statement. I will be happy to answer any questions you may have.

One Page Summary of NIEHS Testimony by John Bucher, Associate Director NTP
Subcommittee on Commerce, Trade & Consumer Protection
U.S. House of Representatives Committee on Energy & Commerce
10 June 2008

I am Dr. John Bucher, Associate Director of the National Toxicology Program (NTP). The NTP has researched phthalates for cancer and reproductive effects in experimental animals, and our Center for the Evaluation of Risks to Human Reproduction (CERHR) has reviewed the literature on seven phthalates and on bisphenol A (BPA) for potential effects on human reproductive health.

BPA has been extensively studied for its ability at very low doses to affect hormonal processes involved in development. The doses of BPA that cause subtle effects on the development of animals are close to estimates of current exposures to the U.S. population.

Based on these animal studies, the NTP CERHR express "some concern" that current exposures of BPA to fetuses, infants, and children could cause neural and behavioral effects, effects on the prostate and mammary gland, and an earlier age at which females attain puberty, and "negligible concern" or "minimal concern" for effects in other segments of the population.

The NTP has conducted many experimental animal studies on various phthalate esters. Not all phthalates produce adverse reproductive effects, but all "active" phthalates cause malformations or cancer in the male reproductive tract of animals exposed during development.

The NTP CERHR expressed "serious concern" that current exposures of male infants to one particular phthalate, di(2-ethylhexyl)phthalate (DEHP), during certain medical treatments could adversely affect development of the reproductive tract. We expressed "concern" for male offspring of women undergoing certain medical treatments during pregnancy or breastfeeding, and for infants less than one year old exposed to DEHP from diet or mouthing of DEHP-containing objects, or undergoing certain medical treatments. We expressed "some concern" for male children who may be exposed to levels of DEHP higher than those to the general population.