October 14, 2005
MEETING SUMMARY
NATIONAL TOXICOLOGY PROGRAM
CENTER FOR THE EVALUATION OF RISKS
TO HUMAN REPRODUCTION

EXPERT PANEL RE-EVALUATION OF DEHP
OCTOBER 10–12, 2005

The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) convened an expert panel to re-evaluate the reproductive and developmental toxicities of di(2-ethylhexyl)phthalate (DEHP). A previous CERHR Expert Panel had evaluated DEHP in 1999-2000. However, since release of the earlier CERHR Expert Panel Report on DEHP, approximately 150 papers relevant to human exposure and reproductive and/or developmental toxicity of DEHP have been published. The CERHR decided to update the evaluation of DEHP because of: (1) widespread human exposure, (2) public and government interest in potential adverse health effects, and (3) the large number of relevant papers published since the earlier evaluation. The expert panel meeting was held October 10-12 in Alexandria, VA. This is the first time a CERHR expert panel was convened to update an evaluation conducted by an earlier expert panel.

Di(2-ethylhexyl)phthalate (CAS RN:117-81-7) is a high production volume chemical used as a plasticizer of polyvinyl chloride in the manufacturer of a wide variety of consumer products, such as building products, car products, clothing, food packaging, children's products (but not in toys intended for mouthing) and in some medical devices made of polyvinyl chloride.

The expert panel was composed of 11 scientists who served as independent experts and not as representatives of their employers or other organizations. The expert panelists reviewed and evaluated the available scientific evidence on DEHP in three primary areas: human exposure, reproductive toxicity, and developmental toxicity. They considered the quality, quantity, and strength of the evidence in their deliberations about the potential for this chemical to cause adverse effects on human reproduction and/or prenatal or postnatal development. Their evaluation was based on the report and conclusions of the earlier expert panel and the newer scientific information. The newer scientific information is the basis for the draft DEHP Update Expert Panel Report released in August 2005. This expert panel confirmed, modified, or added to the conclusions of the earlier expert panel. They also identified data gaps and research needs.

Expert Panel Conclusions on Re-evaluation of DEHP
General adult population

The expert panel has **minimal concern*** that general population exposures adversely affect adult human reproduction. This level of concern is not altered for adults medically exposed to DEHP or MEHP (mono(2-ethylhexyl) phthalate, a metabolite of DEHP). This conclusion is based upon a general population DEHP exposure estimate of 1–30 µg/kg body weight/day. This conclusion concurs with the conclusion of the first expert panel.

Healthy infants and toddlers
If the level of exposure is at the high end of the estimated exposure range for the general population, the expert panel has **some concern** that exposure to DEHP can adversely impact reproductive development in male children older than one year. The expert panel has **concern** that DEHP exposure can adversely affect reproductive development in infants less than one year old. These conclusions are a refinement of the first panel's conclusion of concern for the entire healthy infant/toddler population.

Critically ill infants
Parenteral medical exposure to DEHP of critically ill infants can exceed general population exposure by several orders of magnitude. The expert panel estimated the upper range of DEHP/MEHP exposure from medical procedures in infants to be 6000 µg/kg body weight/day. The expert panel has **serious concern** that such exposures may adversely affect male reproductive tract development and function. The panel believes that the benefits of medical procedures can be significant, but that minimizing exposure to DEHP should be a goal. This conclusion concurs with that of the first expert panel.

Pregnancy and lactation
Estimates of exposure to DEHP for the adult human population range from 1–30 µg/kg body weight/day. Based upon this exposure estimate, the expert panel has **some concern** for the effects of DEHP on male offspring of humans exposed during pregnancy. This is a reduction in the level of concern from the first expert panel due to greater confidence in exposure levels in the general population and to greater confidence in the effect level in experimental animals. Further, this expert panel expressed **concern** for possible effects on male fetuses of women undergoing certain medical treatments where additional exposure to DEHP could occur.

The conclusions noted above are those of the independent expert panel and do not necessarily represent the views of the National Toxicology Program.

* *Levels of concern expressed by CERHR expert panels include negligible concern, minimal concern, some concern, concern, and serious concern.*

Next Steps
The final expert panel report from this re-evaluation of DEHP will be posted on the CERHR web site (*http://cerhr.niehs.nih.gov*) and available in printed text from

the CERHR in November, 2005. The CERHR will solicit public comments on this report through an announcement in the *Federal Register*. Following this comment period, the CERHR will prepare the NTP-CERHR monograph on DEHP, consisting of an NTP brief, expert panel report, and all public comments on that report. The monograph will be available to the public on the CERHR web site and in hardcopy from CERHR. The monograph will be sent to appropriate federal health and regulatory agencies.

Background

The NTP established the CERHR in 1998 as a public resource for providing scientifically based, uniform assessments of the potential for adverse effects on reproduction and/or development caused by man-made or naturally occurring chemicals or chemical mixtures to which humans are exposed. The CERHR convenes independent panels of scientific experts to conduct its evaluations. Expert panel meetings are open to the public and the public is invited to nominate scientists to serve on CERHR expert panels. Following completion of the evaluation of a chemical, the NTP prepares an NTP-CERHR monograph that contains its opinion on the potential for the chemical to be a reproductive or developmental hazard, the expert panel report, and public comments received on the final expert panel report. NTP-CERHR monographs on other chemicals evaluated by CERHR include six phthalates, methanol, 1-bromopropane, 2-bromopropane, ethylene glycol, propylene glycol, fluoxetine (Prozac®), acrylamide, amphetamines, methylphenidate, and styrene and are available on the CERHR web site or in hardcopy from CERHR.

Questions about the expert panel review or CERHR can be directed to Dr. Michael Shelby, CERHR Director at 919-541-3455 or shelby@niehs.nih.gov