MEETING SUMMARY
NATIONAL TOXICOLOGY PROGRAM
TO HUMAN REPRODUCTION

EXPERT PANEL REVIEW OF AMPHETAMINES AND METHYLPHENIDATE
JANUARY 10–12, 2005

The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) convened an expert panel on January 10–12, 2005 in Alexandria, Virginia. The purpose of this meeting was to evaluate the scientific evidence regarding the potential reproductive and/or developmental toxicity associated with exposure to the central nervous system stimulants, amphetamines and methylphenidate. The CERHR selected amphetamines and methylphenidate for expert panel evaluation because of widespread usage in children, availability of developmental studies in children and experimental animals, and public concern about the effects of these stimulants on child development.

Amphetamines evaluated were *d*- and *d,l*-amphetamine and methamphetamine. *d*- and *d,l*-Amphetamine are indicated for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy; methamphetamine is indicated for the treatment of ADHD and for short-term treatment of obesity. The most common proprietary amphetamine preparation is Adderall®, a mixture of *d*- and *l*-amphetamine salts in a 3:1 ratio. *d*-Methamphetamine is used in pharmaceutical preparations in the United States and is also manufactured and used as an illicit drug. Methylphenidate is a central nervous system stimulant indicated for the treatment of ADHD and narcolepsy in persons six years and older. *d*, *l*-Methylphenidate is marketed under the names Ritalin®, Metadate®, Methylin®, and Concerta®. The *d*-enantiomer is marketed under the name Focalin™.

The expert panel, composed of 13 independent scientists, reviewed and evaluated the available scientific evidence on amphetamines and methylphenidate 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 these chemicals to cause adverse effects on human reproduction and/or prenatal or postnatal development.

Expert Panel Conclusions on Amphetamines
The expert panel reached the following conclusions based on its evaluation of the data on amphetamines and methamphetamine.

Amphetamine

1. There is **some concern** with regard to potential neurobehavioral alterations due to prenatal amphetamine exposure in humans both in therapeutic and non-therapeutic settings.

Methamphetamine

1. There is **concern** with regard to potential adverse perinatal outcomes

and neurobehavioral alterations due to prenatal methamphetamine exposure in humans both in therapeutic and non-therapeutic settings.

Expert Panel Conclusions on Methylphenidate

The expert panel reached the following conclusions based on its evaluation of the data on methylphenidate.

1. There is **minimal concern** for methylphenidate-induced growth restriction in humans at standard therapeutic doses.
2. There is **negligible concern** for methylphenidate-induced tics and movement disorders in humans at standard therapeutic doses.

While data were available on other potential effects of the amphetamines and methylphenidate, the expert panel judged those data as insufficient to support sound, evidence-based conclusions.

Next Steps

The final expert panel reports from the evaluations of amphetamines and methylphenidate will be posted on the CERHR web site (http://cerhr.niehs.nih.gov) and will be available in printed text from the CERHR on March 21, 2005. The CERHR will solicit public comments on these reports through an announcement in the *Federal Register*. Following this comment period, the CERHR will prepare two NTP-CERHR monographs, one on amphetamines and one on methylphenidate.

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 its expert panels. Following completion of an expert panel report, the NTP prepares a 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 all 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®), and acrylamide. These are available on the CERHR web site.

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