FDA Drug Safety and Risk Management Advisory Committee Meeting

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Organizations: American Academy of Child and Adolescent Psychiatry & American Psychiatric Association

Presenter: Laurence Greenhill, M.D.

Contact: Stacia Hall, M.P.P.
(Phone: 202-966-7300 ext. 113 or Email: shall@aacap.org)

My name is Laurence Greenhill, MD. I am a child psychiatrist, and the chairman of the American Academy of Child & Adolescent Psychiatry (AACAP) Work Group on Research, who has paid my travel costs. I am also representing the American Psychiatric Association (APA). I much appreciate the opportunity to be able to make a brief public statement to the FDA Drug Safety and Risk Management Advisory Committee today.

The AACAP is a medical membership association established by child and adolescent psychiatrists in 1953. Now over 7,000 members strong, the AACAP is the leading national medical association dedicated to treating and improving the quality of life for the estimated 7 – 12 million American youth under 18 years of age who are affected by emotional, behavioral, and developmental disorders. The AACAP supports research, continuing medical education and access to quality care.

The APA is medical specialty society representing over 35,000 U.S. and international member physicians working together to ensure humane care and effective treatment for all persons with mental disorder, including mental retardation and substance-related disorders. APA promotes a society that has available, accessible quality psychiatric diagnosis and treatment.

As a child psychiatrist, I have participated in NIMH-sponsored research on Attention Deficit Hyperactivity Disorder, serving as a principal investigator in the NIMH MTA Study of school age children and the NIMH PATS study of preschool children with ADHD. Both studies each have treated over 300 children with methylphenidate, the most frequently used medication for this purpose. The MTA employed this medication initially for 14 months under controlled conditions, and then for 4 more years in an ongoing, naturalistic follow up. I have also participated in numerous pharmaceutical industry protocols involving controlled studies of ADHD medications for the treatment of youth and adults with ADHD.

Stimulant medications are some of the most extensively studied medications used for the treatment of behavior disorders in children and adolescents. There have been over 200 controlled

studies over the past 50 years. These drugs produce robust responses in over 2/3 of affected youth by lowering the intensity of their ADHD symptoms. Children with ADHD can sit, concentrate in class and are less often rejected by their peers. ADHD medications constitute the largest group of medications approved for use by the FDA for the treatment of children with behavioral problems. The Centers for Disease Control estimates that approximately 3,500,000 youth in the United States are taking stimulants as part of their treatment plan. For these reasons, I believe that stimulant medications offer many benefits to a wide range of children, and have proven to be safe over a half-century of heavy use.

The advisory committee today will be discussing better ways to predict and identify rare, unexpected, and serious adverse events of sudden death, hypertension, myocardial infarction, and stroke that occasionally appear in registration and post-marketing clinical trials of these medications. This research task is made difficult by the minuscule numbers of these rare events. In contrast to the millions taking ADHD medications each day, less than 20 youth have suffered sudden death while taking these medications over the past 5 years. The numbers of those with other cardiovascular events are correspondingly small.

How can one determine the prevalence of such rare, unexpected, and serious adverse events to better estimate risk? Opportunities for prospective cohort design such as the NIMH/AACAP's CAPTN large simple trials network, the American Academy of Pediatrics ADHD registry among developmental pediatricians, and the NICHD sponsored National Children's Study involving 100,000 youth. CAPTN has recruited over 200 child psychiatrists who are managing thousands of young patients. This practice network will provide protocol-driven, postmarking surveillance for youth treated with ADHD medications to track such low frequency adverse events prospectively. CAPTN also will add a Pharmacogenomic aim to identify the very good responders as well as those rare cases that suffer intense adverse events to determine if these unusual responders have polymorphic alleles that code for central nervous system receptors. Second, the American Academy of Pediatrics, under the leadership of Mark Wolraich, is developing a registry for US developmental pediatricians that will provide long term surveillance of medications used to treat ADHD. Finally, the NICHD-sponsored National Children's Study will be able to estimate these rare events in untreated normals and children with ADHD.

Despite their overall safety, professional organizations realize the importance of identifying rare, unexpected adverse events and determining their prevalence. Only then can the partnership of parent and practitioner make an informed decision regarding the benefit-risk ratio involved in starting medication treatment. In addition, the Academy and APA is aware of the long-term impairments that do occur to children with ADHD when they do not or cannot receive first-line treatments for their disorder. While the evidence base suggests that these drugs are safe for the majority of children, we applaud the FDA's decision to broaden our knowledge about rare risks accompanying these treatments.

Again, I thank the FDA for providing me the opportunity to present this testimony on behalf of the AACAP and the APA.

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