

AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY

FDA Pediatric Advisory Committee Meeting

March 22, 2006

My name is Laurence Greenhill. I am a child psychiatrist, working at the New York State Psychiatric Institute, doing treatment research on the safety and efficacy of medications used to treat ADHD in children, adolescents and adults. I am also the chairman of the Workgroup on Research at the American Academy of Child and Adolescent Psychiatry. The AACAP strives to raise the standards of care and ethical methods in clinical trials of new medications, and studies of medication effectiveness, and open safety studies of marketed medications.

My first point is that the American Academy of Child and Adolescent Psychiatry supports the FDA advisory panels in their efforts to better characterize the safety of medications. This is particularly true because the ADHD disorder can be highly impairing for the patient and very wearing for the family, as we have heard today. Patients and families need to know about effective treatments for ADHD, as well as have full knowledge of their adverse events. My sympathies go out to those families we have heard from today who have suffered.

For gathering safety information, I have seen the pendulum swing from the use of spontaneous patient interview methods which under-report adverse events in small controlled trials to the current full disclosure of every adverse event from the unreliable post marketing reporting system, no matter how rare. A full review of all adverse events, without including an estimate of their risk for occurring, makes it most difficult for families and their physicians to determine the balance of benefit versus risk when selecting a treatment. Professional organizations, including the AACAP and American Academy of Pediatrics, now publish practice guidelines for practitioners to set a standard of care. These guidelines ask practitioners to weigh carefully all common adverse events identified by FDA panels. In addition, the AACAP and its practitioners value standardized assessments in preference to spontaneous, non-systematic MEDWATCH reports.

My second point is to urge both the pharmaceutical industry and the FDA to agree on a standard method for collecting safety information. The FDA today identified design

problems in the stimulant trials, including very short trials, patients pre-selected to have no side effects on stimulants, and data sets that can't be combined across studies. These problems made it difficult to determine the true rate of adverse events associated with a specific medication. In addition, there is no standard way to report adherence to medication treatment, for example practitioners can't tell if families prematurely discontinue medications they prescribe because of mild but highly bothersome adverse events. Physicians conducting the open and controlled trials need to be trained in standard methods about how to ask about adverse events, which family member to ask, what questions yield the best information, and how to code adverse events reliably.

Third, I would urge the advisory panels to recommend the FDA better specify which groups are at risk for specific adverse events, if that is known. At the February 9, 2006 session of the Drug Safety and Risk Management Advisory Committee, they voted by a narrow margin –eight to seven – to recommend that a black box warning about cardiovascular problems be applied to all stimulant medications for all age groups. This was controversial, because at the same meeting, it was noted repeatedly that the cardiovascular risks might be much greater if the patient was an adult. In addition, the reports all came from the FDA's passive surveillance MEDWATCH database, which can not be used as proof that ADHD medications cause heart problems. This is because some patients in the database have pre-existing cardiac disease, some patients are on multiple medications, and there is no information on the number of patients exposed. It would be useful for the groups involved to agree on a predetermined threshold frequency of adverse events that would trigger a review of labeling information.

In closing, I'd like to add that my travel to this meeting has been supported by the American Academy of Child & Adolescent Psychiatry, and I have served as consultants to and received research grants from companies, whose products are being discussed today, including Novartis, McNeil, Cephalon, Eli Lilly, and Shire.

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