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To: Members of the Drug Safety and Risk Management (DSaRM) Advisory
Committee, and Consultants

Subject: February 9-10, 2006 DSaRM Meeting

It is my pleasure to welcome you to the February 9 and 10, 2006 Drug Safety and Risk Management (DSaRM) Advisory Committee meeting. The first day of this meeting will focus on discussion of research approaches that could be used to study whether drugs used to treat Attention Deficit Hyperactivity Disorder (ADHD) increase the risk of adverse cardiovascular outcomes. The second day will provide updates to the Committee on developments in the Office of Drug Safety, the Drug Safety Oversight Board, agency actions on the COX-2 selective Nonsteroidal Anti-inflammatory Drugs (NSAIDs), and the risk management program for the isotretinoin products.

Background

Day 1

At the May 2005 DSaRM meeting, the committee discussed the strengths and limitations of the FDA passive surveillance system for adverse events. At the same meeting, the committee discussed the potential uses of other methods, such as epidemiologic studies using large databases that link pharmacy claims data to medical outcomes to assess the relationship of a drug to an adverse event. The case of a potential increased risk of adverse cardiovascular outcomes associated with drugs used to treat ADHD illustrates the challenges of post-marketing drug safety assessments. While FDA has received case reports of such events in patients taking medications for ADHD, these reports by themselves do not establish a causal relationship between these medications and cardiovascular adverse events. We will ask you to consider the feasibility of various epidemiologic approaches to further investigate this safety signal and to address specific methodological considerations. The briefing package includes a past review by FDA staff as well as medical literature relevant to the discussion.

Day 2

Drug Safety Oversight Board

In February 2005, as part of improvements in drug safety monitoring, FDA announced the creation of a Drug Safety Oversight Board (DSOB) to oversee the management of important drug safety issues within the Center for Drug Evaluation and Research (CDER). The DSOB began meeting in July 2005. An update on the DSOB's structure, function, and activities will be presented.

COX-2 Selective Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

In February 2005, the cardiovascular risks of nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 selective and prescription and non-prescription non-

selective NSAID medications, were discussed at a joint meeting of FDA's Arthritis and Drug Safety and Risk Management Advisory Committees. An update on agency actions will be presented.

Isotretinoin Risk Management Program

At a joint meeting in February 2004, FDA's Drug Safety and Risk Management Advisory Committee and Dermatologic and Ophthalmic Drugs Advisory Committee reviewed the existing risk management programs for isotretinoin, a drug used to treat severe recalcitrant nodular acne, but which carries a significant risk of birth defects with fetal exposure. The joint committee called for major improvements in the risk management program, including mandatory registration to ensure that patients who could become pregnant have negative pregnancy testing and birth control counseling before receiving the drug.

In August 2005, the FDA announced approval of a strengthened risk management program for isotretinoin, called iPLEDGE, aimed at preventing exposure to the drug during pregnancy. The details of this program and progress on its implementation will be presented.