

**Pediatric Advisory Subcommittee Meeting
Open Meetings
June 11 & 12, 2003**

OVERVIEW

At the June 11th session of the Pediatric Advisory Subcommittee meeting, the Committee will be asked to advise the FDA on emerging issues about the management of hyperbilirubinemia in term and near-term newborns. The discussion will focus on the potential role of new drug therapies in the prevention and management of jaundice in this population, how such interventions fit within the treatment paradigm for this condition, and on specific questions about the design of safety and efficacy studies of drugs for the prevention of hyperbilirubinemia. The FDA will use your advice to clarify how to move forward in this newly emerging and complex area of drug development.

To prepare you for these deliberations, you will hear a series of expert presentations on the management of hyperbilirubinemia in the term and near-term newborn. Topics to be covered include: the changing epidemiology of neonatal hyperbilirubinemia; the safety and efficacy of phototherapy; the surveillance of kernicterus; the metalloporphyrin heme oxygenase inhibitor drug class; and the ethical issues surrounding this research. Authors of the Agency for Healthcare Research and Quality January 2003 evidence report on the management of neonatal hyperbilirubinemia will present the design of their study and the findings within their report. You will also hear from a parent of a child with kernicterus, and from a nurse who administers home phototherapy.

This briefing book provides additional background material on these issues, including the full AHRQ report. The AHRQ report is long, approximately 250 pages. We have provided it in its entirety because the findings, conclusions, and recommendations of this report will form a major source of evidence for the updated AAP guidelines, which are currently under development. If you have limited time to prepare, the summary is excellent, and the many evidence tables may help orient you to the relevant literature and issues in a relatively short period of time.

During and following those presentations, we will ask you to deliberate on a series of questions, which are provided in draft form below.

Draft Questions for June 11, 2003

- 1) How has the epidemiology and definition of hyperbilirubinemia changed over the last decade?
- 2) In the context of current medical practice, including phototherapy, should drugs be developed for an earlier intervention to prevent hyperbilirubinemia in newborn infants? In answering this question, please discuss the following:

- How you define the population at high risk for complications of hyperbilirubinemia?
 - What level of safety or other issues need to be addressed for a therapy to prevent hyperbilirubinemia, which inevitably will be given to a large number of infants who would not be at risk for kernicterus?
 - What do you see as the intervention sequence (e.g., more screening, additional monitoring and assessments, phototherapy, hydration, pharmacotherapy, cessation of breast feeding, changes in infant nutrition, home nursing visit, etc.)? Why?
- 3) In today's healthcare setting, does the benefit of drug therapy to prevent hyperbilirubinemia in the newborn population as a whole outweigh the risk to individual newborns, the majority of whom require no intervention?
- 4) Assuming that hyperbilirubinemia only requires therapeutic intervention with phototherapy approximately 3 to 5 percent of the time, what safety information would you require from a sponsor for a new molecular entity before it could be introduced into the newborn population?

At the open session on the afternoon of June 12th, you will hear from Dr. Solomon Iyasu, Medical Team Leader with the Division of Pediatric Drug Development. Per section 17 of the Best Pharmaceuticals for Children Act, Dr. Iyasu will report on adverse events for the following drugs that were granted market exclusivity under 505A of the Federal Food, Drug, and Cosmetic Act: Zoloft (sertraline) and Ditropan (oxybutynin). Dr. Iyasu will also provide interim updates on Lipitor (atorvastatin) and Zocor (simvastatin).

The FDA relies on the knowledge, judgement, experience and wisdom of scientists and practitioners like you to help determine how to move forward and address newly emerging issues related to drug development. Thank you for your time and effort, and we look forward to seeing and hearing from you on June 11th.

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