MINUTES OF THE
PEDIATRIC ETHICS SUBCOMMITTEE
of the PEDIATRIC ADVISORY COMMITTEE
Monday, March 23, 2015

Members Present
Steven Joffe, M.D., M.P.H. *(Acting Chair)*
Norman Fost, M.D., M.P.H
Leonard Glantz, J.D.
Douglas Diekema, M.D., M.P.H.
Loretta Kopelman, Ph.D.
Alexander A. Kon, M.D.
Sara Goldkind, M.D., M.A.

Temporary Members
Kenneth Towbin, M.D. *(Pediatric Advisory Committee Representative)*
Susan Baker, M.D., Ph.D. *(Pediatric Advisory Committee Representative)*
Mark Hudak, M.D. *(Pediatric Advisory Committee Representative)*
Michael White, M.D., Ph.D. *(Pediatric Advisory Committee Representative)*
Randall Flick, M.D.
Keith Kocis, M.D., M.S.
Geoffrey Rosenthal, M.D., Ph.D.
Marla Birzescu, M.D.
Gary Walco, Ph.D.

Designated Federal Official
Walter Ellenberg, Ph.D.

U.S. Food and Drug Administration (FDA) Participants
Robert Nelson, M.D., Ph.D.
Michelle Roth-Cline, M.D., Ph.D.

Other Invited Participants (Speakers)
David Wendler, Ph.D. (NIH)
Joseph Cravero, M.D. (Boston Children's Hospital)

Pediatric Ethics Subcommittee Meeting

The meeting was convened at approximately 8:32 a.m.

Welcome and Introductory Remarks
Steven Joffe, M.D., M.P.H., Acting Chair of the Pediatric Ethics Subcommittee

Walter Ellenberg, Ph.D., Designated Federal Official, Pediatric Advisory Committee, Office of Pediatric Therapeutics, Office of Special Medical Programs, FDA

Presentations

Agenda Overview
Robert Nelson, M.D., Ph.D. OPT/OC/FDA

Ethical Analysis of Clinical Trial Protocols, Component Analysis, and Examples of Protocols Involving Sedation for Non-Beneficial Procedures
Robert Nelson, M.D., Ph.D. OPT/OC/FDA and
Michelle Roth-Cline, M.D., Ph.D. OPT/OC/FDA

Pediatric Procedural Sedation
Joseph Cravero, M.D.

Policy Implications of Decisions About the Appropriate Risk Level of Pediatric Procedural Sedation Under 21 CFR 50 Subpart D
David Wendler, Ph.D.

Open Public Hearing
No speakers

Presentation of Questions and Charge to the Subcommittee
Michelle Roth-Cline, M.D., Ph.D. OPT/OC/FDA

Summary of FDA Questions and Committee Discussion

FDA Question

Please discuss the factors which should be taken into account when designing a protocol to provide procedural sedation for nontherapeutic procedures in pediatric clinical investigations. Among the factors that may be considered are: the American Society of Anesthesiology (ASA) risk classification, the therapeutic index of the different drugs commonly used for procedural sedation, the availability of reversal agents for those drugs and/or the speed with which the drug effect dissipates, the nature and seriousness of the adverse events associated with the different drugs, the targeted depth of sedation needed to complete the procedure, the type of airway support that may be necessary, the planned monitoring, and the skill of the practitioner(s) and context of use. In light of these (and any other) factors, please comment on how the risks of procedural sedation may be minimized. In addition, please comment on how these factors may influence your assessment of whether one or more approaches to procedural sedation may be considered a minor increase over minimal risk.

Subcommittee Discussion

The Subcommittee generally agreed that (1) procedures should be performed at a high volume center with a dedicated pediatric sedation service; (2) there should be rigorous scientific

justification for the need for the nontherapeutic procedures; (3) the approach to procedural sedation and risk minimization procedures should be described in the protocol; (4) children with chronic conditions that may place them at higher risk from procedural sedation should be carefully evaluated and potentially excluded from the protocol; (5) the nontherapeutic procedure should be terminated if complications of sedation arise or the level of sedation is inadequate as it would be inappropriate to escalate the approach to procedural sedation beyond what would be considered a minor increase over minimal risk rather than to stop the procedure; (5) if a particular procedure in a particular patient population is normally accompanied by sedation when performed for clinical reasons, sedation should not be withheld in the nontherapeutic research setting to avoid its risks and thereby enhance the procedure's approvability under federal research regulations; and (6) there should be clear communication with potential subjects (and their parents) regarding the nontherapeutic nature of the procedures and procedural sedation in child assent and parental permission documents.

FDA Question

Assuming the risks have been minimized, are there one or more approaches to procedural sedation that would present no more than a minor increase over minimal risk? (Yes/No)

Following the vote you will have the opportunity to comment individually on the factors you considered in making your assessment.

Committee Vote and Discussion

YES: 7 NO: 9

The Subcommittee was not able to agree on whether one or more approaches to procedural sedation would present no more than a minor increase over minimal risk. Among Subcommittee members voting yes, members cited the importance of limiting nontherapeutic procedural sedation to high-volume centers with highly experienced providers, and to children for whom procedural sedation would not pose elevated risks (e.g. based on ASA risk classification). Members voting no commented that procedural sedation posed greater risks than those allowed under a minor increase over minimal risk category or were concerned about the likelihood that nontherapeutic procedures requiring sedation would be allowed in situations that posed greater risk to children.

Adjournment

The meeting was adjourned at approximately 4:13 p.m.