11/4/03 FINAL MINUTES

INITIAL REVIEW:

(A) Principal Investigator:
Protocol Title: Effects of Single Dose of dextroamphetamine in Attention Deficit Hyperactivity Disorder

Protocol summary: This study includes a double-blind, placebo-controlled administration of a single low dose of oral dextroamphetamine (10mg) in 14 healthy control children, 14 ADHD children and 12 pairs of monozygotic and dizygotic children discordant for ADHD. An fMRI will follow the medication administration to examine differences between groups.

NOTE: Prior to the meeting Dr. Rosenstein circulated a report from NHRPAC (National Human Research Protections Advisory Committee) clarifying specific portions of 45 CFR 46 Subpart D that governs Children's Research.

DISCUSSION:

[This protocol was initially discussed at the 10/28/03 IRB meeting, at which time the board voted to resume discussion on the protocol at the next IRB meeting. This protocol was the first item on the agenda for the meeting.]

DISCUSSION IN EXECUTIVE SESSION:

At the previous meeting the board had deferred a final vote on this protocol to the Nov. 4th meeting. The discussion resumed with individual board members providing their perspective on this issue related to the risk assignment for this study. The following notes summarize the views expressed:

- The Common Rule for the protection of human research subjects (45 CFR 46) defines minimal risk as being "not greater than…those ordinarily encountered in daily life." One member suggested that exposure of healthy children to similar medications is common, particularly with the prevalence of ADHD in children who are prescribed stimulant medications for symptoms of ADHD or difficulties in school. Presumably a percentage of these children may not actually have ADHD and are erroneously prescribed the medication. Thus, in the mind of this member the study could be considered minimal risk.
- Another member identified that one of the board's concern was the potential to put subjects at risk for subsequent experimentation/abuse of these stimulant medications. This member suggested that the board could make stipulations that would make this risk more explicit in the consent forms but still permit the approval of this study as minimal risk.
- A third member expressed concern that there is very little known regarding the risk of a single dose of dextroamphetamine in healthy children. In the absence of data establishing the risks, one member suggested the board should err on the side of subject protections and forward this protocol to the 407 panel for review.
- The concern regarding the potential for later abuse of similar substances based on this single exposure was also discussed. Is it possible that a single exposure to dextroamphetamine might somehow reset a subject's physiology and thereby increase their susceptibility toward a tendency of abuse? This did not seem likely to the member raising the issue, but it remains an unknown. Another member

posed that the board could stipulate that this “unknown risk” be clearly outlined in the consent forms thus making the study approvable as a minimal risk study.

- Members of the board expressed concern regarding the amount of compensation for subjects participating in this study (total possible study compensation: $570).
- One member felt giving a child a controlled substance (in the absence of a medical indication) could not be justified, and therefore the protocol could not be approved.
- Other members felt that in the absence of relevant data on the risk of subsequent abuse by subjects, the Board should err on the side of caution and consider this study to be a minor increment over minimal risk.

DECISION AND VOTE:

A motion was made to designate this protocol as a minimal risk study. There were 5 votes for the motion and 7 votes against the motion, thus the motion failed.

A motion was made to forward this protocol to a 407 panel for expert review. There were 10 votes for this motion and 2 abstentions.

STIPULATIONS:
None, the protocol was tabled for forwarding to a 407 panel

RECOMMENDATIONS:
None, the protocol was tabled for forwarding to a 407 panel.