15. Institutional Review Board meeting minutes dated January 11, 2005.

IRB Meeting Minutes of January 11, 2005

Protocol #: **13472A** – Revised Pending-Conditional

Principal Investigator: Robert Rosenfield

Title: Gonadotropin Releasing Hormone (GnRH) Agonist Test in Disorders of Puberty

Summary of protocol:
This study was originally reviewed at the IRB meeting of November 9, 2004 and received Pending-Conditional status. The Committee determined that the study could be approved in adults (both with and without a pubertal disorder) and in children with a pubertal disorder, pending a response to editorial changes in the consent form and response from the FDA regarding the IND status of the study drug, leuprolide. The Committee also determined that the study was not approvable in children without a pubertal disorder and should be sent to OHRP for 407 review consideration. The PI informed the IRB in late December that the protocol also underwent review by the General Clinical Research Center (GCRC), who granted approval pending a satisfactory response to issues identified by the reviewers. As the GCRC issues had not received review at the last IRB meeting, the IRB staff determined that the protocol had to come back before the Committee to review the PI's response to the pending conditional letter and the issues raised by the GCRC.

GCRC Comments: The GCRC comments included recommendations to augment sample size and to include other samples to increase statistical power; notation that the total number of subjects is not consistent in different parts of the protocol; request to modify the DSMP requesting clarification of amount of blood to be drawn from the subjects and a request to match genetic material with only an ID number to protect confidentiality. The PI revised the protocol and DSMP plan to accommodate the GCRC comments.

Additional changes the PI made to the protocol and consent form, in response to the GCRC include:

- Background information, including reference, has been added about the status of knowledge about the genetics of common disorders of puberty
- Methodology update for the CRC Core Laboratory's current method of DNA preparation
- The GCRC asked the PI to consider adding more centers. The PI's responded by clarifying that Carol Foster at University of Michigan hopes to conduct a similar study. However, she is waiting for her grant to be approved by the NIH (the PI has a subcontract on her contract). If she receives NIH funding and U of M IRB approval, the PI will amend the protocol in order to pool his data together with her data.
- The PI changed the wording in the consent form regarding DNA analysis in order to harmonize it with another protocol (#13528B). Upon request by the IRB staff,

the PI further revised the wording to make it easier to understand. The Committee agreed that the revisions were appropriate.

The PI plans to submit his response to the GCRC once IRB approval has been received.

Editorial Corrections to the Consent Forms and Assent Forms: The changes outlined in the Pending-Conditional letter regarding the consent and assent forms were addressed by the PI. Upon review of the revised consent forms, the IRB staff noted that the consent form for adults did not contain information pertinent to the healthy adult volunteers. Upon request by the IRB staff, the PI provided a separate consent form for this population. This consent form differs from the consent form for adult patients in that it includes a description of monetary compensation (note that adults with a disorder are not being paid), clarification that there is no direct benefit and no other alternative except to not participate.

IND status for Leuprolide: At the prior IRB meeting, the IRB had been under the impression that the PI had already submitted his IND application for leuprolide to the FDA. In the PI's response to the Pending-Conditional letter, he clarified that the application had accidentally been left on his secretary's desk and had not been mailed out when he had originally thought. Upon discovery of this incident, the application was immediately submitted. He has now informed the IRB that the 30 day waiting period for a response from the FDA has now passed without response. Thus, it appears an IND# is not required by the FDA for the use of leuprolide as a diagnostic agent in this study.

Discussion: The Committee agreed the PI appropriately addressed the issues outlined in the Pending-Conditional letter as well as follow-up IRB comments for the additional consent form for healthy adults, and additional changes in the consent forms regarding the collection of blood for DNA and cell line creation. The consent forms and assent forms are appropriate and no further changes are necessary. The Committee reviewed the changes requested by the GCRC and found them appropriate. No other changes to the protocol are necessary.

Issues: None

Risk Determination:
Adults-Greater than minimal risk
Children with a pubertal disorder- Minor increase over minimal risk with a prospect of direct benefit
Children without a pubertal disorder-Minor increase over minimal risk, with no prospect of direct benefit, and the research is not likely to yield generalizable knowledge about the subject's disorder or condition, since the healthy kids have no disorder. Review by a 407 panel is needed before IRB approval can be granted.

Recommendation: Full approval in all adults and in children with a pubertal disorder for 12 months. Not approvable in normal child volunteers; recommend sending this portion of the study to Mary Ellen Sheridan for 407 review consideration.

Vote: 9 For 0 Against 0 Abstaining 9 TOTAL