December 7, 2004

Robert Rosenfield, M.D.
Department of Pediatrics
[redacted]

RE: New protocol 13472A– ***Gonadotropin Releasing Hormone (GnRH) Agonist Test in Disorders of Puberty***

Dear Dr. Rosenfield:

At its Thursday, November 18, 2004, meeting, the CRC Advisory Committee reviewed and approved the above-referenced protocol, subject to satisfactory response to the following questions and recommendations:

1) This protocol has potential to provide a unique means by which to confirm disorders of puberty in a convenient, cost-efficient manner. However, the studies are underpowered at least in part because of the relatively low frequency of these conditions in the population. This protocol will provide descriptive results, but strong consideration should be given to inclusion of other centers and to expanding the sample size to augment the statistical power.

2) The total number of subjects to be enrolled is inconsistent throughout the proposal. On the face page and in the planned enrollment table 240 subjects are listed, yet in the narrative of the research plan under the methods section a total of 280 subjects are listed. Please clarify.

3) Please revise the third paragraph in the Confidentiality section on page 3 of the consent form. A home visit is described that is not included in this study.

4) Please make the following changes to the Data and Safety Monitoring Plan.

   a. On page 2 of 6 under "Safety Level 2 Risk" the box for venipuncture with removal of >5% and <10% of blood volume (for minors) is checked, however, in the adverse event reporting section on page 4 of 6 item #1 states that <5% of the blood volume will be taken. Please clarify what percentage of the blood volume will be taken from the subjects.

   b. Add the following statement or a variant of it to section 3A (Identify adverse events or toxicities that may result from participation in this study): "Breach of confidentiality concerning genetic testing will be minimized by using only an ID number to identify the participant's blood samples and test results."

c. Since this is not a study that includes treatment, a more detailed response as to how subject withdrawals/dropouts prior to study completion will be reported is required. Please revise item 6 on the last page.

5) The Committee supported the recommendations of statistician [redacted]. His comments are enclosed for your reference.

6) Please provide the CRC Administrative Office with a copy of the Institutional Review Board's approval certification and any revisions to the protocol and informed consent documents they may require as soon as they are available.

We are very pleased to have your ongoing participation, and welcome any comments that you may have.

Sincerely,

Ronald Cohen, M.D.
Acting Chairman, CRC Advisory Committee

Encl.
cc: Protocol File