The University of Chicago

Division of Biological Sciences • The Pritzker School of Medicine
The University of Chicago Hospitals

Institutional Review Board
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INSTITUTIONAL REVIEW BOARD CERTIFICATION

Principal Investigator:	Robert Rosenfield
Facex:	[redacted]
IRB Protocol Number:	13472A
Type of Submission:	New
Meeting Date:	11/09/2004
Informed Consent:	Written
Special Population:	Children
Advertisement(s) Used:	Yes
Protocol Title:	Gonadotropin Releasing Hormone (GnRH) Agonist Test in Disorders of Puberty

In order for this protocol to receive full IRB approval, you must respond to each of the items listed below by 60 days from the date of this certification. If you do not respond by this date, your protocol will be terminated, unless we are informed of extenuating circumstances which satisfy the IRB. All responses must be either highlighted or in bold print.

STATUS: Pending-Conditional

I. The Committee discussed the level of risk that the study procedures present to both healthy children and children with a pubertal disorder. The Committee concluded that the administration of leuprolide in an off-label manner represents a minor increase over minimal risk. In children with a pubertal disorder there might be benefit if the study provides a better diagnostic characterization of their disorder. The Committee also agreed that the study procedures are similar to those that a child with pubertal disorder would undergo during routine clinical treatment. Thus, the Committee found that in children with a pubertal disorder, the research could be approved under 45CFR46.405, research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. In regards to healthy children, the Committee found that the research represents a minor increase over minimal risk as it is being used in an off-label manner and there is no definitive data about its effect in healthy kids. The Committee also agreed that there is 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. Thus, the Committee found that in healthy children, this research must undergo 407 review as it is research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. The IRB also found that for healthy children, the permission of both parents must be obtained unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care custody of the child.

II. The Committee discussed if an IND# is needed for the use of leuprolide. It was noted that the PI had sent the FDA an IND annual report informing them of the change to leuprolide acetate. Please inform the IRB if a response from the FDA was received regarding this matter. If so, please forward the response from the FDA for our review.

III. Please revise the consent forms and assent forms as outlined below. A copy of all revised documents should be submitted to the IRB for review.

A. Please revise the assent forms for healthy children and patients by adding the IRB protocol number to the top of the forms.

B. Please revise all of the consent forms (for adults and parents) to include the following changes:
   1. On page 2, 2nd paragraph, the Committee agreed that the following phrase was not written in lay language: "...recently discovered potential regulators and markers of pubertal development when the technology becomes available (such as activin, inhibin and free alpha subunit)" Please revise this phrase by using lay language.
   2. On page 3, in "What are the risks of the study" section, 5th bullet, please change "We have performed 457 leuprolide diagnostic tests..." to "We have performed **over 400** leuprolide diagnosic tests..."

C. Please revise the consent form for parents of healthy children to also include the following changes:
   1. On page 4, in "What other options are there?" section, please remove the phrase "...or to have the standard test (with natural GnRH, marketed as Factrel if it is available within a reasonable period of time, or with GnRH agonist (leuprolide) test performed commercially". The Committee agreed that this phrase is not applicable to the healthy volunteers.
   2. As the Committee determined that the signature of both parents should be obtained for healthy volunteers, please revise the "Consent" section on page 6 to include an additional signature line for the 2nd parent.

D. In regards to parents of children with a condition as well as adults with a condition, it was unclear to the Committee if parking stickers will be provided for

the subjects. If so, please revise the consent forms to include this information in the section "Will I be paid for my participation?"

THE RESEARCH PROTOCOL AND/OR CONSENT FORM DESCRIBED ABOVE HAVE BEEN REVIEWED BY THE IRB WITH THE RESULTS AS INDICATED.

Date: NOV 2 3 2004 Signature of Chair

Jonathan Moss, M.D., Ph.D.

Federal regulations require that any severe drug reaction and unexpected or adverse occurrence to subjects during the conduct of this research be reported to the IRB. Any changes to this protocol must be submitted for review to the IRB.