Revised - Response to Pre-Review

THE UNIVERSITY OF CHICAGO

PROTOCOL SUBMISSION FORM
INSTITUTIONAL REVIEW BOARD
OFFICE OF RESEARCH SERVICES
Room S138 MC 1108
5841 S. Maryland Ave., Chicago, Illinois 60637
Phone: 773-702-6505 / Fax 773-834-0659
http://ors.bsd.uchicago.edu/IRB/irb_forms.html

For Office Use Only
Received date 10-13-04 Protocol # 13472A Meeting Date 10-19-04

PROTOCOL TITLE

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

PRINCIPAL INVESTIGATOR

Last Name: Rosenfield First Name: Robert

Degree: [X] M.D. [ ] Ph.D. [ ] Other Faculty Rank: Professor

Department: Pediatrics Section: Endocrinology

Mail Code/Campus Mailing Address: MC5053 E-mail address: robros@peds.bsd.uchicago.edu

Campus Phone Number: 773-702-6432 Fax Number: 773-702-0443 Pager: Unique ID#:

PRIMARY CONTACT - Investigators wishing to appoint a contact for IRB communications should complete all the contact information requested below.

Last Name: Walsh First Name: Deborah

Degree: [ ] M.D. [ ] Ph.D. [X] R.N. [ ] Other Title: Research Nurse Associate

Department: Peds Endocrinology E-mail address: dwalsh@peds.bsd.ucnicago.edu

Campus Phone Number: 773-702-6432 Fax Number: 773-702-0443 Pager: 6047 Unique ID#: 69-118

CO-INVESTIGATORS/OTHER RESEARCH PERSONNEL

Please utilize supplemental forms A and B to list all participating co-investigators and other research personnel.

LEVEL OF REVIEW

[X] FULL [ ] EXPEDITE - Attach Supplemental Form E to request expedited review

FUNDING SOURCE

☐ Internal Funding (Department Chair's signature required)

☒ External Funding

☒ Grant, Contract or Cooperative Group

Agency/Sponsor: GCRC

Agency/Sponsor ID#: USPHS RR-00055

TRACS ID#:

Funded (Y, N, Pending):

A copy of the entire grant application or sponsor protocol MUST be included with the submission.

☐ Non-Cash Support from Manufacturer/Sponsor

Manufacturer/Sponsor:

Type of support:

PERFORMANCE SITES

Identify each site other than the University of Chicago Hospitals where research procedures will be performed (i.e., where recruitment or interaction with subjects, specimens or data will take place).

☐ Weiss Memorial Hospital

**Approval from Weiss Hospital IRB will be required before initiating work at this site. Please submit a copy of the approval from the Weiss IRB.*

☐ LaRabida Children's Hospital

☐ Friend Family Health Center

Approval from Friend Family Center will be required before initiating work at this site.

☐ Offsite Clinic

Please name off site location:

ADDITIONAL PERFORMANCE SITES

Please list below any additional sites other than the University of Chicago Hospitals where the research will be performed **under the direction** of the University of Chicago principal investigator or co-investigator.

Please list any additional sites where the research will be performed.	**Provide certification or letter of IRB approval (non-cooperative group studies)**	**Provide letters of cooperation or support (as appropriate)**
	☐ Attached ☐ Will Follow ☐ N/A	☐ Attached ☐ Will Follow ☐ N/A
	☐ Attached ☐ Will Follow ☐ N/A	☐ Attached ☐ Will Follow ☐ N/A
	☐ Attached ☐ Will Follow ☐ N/A	☐ Attached ☐ Will Follow ☐ N/A

ADDITIONAL REVIEWS REQUIRED

Final approval by the IRB may include review by other University of Chicago committees. Indicate if review and approval by these committees is necessary, and the date of approval. Please provide documentation of review and approval.

	Review Required		Date of Approval
General Clinical Research Center	☒ Yes	☐ No	
Clinical Trials Review Committee *Reviews research involving cancer patients, cancer treatments, or requiring support from the Cancer Research Center*	☐ Yes	☒ No	
Institutional Biosafety Committee *Reviews the research use of recombinant DNA and its derivatives (biohazardous agents)*	☐ Yes	☒ No	
RDRC Committee *Reviews the use of radioactive drugs as well as the purchase and use of radioisotopes in humans (including research and routine)*	☐ Yes	☒ No	
Nursing Research Committee	☐ Yes	☒ No	
Is the scientific merit of this research project subject to peer review by another agency, sponsor or committee? Name of agency or committee:	☐ Yes	☒ No	

PURPOSE OF STUDY

Please summarize the purpose of the study using non-technical language.

The purpose of the study is to evaluate the effectiveness of the drug, leuprolide, in finding the causes of various disorders of puberty.

DESCRIPTION OF HUMAN SUBJECT POPULATION

As per 45 CFR 46 human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains
(1) data through intervention or interaction with the individual, or
(2) identifiable private information (i.e., pathological specimens, medical records, etc.)

Please answer the questions below for the subject population to be enrolled at the University of Chicago sites.

1. **Number of evaluable subjects to be enrolled** | | | 2 | 8 | 0 |

2. **Estimated total number of individuals who would be consented for the study to obtain the number of evaluable subjects** | | | 3 | 2 | 0 |

   Individuals who go through the consent process fall under the protection of the IRB even if they have no further participation in the study (i.e., include any screen failures, individuals who decline participation, etc. in this number)

3. **Age Range** (check all that apply)

   ☒ 0-6 yrs. (submit consent form and Supplemental form C)

   ☒ 7-17 yrs. (submit parental consent form, child's assent form, if applicable, and Supplemental form C)

   ☒ 18-58 yrs.

   ☐ 59+ yrs.

4. **Type of Subjects:**

   ☐ inpatients

   ☒ outpatients

   ☒ healthy volunteers

   ☐ UC employees

   ☐ UC Students (Dean of Students approval is required)

   ☐ other: specify _____

5. **Describe populations to be excluded from the research.** Please describe procedures to assure equitable selection of subjects. Researchers should not select subjects on the basis of discriminatory criteria. Selection criteria that excludes one sex or racial or ethnic group requires a clear scientific rationale for the exclusion.

Chronic disease (exclusion of chronic systemic, metabolic, and endocrine disease determined by history, physical examination, complete blood count, erythrocyte sedimentation rate, comprehensive metabolic panel, thyroxine, and somatomedin-C determinations) or sex hormone usage within 2 months.

6. **Special populations to be included in the research** (check all that apply):

- [x] minors under age 18 - Supplemental form C must be included
- [ ] pregnant women
- [ ] fetus/fetal tissue
- [ ] prisoners
- [ ] economically disadvantaged
- [ ] decisionally impaired
- [ ] individuals with mental retardation
- [ ] illiterate
- [ ] Non-English speaking

7. **Provide rationale for using special populations**
The groups listed in (6) above are considered "vulnerable" and require special consideration by federal regulatory agencies and/or the IRB.

SCREENING PROCEDURES - *If oral consent will be obtained, skip question 3 of this section.*

1. **Will the investigative staff have any contact with the study subjects?**

[x] Yes [ ] No If No, please attach the "Waiver of Consent/ Authorization" form and skip to "Informed Consent" section on page 6.
If Yes, continue on to question 2.

2. **Describe how subjects will be identified for participation in this study.**

Patients will be those presenting to the Pediatric Endocrinology Clinics of the University of Chicago Medical Center. We will attempt to recruit all subjects meeting eligibility criteria by informing them of the study while they are in clinic. Volunteers will be obtained via advertisements in the form of fliers posted throughout the University, and ads in newspapers, magazines, and other publications.

3. **The HIPAA Privacy regulations define screening procedures under two categories. Screening procedures are the procedures performed to identify potential study subjects and obtain information in order to contact these individuals regarding study participation. If your protocol involves pre-screening, please identify whether or not the data would be shared outside of the University of Chicago and check the corresponding screening option. If your study does not involve pre-screening, please check "this protocol does not involve pre-screening."**

- [ ] Screening data will NOT be shared with individuals outside of the University of Chicago. "Preparatory for Research" form attached.
- [ ] Screening data WILL be shared with individuals outside of the University of Chicago. "Waiver of Authorization" form attached.
- [x] This protocol does not involve pre-screening. All subjects are either recruited through advertisements or through direct contact with patients. There is no prior review of the patient's medical record other than standard of care.

RECRUITMENT PROCEDURES

1. **Will advertisements be used to recruit subjects?** ☒ Yes* ☐ No

   *If yes, check the types of documents you will use in this process and append these documents to the IRB application (check all that apply).

   ☐ Brochures
   ☐ Newsletters
   ☒ Flyers Posters
   ☐ Radio
   ☐ Television
   ☐ Contact letters (physicians, teachers, etc.)
   ☐ Internet
   ☒ Other newspapers, magazines

2. **Describe who will make initial contact with the potential subject.**
   Please note: Patients may not be approached for participation in a research study without the assent and/or involvement of the patient's treating physician.

   The endocrinologist seeing the patient in clinic will approach the patient about the research study.

   All flyers are the same as the advertisements placed in newspapers and magazines (see attached ad).

INFORMED CONSENT

1. **Will you obtain informed consent from subjects participating in this study?**
   ☒ Yes ☐ No*

   **If no, please submit Supplemental Form W "Waiver of Consent/ Authorization" and skip to page 8 "Description of Study".*

2. **How will informed consent be obtained from potential study participants?**

   ☐ Oral consent script
   Complete and submit Supplemental form O, "Use of Oral Consent."

   ☒ Written informed consent form

   Attach the written consent form to be used in this study. Consent forms should be written in simple declarative sentences. The forms should be jargon free. Foreign language versions should be prepared for applicable research.

   The current consent form template is available on the IRB web site at http://ors/HS/newirbforms/index.html.

INFORMED CONSENT PROCESS

Simply giving a consent form or reading a consent script to a subject does not constitute informed consent. The following questions pertain to the process.

1. **Will adult subjects have the capacity to give informed consent?** ☒ Yes ☐ No*

   *If not, describe the likely range of impairment and explain how, and by whom, their capacity to consent will be determined. Individuals who lack the capacity to consent may participate in research only if a legally authorized representative gives consent on their behalf or the Illinois Surrogate Act is followed. Please utilize Supplemental Form P if proxy consent will be sought.

2. **How will you determine whether the subject understands the study? Throughout the course of the study, how will you continue to ensure the subject understands the study?**

The nature and purpose of the study and the risks and benefits of participating in the study will be explained in detail to the patient and family. Special attention will be given to ensure that the study is explained to the patient at a level that he or she can understand. In order to assure that the patient understands the information given, the doctor or nurse obtaining consent will ask that the patient explain the study in his or her own words back to the person obtaining consent. The patient will specifically be asked whether he or she would like to participate in the study. All procedures associated with the study will be explained and answers to any questions or concerns will be given. Any patient declining participation will not be included in the study, whether or not the parents want him or her to participate. A copy of the signed consent and assent forms that explain the study will be given to the patients and families for their record. Phone numbers for research personnel and the IRB will be included in the consent in the event that patients have questions or concerns at a later date.

3. **In relation to the actual data gathering, when and where will consent be discussed and documentation obtained (for example, pre-operatively or several days before study procedures commence)?** Be specific.

The principle investigator or M.D. or R.N. associate will obtain written consent after informing subjects about the study, procedures associated with it and all experimental procedures, prior to any procedures or tests being initiated.

DESCRIPTION OF STUDY

1. **Describe the tasks/tests or procedures subjects will be asked to complete or undergo using non-technical language.** (Suggestion: explain step by step what the subjects will be asked to do and distinguish those which are experimental from those which comprise routine clinical care.)

See attached protocol.

The subject will be admitted to the Clinical Research Center at the University of Chicago Hospitals at approximately noon on Day 1. Height (via Harpenden stadiometer) and weight will be obtained by nurses in the Clinical Research Center. Pubertal stage will be assessed by the pediatric endocrinologist via physical exam. An IV will be placed in the arm at approximately 1700 hours to begin the study. (Routine Clinical Care)

Sleep Test. Blood sampling will begin at approximately 1900 hours via continuous withdrawal pump and continue for 12 hours to 0700 hours. Approximately 2.5 cc heparinized blood will be collected for LH, FSH, and sex steroids over sequential 20 minute intervals from an indwelling intravenous line by constant withdrawal pump. (Experimental)

GnRH agonist test. Leuprolide acetate injection dose of 10 mcg/kg is given at approximately 0700 hours. Blood sampling will begin at approximately 0700 hours. Samples will be obtained before (at 20 minute intervals x 4) and after the leuprolide dose: 0, 0.5, 1, 2, 3, 4, 8, 12, 16, 20, and 24 hours. LH and FSH will be measured in all samples; testosterone (boys) and estradiol (boys and girls) at 0, 16, 20, and 24 hours. (Experimental)

Blood will be withdrawn (15-30 cc) for DNA. (Experimental)

Bone age radiograph will be obtained for classification purposes. (Routine Clinical Care)

Patient will be discharged on prophylactic ferrous sulfate (300 mg daily for 1 month) at completion of the study. (Routine Clinical Care)

2. **Does this research involve the use of any DRUGS?** ☒ Yes* ☐ No

*If yes, complete and submit Supplemental Form D and the investigational brochure or package insert.

3. **Does this research involve the use of any DEVICES?** ☐ Yes* ☒ No

*If yes, complete and submit Supplemental Form F and the investigational brochure.

4. **Does the research involve (Check all that apply):**

- ☐ any surgical procedure
- ☐ use of radioisotopes or radioactive agents (Submit Supplemental Form H)
- ☐ administration of physical stimuli
- ☐ changes in diet or exercise
- ☒ use of private records (medical or educational records)
- ☒ possible invasion of privacy of subject or family
- ☐ deprivation of physiological requirements such as nutrition or sleep
- ☐ manipulation of psychological or social variables
- ☐ collection of personal or sensitive information in surveys or interviews
- ☐ use of a deceptive technique
- ☐ materials that subjects might consider offensive, threatening or degrading
- ☐ Other risks: specify

5. **Does the study involve blood drawing, marrow biopsy sampling, biopsy of other tissues, etc?** ☒ Yes* ☐ No

*If yes, state how much and how often the samples are taken. In addition, clarify whether the samples would retain identification that could be linked to study subjects.

Sleep test--Blood samples (2.5 cc each) will be taken every 20 minutes for 12 hours (total, 90 cc). Leuprolide test-- Four blood samples (3 cc each) and one (7 cc) sample will be taken prior to the test. Eleven (7cc each) samples, two (20cc each) samples, and one (30 cc) sample will be taken during the test (total, 166 cc). Samples will retain subject identification including names and MR numbers to allow for results to be included in the medical record.

6. **Will material be collected for genetic analysis?** ☒ Yes* ☐ No

*If yes, please complete and attach Supplemental form G

PROTECTED HEALTH INFORMATION

Indicate the information that will be collected about study subjects during participation in this study.

- [x] Names
- [x] Addresses
- [x] Employers' Names or Addresses
- [x] Relatives' Names or Addresses
- [x] Dates (except for years)
- [ ] Ages (only if >89)
- [x] Telephone and /or Fax Numbers
- [x] E-mail Addresses
- [x] Social Security Numbers
- [x] Medical Record Numbers
- [ ] Certificate Numbers (including device serial numbers for implants)
- [ ] Health Plan Beneficiary Numbers
- [ ] Member or Account Number
- [ ] Vehicle Identifiers & Serial Numbers (e.g. VINS, License Plate #)
- [ ] Voiceprints
- [ ] Fingerprints
- [ ] Full face photos and comparable images
- [ ] Any other unique identifying number, characteristic or code

Describe

CONFIDENTIALITY

1. **Describe provisions made to maintain confidentiality of data.** Who will have access to raw data? Will raw data be made available to anyone other than the Principal Investigator and immediate study personnel? If yes, who, how, and why? Describe the procedures for sharing data. Describe how the subject will be informed that the data may be shared.

A coded number will identify DNA. The record linking the ID number to the patient will be kept locked in the Clinical Research Center and the offices of Dr. Rosenfield and only personnel directing the research will have access. All other data is stored as paper files and a computerized database in a secured and locked area to which only the investigative team has access. Patient names will not be used in any scientific or other publications without their written approval. Records may be reviewed by federal agencies including the Food and Drug Administration and Office of Human Research Protections, and by the Institutional Review Board at the University of Chicago. Subjects will be informed of the above during the consent process and through our providing them with a copy of the written consent form.

2. **Where will the data be kept and for how long?** If audio or videotapes will be used, how will they be disposed of?

Data will be kept indefinitely as paper records and computer database in a locked, secured area to which only the investigative team has access.

RISKS OF THE RESEARCH

1. Identify the risks (current and potential) and describe the expected frequency, degree of severity, and potential reversibility. Include any potential late effects.

The following are risks associated with the study:

1. The IV needle may cause irritation or bruising at the IV insertion site, redness or swelling of the vein or infection. This happens infrequently and is reversed by removing the IV.

2. The amount of blood taken is equal to about a half-pint, less than 10% of blood volume over a 36 hour period. This amount of blood is normally not enough to cause a low blood count. Although the amount of blood drawn is not dangerous, it may be enough to cause temporary dizziness. Dizziness occurs rarely and can be prevented by ensuring the fluid intake of the subject is adequate.

3. Heparin is used to prevent clotting in the IV. The amount of heparin used is too little to cause excessive bleeding from the vein.

4. Leuprolide has no known direct or permanent side effects. In adult women the changes in hormones may cause temporary premenstrual-type symptoms and/or delay ovulation by about a week after the test is performed. Premenstrual symptoms include nausea, breast tenderness, and mood swings. Delayed ovulation can delay the onset of the next period. Leuprolide is mixed in a preservative called benzyl alcohol to which some people are allergic. Allergic reactions vary from one person to another and may include redness, rashes, and swelling. We have performed 457 leuprolide diagnostic tests in children and adults with no adverse events.

5. Unforeseeable side effects or adverse reactions, such as allergic reactions could occur. Allergic reactions are rare (1 case report) and unheard of in response to the short-acting form used for these studies. We have performed 475 leuprolide diagnostic tests in children and adults with no adverse events.

6. Anxiety symptoms may occur related to the needle sticks required to draw blood samples. These include numbness or tingling of the hands or feet, and constipation.

2. **Describe the precautions taken to minimize risk, including rescue provisions:**

The following will be done to minimize risks:

1. All blood draws and IV insertions will be done with aseptic technique with patient comfort in mind.

2. Blood sampling will be performed after the subject is admitted to the Clinical Research Center of the University of Chicago Hospitals on a General Pediatric Service, with a nurse in constant attendance, a resident in Pediatrics available in-house, and the Pediatric Endocrinology service on call. Subjects will be well-hydrated by the CRC nursing staff and monitored when getting out of bed to assess for dizziness and ensure safety. Iron stores will be repleted by prescribing ferrous sulfate.

3. The Clinical Research Center is equipped with rescue medications and equipment in the event that a subject would experience an adverse event during one of the tests. Experienced nurses and physicians monitor all subjects during their participation in the study.

3. **Why are the identified risks reasonable?** Please justify the risks in relation to the anticipated benefits to the subjects and in relation to the importance of the knowledge that may reasonably be expected to result from the research.

Patients with disorders of puberty benefit from the diagnostic accuracy of the sleep test for the subtle hormonal changes of early puberty, as well as the interpretation of the results of the Leuprolide (GnRHag) test. There is often not an available alternative to the GnRHag test because the Factrel (GnRH itself) supply is erratic, and often unavailable at the time of need for prompt diagnosis. Factrel is the standard diagnostic agent used by pediatric endocrinologists to attempt to distinguish among disorders of puberty.

This study is potentially beneficial to society by improving diagnostic accuracy of disorders of puberty, as well as providing for the pressing need for sex-, age-, and pubertal stage-specific normative data to be used as comparison data. Such comparison data will better enable us to determine what is normal versus what is not and assist with the earlier diagnosis and treatment for patients with pubertal disorders. Adverse events associated with the study are infrequent or rare and easily reversible. Therefore, the risks are reasonable for healthy volunteers.

DATA AND SAFETY MONITORING PLAN

1. **Is there a data safety monitoring board/committee to review this study for safety and adherence to the study protocol?** ☐ Yes ☒ No

   NOTE: Regardless to the response to this question, all subsequent questions in this section must be addressed.

2. **Provide a general description of the data and safety monitoring plan which must include, at a minimum, a description of the reporting mechanism of serious/unexpected adverse events to the IRB, the study sponsor (if applicable) and the FDA.**

Overall level of risk of the study is low. The PI will perform safety monitoring annually, along with Dr. Elizabeth Baumann through review of the data. Adverse events will be graded according to the 0-5 scale shown in the DSM guidelines. Adverse events will be reported in writing to the IRB and CRC. The FDA will also receive adverse event reports within 7 days of site notification. Treatment would be stopped in the event of severe allergic reaction or if IV access was not possible to achieve. Subject withdrawals/dropouts prior to study completion will have intent to treat statistical analysis performed.

3. **Describe plans for monitoring the progress of the study and the safety of study participants (e.g. timing of data and safety monitoring reviews and reports, planned interim analysis, etc.)**

Participants will be monitored closely while in the study for any adverse events. Data will be reviewed as it is available and also annually to determine safety of the study. Any adverse events will be reported in writing to the IRB, the CRC, and the FDA.

BENEFITS OF PARTICIPATION

List any anticipated direct benefits of participation in this research project. If none, state that fact here and in the consent form. Remunerations should not be described as a benefit.

Patients with disorders of puberty directly benefit from the diagnostic accuracy of the sleep test for the subtle hormonal changes of early puberty, as well as interpretation of the results of the GnRHag test. Factrel (GnRH itself), the standard diagnostic agent used by pediatric endocrinologists to attempt to distinguish disorders of puberty, is not always available at the time prompt diagnosis is needed.

There is no direct benefit to volunteers.

ALTERNATIVES TO PARTICIPATION

List appropriate alternative clinical procedures or courses of treatment available to subjects. If there are no clinical alternatives, please state that participation is voluntary.

The GnRH agonist (leuprolide) test may be performed commercially.

COMPENSATION FOR PARTICIPATION

1. **Will subjects be paid or otherwise compensated for participation?** ☒ Yes* ☐ No**

   ** If yes, please continue to answer questions 2, 3, and 4 of this section.*
   ***If no, please skip to the "Costs" section.*

2. **What gifts, compensation, travel money or other reimbursement will be given to the subjects? Please provide a dollar amount if applicable.**

Volunteers are compensated $50 for completion of the leuprolide test, $50 for completion of the sleep test, or $150 for completing both the sleep test and the leuprolide test via a check from the University. They are also given free parking for each day they are in the CRC for the study.

Patients are not compensated for participating

3. **When will subjects receive compensation?**

Subjects will receive compensation after completion of the study, as soon as the check is available from the University.

4. **Please either describe a plan for prorating payments if a subject withdraws from the study early or provide a justification as to why prorated payment is not being offered.**

Payment is prorated. Subjects are paid $50 for completing the sleep test, $50 for completing the leuprolide test, or $150 for completing both the sleep and leuprolide tests.

COSTS

1. **Will the subjects be charged for research-related procedures?** For example, will subjects be charged for extra tests related to the research, i.e., lab tests, EKG, etc.? ☐ *Yes ☒ **No

**If yes, please explain the charges and answer question #2.*
***If no, please skip to the Conflict of Interest Section.*

2. **Are there any costs indicated above that are considered experimental by the Centers for Medicare & Medicaid Services and therefore not likely to be covered or reimbursable by the subject's health insurance?** If yes, please specify below. Note that the consent form must disclose to subjects that there may be charges which, because of their experimental nature, cannot be billed to or be reimbursed by their insurance. ☐ Yes ☐ No

N/A. Subjects will not be charged for tests related to the research.

CONFLICT OF INTEREST

Is there a potential conflict of interest associated with this protocol? ☐ Yes* ☒ No

*If yes, please explain in a separate letter to the Committee the conflict associated with the P.I. or any other participant. Conflict of interest is defined in The University of Chicago policies. Please contact University Research Administration (www.uchicago.edu/adm/ura/coi/coipolicy.html) or the BSD Office of Research Services for further information.

LITERATURE REVIEW

Please include your biobliography or attach the results of a literature search which justify the involvement of human subjects in this research project.

OTHER MATERIALS

Please ensure all corresponding materials are enclosed in your protocol submission, including a separate protocol document. See the "Protocol Application Contents" section of the IRB Policy and Procedure Manual for a complete description (http://ors/IRB/hs_policy_manual.html).

INVESTIGATOR'S ASSURANCE

I certify that the information provided in this application is complete and correct.

I understand that as Principal Investigator, I have ultimate responsibility for the protection of the rights and welfare of human subjects, conduct of the study and the ethical performance of the project.

I agree to comply with all University of Chicago policies and procedures, as well as with applicable federal, state and local laws regarding the protection of human subjects in research, including but not limited to, the following:

* The protocol will be performed by qualified personnel according to the University of Chicago IRB approved protocol,
* No changes will be made in the protocol or consent form until approved by the University of Chicago IRB,
* Legally effective informed consent will be obtained from human subjects if applicable, and
* Adverse events will be reported to the IRB per the IRB Adverse event reporting policy.

I further certify that the proposed research is not currently being conducted and will not begin until IRB approval has been obtained.

Principal Investigator

09 - 07 - 2004

Date

DEPARTMENT CHAIR SIGNATURE

The signature of the Department Chair is required when the study is not externally funded.

Department Chair

__ - __ - ____

Date