

OFFICE FOR THE PROTECTION OF RESEARCH SUBJECTS

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A MESSAGE FROM THE DIRECTOR OF THE OFFICE FOR THE PROTECTION OF RESEARCH SUBJECTS

As a UIC researcher I have often faced the impending Continuing Review application deadline with annoyance and aggravation. I understand the many demands placed on UIC faculty and appreciate the conflicting deadlines that often arise.



James H. Fischer
Director, OPRS

However, the regulations for human subject research allow no extension of the continuing review deadline set by the IRB. Thus, no matter what other interests may interfere with an application deadline for continuing review, a lapse in IRB approval represents noncompliance with the federal regulations and UIC policy and requires that all research activities be stopped unless an exception is granted by the IRB to prevent harm to subjects. Repeated lapses of human subject research by an investigator may result in a determination of continuing or serious noncompliance. This month in the newsletter we examine what happens when a protocol lapses, what the UIC and OHRP requirements are in this situation, and the implications for the investigator.

What type of untoward events require reporting, what types of protocol violations require prompt reporting, when do I need to report an incident of noncompliance? What adverse effects occurring at UIC need to be promptly reported? These questions commonly arise with researchers. Please see this month's article on events requiring Prompt Reporting.

OPRS looks forward to hearing from you.

Jim Fischer
Director OPRS

OFFICE FOR THE PROTECTION OF RESEARCH SUBJECTS (OPRS) 2008 HOLIDAY SCHEDULE

The Office for the Protection of Research Subjects (OPRS) will observe the reduced service schedule for non-essential services for the holidays. Therefore, the OPRS will be closed from 5:00 PM on Tuesday, December 23, 2008, and will reopen at 8:30 AM on Monday, January 5, 2009. In addition, the east side OPRS satellite office will be closed beginning December 22nd.



NEWS FOR INVESTIGATORS

DON'T LET YOUR IRB APPROVAL EXPIRE!

A lapse in IRB approval represents noncompliance.

OPRS issues 90, 60 and 30 reminders that you are approaching your expiration date. Investigators must file a Continuing Review application for all active research.

Investigators must file a Final Research Report to request study closure with OPRS for every IRB approved study within 30 days of the completion of the study.

If you do not file a Continuing Review or a Final Research Report by the IRB assigned expiration date **your research activities must stop!**

This includes:

- any research related interventions
- recruitment
- data collection
- data sharing/reporting and analysis of identifiable data
- subject enrollment

Also, you need to report to the IRB within 5 days on the status of research subjects.

When the investigator feels it is in the best interest of a subject to continue research activities during the lapse, a request to continue the research should be submitted to the IRB using the UIC OPRS Protocol Exception form.

If a Continuing Review application or Final Research Report is not submitted by the expiration date, the consequences are:

- research activities must stop, unless an exception is granted by IRB, protocol is classified as “lapsed in IRB approval”;
- research is closed if continuing review not obtained within 14 days;
- a determination of noncompliance is made by the IRB;
- additional education/training may required of the PI before submitting new protocols;
- noncompliance will be reported, as applicable, to the appropriate federal agencies and sponsors;
- Department Head is notified;
- the Vice Chancellor for Research is notified; and
- UIC Grant and Contracts is notified and funding may be terminated.

Please review the new policy [Study Closure, Lapse in IRB Approval and Withdrawal of Research](#) and the [flow chart](#) to better understand your responsibilities, what to do if your research is greater than minimal risk, and, most importantly, how to best ensure the safety of your subjects.

*“If you do not file a Continuing Review or a Final Research Report by the IRB assigned expiration date **your research activities must stop!**”*

HUMANITARIAN USE DEVICE (HUD)

Humanitarian Use Device (HUD) refers to a medical device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year (21 CFR 814.3(n)). The HUD category was developed to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations. Unlike other significant risk medical devices, the application submitted to the FDA for approval of the HUD (referred to as a humanitarian device exemption (HDE)) is not required to show that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Other facts concerning the use of HUDs include:

- An HUD may only be used after the sponsor (i.e., holder of the HDE) has received FDA approval of the HDE and the IRB at the institution has approved its use.
- Even though use of the HUD for its approved indication(s) does not represent research, FDA regulations require initial and continuing (at least annually) review by an IRB.
- Initial review by the IRB must occur at a convened meeting; continuing review however may follow expedited review procedures.
- FDA regulations do not require informed consent; however the IRB may, on its discretion, require informed consent. Typically, a patient information sheet containing information to allow the subject to make an informed decision suffices.
- An HUD-specific IRB application will be available by March, 2009, until then please contact the OPRS staff for help in preparing the IRB application.
- The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.
- HDE holders may charge for the HUD to recover costs (including research & development, fabrication, and distribution), but are prohibited from making a profit except in limited indications for pediatric use.

Use of a HUD outside its approved indication(s) (i.e., of-label) can only occur under emergency or compassionate use situations. Emergency use of an HUD must follow the same policies that govern the use of unapproved devices, drugs, and biologics. For emergency use, the patient must meet the following criteria:

- A life-threatening situation exists requiring treatment with the test article;
- no standard acceptable treatment is available; and
- insufficient time is available to obtain IRB approval at a convened meeting.
- the activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.

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“The FDA expects the physician to follow as many human subjects protection procedures as possible.”

HUMANITARIAN USE DEVICE (HUD) CONTINUED FROM PAGE 3

Additionally, the FDA expects the physician to follow as many human subjects protection procedures as possible, including:

- Obtaining an independent assessment by an uninvolved physician;
- obtaining informed consent from the patient or a legal representative in accordance with and to the extent required by 21 CFR 50;
- documenting informed consent in writing;
- notifying institutional officials as specified by institutional policies;
- notifying the Institutional Review Board (IRB); and
- obtaining authorization from the HDE holder.
- UIC policy requires physicians, at a minimum, to fulfill procedures 2, 4, 5 and 6.

After an HUD is used in an emergency use situation, the physician should:

- Report to the IRB within five business days;
- evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts with the sponsor to obtain FDA approval for a compassionate use supplement to the HDE; and
- notify the sponsor of the emergency use and provide a written summary of the conditions constituting the emergency, subject protection measures, and results.

If the situation is not an emergency, an HUD may be employed using compassionate use procedures. This requires that the HDE holder submit a HDE supplement to the FDA requesting approval for compassionate use. Compassionate use typically involves following many of the patient protection measures listed above for emergency use.

For assistance concerning emergency or compassionate use, please contact the UIC OPRS at 312-996-1711.

For FDA guidance on HDE regulations: <http://www.fda.gov/cdrh/ode/guidance/1668.html>

UIC Guidance on emergency use is available at:
<http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0287.pdf>.

New Forms and Policies for Researchers

UIC UNIVERSITY OF ILLINOIS
AT CHICAGO

FORM - Determination of Whether an
Activity Represents Human Subjects
Research

Version: 2.0
Date: 10/16/08

DETERMINING WHETHER OR NOT AN UNANTICIPATED PROBLEM OR OTHER EVENT REQUIRES PROMPT REPORTING

Human subjects research is predictably unpredictable. Many times unanticipated problems or adverse events occur.

On October 15, 2008 OPRS released a revised “Unanticipated Problems and Other Events Requiring Prompt Reporting” policy. It is important that all investigators take a few minutes to review this policy, which is available on-line at the following web-site: <http://tiger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0279.pdf>

The revised policy categorizes events in three basic ways: a) Internal vs. External; b) Anticipated vs. Unanticipated; and c) Related vs. Unrelated.

Internal Events:

- Occur at UIC, JBVAMC, or other sites where the UIC IRB has oversight responsibility for the research;
- are far more likely to require prompt reporting than external events; however,
- some external events must also be promptly reported, such as external adverse events determined by the investigator, sponsor, coordinating center or DSMB/DMC to represent an unanticipated problem (i.e., unanticipated, related, and increased risk of harm).

Unanticipated Problems:

- Problems, events or information items that are not expected, given the nature of the research procedures and the subject population being studied; and
- suggest that the research places subjects or others at a greater risk of harm or discomfort related to the research than was previously known or recognized.
- Anticipated problems and how they will be handled will have already been explained to the IRB in the research protocol and/or Initial Review Application.

Related Problem:

- An event is related or possibly related to participation in the research if the event is more likely than not to have been caused by the procedures associated with the research.
- Related events are far more likely to require prompt reporting to the IRB.

Specific information regarding what events and problems need to be reported are provided in Section IV of the revised “Unanticipated Problems and Other Events Requiring Prompt Reporting” Policy.

OPRS frequently hears from investigators that events do not fall neatly into categories. When in doubt, call OPRS at 312-996-1711 and ask to speak with the Assistant Director assigned to your IRB of record.

Responding appropriately and promptly to an unanticipated problem or adverse event will not diminish the value of your research; however, not responding appropriately and promptly will.

Contributed by Charles Hoehne, Assistant Director Educational Initiatives

*“Human subjects
research is predictably
unpredictable.”*

TIMELINES AND REPORTING PROCEDURES FOR REPORTABLE EVENTS

Timelines for reporting unanticipated problems and other events to the IRB:

- Reporting is required within five working days of becoming aware of the event for:
 - a. Internal adverse events considered serious as defined above (e.g., death, life threatening injury);
 - b. changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects.
- Reporting is required within ten working days of discovering or being notified of the event for all other incidents listed in section IV of the “Unanticipated Problems and Other Events Requiring Prompt Reporting” policy: <http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0279.pdf>
- Investigators are also responsible for reporting adverse events and problems to the sponsor and any other agencies as specified in the protocol, data safety monitoring plan or other agreements.

How to report an unanticipated problem or other event to the IRB:

- The investigator informs the IRB of a potential unanticipated problem/event by submitting the UIC OPRS “Prompt Reporting to the IRB” form.
- Unanticipated problems/events occurring at the Northwestern University (or an NU affiliate) performance site for research approved by the Collaborative IRB (UIC IRB#4) are:
 - a. Reported by investigators to the NU OPRS.
 - b. These reports are forwarded by NU OPRS to UIC OPRS and the Collaborative IRB.
 - c. All other performance sites where the UIC IRB has oversight responsibility, the reports are forwarded directly to the UIC OPRS.

Materials that need to be included with the submission of the prompt report:

- “Prompt Reporting to the IRB” form; and
- examples of materials that should be submitted with the prompt reporting form include, when available, case report forms, DSMB/DMC reports, updated investigator brochures, amendment applications with revised protocol or consent form, or sponsor communications.

What happens after the report is submitted?

- OPRS staff reviews the report to determine if it meets the following criteria:
 - a. The event is unexpected in nature, severity or frequency given the research procedures and subject population;
 - b. the event is related or possibly related to participation in the research; and
 - c. the event caused harm or placed the subjects or others at greater risk of harm or discomfort than was previously known or recognized.
- If all three criteria are met:
 - a. If minimal risk, the event is referred to the IRB Chair or designee for review.
 - b. If greater than minimal risk, consult with IRB Chair or designee and refer event to the convened IRB for review.
- The IRB Chair/Designee or convened IRB (depending upon risk level) then:
 - a. Considers whether the event meets the prompt reporting criteria and assesses the risk level associated with the event; and
 - b. considers possible corrective actions.
 - c. The OPRS staff communicates the IRB determinations to the IRB.



CONTINUING EDUCATION OPPORTUNITIES FOR INVESTIGATORS

OPRS requires that investigators and key research personnel take initial training before conducting research. Training also needs to be updated every two years with two Continuing Education credits.

Need CE Credit?

- Does your department hold lectures that would be appropriate for Human Subjects Research Education credit?
- Have you heard of a program that you would like to see offered for Human Subjects Research Education credit?
- Will you be attending a conference that would apply to Human Subjects Research?

Please contact Laurie Kennard at (312) 413-9175 to see if your program might apply.

Are there issues you need to know more about? How can OPRS help you in the IRB process?

Is there a lecture on campus that would qualify for Human Subjects Research Continuing Education? A posting on our website and a write-up in the OPRS newsletter can get the word around campus.

OPRS welcomes your thoughts on Continuing Education issues. Please contact Laurie Kennard at lkennard@uic.edu if you or your department has a presentation that may qualify for continuing education credit.

Office for the Protection of
Research Subjects (OPRS)

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[http://tiger.uic.edu/depts/
over/research/
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