



# ST. JOHN HOSPITAL & MEDICAL CENTER

Winter, March, 2007  
Issue 7

## Research Quarterly

News for and by the IRB and Research Professionals of St. John Healthcare System

### **IRB NEWS**

by  
Peter A. Nickles, M.D.

**Chairman, IRB**

### **New Forms - REMINDERS**

The IRB application, continuing review form, revision application, and serious adverse event reporting forms have been revised, and the consent form skeleton has been updated. Please contact our office if you need the new versions.

We also want to encourage electronic submission of application materials. If electronically submitted, a signed copy of the application form still needs to reach us in a timely fashion.

*Outdated and/or unsigned forms received by the IRB will be returned which may delay your project.*

\*\*\*\*\*

Any materials describing an IRB-approved study that will be viewed by the general public (i.e. flyers, newspaper or newsletter articles, interviews, media events) must be submitted to the IRB for prior review and approval.

The IRB's responsibility is to protect the rights and welfare of human subjects. The IRB reviews and oversees research to ensure that it complies with federal regulations pertaining to human subject protection, as well as the good clinical practice (GCP) guidelines of the International Conference on Harmonization. No interaction with human subjects in research (including chart review) may begin until the IRB has reviewed and approved the protocol.

### **IRB Standard Operating Procedures (SOPS)**

The IRB SOPs are printed and available as a resource document. If you have not received a copy please call 3-8314 or 3-3863.

**NEW STUDIES** - Four (4) copies of the protocol and of the Investigator Brochure, plus two (2) copies of the application and all other materials are required.

**ALL OTHER SUBMISSIONS** – Two copies of all other submissions, (Continuing Review, adverse events, amendments, updated Investigator Brochures, memorandums, etc), are required.

Please use the IRB # (e.g. SJ 1010-01) when referring to your Protocol. The IRB # will assist us in locating the file and answering your questions quickly.

The IRB office is your resource center and will always be available to provide information or assistance.

\*\*\*\*\*



### **IRB 2007 Meeting Dates**

All meetings occur monthly on the third Thursday at 7:30 AM in the Mack Office Building, Suite 390.

- January 18, 2007
- February 15, 2007
- March 15, 2007
- April 19, 2007
- May 17, 2007

June 21, 2007  
July 19, 2007  
August 16, 2007  
September 20, 2007  
October 16, 2007  
November 15, 2007  
December 20, 2007

### **IRB Administrative FEE Increase in 2007**

Effective January 2, 2007, the one-time IRB Administrative Fee to review externally sponsored projects was raised from \$1500.00 to \$2000.00.

Please alert all sponsors to this increase and make sure the new fee is included in all contracts.

### **Congratulations**

Mary Barnhart, IRB Coordinator, was featured in the Michigan Ethics Research Network (MERN) Newsletter with an article titled "The Role of Ethics Committees, Ethics Consults, and IRBs in Recognition and Protection of Patient Rights." Congratulations and well done!

**INVESTIGATORS:** Anyone working on your research study must complete the NIH computer-based training modules found at:

<http://cme.nci.nih.gov>

**Anyone** consenting subjects or collecting data in a research trial **must** be reported to the IRB. Research Office. Research Coordinators often change projects, and the IRB Office needs to be informed.

***Remember, any changes to your protocol or studies must be reported to the IRB.***

### **EDUCATIONAL PROGRAMS FOR INVESTIGATORS AND RESEARCH STAFF**

Wednesday, January 25, 2007, Patti Webber, RN., BSN, Education Coordinator for Wayne State University presented "The Informed Consent Process". The program was well attended and the presentation was well done. Thank you to Denise Cunningham who has been spearheading these educational programs.

**Save the date!** September 27, 2007 from 8:00 AM to 4:00 PM is the date for the Research Summit sponsored by the St. John Hospital & Medical Center IRB, St. John Providence Hospital IRB, and Hall, Render, Killian, Heath & Lyman, PLLC at the Grosse Pointe War Memorial Center. This is one

you will not want to miss! So, plan on attending, and look for further details in upcoming publications.

If you have suggestions for topics or speakers, please call the IRB office at 313-343-8314 or 313-343-3863.

### **IRB INFORMATION CORNER**



### **Unanticipated Problems in HHS Clinical Trials Must Be Reported**

ALL "unanticipated problems" affecting participants in clinical trials sponsored or supported by HHS must be reported under Office of Human Research Protections (OHRP) new guidance.

These are not the same as adverse events, although there is some overlap: adverse events must be reported if they meet the definition of serious or unexpected and are also unanticipated problems. The guidance states, "Only a small subset of adverse events occurring in human subjects participating in research are unanticipated problems that are not adverse events and yet must be reported."

Federal regulations contain the phrase "unanticipated problems involving risks to subjects or others", but do not explain what it means. The new guidance says that OHRP considers any incident, experience or outcome an unanticipated problem if it:

- Is of an unexpected nature, severity or frequency given the research procedures described in the IRB-approved research protocol or informed consent or related documents, taking into account the characteristics of the subject population;
- Is or may be related (with "reasonable possibility") to participation in the clinical trial; and
- May place trial participants at risk of physical, psychological, economic, or social harm than was previously known or recognized.

Difficult though it is to determine what is unexpected and what may be related to the clinical trial, the

guidance states that when any unanticipated problem meeting the above criteria occurs, the PI should consider taking corrective action. Such actions could include: changing the protocol; modifying inclusion/exclusion criteria and/or the informed consent; suspending new subjects, and/or modifying study procedures to minimize risks. Reportable unanticipated problems that are not adverse events may involve harm that is social or economic, instead of physical or psychological (as with adverse events), or may place research participants or others at increased risk of social or economic harm (and again, since no actual harm occurs, this is not an adverse event). The guidance gives three examples of “unanticipated problems” that would result in increased risk of harm.

1. An investigator surveys college students about their illicit drug use and other illegal behavior, and stores this individually identifiable sensitive information on a laptop computer that is then stolen from his car.
2. A pharmacy technician makes a processing error that results in a participant in a multi-center clinical trial receiving a dose of experimental drug 10 times higher than that dictated by the IRB-approved protocol. The result is increased risk of toxicity to the participant, but no actual harm occurs.
3. An audit of a clinical trial uncovers the fact that an investigational biologic agent derived from human sera has been given to cancer patients without appropriate screening and testing of donors for potential viral contaminants, including HIV and hepatitis B.

The common thread is that the problems were unexpected, related to participation in the research, and placed subjects at a greater risk of physical, psychological, or social harm than was previously known or recognized.

The guidance can be accessed at:

[www.hhs.gov/ohrp/policy/AdvEventGuid.html](http://www.hhs.gov/ohrp/policy/AdvEventGuid.html)

### **FDA Guidance Roles and Responsibilities of Sponsors in Device Trials**



#### FDA Definitions:

**“Sponsor”** means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator and the employees are investigators.

**“Sponsor-Investigator”** means an individual who both initiates and actually conducts, alone or with others, an investigation, that is under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than the individual. The obligations of a sponsor-investigator under this part include those of an investigator and those of the sponsor.

**NOTE: If you fit the criteria of a sponsor-investigator you must meet both sponsor and investigator responsibilities.**

### **Sponsor Responsibilities for Significant Risk Device Studies**

#### General responsibilities (§812.40)

Sponsors are responsible for selecting qualified investigators and providing them with the information that they need to conduct the investigation properly. They must also ensure proper monitoring of the investigation and IRB review and approval, submit an IDE application to FDA for significant risk device studies, and inform the IRB and FDA promptly of any significant new information about the investigation.

#### FDA and IRB approval (§812.42)

A sponsor cannot begin an investigation or any part of an investigation until an IRB and FDA have both approved the application or supplemental application.

#### Selecting Investigators (§812.43)

A sponsor is responsible for selecting investigators qualified by training and experience to investigate the device.

#### Selecting Monitors (§812.43)

A sponsor must select monitors qualified by training and experience to monitor the

investigational study in accordance with the IDE and other applicable FDA regulations.

#### Device Control (§812.43)

A sponsor can ship investigational devices only to qualified investigators participating in the investigation.

#### Investigator Agreements (§812.43)

A sponsor must obtain a signed agreement from each participating investigator that includes:

- the investigator's curriculum vitae
- a statement of the investigator's relevant experience, including the dates, location, extent, and type of experience, where applicable
- an explanation of the circumstances that led to termination of a study if the investigator was involved in an investigation or other research that was terminated
- a statement of the investigator's commitment to:
  - conduct the investigation in accordance with the agreement, the investigational plan, the IDE and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA
  - supervise all testing of the device involving human subject, and
  - ensure that the requirements for obtaining informed consent are met.
- sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under 21 CFR 54, Financial Disclosure by Clinical Investigators. The sponsor shall also obtain a commitment from the clinical investigator to promptly update this information if any relevant changes occur during the course of the investigation and for one year following completion of the study. (The financial certification or disclosure is submitted in the PMA or Premarket Notification 510(k) application. It should not be submitted in the IDE application.)

#### Informing investigators (§ 812.45)

A sponsor must supply all investigators participating in the investigation with copies of the investigational plan and a report of prior investigations of the device.

#### Monitoring (§ 812.46)

##### Securing Compliance

A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the IDE requirements, any other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA must promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor must also require that the investigator dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

##### Unanticipated Adverse Device Effects

The sponsor must immediately conduct an evaluation of any unanticipated adverse device effect. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects must terminate all investigations or parts of the investigations presenting that risk as soon as possible. Termination must occur no later than 5 working days after the sponsor makes this determination and no later than 15 working days after the sponsor first received notice of the effect.

##### Resumption of Terminated Studies

For significant risk device investigations, a sponsor may not resume a terminated investigation without IRB and FDA approval. For a non-significant risk device investigation, a sponsor may not resume a terminated investigation without IRB approval. If the non-significant risk study was terminated for unanticipated adverse device effects, the sponsor must also obtain FDA approval.

#### Sponsor records (§ 812.140)

The sponsor must maintain accurate and complete records relating to the investigation. These records include:

- all correspondence including required reports,
- records of shipment of the device,
- records of disposition of the device
- signed investigator agreements including financial disclosure information,

- records concerning complaints and adverse device effects whether anticipated or not,
- any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

See Records for additional information on recordkeeping requirements.

#### Sponsor Reports (§812.150)

The sponsor must provide the following reports in a timely manner to FDA, the IRB's, and/or the investigators.

- Unanticipated Adverse Device Effects
- Withdrawal of IRB Approval
- Withdrawal of FDA Approval
- Current List of Investigators
- Progress Reports
- Recalls and Device Disposition
- Final Report
- Informed consent
- Significant Risk Device Determination
- Other Reports

#### Labeling (§812.5)

Under §812.5 an investigational device or its immediate package must bear a label with the following information:

- the name and place of business of the manufacturer, packer, or distributor
- the quantity of contents, if appropriate; and
- the statement, "CAUTION Investigational device. Limited by Federal (or United States) law to investigational use."

The label must also describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

The labeling of an investigational device must not contain any false or misleading statements nor imply that the device is safe or effective for the purposes being investigated.

The sponsor should provide detailed information on device labeling in the investigational protocol. This information may vary depending on the device and the nature of the study. Product labeling should be sufficient to ensure stability of the test article for the duration of the study (storage requirements, calibration procedures), bear sufficient directions for proper administration, and detail procedures to follow in the event of patient injury.

#### Promotion of Investigational Devices (§812.7)

Under §812.7, a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator cannot:

- Promote or test market an investigational device, until after FDA has approved the device for commercial distribution.
- Commercialize an investigational device by charging the subjects or investigators a higher price than that necessary to recover costs of manufacture, research, development, and handling.
- Unduly prolong an investigation. If data developed by the investigation indicate that premarket approval (PMA) cannot be justified, the sponsor must promptly terminate the investigation.
- Represent that an investigational device is safe or effective.

However, the sponsor may advertise for research subjects to solicit their participation in a study. Appropriate advertising methods include but are not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects.

Advertisements should be reviewed and approved by the IRB to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. No claims should be made, either explicitly or implicitly, that the device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other device.

FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process.

Additional guidance is available in the following guidance documents:

"Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators, 1998 - Recruiting for Study Subjects"

<http://www.fda.gov/oc/ohrt/irbs/toc4.html>

Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects

<http://www.fda.gov/cdrh/comp/2229.html>

<http://www.fda.gov/cdrh/comp/2229.pdf>

## **FAMILY PRACTICE RESIDENCY NEWS**



### **Masonic Medical Center Participates in National Research Study**

Postpartum depression is a common serious problem among women who have recently had babies. As many as 1 in 8 women will experience postpartum depression. Currently it is often under recognized and under treated.

The St. John Hospital – Masonic Medical Center is participating in a large national study of postpartum depression. This study is funded by the Agency for HealthCare Research and Quality, a federal research group similar to the National Institutes of Health and part of the Department of Health and Human Services. This 5-year study will include 30 family medicine practices around the United States who are members of the American Academy of Family Physicians National Research Network. Masonic Medical Center is the only Michigan site. The results from this study could change the medical care of all postpartum women in the US.

Women who receive their care at Masonic Medical Center and have had babies in the past 5 to 12 weeks will be asked to consider enrolling. The women will only be asked to complete 3 sets of questions that require about 15 minutes to complete at the enrollment visit and when their babies are 6 and 12 months old. Women will receive a small thank you gift for answering the questions.

This is an honor and a big responsibility for the participating practices and is an excellent example of research at the practice level. This is the type of research that can move new information into everyday practice.

The principal investigator for the Masonic site is Rachel O'Byrne, MD and the study coordinator is Patricia West, PhD, RN. You can contact them at 586-296-6213.

The study principal investigator is Barbara P. Yawn, MD MSc, Director of Research at the Olmsted Medical Center in Rochester, MN. She can be contacted at (507) 287-2758.

### **IRB Office Information**

#### **Hours of Operation:**

Monday through Friday, 8:00 AM – 4:30 PM

313-343-8314 – Mary Barnhart

313-343-3863 – Lee Booze-Battle

313-343-7813 – Denise Cunningham

Fax Number: (313) 343-7840

The IRB Office is your research resource center. Please do not hesitate to call us if you need information, or assistance.