

CLINICAL INVESTIGATION/ RESEARCH COMPLIANCE



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New Faculty Orientation

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OUTLINE



- Take home message
- Magnitude of clinical research at Hopkins
- The nuts and bolts of human research
subject protection
- Compliance challenges

Take home message



- PI has the responsibility for all aspects of study, including subject protection
- Need to understand your regulatory responsibilities as an investigator
- The IRB is here to help and protect human subjects (and indirectly the investigators)

Magnitude of Clinical Research at Johns Hopkins



- About 70% of funded research has IRB review or exemption, indicating involvement of human materials or subjects
- 2,100 active protocols at Johns Hopkins Medicine IRBs (not including exempt research)
- 651 protocol approved by WIRB for JHM

Code of Federal Regulations



- Divided into 50 titles, representing broad areas subject to Federal regulation.
- Each title divided into chapters, usually bearing the name of the issuing agency
 - TITLE 1 GENERAL PROVISIONS
PUBLIC WELFARE

Code of Federal Regulations



TITLE 45

PUBLIC WELFARE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PART 46

PROTECTION OF HUMAN SUBJECTS

TITLE 21 FOOD & DRUGS

PART 50

PROTECTION OF HUMAN SUBJECTS

Your Responsibility



- To understand and follow the federal regulations that relate to human subject research
- IRBs and investigators speak two different languages: regulation vs. science
- The IRB is your friend—it protects the participant, the institution, and YOU

Federal Oversight Actions



- Beginning 1999, DHHS Office of Human Research Protections oversight program began to sanction academic institutions
- Sanctions continue today
- 2005 – University of Washington Health Sciences shutdown and restrictions remain in place

Impact of OHRP/FDA Oversight at institutions



- Numbers of policies and procedures expanded
- Very complicated review process
- Detailed information required at submission to IRB

Accomplishment 2005

JHM Human Subjects Protection Program accredited by the Association for Accreditation of Human Research Programs, Inc.

Accredited for three years



IRB Review Agreements



- JHH and JH Bayview
- JHM and BSPH
- JHM IRB and Homewood IRB
- JHM and MedStar
- JHM and NCI Central IRBs
- JHM and NIDA & NIA
- JHM and Balto City Health Dept (2006)

Accomplishments



- Better communication with faculty and staff about rules and regulations
 - IRB website updated regularly – contains all policies and updated guidances
 - eIRB application system – allows PI to track review process
 - Compliance monitoring program – monitors available to assist in development of study SOPs or case report documentation

Compliance Challenge: FDA Inspections



JHM PIs cited for failure to:

- prepare or maintain adequate case histories with respect to observations and data pertinent to the investigation. (Lack of documentation)
- report promptly to the IRB all unanticipated problems involving risks to human subjects or others.
- conduct the clinical investigation in accord with the investigational plan. (Protocol deviations not requested or documented from sponsor/IRB, and inclusion/exclusion criteria not followed).
- obtain informed consent from subjects prior to their participation
- maintain records on the condition of each subject upon entering and during the course of the investigation
- maintain records of device receipt and repair.

Recent FDA citations: PI Responses



- “That is not my job.”
- “I have a great person who takes care of this for me.”
- “We did get informed consent.”
- “We always do a biopsy (insert favorite procedure) when a patient develops this problem.”
- “No one ever told me this before.”

Institutional Review Boards (IRBs)



IRB Does not = Institutional Approval

Who has final approval authority?



- If the IRB disapproves a project, no appeal to Institutional Administration is possible.
- If the IRB approves a project, Institutional Administration may determine the project may not be conducted at JHM.

Who is responsible for compliance?



- Faculty have the responsibility to understand policies and procedures and comply with them
- IRBs and Institutions have responsibility to comply with state laws and federal regulations

Who may obtain consent from potential research subjects?



- Principal investigator
- Co-investigators listed on the application
- Consent designees:
 - Approved by the IRB & trained by PI

Regulations followed by the IRBs and JHM Administration




- DHHS regulations
- FDA regulations

What is the definition of research?



- DHHS and FDA regulations contain different definitions:
 - DHHS: The systematic collection of data designed to contribute to generalizable knowledge
 - FDA: “Clinical investigation” - Any experiment that involves a test article and one or more human subjects that must be submitted to the FDA.

What are the three review categories?



- Exempt
- Expedited (which does not equate to a fast review) - project must be judged by the IRB to be minimal risk **and** on the list published in the federal regulations
- Convened full board review

JHM Limitations on Exempt Research Categories



- The research involves interaction or intervention (excluding chart and record reviews) with hospitalized patients, institutionalized patients, outpatient clinic patients, or employees of JHHS, JHUSOM, or JHUSON

Must one submit an application before starting research?



- Yes
- Exempt research designation must be granted by the IRB before beginning a project considered exempt under DHHS regulations

What is the policy on recruitment of employees and students?




- Recruitment is allowed but restrictions apply
- IRBs consider the issue on a case-by-case basis
- Investigators may not recruit or enroll individuals who report directly to them
- May not solicit directly on a personal basis
- Strict protections must be in place to protect confidentiality

JHM IRBs that review research proposals



- East Baltimore campus: JHM IRBs 1, 2, 3, & X
- Bayview campus: JHM IRB 5
- Western Institutional Review Board (WIRB) - Olympia, Washington

What are the presubmission requirements for internal JHM IRBs



- Completion of JHUSOM on-line human subjects, HIPAA, and CCOI training courses
- All PIs of IRB applications must complete the C.O.R.E. by January 1, 2007 – New faculty have one year to complete
- Department chair signatures, when applicable
- Cancer treatment trials - review by the Oncology Center CRO, regardless of department of origin
- CCOI, P&T, CRRC, and IBC reviews performed concurrently

What are the WIRB presubmission requirements?



- Completion of the required JHUSOM on-line training courses
- Department chair signatures (but not all departments)
- Cancer treatment trials - review by the Oncology Center CRO, regardless of dept of submission
- CCOI review
- Clinical Radiation Research Committee (CRRC)
- Pharmacy & Therapeutics Committee (P&T)
- Institutional Biosafety Comm.

Internal JHM IRB Review vs WIRB Review



- WIRB - Olympia, Washington
 - Under contract to review a subset of new commercially funded projects, but only until January 1, 2007

Where to submit materials?



- Internal JHM IRBs – submit using e-IRB system
- WIRB
 - WIRB JHU Liaison located in Reed Hall 130-B. The liaison coordinates all required pre-reviews and sends applications to Olympia. Electronic submission or direct submission to Olympia not allowed.

When to submit human subject research proposals?



- Federally funded:
 - Just in time - After Study Section review & receipt of notice of a fundable score
- Commercially funded:
 - in parallel with contract submission to Office of Research Administration
- EXCEPTIONS:
 - Foundations & select federal sponsors that require IRB approval before submission of a funding application.

When is it too late?



- Manuscript submitted to journal and journal requests IRB approval date
- Approval required between convened meeting dates

Is there a deadline for submission of applications for IRB review?



- No
- eIRB applications are assigned to an IRB as received and staff determine application is complete

Retroactive approvals - Not possible



"I am writing to request an expedited review of a study regarding... I must ask forgiveness for submitting this now but the study was performed in the spring before the heightened awareness of the need for IRB approval for this type of study."

How to submit for IRB review



- e-IRB submission
- Website address is: <https://e-irb.jhmi.edu>
- Training available through OHSR

How to obtain answers to IRB process questions



- Generic questions may be sent to the office e-mail site at: jhmirb@jhmi.edu
- Contact: IRB Associate Managers, Director or Human Subjects Specialists at 5-3008
- Contact the Assistant Dean for Human Subjects Research Compliance or a member of the regulatory team
- Contact the IRB Chairs/Co-Chairs
- Contract information is on the IRB web site. Website address is: <http://irb.jhmi.edu>

How to Contact eIRB

Contact Information

jhmeirb@jhmi.edu
or
410.955.3008

eIRB Account

- All users of eIRB must be assigned an account.
 - Johns Hopkins affiliated study team members: send your full name, JHED ID, and current email address to the eIRB Help Desk at jhmeirb@jhmi.edu.
 - Non-affiliated study team members: send the full name, affiliation, working email address, and working phone number to the eIRB Help Desk at jhmeirb@jhmi.edu.
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IRB/eIRB Internet Addresses

- IRB Website – <http://irb.jhmi.edu/>
- eIRB Home Page – <http://irb.jhmi.edu/eIRB/>
- eIRB Login – <http://e-irb.jhmi.edu>

How to slow down the IRB review process



- Send information to the office of a JHM IRB chair
- Unhelpful responses

Perception vs reality



Good research intentions

VS

Community attitudes

Good research intentions



- Improve health & health care delivery services
- Advance knowledge
- Engage patients in research process

Community perceptions about JHM and research



- Hopkins Historical perspective: bad feelings
 - Community residents are guinea pigs
 - Adverse publicity fuels distrust
 - The New York Times 2/27/2005 "Abuses Endangered Veterans in Cancer Drug Experiments"
 - U.S. Attorney's Office News Release 2/2005 "U.S. Settles Case of Gene Therapy Study that ended in Teen's Death"
 - KY Lexington Herald-Leader May 2005 "Shame on us for experimenting on defenseless children"

Summary



- Start completing the required training as soon as possible
- Go to the Johns Hopkins IRB website (irb.jhmi.edu) and familiarize yourself with how the information is organized
- Consult with the OHSR staff if you have any questions about whether you are actually engaged in research that might need review