New Study Submissions to the IRB

Tufts-New England Medical Center
Tufts University Health Sciences

IRB Education Series
2006

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We all need to speak the same language...
What is human subject research?

Definitions:

“Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.” (45 CFR 46.102(d))
Definitions continued:

“Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains (a) data through intervention or interaction with the individual, or (b) identifiable private information.” (45 CFR 46.102(f))
Definitions continued:

“Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.” (45 CFR 46.102(f))
Definitions continued:

“Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” (45 CFR 46.102(i))
Definitions continued:

“Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.” (45 CFR 46.102(c))
Is it human subject research?

Testing whether or not animals "kiss"
The IRB decides!

- Human research may involve *direct* interaction or intervention with a human subject (specimen collection, new drug/device investigation).

- Human research may also involve *indirect* activities (e.g., medical record review, specimen analysis, observation of behavior).

“There I was—asleep in this little cave here, when suddenly I was attacked by this hideous thing with five heads!”
Does Not Constitute Human Subjects Research

• 10 August 2004 Office for Human Research Protections (OHRP): “Guidance on Research Involving Coded Private Information or Biological Specimens”

• Certain coded or de-identified analyses

• Determination is not to be made by the Investigator

• Provide a detailed letter of activities to the IRB; a determination is returned to the Principal Investigator

• http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf (copy provided)
“What the? ... This is lemonade! Where’s my culture of amoebic dysentery?”
Human subject interventions!

On Oct. 23, 1927, three days after its invention, the first rubber band is tested.
Belmont Report

- **Respect for Persons**
  - Individuals should be treated as “autonomous agents”
  - Protect those with “diminished autonomy”

- **Beneficence**
  - Do not harm
  - Maximize possible benefits and minimize possible risks

- **Justice**
  - Treat subjects fairly
  - Distribute risks and benefits equally
Applying Ethical Principles

• **Respect for Persons**
  • Informed consent
  • Voluntary participation
  • Freedom to withdraw from a study without penalty
  • Protect privacy and confidentiality

• **Beneficence**
  • Risks are minimized
  • Benefits are maximized
  • Risks are justified by potential benefits
  • Conflicts of interest are managed or eliminated

• **Justice**
  • Protection of vulnerable populations
  • Those who may benefit are not excluded
Human Subject Research Review at Tufts University and Tufts-NEMC

- **Scientific review**
  - Not required by laws governing IRBs, but a logical necessity!
  - Historically and typically the responsibility of an IRB; increasing national trend to create scientific review committees.
  - Concentrate on scientific merit, study design, etc.
  - Institutional Scientific Review Committee (SRC)

- **Ethical review**
  - IRB
So, it’s human subject research...
c. **Full IRB**

- Form I
- Protocol
- ICF(s)
- Education requirements satisfied
- Advertisement(s)
- Questionnaire(s)
- Form II (drug/compound)
- Form III (device)
- Form IV (research radiation)
- Form VI (tissue-banking)
  - Optional TB ICF
- HIPAA documentation
FORM I

“Submit an original and TWO (2) copies of all documentation (protocol, ICF(s), Forms II, III, IV, VI, as applicable, and all necessary supporting documentation) to the IRB office, Box 817. Ensure that at least one set of copies is single-sided. This, and all forms submitted to the IRB office, should be typed.”

• Please DO NOT write “see protocol”

• http://www.tufts.edu/central/research/msword/IRB/Form%20I%20version%2012.0.doc
C. Enrollment Goals

Number of subjects needed to complete the study at this site:

Number of Tufts–NEMC/TUHS subjects needed to be consented\[^{1}\] to achieve research goals:

\[^{1}\] The IRB will count every subject who has signed an informed consent form (ICF) as enrolled, whether or not that subject completes the study. In determining the number of subjects to be enrolled the investigator should take into consideration the likely subject attrition rate. Screening to determine eligibility should not be counted in determining the number to be enrolled.
F. Mandatory Human Subject Protection Education

• The completion of the education modules is mandatory for each research team member.

• Research Team Members: Those who are responsible for the design, conduct, or reporting of this research, such as the Principal and Co-Investigators, Research Nurses and Coordinators, Project Managers, etc.

• Based on an individual’s role (e.g., Co-I, coordinator)

• Education requirements and modules are accessible at: http://www.tufts.edu/central/research/IRB.htm#req
Education Modules

• OHRP Investigator 101

• Barnes lectures
  • September lecture, Research Compliance: Basic Requirements and Accurate Record Keeping
  • October lecture, Recognizing and Reporting Adverse Events During a Clinical Trial
  • November lecture, The Impact of HIPAA on Clinical Research; OR lecture given by Steven D. Schwaitzberg, MD, A Practical Guide to HIPAA Issues for Research at T-NEMC and TUHS
  • December lecture, What Researchers need to Know about Investigational Drugs and Devices under FDA Regulations (INDs/IDEs)
You might be ready for this right about now…
FORM II

- For any drug, substance, or biologic *administered as part of the research*.
- Don’t leave ANY blank fields – “N/A”
- Need the:
  - Investigator’s Brochure
  - Package insert information – don’t send the actual insert!
  - Micromedex® printout
  - MSDS sheets
- [http://www.nemc.org/resadmin/Forms/HIRC/form2.doc](http://www.nemc.org/resadmin/Forms/HIRC/form2.doc)
FORM III

- For any device used as part of the research.
- Don’t leave ANY blank fields – “N/A”
- If there is FDA correspondence/documentation, submit a copy
- Need the:
  - Investigator’s Brochure
  - Operator's Manual
  - User’s Guide
FORM IV

- For any radiation exposure *as part of the research.*
  - X-ray
  - CT scan
  - Fluoroscopy
  - PET scan
  - Nuclear medicine scan
- MUST be signed by the Radiation Safety Officer
FORM VI

- For ANY sample banking
- *Please* read the banking policy/guidelines
  - [http://www.tufts.edu/central/research/msword/IRB/TissueBankingPolicy.doc](http://www.tufts.edu/central/research/msword/IRB/TissueBankingPolicy.doc)
- MUST be optional, unless the entire study is about storing the sample
- Need an optional tissue banking ICF
- Question 10
  - Attach a copy of the tissue bank's written policies...
  - If you need help with this, CALL THE IRB OFFICE! We have an informal, unofficial template!
- [http://www.tufts.edu/central/research/msword/IRB/FormVI.doc](http://www.tufts.edu/central/research/msword/IRB/FormVI.doc)
Basic Elements of a Protocol*

- Aims/objectives, hypothesis
- Research plan
  - experimental design
  - sample size, statistical analysis
  - subject population
    - inclusion, exclusion criteria
    - vulnerable populations
    - recruitment methodology
  - payment
  - risk:benefit assessment
  - methods/procedures
  - safety assessment and monitoring/adverse event reporting
  - consent
  - confidentiality measures

* Copy provided.
Some regulations seem like...

What we say to dogs
Okay, Ginger! I've had it!
You stay out of the garbage!
Understand, Ginger? Stay out of the garbage, or else!

What they hear
Blah blah GINGER blah
Blah blah blah blah blah
Blah blah GINGER blah
Blah blah blah blah...
The Health Insurance Portability and Accountability Act of 1996 (HIPAA)

- National standards to protect the privacy of protected health information (PHI) of individuals
- Detailed requirements for the use/disclosure of PHI
- HIPAA applies to health care providers and employer group health plans: covered entity
- Use/disclosure of PHI within a covered entity is permitted for treatment, payment, operations
- Effective 14 April 2003
HIPAA At Tufts-NEMC and Tufts University

- ALL of Tufts-NEMC
- TUSDM
- Student services on the Medford campus
- If you interact with a covered entity
Common HIPAA Terms

- **Covered entity**: Health care providers and employer group health plans (Tufts-NEMC)
- **Privacy Board**
- **PHI**
- **Treatment, payment, operations** ("T, P, O")
- **Use** (Exchange of PHI for T, P, O)
Common HIPAA Terms

- Disclosure (Exchange of PHI for non-T, P, O)
  - Research authorization
  - Waiver of research authorization
    - Accounting requirements
  - De-identified
  - Limited Data Set (data use agreement)
- Minimum necessary standard
Ways to satisfy HIPAA

- Data are de-identified
- Research Authorization Form (RAF)
- Waiver of Research Authorization
- Limited Data Set
- Decedent Records
- Review Preparatory to Research
Definition of de-identified

• None of the 18 HIPAA-defined identifiers may be contained in the information and no one accessing the information has actual knowledge that the information could be used – alone or in combination with other information – to identify any individual.

• http://www.tufts.edu/central/research/msword/HIPAAADeIdData031403.doc
18 Identifiers

1. Name
2. Geographic subdivisions smaller than a state (includes street address, city, county, precinct, zip code and equivalent geo codes – except the first three digits of zip codes unless the population density is under 20,000)
3. All date elements other than year related to an individual (includes birth date, admission date, discharge date, date of death)
4. Telephone numbers
5. Fax numbers
6. E-mail addresses
7. Social security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
18 Identifiers continued

11. Certificate/license numbers
12. Vehicle identifiers and serial numbers (includes license plate numbers)
13. Device identifiers and serial numbers
14. Web universal resource locators (i.e., URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers (includes finger and voice prints)
17. Full face photographs
18. Any other unique identifying number, characteristic or code and the covered entity does not have knowledge that information could be used alone or in combination to identify an individual.
RAF Elements

- Disclosures: Who, what, and where?
- RAF is to be signed at the same time as the ICF
- Follow the template: Tailor it!
- http://www.tufts.edu/central/research/msword/IRB/RAF11-05-03.DOC
What we say to dogs
Okay, Ginger! I've had it! You stay out of the garbage! Understand, Ginger? Stay out of the garbage, or else!

What they hear
Blah, blah, blah, GINGER, blah, blah, blah, blah, blah, GINGER, blah, blah, blah, blah, blah...

Do you see what I mean...?
Waiver of Research Authorization

- Only HIPAA document that is “approved.”
- General rule: if you will directly interact with the subject (written consent is obtained) a waiver is not appropriate.
- Termination date required
- Accounting requirements
  - 50 or fewer: Names!
  - 50 or more: Profile
- [http://www.tufts.edu/central/research/msword/WaiverWeb031303.DOC](http://www.tufts.edu/central/research/msword/WaiverWeb031303.DOC)
- [http://www.tufts.edu/central/research/msword/WaiverTrackingFormWeb031303.doc](http://www.tufts.edu/central/research/msword/WaiverTrackingFormWeb031303.doc)
Limited Data Set

• Permits dates and elements of geography
  • Zip code
  • Geocode
• Requires execution of a Data Use Agreement
  • http://www.tufts.edu/central/research/msword/RevisedDataUseAgreement.doc
Research on Decedents

- No privacy rights for the deceased
- May be asked to provide copy of the death certificate(s)
- May not use or request to use a decedent’s medical history to obtain information about another living person(s), such as a decedent’s living relative(s).

http://www.tufts.edu/central/research/msword/HIPAAADecedents031403.doc
Review Preparatory to Research

- *Preparation of research*
- http://www.tufts.edu/central/research/msword/ReviewPreparatory031403.doc
HIPAA Privacy Officers for Research

- Tufts-NEMC: Jeffrey Weinstein (617.636.2815)
- TUSDM:
- Tufts University:
For more information on HIPAA

- http://www.cms.hhs.gov/hipaa/
- http://www.hhs.gov/ocr/hipaa/
- http://aspe.hhs.gov/admnsimp/pl104191.htm
What *really* happens...
New studies:

- Logged into IRB database
- Assigned a unique IRB #
- Pre-reviewed for:
  - Completeness (including education requirements)
  - Accordance with federal and state regulations and institutional policies
Full IRB

Assigned to an IRB agenda
Assigned a Primary and Secondary Reviewer

Reviewed at a convened IRB meeting

IRB comment letter sent to PI within 2 weeks of the meeting
Principal Investigator responds to IRB review stipulations/requests for clarification:

Submission is reviewed by “expedited review procedures.”

If necessary, additional information, etc., is requested from the PI.

Approval letter is generated, signed, and sent to the PI. IRB members are notified.
Sometimes unanticipated things happen...
Common Problems

• Requested change/stipulation/clarification not addressed
• ICF too technical
• Requested documents not provided
• Forms not complete or inaccurate info on forms
• No HIPAA documentation
• Signature of PI not provided
• Education requirements are not satisfied
• Protocol is not sufficiently detailed
• All risks listed in the template (sponsor’s) ICF are not in the ICF submitted for review
Helpful Tips:

- Address all issues.
- PI signatures present as required.
- If applicable, provide a copy of the grant.
- Answer the questions on the forms.
- Provide requisite supporting documentation.
- ICF is written at an 8th grade reading level.
- Provide tracked and untracked copies of revised documents.
- Include a version date or number on all documents.
- Ensure education requirements are satisfied.
More Information

- **FDA**: http://www.fda.gov/default.htm
  - FAQ
    - http://www.fda.gov/oc/ohrt/irbs/faqs.html#IRBOrg
- **OHRP**: http://www.hhs.gov/ohrp/
  - ICF checklist
    - http://www.hhs.gov/ohrp/humansubjects/assurance/consentckls.htm
  - Code of Federal Regulations
    - http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
  - ICF Tips
    - http://www.hhs.gov/ohrp/humansubjects/guidance/ictips.htm
- **NIH**
  - Protocol Review Standards
  - http://www.irbforum.org/
IRB Leadership

- IRB Chair: David P. Chelmow, MD
- IRB Vice-Chairs: Edward L. Decker, PharmD
  Judith A. Frazier, RN, MEd
  Nicholas G. Guerina, MD, PhD
- IRB Members are from more than 17 divisions at Tufts-NEMC and Tufts University, including TUSM, TUSDM, HNRCA, etc., and community representatives who are not affiliated with either institution.
IRB office

• IRB Admin. and Operations Manager: Jennifer A. Graf
• IRB Coordinators: Julie Morelli Novak (IRB-RED)
  Elizabeth Kervis (IRB-BLUE)
• Continuing Review Coordinators: André Briola
  TBA
• Assistant IRB Coordinator: Kelly J. Shipman
• Administrative Assistant: Jennifer C. Coes
IRB Office
Box 817
(617) 636-7512

http://www.tufts.edu/central/research/IRB.htm