Submitting Requests for Exemption and Expedited Review to the IRB

Tufts-New England Medical Center
Tufts University Health Sciences

IRB Education Series
2006

Presentation may only be reused or reprinted with written permission from the Tufts-New England Medical Center/Tufts University IRB office.
What is Exempt/Expedited Review?
Research studies that qualify for Exempt/Expedited review are reviewed in the IRB office by either the IRB Chair, an IRB Vice-Chair, or an IRB member designated by the Chair.

Exempt/Expedited studies do not extend beyond minimal risk, as defined by federal regulations:

“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))
What is an Exemption?

- Human subjects research is granted exempt status when it falls into one of the six (6) categories of Exemption, as defined by DHHS (Department of Health and Human Services) in 45 CFR 46, also known as “the Common Rule”
- Exempted research is not subject to annual continuing review, but... if the scope of the research changes from the time of initial exemption granted, let the IRB know!
- No correspondence will be sent from the IRB office to “renew” an exemption
Research may not be exempted if...

...research involves prisoners, pregnant women, human fetuses and neonates, individuals with psychiatric, cognitive, or developmental disorders, or substance abusers

...research involves children (sometimes)

...research includes both exempt and non-exempt activities
How to Apply for an Exemption

- If you suspect your research may qualify for exempt status, please consider the following six (6) categories:

1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(45 CFR 46.101(b)(1))
2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation.

(45 CFR 46.101(b)(2))
3) Research involving use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph...(2), if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(45 CFR 46.101(b)(3))
4) Research involving the collection or study of existing data, documents, records, pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(45 CFR 46.101(b)(4))
5) Research and demonstration projects which are conducted by or subject to the approval of Department of Agency heads, and which are designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs;
(ii) procedures for obtaining benefits or services under those programs;
(iii) possible changes in or alternatives to those programs or procedures; or
(iv) possible changes in methods or levels of payment for benefits or services under those programs.

(45 CFR 46.101(b)(5))
6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a good is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S.D.A.

(45 CFR 46.101(b)(6))
The Exemption Form

- **Question # 1: Exemption claimed**
  - See IRB website for a list of exemption categories

- **Question # 2: Describe how research fits within exemption claimed**
  - Please be specific; do **not** simply state category

- **Question # 3: Describe the nature of subject involvement**
  - Is actual human subject interaction involved, or will data/samples be sent to you?
  - If de-identified data/samples to be sent, **please** include letter of approval from outside institution or letter that explains that identifying subject information will/will not be sent to you
Question # 4: Will subjects be recruited?
- Includes advertising and referrals
- If recruiting students, please include letter of support from applicable Dean
- Please include recruitment ads, e-mails, etc.

Question # 5: Does this research involve human embryonic stem cells?
- Research is exempt if only aspect of study is to receive de-identified cells

Question # 6: Attach a copy of protocol or research plan
- Please at least include: procedures involving subjects, confidentiality measures, and some background
Things to Remember

- If applicable, provide enough information for the IRB to make an assessment as to category of HIPAA (Health Insurance Portability & Accountability Act) satisfaction
  - Potential HIPAA categories for Exemptions: Limited Data Set, De-identified, Waiver of Research Authorization

- If study funded by a grant, please include copy of grant

- Education Requirements: Human Subjects Training
  - Investigators participating in exempt studies are NOT required to complete human subjects training for Tufts-NEMC/TUHS IRB office (but it is recommended!)
What is Expedited Research?

➢ Research may qualify for expedited review if it…
  ➢ Does not exceed minimal risk
  ➢ Falls into one of the 9 new study expedited categories of review

BUT…

➢ According to federal guidance, it is at the discretion of the Reviewer (IRB Chair/Vice-Chairs) to refer research to the full IRB for review even if the research qualifies for expedited review.
Criteria, as indicated by DHHS, for IRB Approval of Research (45 CFR 46.111)

- Procedures must be consistent with sound research design
- Risks of research must be reasonable in relation to the anticipated benefits
- Subject selection must be equitable
- Informed consent must be sought and documented unless a waiver of consent and/or documentation of consent has met waiver criteria (45 CFR 46.116(d) and 117(c))
As Defined by DHHS, Categories of Expedited Review for New Research Studies (45 CFR 46.110(a))

1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(45 CFR 46.110(a)(1))
2) **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:**

(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; **or**

(b) from other adults and children\(^2\), considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

(45 CFR 46.110(a)(2))
3) Prospective collection of biological specimens for research purposes by noninvasive means.

- Examples:
  - Hair and nail clippings in a nondisfiguring manner;
  - Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction
  - Permanent teeth if routine patient care indicates a need for extraction
  - Excreta and external secretions (including sweat)
  - Placenta removed at delivery

(45 CFR 46.110(a)(3))
4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

- Examples:
  - Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy
  - Weighing or testing sensory acuity
  - Magnetic resonance imaging

(45 CFR 46.110(a)(4))
5) *Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).* (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

(45 CFR 46.110(a)(5))
6) Collection of data from voice, video, digital, or image recordings made for research purposes.  
   (45 CFR 46.110(a)(6))

7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)
   (45 CFR 46.110(a)(7))
Categories of Expedited Continuing Review

8) Continuing review of research previously approved by the convened IRB as follows:
(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
(b) where no subjects have been enrolled and no additional risks have been identified; or
(c) where the remaining research activities are limited to data analysis. 45 CFR 46.110(a)(8)

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. 45 CFR 46.110(a)(9)
How to Prepare a New Expedited Submission for Review

- If you think your study does not exceed minimal risk, does not qualify for exemption, and does fit into one of the first seven (7) expedited categories, please submit:
  - Form I
  - Protocol document

And…
If applicable:

- Form II
  - Only commercially available drugs to be used as indicated
- Form III
  - Only commercially available devices to be used as indicated
- Form VI, Optional Tissue Banking ICF
  - Tissue Banking: Biological materials stored in central place for specified/unspecified future use
- Informed Consent Form(s)
- HIPAA Documentation
  - Possible HIPAA findings: Research Authorization Form, De-Identified, Limited Data Set, Waiver of Research Authorization
If applicable:

- Letters of Support
  - Recruiting Students? Letter from applicable dean
  - Recruiting Employees? Letter from head of applicable division/department

- Other institutions’ IRB approval letters
  - If study also taking place or has taken place at another institution

- Other documentation from outside institutions
  - If receiving de-identified samples/data
  - If Data Use Agreement has been executed at outside institution

- Advertisements/Recruitment materials

- Contact Letters to Subjects, Questionnaires, etc.
Form VII,
Medical Record/Chart Review/Clinical Database
Research Study

- May qualify for either Exempt or Expedited review
  - Important question: Will you be obtaining identifying information? If no identifiers involved, research is exempt
  - If retaining identifying information (name, medical record number, etc.) for any amount of time, provisions must be in place to maintain confidentiality of subject information
  - The IRB reviewer of the research (not office staff) makes the final determination as to whether research is exempt or expedited
Common Reasons Research Would NOT Qualify for Expedited Review

- Form IV, “Application for Investigation in Humans, Procedures Involving Radiation,” is submitted
  - According to federal regulations, research studies involving radiation must be reviewed by full IRB committee (45 CFR 46.110(a)(4))
- X-rays for research are involved
  - e.g., if you plan to take 10 clinical x-rays and 1 for research, research must be reviewed by full IRB committee (45 CFR 46.110(a)(4))
- Vulnerable populations are to be included in research (sometimes)
  - Research involves prisoners, children, pregnant women, human fetuses and neonates, individuals with psychiatric, cognitive, or developmental disorders, or substance abusers
Other Considerations

- **Education Requirements** (Expedited Research only)
  - If taken prior to March 2004, NIH or University of Rochester human subjects training certificates accepted
  - After March 2004, Investigator 101 human subjects training accepted [developed and copyrighted by Office of Human Research Protections/Public Responsibility in Medicine & Research (OHRP/PRIM&R)]
  - Barnes lectures
    - September, “Recordkeeping” and October, “Adverse Events” must be completed by all research team members whose responsibilities involve these areas
    - November, “HIPAA” must be completed by research team members who work in a covered entity or who use patient information from a covered entity
    - December, “IND/IDEs” must be completed by research team members involved in FDA-regulated research
Other Considerations

- In order to serve as Principal Investigator, one must have an appointment at Tufts University or Tufts-NEMC

- HIPAA (Health Insurance Portability & Accountability Act)
  - Only applies to covered entities (Tufts University School of Dental Medicine, Student Services on Medford Campus, & NEMC Hospital)
  - Only applies if Protected Health Information (PHI) is used, received, and/or disclosed
Other Considerations

- Principal Investigator must sign all study correspondence.

- Research Risks vs. Clinical Risks
  - e.g., an anonymous questionnaire is sent to all patients who received a kidney transplant at Tufts-NEMC during February 2006 – no identifiers are collected.
  - The clinical risks are not minimal, but the research does not involve activities that exceed minimal risk.
More Information

- OHRP: http://www.hhs.gov/ohrp
  - Expedited Review Categories (copy provided)
    - http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm
  - Exempt Review Categories (copy provided)
    - http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.101
  - Code of Federal Regulations
    - http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
IRB Leadership

- **IRB Chair:** David P. Chelmow, MD

- **IRB Vice-Chairs:**
  - Edward L. Decker, PhD
  - 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 A. Kervis (IRB-BLUE)

Continuing Review Coordinators: Andre Briola, MPH  
TBA

Assistant IRB Coordinator: Kelly J. Shipman

Administrative Assistant: Jennifer C. Coes
IRB Office
NEMC Box 817
(617) 636-7512

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

According to federal regulation 45 CFR 46.116(d):

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
(1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
Informed Consent

According to federal regulation 45 CFR 46.117(c):

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:
(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.