Protecting Human Subjects
In Social-Behavioral-Educational Research:

Working with the IRB

Lloyd Byrd, MS
Vice Chair, VCU IRB Panel B

Monika S. Markowitz, Ph.D.
Director, Office of Research Integrity and Ethics
Vice President’s Office for Research

Virginia Commonwealth University
November, 2011
History of Research Transgressions

- Medical war crimes
  - Nuremberg Code 1947
- Tuskegee Syphilis Study
- Jewish Chronic Disease Hospital
- Willowbrook
- Tea Room study
- Milgram’s deception study

Leads to research oversight by the federal government

- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1974
- Belmont Report 1978
Belmont Principles (1978)

The ethical foundation of federal regulations for research

- Respect for persons  →  informed consent
  privacy & confidentiality

- Beneficence  →  benefit/risk or burden assessment

- Justice  →  distribution of risk and benefit inclusion/exclusion
Federal Regulations and Policy Stemming from Belmont Principles

45 CFR 46 – DHHS Policy for Protection of Human Research Subjects - Subpart A

 Originally adopted January 13, 1981
 Revised June 18, 1991

 “The Common Rule” – adopted by 17 federal agencies, including FDA-regulated research in 1991
Protective Mechanisms Established by the Common Rule

- Institutional Assurances of compliance with regulations

- Review of research by an Institutional Review Board (IRB) or Ethics Committee

- Informed consent of subjects
Institutional Review Board (IRB)

- Established to provide ethical review of research
- Assure that federal regulations are followed
- Members include researchers, non-researchers and members of the local community
- 4 IRB panels at VCU
  - other IRBs of record: WIRB, CIRB
Activities needing IRB approval

☐ RESEARCH –
   A systematic investigation designed to develop or contribute to generalizable knowledge. 45 CFR 46.102(d)

☐ HUMAN SUBJECT –
   A living individual about whom an investigator…conducting research obtains
   1) data through intervention or interaction with the individual, or
   2) identifiable private information. 45 CFR 46.102(f)

☐ HIPAA – IRB approval or acknowledgement
   Research that involves the use of protected health information 45 CFR 160
Start with ‘research’

- ‘Systematic’: use of statistical analyses, scientific methods

  AND

- What about ‘generalizable’?

  Is the intent of this project to contribute to knowledge in the field or discipline?
  Are there hypotheses or research questions?
  Will analysis of data lead to generalizable claims, inform policy?

  Is there an intent to publish or present the project as research?

  If ‘yes’ >>>>>> the project is research
Generally Not ‘Generalizable’

- Quality improvement projects – designed with goal of improving institutional/organizational practice
- Quality assessment/assurance projects
- Case report or case series – if no systematic investigation, i.e. no statistical or data analysis; no outcome measures
- Public health practice – surveillance, program evaluation
- Education, in and of itself – intended to only provide a perspective or report on non-experimental methods
- Survey/questionnaire development – no data retained for research purposes
- Oral histories ~ controversial

i.e. Not defined as research needing IRB approval
What about ‘human subjects’?

- More straightforward
  - Interventions or interactions with persons
  - Access to identifiable personal data

- Secondary data sets without ANY identifiers or codes generally do not involve human subjects

Note difference between anonymous (absolutely no links) and de-identified (codes are retained)

- Suggestion: Refrain from the word ‘research’ if project not to be considered human subjects research under IRB purview
Guidance on “Activities needing IRB Approval”

- VCU IRB website -
  http://www.research.vcu.edu/irb/wpp/flash/wpp_guide.htm#II-2.htm

- Refer to this PowerPoint presentation for more information and examples:
  "How do I determine if my project is 'human subjects research?'"

- Guidance from the Office of Human Research Protections (OHRP):
  OHRP Human Subject Research Decision Charts
  OHRP Guidance Document: Engagement of Institutions in Research
  OHRP Guidance Document: Coded Private Information or Biological Specimens
  OHRP Quality Improvement Frequently Asked Questions
Social-behavioral-educational projects that will likely require IRB submission

- Interviews – quantitative or qualitative approaches
- Focus groups
- Pretest / intervention / post-test - (e.g., analysis of writing samples)
- Surveys - including Internet-based surveys
- Randomized intervention and control group
- Data analysis of primary or secondary data that contain identifiers or codes
- School-based research
Who makes the determination?

At VCU, the PI determines if a project is human subjects research (but the IRB determines if ‘exempt’ applies):

☐ IF...
- there is a question
- a project *might* become research
- there is *potential* to publish or present as research

☐ THEN...
- submit to the IRB (or at least ask!): *presumption of human subjects research for faculty and dissertation projects*
Assessing Protocol for ETHICAL Treatment of Research Subjects

- Respect for persons
  - Are individuals free to say no to all or some participation?
  - Is the consent form clear and understandable to this population? Is there an on-going consent process?
  - Does the consent process include all the necessary information about the study?

- Beneficence
  - What is the balance of risks/burdens to benefits?
  - Have burdens and risks been minimized?
  - Does the ‘science’ justify the potential risks or burdens?

- Justice
  - Are participants fairly selected for the study?
  - Who benefits from the study and who bears the risks/burdens?
Types of IRB Review

- Level of potential risk to subjects determines type of review

Exempt ---- Expedited ---- Full Board

Low risk  ---\Rightarrow--- High risk

- Click on “forms” on the IRB website to receive guidance on determining review type:
  www.research.vcu.edu/forms/vcuirb.htm
“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 examination or tests.

45 CFR 46.102(i)
Risk/Benefit Assessment

IRB considers the risk of criminal/civil liability, financial risk, employment risk, stigmatization, insurability, and embarrassment in deciding if risk is truly minimal.

IRB are also concerned about risk to community.
Privacy and Confidentiality

- “When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data”
  45 CFR 46.111(a)

- Breaches of privacy and/or confidentiality are the main risk in social-behavioral-educational research or research that is no greater than minimal risk
Populations specifically protected in federal regulations

- Pregnant women – Subpart B
- Prisoners – Subpart C
- Children – Subpart D

45 CFR 46.200-46.409
Other considerations may also contribute to ‘vulnerability’

- Language
- Culture
- Current Events or Incidents
- Age (elderly)
- Age (adolescents)
- Educationally, economically disadvantaged
- Transient or Permanent Cognitive Impairment
- Substance Use
- Health Status
- Students
- Employees
<table>
<thead>
<tr>
<th>IRB Review Type:</th>
<th>Exempt</th>
<th>Expedited</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimal risk</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>One IRB reviewer</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Does not include identifiers, with some exceptions</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Topic generally not sensitive</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Non-vulnerable populations, with some exceptions</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Minimal risk research</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>One IRB reviewer outside of convened meeting</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>May include identifiers (direct or indirect)</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Topics not sensitive OR may include some sensitive topics, but confidentiality securely protected</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Populations may include regulated vulnerable &amp; others with adequate protections</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>IRB Review Type:</td>
<td>Exempt &lt;&lt;&lt;</td>
<td>Expedited &gt;&gt;&gt;&gt;</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------</td>
<td>------------------</td>
</tr>
<tr>
<td>1. Exempt from formal informed consent requirement, but subjects deserve to know about the research</td>
<td>1. Consider a formal informed consent process OR justify a waiver of consent</td>
<td></td>
</tr>
<tr>
<td>2. Exempt from continuing IRB review</td>
<td>2. Requires IRB continuing review at least annually</td>
<td></td>
</tr>
<tr>
<td>3. Fits one of 6 exempt categories</td>
<td>4. Fits one of 7 expedited categories</td>
<td></td>
</tr>
</tbody>
</table>
Six ‘Exempt’ Categories

- 1. Typical educational practices
- 2. Educational tests, surveys, interviews, or observation of public behavior (cannot include minor subjects)
- 3. Research with elected public officials, appointed public officials, candidate for public office
- 4. Existing data, documents, pathological specimens, if publicly available or rendered unidentifiable
- 5. Evaluation of public benefit service programs
- 6. Taste and food quality evaluation and consumer acceptance studies

45 CFR 46.101(b)
Typical Problems with Exempt Submissions

- Interaction with subjects (Category 1)
- Children/minors in study (Category 2)
- Prospective data collection (Category 4)
- Identifiable data (Category 4)
- Missing documents – surveys, emails, information sheets, etc. (i.e., any communication or document sent or given to subjects)
- Missing notification about research, that it is voluntary, that skipping questions is allowed
- Exempt deals with agreement; consent is never implied
Informed Consent for Exempt Studies

- No formal consent document needed for ‘exempt’ research >> collection of identifiers restricted, none in #4
- But...subjects deserve to know they are participating in VCU research project, their participation is voluntary, and they do not need to answer every question
- Include these consent “elements” with a survey or questionnaire.
Categories for Expedited Review

☐ 1. Clinical studies: IND/IDE NOT required
☐ 2. Blood sample collection (routine methods – small amounts)
☐ 3. Prospective collection of biological samples— noninvasive means
☐ 4. Data collected though noninvasive means (routinely practiced in clinical settings)

☐ 5. Materials (data, documents, specimens etc.) have been collected or will be collected for non-research purposes
☐ 6. Collection of voice, video or digital data for research purposes
☐ 7. Individual or group behavior, surveys, interviews, oral histories

45 CFR 46.110(b) (Initial Review)
Full Board Review

- If the research does not meet criteria for exempt or expedited review, it is classified as a Full Board study (it likely is greater than minimal risk)

- Discussed and approved at convened monthly meeting of an IRB panel; modifications also require approval

- Requires ‘continuing review’ at least annually
Basic elements of informed consent

Expedited and Full Board Reviews

☐ Statement that the study involves research
☐ Reasonably foreseeable risks/discomforts
☐ Reasonably expected benefits
☐ Disclosure of appropriate alternative procedures
☐ Confidentiality of identifiable records
☐ For high risk, what happens if injured in research
☐ Contact about research, problems, or concerns
☐ Voluntary participation, may refuse participation, and discontinue participation at any time

45 CFR 46.116(a)
Waiver of some or all elements of informed consent

IRB may approve a waiver if:

☐ (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.

45 CFR 46.116(d)
Waiver of documentation

An IRB may waive documentation of consent 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.

45CFR46.117(c)
Conducting Research in the Schools—
Working with the Schools and the VCU IRB

- School constraints of timing, appropriateness of project, diversity of student/parent population.
- Federal regulations - FERPA, PPRA
- School-based research is often expedited review
- Informed consent - student’s assent and parental permission - must be considered
- May be waived by the IRB if school permits parental ‘opt out
- PowerPoint tutorial at: http://www.research.vcu.edu/irb/ResearchInSchools.ppt
IRB and HIPAA for Research

The IRB is also required to review research for compliance with HIPAA regulations.

- Protected Health Information (PHI) is individually identifiable health information that is obtained or used for treatment, payment or health care operations within the VCU Affiliated Covered Entity. PHI must be maintained and used in compliance with the Privacy Rule (45 CFR 160)

See: http://www.research.vcu.edu/irb/hipaa-guidance.htm
Private Health Information (PHI) Identifiers

- Health information is considered **individually identifiable** when it is associated with any of the following identifiers:

1. Names
2. Geographic subdivisions smaller than state, except 3 initial zip code digits
3. All elements of dates (except year) and **all ages over 89**
4. Telephone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social security numbers
8. Medical Record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers & serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographs and any comparable images
18. Any other unique identifying number, characteristic or code
Protective Mechanisms Established by the Privacy Rule

- The Privacy Rule was designed to protect private health information from incidental disclosures. The regulations specifically apply to health care providers, health plans, and health care clearinghouses that transmit health information electronically.

- The use of health information for research has been impacted by the Privacy Rule by limiting the ways in which researchers may obtain or use health information that is Protected Health Information (PHI).
HIPAA Research Pathways

- Individuals who have involvement in conducting treatment, payment, or health care operations have access to PHI for business purposes. Having the ability to create or use PHI through standard operations does **not** allow for the use of PHI for research purposes without following one of the allowable pathways.
  - De-Identified Data
  - Review Preparatory to Research*
  - Limited Data Set and Data Use Agreement
  - Research with Decedent PHI*
  - Waiver of Authorization
  - Signed HIPAA Authorization

*VCU PHI only
VCU and VCUHS are jointly covered by HIPAA regulations under what is termed the **VCU Affiliated Covered Entity (VCU ACE)**. All of the units included in the VCU ACE may have access to Protected Health Information through the conduct of standard business operations. The VCU ACE includes the following units:
- VCU Health System (VCUHS) and all satellite clinics
- Schools of Medicine, Pharmacy, Nursing and Dentistry
- VCU Employee Health
- VCU Telecommunications
- VCU Audit & General Management
- VCU Police Services
- VCU Office of General Counsel
- VCU Office of Research
More Information about HIPAA at VCU

- HIPAA for Research and the IRB: A New Partnership for Privacy Protections
  www.research.vcu.edu/.../20110325_ Stickler_HIPAA_IRB _What_you_need__to_know.pdf

- What is Covered By HIPAA at VCU
  www.research.vcu.edu/irb/Understanding+HIPAA+&+Research+at+VCU.pdf

- HIPAA Decision Tree
  www.research.vcu.edu/irb/Decision+Tree+1-++HIPAA+Determination.pdf

VCU IRB process

- Complete application (from website), get appropriate signatures and submit to IRB office (800 E. Leigh St.)
- Assigned to one of 4 VCU IRB panels (A,B,C,D)
- Assigned to a “primary reviewer” (& secondary reviewer for Full Board)
- IRB approval to begin research = formal written approval letter via email (pdf)
- Conduct of research reflects the protocol approved by the IRB
- Any changes to the protocol are prospectively reviewed and approved by the IRB
- Report unanticipated problems to the IRB – if relevant, use “Change in Research” form when reporting UP
What you can do to facilitate the IRB review process

- Complete CITI training – note a new Refresher requirement
- Assure a high quality submission
  - Submission forms - completed fully & accurately
  - Research synopsis - clear and complete
  - All supplementary materials included - (e.g., recruitment ads, letters/emails to participants, questionnaires/surveys, focus group questions, consent forms (if needed), etc.)
- Clearly describe other non-VCU entities who are ‘engaged’ in the research
- Respond promptly to IRB communications
When you prepare your IRB submission

- Find out who is on the IRB from your school/department and seek consultation
- Review the WPPs and IRB guidance on the VCU website
- Call the IRB office for consultation
- Good planning makes a good submission!
Criteria For IRB Approval

- Minimized risks
- Reasonable risk/benefit relationship
- Equitable subject selection
- Informed consent process
- Informed consent documentation
- Data monitored for safety, if appropriate
- Confidentiality/privacy maintained
- Vulnerable populations protected

45 CFR 46.111

Also: Compliance with HIPAA for research
Questions?

- Faculty PI
- IRB members in your department
- Office of Research Subjects Protection
  828-0868 – IRB submission and review process
- Office of Research Integrity and Ethics
  827-2157 – ethical issues, including design, informed consent process, recruitment, etc., research problems, conflicts of interest