Applying the Approval Criteria and Inner Workings of an IRB

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“Let us all remember that a slower progress in the conquest of disease would not threaten the society, grievous it is those who deplore that particular disease be not yet conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possible caused by too ruthless a pursuit of scientific progress, would make its most dazzling triumphs not worth having”

Jones H Philosophical reflections on experimenting with human subjects
History of Human Subject Protection

“What seem to be breaches of ethical conduct in experimentations by no means rare, but are almost one fears universal.. A particular pernicious myth is the one that ends justify the means....Whoever gives the investigator the god like right to choose martyrs'... ?”

Beecher NEJM 1966
Objectives

I. Differences between Practice & Research
II. IRB Review Categories
III. Functions of the IRB
IV. Identifying Risks
V. Subject Selection
VI. Informed Consent
VII. Privacy & Confidentiality
VIII. Vulnerable Populations
IX. Interesting case studies
HSRO
Work Load
Number of Submissions Processed by University of Miami - HSRO/IRB in FY 12

- New Study: 6032
- Amendment: 2645
- Continuing Report: 1456
- Final Report: 609
- Reportable Events: Notifications, Adverse Events, Deviations, Exceptions: 752

Total: 11,494
Number of Submissions Processed by University of Miami - HSRO/IRB in FY 12

Top Ten

- Medicine: 5377
- Pediatrics: 1328
- Ophthalmology: 529
- Surgery: 456
- Psychology: 406
- Psychiatry and Behavioral Sciences: 374
- Anesthesiology: 277
- Obstetrics and Gynecology: 251
- Dermatology and Cutaneous Surgery: 217
- Epidemiology and Public Health: 216
<table>
<thead>
<tr>
<th>Review Type</th>
<th>Total</th>
<th>Exempt Review</th>
<th>Expedited Review</th>
<th>Full Board Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2809</td>
<td>668</td>
<td>959</td>
<td>1182</td>
</tr>
<tr>
<td>Federally-funded</td>
<td></td>
<td>71</td>
<td>191</td>
<td>442</td>
</tr>
<tr>
<td>Foundation</td>
<td></td>
<td>12</td>
<td>45</td>
<td>58</td>
</tr>
<tr>
<td>Gift</td>
<td></td>
<td>5</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Industry-funded</td>
<td></td>
<td>7</td>
<td>47</td>
<td>316</td>
</tr>
<tr>
<td>No funding*</td>
<td></td>
<td>573</td>
<td>667</td>
<td>364</td>
</tr>
</tbody>
</table>
### Top 10 Percentage Breakdown by Department based on potential and actual HSRO/IRB Revenue stream for FY 12

<table>
<thead>
<tr>
<th>Department</th>
<th>Federally/State-funded</th>
<th>Industry-Funded</th>
<th>Unfunded*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine</td>
<td>5.97%</td>
<td>12.67%</td>
<td>7.53%</td>
<td>26.17%</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>6.96%</td>
<td>1.22%</td>
<td>3.27%</td>
<td>11.45%</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>1.08%</td>
<td>1.10%</td>
<td>5.07%</td>
<td>7.25%</td>
</tr>
<tr>
<td>Arts &amp; Sciences</td>
<td>2.92%</td>
<td>0.00%</td>
<td>3.61%</td>
<td>6.52%</td>
</tr>
<tr>
<td>Surgery</td>
<td>0.93%</td>
<td>1.00%</td>
<td>3.22%</td>
<td>5.14%</td>
</tr>
<tr>
<td>Neurology</td>
<td>1.44%</td>
<td>1.49%</td>
<td>1.42%</td>
<td>4.35%</td>
</tr>
<tr>
<td>Anesthesiology</td>
<td>0.15%</td>
<td>1.00%</td>
<td>2.13%</td>
<td>3.28%</td>
</tr>
<tr>
<td>Psychiatry and Behavioral</td>
<td>1.68%</td>
<td>0.36%</td>
<td>1.12%</td>
<td>3.15%</td>
</tr>
<tr>
<td>Sciences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiology and Public</td>
<td>2.37%</td>
<td>0.00%</td>
<td>0.69%</td>
<td>3.06%</td>
</tr>
<tr>
<td>Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological Surgery</td>
<td>0.71%</td>
<td>0.10%</td>
<td>2.12%</td>
<td>2.93%</td>
</tr>
<tr>
<td><strong>Total out of 100% for FY 12 of top 10</strong> =&gt;</td>
<td><strong>24.19%</strong></td>
<td><strong>18.92%</strong></td>
<td><strong>30.17%</strong></td>
<td><strong>73.29%</strong></td>
</tr>
</tbody>
</table>
HSRO Compensation to the Departments for the efforts of the IRB Members similar to work RVUs

<table>
<thead>
<tr>
<th>Department/School</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology</td>
<td>0.52%</td>
</tr>
<tr>
<td>Medicine</td>
<td>33.45%</td>
</tr>
<tr>
<td>Neurological Surgery</td>
<td>4.70%</td>
</tr>
<tr>
<td>Neurology</td>
<td>9.73%</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynecology</td>
<td>6.64%</td>
</tr>
<tr>
<td>Pathology</td>
<td>3.49%</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>7.85%</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>5.31%</td>
</tr>
<tr>
<td>Psychology</td>
<td>10.54%</td>
</tr>
<tr>
<td>Radiation Oncology</td>
<td>9.21%</td>
</tr>
<tr>
<td>Research Pharmacist</td>
<td>5.09%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.00%</strong></td>
</tr>
</tbody>
</table>
IRB Purview
45 CFR 46.111 and 21 CFR 56 Criteria

1. Research Relevance
2. Minimization of Risks
3. Reasonable Risk/Benefit Ratio
4. Equitable Selection of Subjects
5. Quality Informed Consent Forms
6. Adequate Safety Monitoring and Provisions for Privacy and Confidentiality
7. Protection of Vulnerable Subjects
8. Conflict of Interest
9. Investigator's qualifications
Basic differences between Practice & Research (Provider vs. Investigator)

• **Practice**: Actions taken by the clinician/practitioner/doctor intended to benefit the *patients and* have a reasonable expectation for success

• **Research**: Actions taken by the investigator/researcher intended to answer the research objectives (test a hypothesis) and advance knowledge (generalizability)
Basic differences between Practice & Research  
(Provider vs. Investigator)

- The “provider/investigator” – a difficult balance of role. If there is any element of research in an activity, that activity should undergo review
IRB Purview

**Research**: A systematic investigation including research development, testing, evaluation designed to develop or contribute to generalizable knowledge

**Human Subject**: A living individual about whom an investigator obtains data through intervention or interaction with the individual; OR Identifiable private information
IRB Review Categories

Full Board, Expedited or Exempt

- Exempt
  - Studies conducted in established educational settings on normal education practices
  - Research involving educational tests such as cognitive, aptitude etc. unless information is collected with identifiable information direct or indirect
  - The release of this information may lead to criminal or civil damages, financial losses etc.
IRB Review Categories

- Expedited review:
  - Can only be for approval but if disapproved has to come to full board
  - This has to be no more than minimal risk
  - The drug or device is already approved and does not need an exemption for IND/IDE
  - Collection of blood < 550 cc or less than 2 times a week. In children < 3ml/kg in 8 weeks
IRB Review Categories

- Expedited review:
  - Prospective collection of biological samples in a non invasive manner
  - Collection of data in a non invasive manner routinely involved in clinical practice
  - Research involving material (data, documents, records, specimens that are collected solely for non research purposes.)
“The Other Players”

- **OHRP/FDA**
- **Participation**
- **The Institution**
- **IRB**
- **The Sponsor**
- **Investigator**

The diagram illustrates the roles and stakeholders involved in research, with a focus on the Investigator's participation within the context of the Institution, OHRP/FDA, and the Sponsor.
Federal Wide Assurance

- Applies when an institution receives federal funding: OHRP grants the institution an “FWA”
- The “FWA” mandates the institution form an “ethics review board”
- More often this board is referred to as an “Institutional Review Board” – IRB
**The “Institutional Review Board”**

• “An independent body of medical, scientific, and non-scientific members designated by an institution to review and approve behavioral and bio-medical research involving human subjects…”

• The purpose of IRB review is so… “appropriate steps are taken to protect the rights and welfare of humans participating as subjects.”

• The regulations require…“diversity of members, including consideration of race, gender, cultural backgrounds and sensitivity to such issues as community attitudes.”
IRB Membership

- Must have at least 5 members
- Need diversity
- At least one member should be: Non-Scientist and non-institutional
- Special Population Experts should be included: Pediatrician, Prisoners, OBGYN
Functions of the IRB

- Verify integrity- (“experience”)
- Assess scientific merit
- Evaluate recruitment plan
- Determine risk/benefit ratio
- Review consent process and consent documents
- Examine plan for monitoring
  - Data integrity
  - Participant’s safety
- Appraise confidentiality
Functions of the IRB

- Risks to subjects are minimized
- Risks are reasonable in relationship to anticipated benefits
- Selection of subjects is equitable
- Informed consent is sought from each subject
- Informed consent is appropriately documented
- Data collection is monitored to ensure subject safety
- Privacy and confidentiality is protected
- Additional safeguards are included for vulnerable populations
Risks to the Subjects

- IRB should not rely solely on investigators to identify risks. No one can be objective about their own work.
- People underestimate the risks involved in things they are very familiar with and overestimate the benefit of things that are important to them.
- The risks involve the magnitude and the probability of harm.
Risks to the Subjects

- Identifying risk requires scientific expertise on the part of the IRB.
- When the IRB does not have necessary expertise it must use outside consultants.
- A IRB that reviews research without the necessary expertise is not in compliance with the regulations.
- The investigator has the right to have the research reviewed by someone with the appropriate expertise.
Subject Recruitment

- Justice requires equitable distribution of both the burdens and benefits of research
  - Individuals and groups that bear the burden should also share in the benefit
  - Individuals and groups that benefit from the research should share in the burden
- Selection of subjects should be justified by the science
- IRBs should not overprotect vulnerable populations so that they are excluded from participating in beneficial research
- If the study is funded by NIH, exclusions of women, minorities and children must be justified
Subject Recruitment

- Subject recruitment is part of the consent process
  - Information in recruitment should be consistent with the protocol
  - Recruitment should not be coercive or unduly enticing
  - Recruitment should clearly indicate that it is for research and not make unfounded claims

- IRBs must review recruitment procedures, including any ads
Informed Consent - Beyond the ICF

- Consent is a PROCESS not a single event or a form to be signed
- The basic components of informed consent include:
  - Full disclosure of the nature of the research and the subject’s participation
  - Adequate comprehension on the part of the subjects
  - The subject’s voluntary choice to participate
Procedures for Obtaining Consent

- Subject has the legal and mental capacity to give consent
- Sufficient time to decide
- Possibility of coercion or undue influence is minimized
- Language is understandable
- The ICF is the documentation
Data management

- All CRFs must be submitted
- Oversight of validity and integrity of data
- Some trials require a DSMB
  - Internal or external
  - Stopping rules
Privacy & Confidentiality

Privacy: a person’s interest to keep information from others
- Identify, Personal, Sensitive

Confidentiality:
- Our right that others will keep private information they learn about us secret
- Our expectation that others will share the private information about us only when they need to know
Risks from a breach in confidentiality

Psychological
Social
Economic
Legal
Vulnerable Populations

- 45 CFR 46
  - Subpart B - Pregnant Women
  - Subpart C - Prisoners
  - Subpart D - Children
Other Vulnerable Populations

- Cognitively impaired
- Mentally ill
- Economically disadvantaged
- Non-English speaking
- Severely ill
- Educationally disadvantaged
- Students
- Employees
An investigator is doing a study in Diabetes and he finds that the protocol is not ethical from his standpoint.

He started practicing standard of care because it is the correct thing to do for patient safety.

He is reported to the IRB.

Before that he alters the records as he is scared to the repercussions.
Interesting Case Studies

- An investigator is doing a study with a new device which he knows will save lives later.

- He has adverse events in the study and decides to blame it on the disease rather than the intervention as he is nervous that the IRB will stop the study.

- He is reported to the IRB.
Interesting Case Studies

- An investigator is doing a study with a new drug and trusts the Study coordinator.
- He has adverse events in the study and realizes that his study coordinator has not reported them to the IRB.
- The PI reports the study to the IRB on his own.
Interesting Case Studies

- An investigator is doing a study with a new drug in the ICU and trusts the coordinator.
- He has had over 100 deviations in the study and does not realize that his study coordinator has not reported them to the IRB but he was informed.
- The study is also monitored by a Pharma company and does not do a proper job. IRB picks this up on an routine audit.
## Comparison of IRB 7.2 and eProst

<table>
<thead>
<tr>
<th></th>
<th>eProst</th>
<th>IRB 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Length of SmartForms</td>
<td>70 pages for new study</td>
<td>10 pages for new study</td>
</tr>
<tr>
<td>Study Team Members</td>
<td>Must be added individually to each new study</td>
<td>PI has the option of setting up a “standard” study team so study team members will be pre-populated in each new study (with the option to remove individuals as needed)</td>
</tr>
<tr>
<td>Protocol form vs. sponsor protocol</td>
<td>Must copy/paste text from sponsor protocol into eProst forms</td>
<td>Simply upload the sponsor protocol – IRB 7 is more document-centric</td>
</tr>
<tr>
<td>Continuing Reports/Amendments</td>
<td>Must be submitted separately</td>
<td>Can be submitted as a single submission</td>
</tr>
<tr>
<td>Department-level Review</td>
<td>Mandatory and must be completed before submission can move forward to</td>
<td>Optional and can be completed in parallel with ancillary and HSRO/IRB reviews</td>
</tr>
<tr>
<td></td>
<td>Ancillary review</td>
<td></td>
</tr>
<tr>
<td>Ancillary Committee Reviews</td>
<td>Must be completed after department review and before HSRO/IRB review</td>
<td>Can be completed in parallel with ancillary and HSRO/IRB review</td>
</tr>
<tr>
<td>Parallel Amendments</td>
<td>Not possible in eProst; limited to one amendment at a time</td>
<td>May have two Amendments open at a time; one for study team changes, the other for changes to any other aspect of the study</td>
</tr>
<tr>
<td>Reportable Events</td>
<td>A reportable event associated with multiple studies must be created for</td>
<td>A single reportable event can be tied to multiple studies</td>
</tr>
<tr>
<td></td>
<td>each study individually</td>
<td></td>
</tr>
</tbody>
</table>
IRB 7.2 Basic Work Flow

For New Study submissions

Study Team

- PI submits
- Study team makes changes, if requested

HSRO/IRB

- HSRO requests changes
- Study team submits changes
- HSRO Pre-Review
- IRB Review (Committee Review or Non-Committee Review; can send back to study team for changes)
- HSRO Post-Review (send determination letter or send back to study team for changes)

Ancillaries/Dept Approvers

- Ancillary Committee Review
- Department Review
Study Process Overview
Modification / CR Process Overview

The process flows as follows:

1. **Pre-Submission**
   - IRB Pre-Review
   - Clarifications Requested

2. **IRB Review**
   - Clarifications Requested
   - Modifications Required

3. **Post-Review**
   - Review Complete

   *This transition can change the content or state of the parent study.*

**Exploded View of IRB Review**

- **Committee Review?**
  - Yes: Non-Committee Review
    - Clarifications Requested
  - No: Go to Post-Review above

Legend:
- Roles responsible: PI and study team, Reviewers, IRB staff

**UHealth**

**University of Miami Health System**

**Miller School of Medicine**
COI Management with IRB 7

• COI disclosure will take place exclusively in the Disclosure Profile System (DPS)
• HSRO will have access to the DPS back end
  – Compliance Assessment Management System-CAMS
• ICOIC (Institution) will review only PHS funded studies that meet the reporting threshold
• HSCOIC (HSRO) will review industry supported trials, as well as institutional COIs, IP etc.
  – will alert ICOIC when their review is required
Grants and Contracts

• Standard language for contracts
• CRIS office will incorporate template language consistently, moving forward
• CRIS will alert as to any changes required to ICF language upon contract execution
• The current plan, which depends on the capabilities of the University's new document management system, is to link to the executed contract pertaining to the study. If we have such linkage the executed contracts will not be uploaded in IRB 7
Velos

- This is the clinical trials tracking system not just a billing compliance system
- We will include this in our IRB 7.2 training to make sure that all study teams enroll their subjects when applicable. It will be mandated by the IRB
- We will force study teams to report to us from the Velos on subject enrollment at the time of continuing review, failure to do so will have consequences
AAHRPP

• Association for the Accreditation of Human Research Protection Programs (AAHRPP)
• An independent, non-profit accrediting body
• Voluntary, peer-driven, educational model
Customer Satisfaction Initiative

- Feedback mechanism pre / post IRB 7
- Survey runs from 7.22.13 – 8/9/13
- Plan to have computer based chat line for PI’s
  – To address issues ‘real time’
- Partnering with CTSI and RSQA
Customer Satisfaction Initiative

Compare your level of satisfaction with the HSRO/IRB within the past 6 months to that of a year ago

- Significantly better: 16%
- Better: 30%
- Same: 41%
- Worse: 8%
- Significantly worse: 5%

6% of the total eProst users have completed the survey.
What is your level of satisfaction with the online protocol submission system (eProst)?

- Very satisfied: 23%
- Somewhat satisfied: 26%
- Neutral: 23%
- Somewhat Dissatisfied: 17%
- Very Dissatisfied: 11%

6% of the total eProst users have completed the survey.
Thank you

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Faculty Member AETC Florida
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