Applying the Approval Criteria and Inner Workings of an IRB

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Philip J. Candilis, Charles W. Lidz, Paul S. Appelbaum, Robert M. Arnold, William Gardner, Suzanne Garverich, Albert J. Grudzinskas Jr, and Lorna J. Simon. The Silent Majority: Who Speaks at IRB Meetings? IRB. 2012 ; 34(4): 15–20.

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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

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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

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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

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HSRO
Work Load

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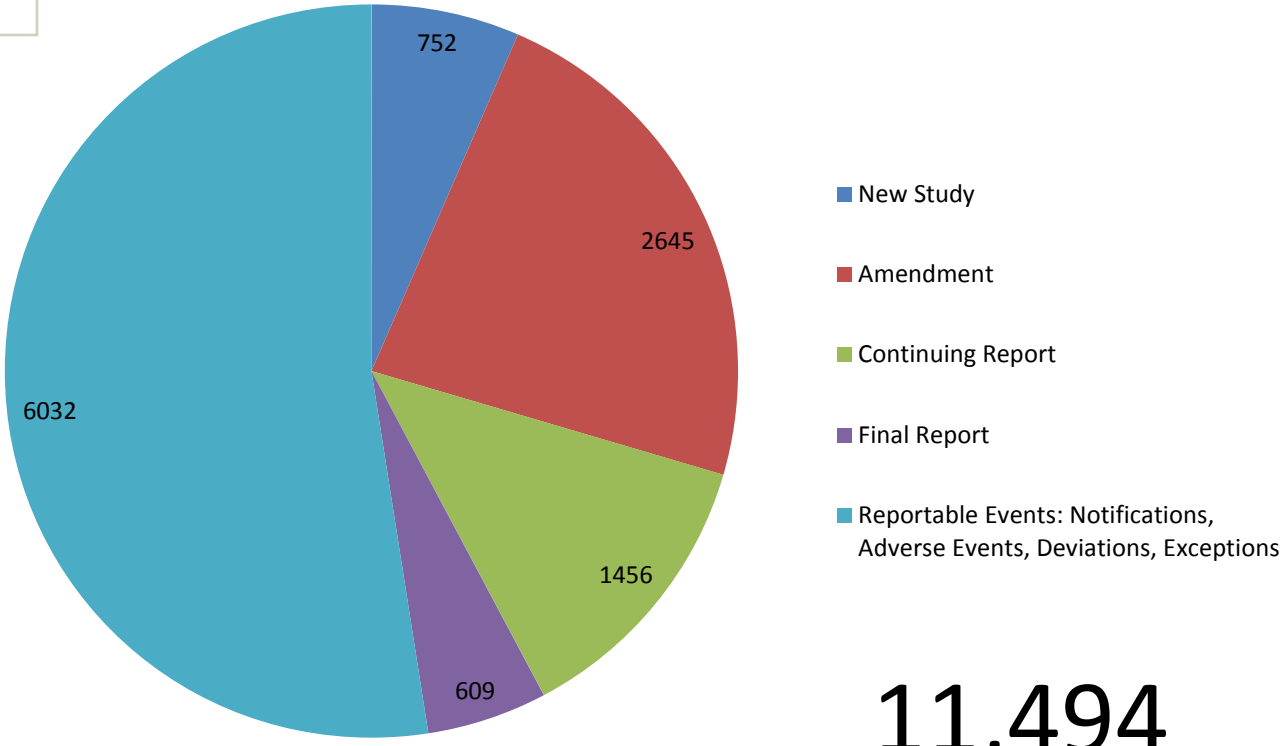
Number of Submissions Processed by University of Miami - HSRO/IRB in FY 12



11,494

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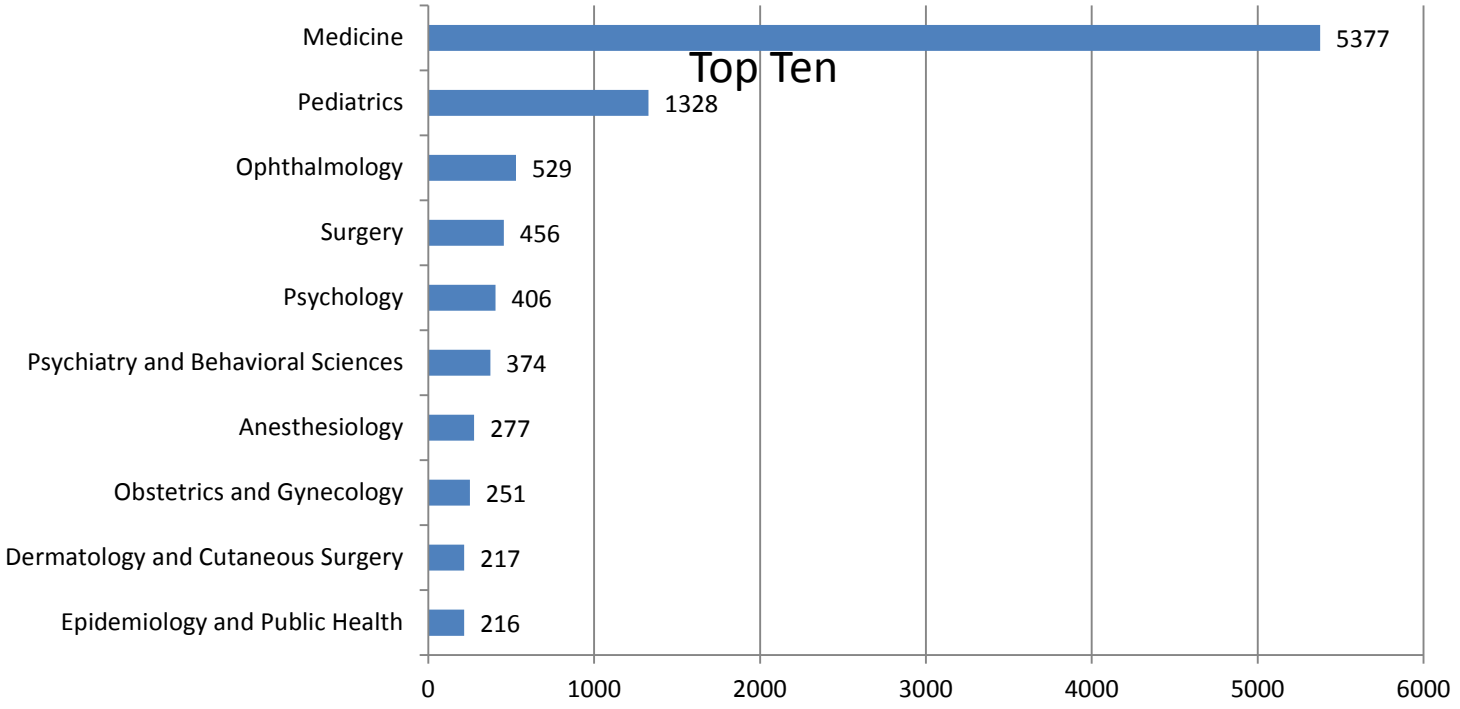

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HSRO-Total Number of Active Studies, by Review Type and Funding As of June 1st, 2012

	Total
Exempt Review	**668**
Federally-funded	71
Foundation	12
Gift	5
Industry-funded	7
No funding*	573
Expedited Review	**959**
Federally-funded	191
Foundation	45
Gift	9
Industry-funded	47
No funding*	667
Full Board Review	**1182**
Federally-funded	442
Foundation	58
Gift	2
Industry-funded	316
No funding*	364
Total	**2809**

Top 10 Percentage Breakdown by Department based on potential and actual HSRO/IRB Revenue stream for FY 12

Department	Federally/State -funded	Industry-Funded	Unfunded*	Total
Medicine	5.97%	12.67%	7.53%	26.17%
Pediatrics	6.96%	1.22%	3.27%	11.45%
Ophthalmology	1.08%	1.10%	5.07%	7.25%
Arts & Sciences	2.92%	0.00%	3.61%	6.52%
Surgery	0.93%	1.00%	3.22%	5.14%
Neurology	1.44%	1.49%	1.42%	4.35%
Anesthesiology	0.15%	1.00%	2.13%	3.28%
Psychiatry and Behavioral Sciences	1.68%	0.36%	1.12%	3.15%
Epidemiology and Public Health	2.37%	0.00%	0.69%	3.06%
Neurological Surgery	0.71%	0.10%	2.12%	2.93%
Total out of 100% for FY 12 of top 10 =>	**24.19%**	**18.92%**	**30.17%**	**73.29%**

HSRO Compensation to the Departments for the efforts of the IRB Members similar to work RVUs

Department/School	Percent
Anesthesiology	0.52%
Medicine	33.45%
Neurological Surgery	4.70%
Neurology	9.73%
Obstetrics & Gynecology	6.64%
Pathology	3.49%
Pediatrics	7.85%
Psychiatry	5.31%
Psychology	10.54%
Radiation Oncology	9.21%
Research Pharmacist	5.09%
Total	**100.00%**

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IRB Purview

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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.

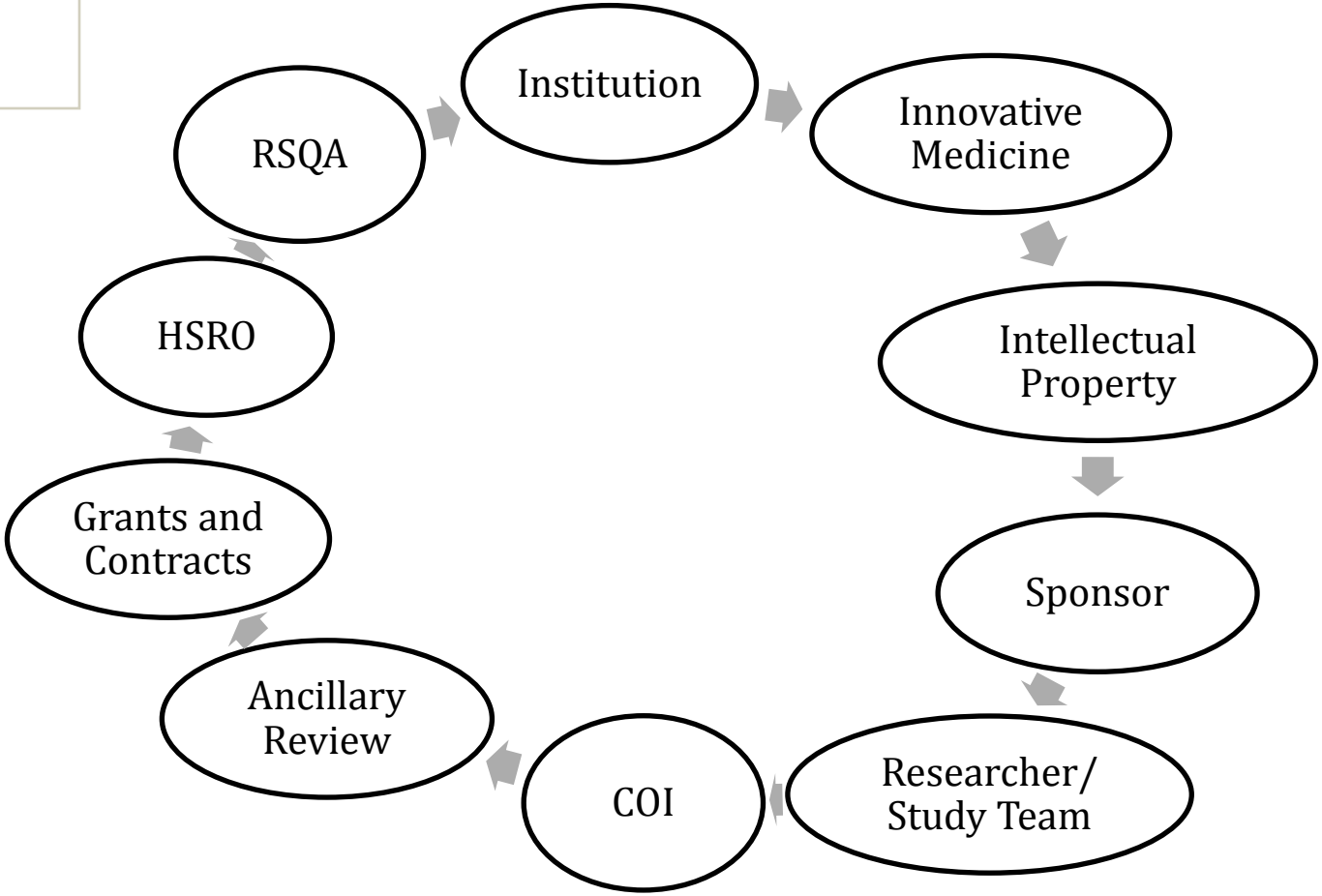
IRB Review Categories

- Expedited review:
  - Can only be for approval but if disapproved has to come to full board
  - This has to be no more that minimal risk
  - The drug or device is already approved and does not need a 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.

Stake Holders in HRPP



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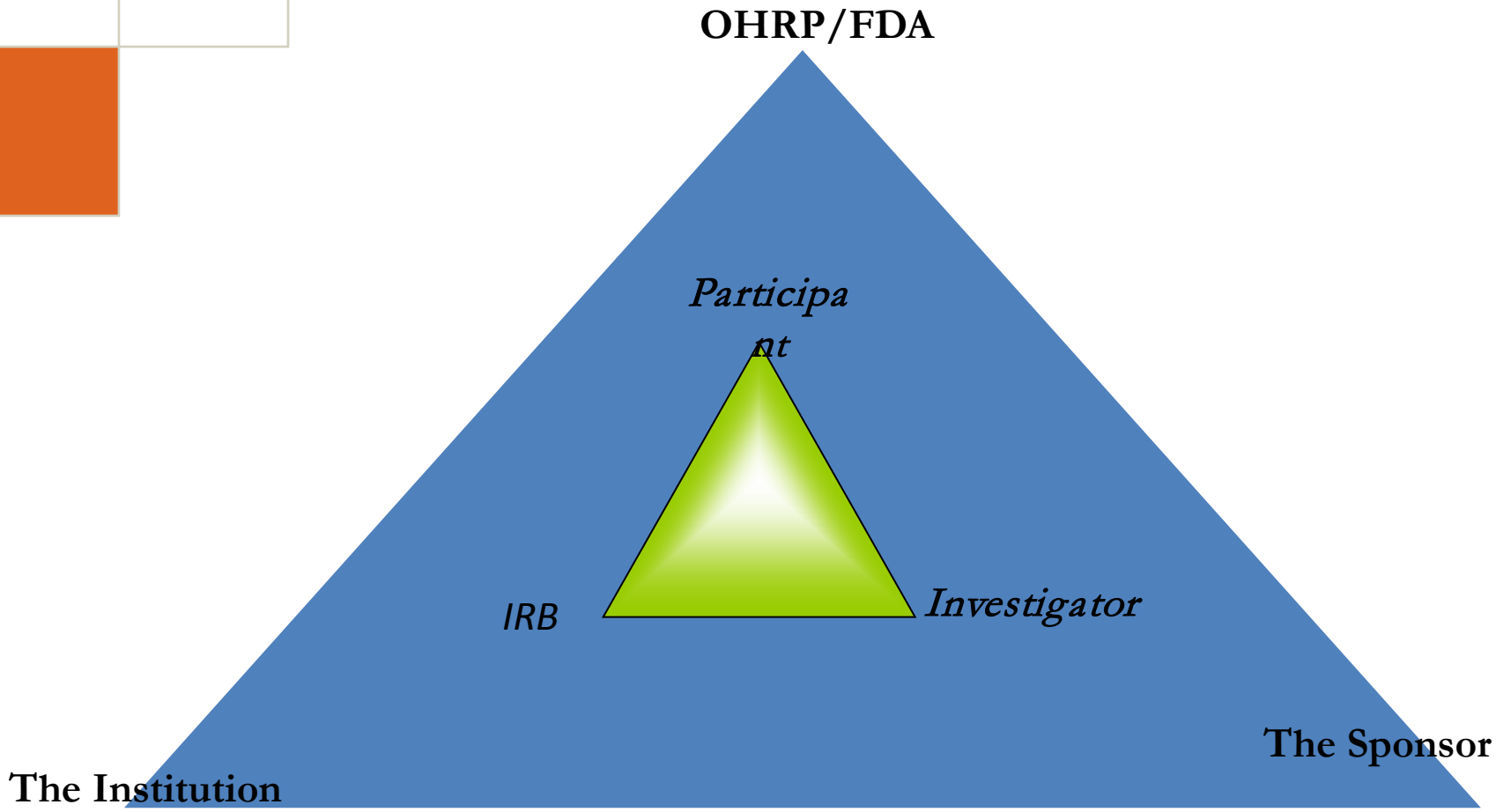
“The Other Players”



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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."

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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

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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 involves 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

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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

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Risks from a breach in confidentiality

Psychological

Social

Economic

Legal

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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

Interesting Case Studies

- 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 that will save life's later
- He has a 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 a 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

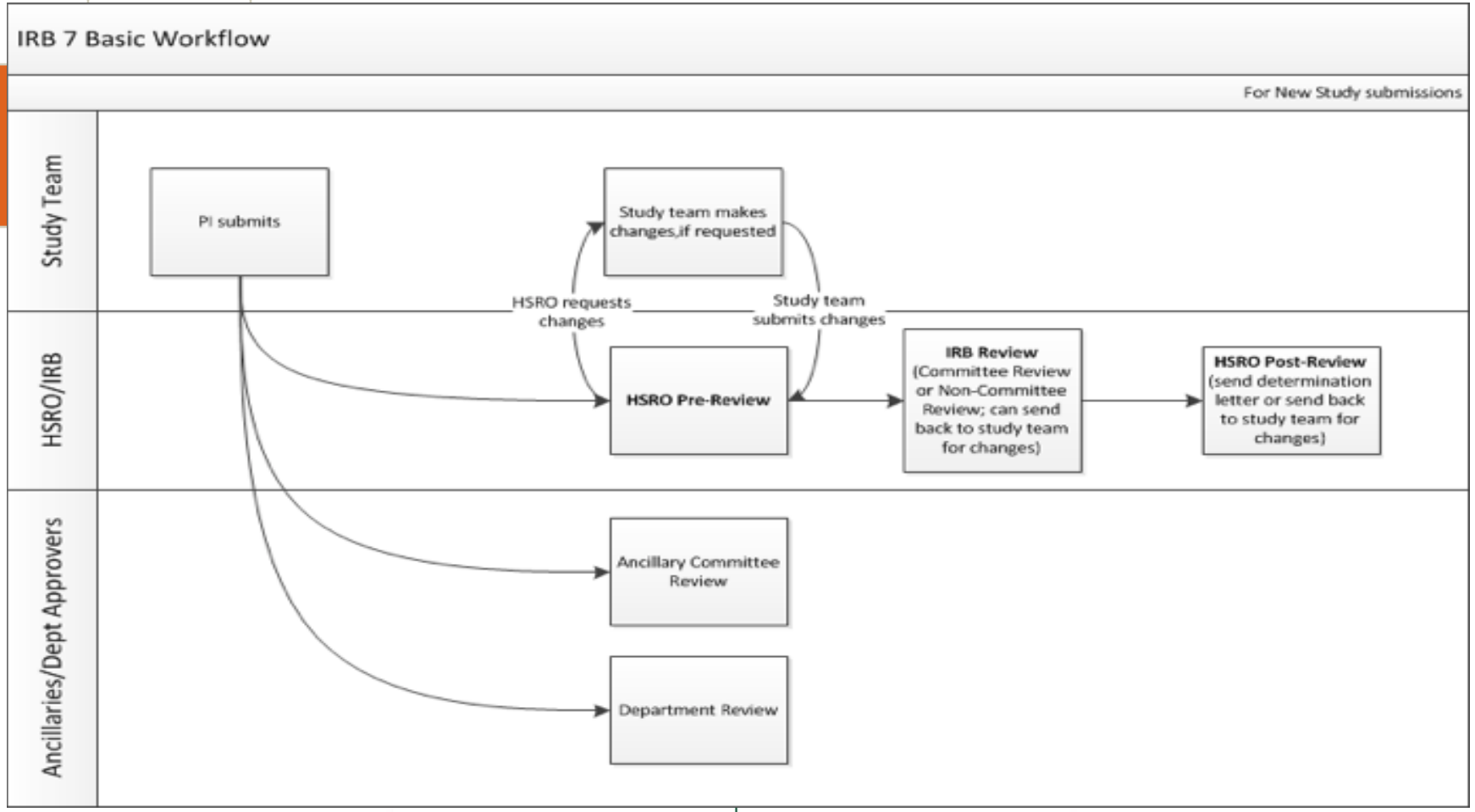
Interesting Case Studies

- 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

	eProst	IRB 7
Maximum Length of SmartForms	70 pages for new study	10 pages for new study
Study Team Members	Must be added individually to each new study	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)
Protocol form vs. sponsor protocol	Must copy/paste text from sponsor protocol into eProst forms	Simply upload the sponsor protocol – IRB 7 is more document-centric
Continuing Reports/Amendments	Must be submitted separately	Can be submitted as a single submission
Department-level Review	Mandatory and must be completed before submission can move forward to Ancillary review	Optional and can be completed in parallel with ancillary and HSRO/IRB reviews
Ancillary Committee Reviews	Must be completed after department review and before HSRO/IRB review	Can be completed in parallel with ancillary and HSRO/IRB review
Parallel Amendments	Not possible in eProst; limited to one amendment at a time	May have two Amendments open at a time; one for study team changes, the other for changes to any other aspect of the study
Reportable Events	A reportable event associated with multiple studies must be created for each study individually	A single reportable event can be tied to multiple studies

IRB 7.2 Basic Work Flow



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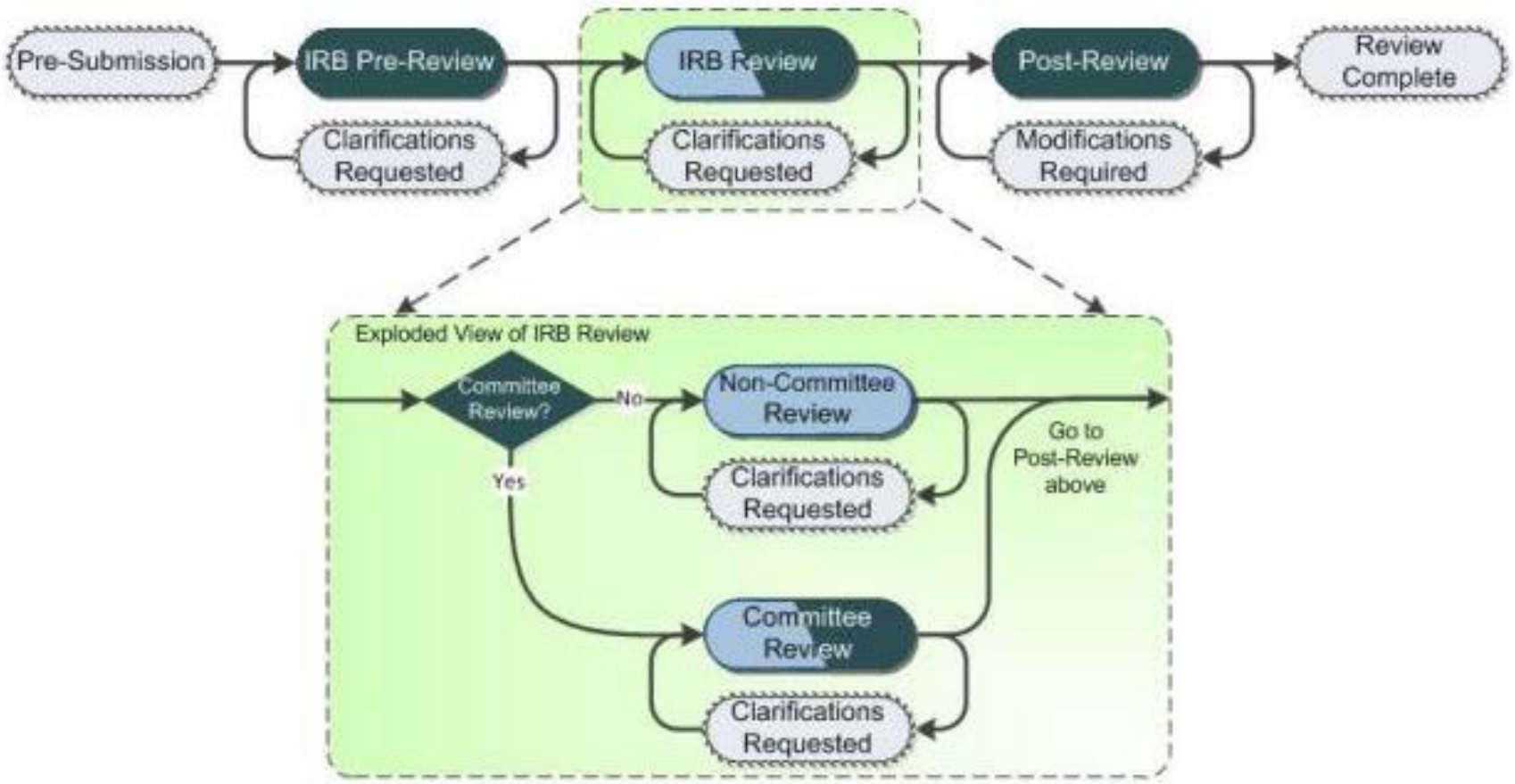
Study Process Overview



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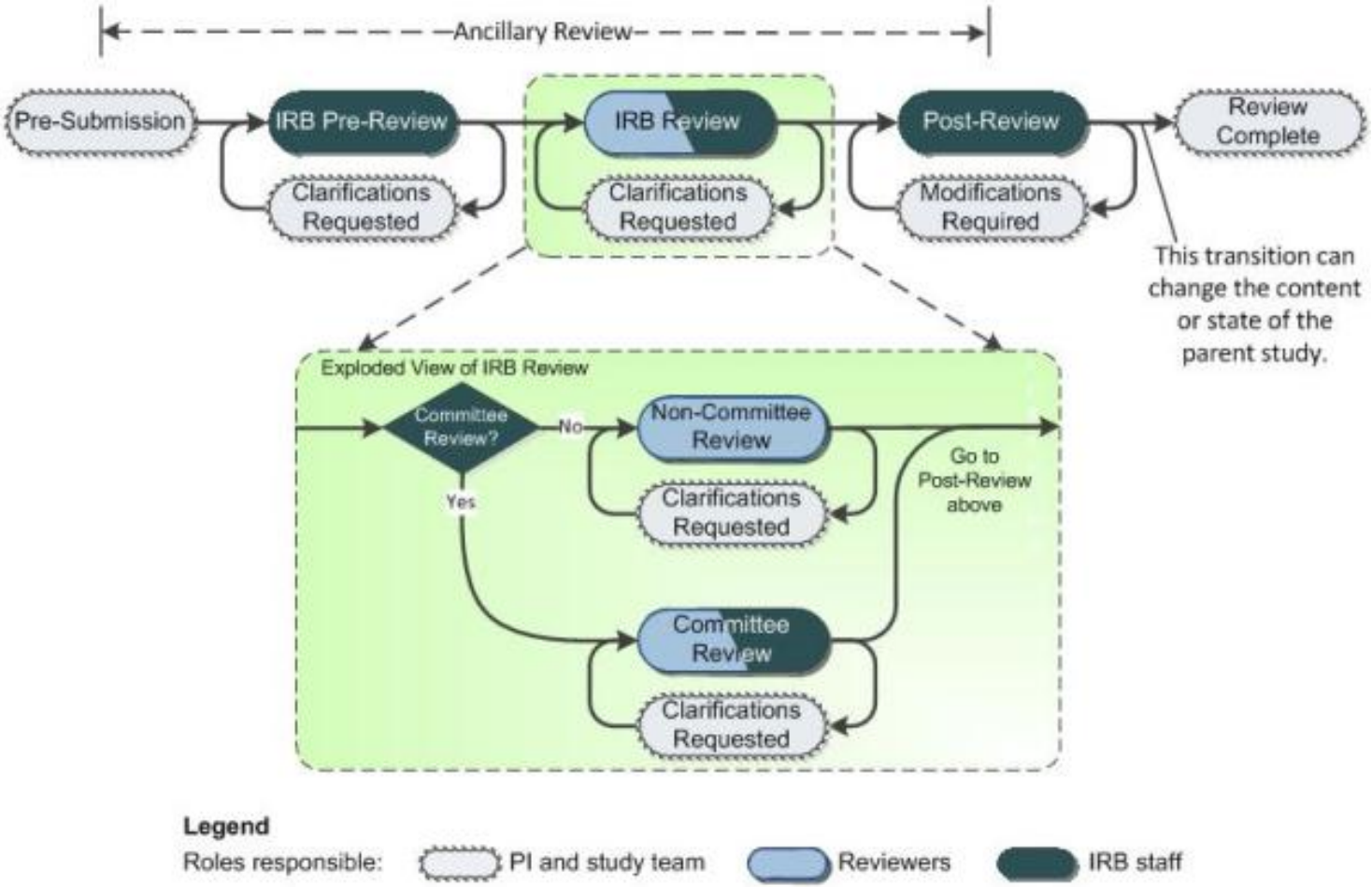
Modification / CR Process Overview



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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

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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

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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

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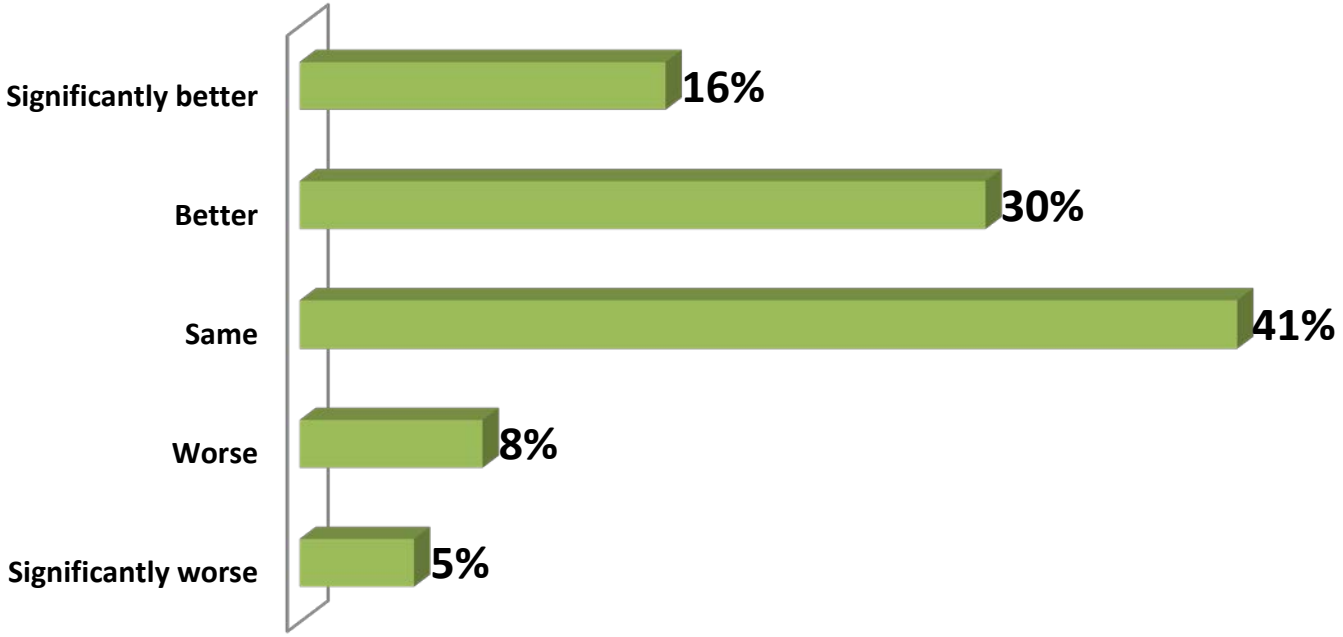
Customer Satisfaction Initiative

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



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

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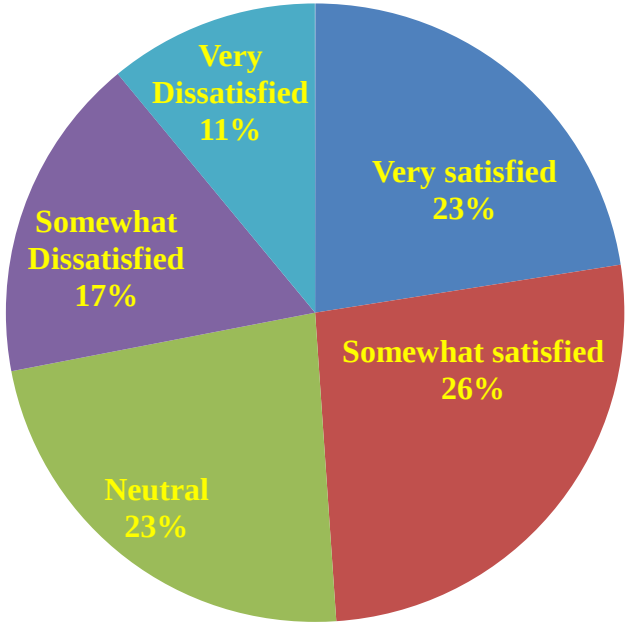
What is your level of satisfaction with the online protocol submission system (eProst)?



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