New IRB Member Orientation

Part VI: IRB Operations

Primary Role of Any IRB

To protect the rights and welfare of human research subjects.

IRB Member Responsibilities

1. Recuse yourself if you have a conflict of interest
2. Be prepared
3. Make an organized presentation to the group
4. Enter your stipulations, if any, in the appropriate section
5. Allow for other perspectives and viewpoints
6. Maintain focus
7. Seek consultation, when needed
8. Honor the hair on the back of your neck
9. Don’t take yourself too seriously
10. Understand IRB’s power – IRB is a partner in the research process and we want to propose solutions when possible!

IRB Membership - OHRE SOP 4.0

- Key Role:
  - Protect the Rights and Welfare of Human Subjects
  - Ensure that the study meets the federally mandated criteria for approval
- IRB members are appointed for a 3-year term which may be renewed
- IRB member performance is reviewed annually
- IRB member actions are covered by the UNC-CH liability coverage

Conflict of Interest and the IRB Member

OHRE SOP 4.0

- No IRB member may vote for any study in which the member has a conflict of interest (COI)

- COI includes if the IRB member or anyone in the member's immediate family:
  - Serves as an investigator
  - Has significant equity, stock options, or other financial interest related to the research ≥$5000
  - Receives compensation related to the research
  - Has a proprietary interest related to the research
  - Has any board or executive relationship related to the research

- Upon receiving the agenda, notify the Chair if you will need to recuse yourself for any submission since this could affect quorum

- At the beginning of each IRB meeting, members are reminded to recuse themselves for the discussion of any submission with which they have a COI

Confidentiality and the IRB Member

OHRE SOP 4.0

- Keep confidential the proceedings of an IRB meeting
- IRB minutes may be subject to public disclosure laws
- As a general rule, we do not disclose to investigators the identity of primary or secondary reviewers
- However, an IRB member may contact a PI to ask questions or seek clarification about the submission
- IRB members sign a confidentiality agreement
- All guests & consultants at IRB meetings sign a confidentiality agreement

IRB Meeting Quorum - OHRE SOP 11.0

- Regulations require that a majority of voting IRB members (quorum) be present
- A quorum must include one member who is a non-scientist [45 CFR 46.108(b)]
- Inform the IRB Office as far in advance as possible if you are unable to attend a meeting or if there is a conflict of interest for a specific submission

Conduct of the IRB meeting

OHRE SOP 11.0

Role of the Chair

- Calls the meeting to order
- Calls for motions and votes
- Ensures that all members have an opportunity to express their opinions

Attendance by investigators

- May be invited to attend at the time their study is discussed
- Should not be present for the final deliberation and vote

Attendance by guests & consultants

- May be permitted to attend, for example, to learn about the IRB process
- Sign the confidentiality agreement prior to the start of the meeting
- May observe only and may not participate in discussions

IRB Meeting Agenda and Review Materials

OHRE SOP 11.0

- Received by IRB Members ≥ 1 week in advance
- Agenda includes the following submissions:
  - Reconsiderations of previously deferred submissions
  - Initial submissions
  - Changes to approved studies (“modifications”)
  - Continuing review of ongoing studies ("renewals")
- Review Materials will also include:
  - Minutes of the last convened meeting (for corrections only, no action required)
  - List of approved expedited studies (informational)

IRB Meeting Quorum Requirements

- Must have more than ½ of the rostered members present throughout the entire meeting.
- Must always have at least 1 non-scientist present throughout the entire meeting.
- Be sure IRB Coordinator knows you are leaving the room BEFORE leaving.

Voting

- Don’t vote if you have a Conflict of Interest:
  - Your study
  - Your spouse’s study
  - Your student’s study
  - You have a conflict with the study sponsor

VotingIs this UNC Practice?

- Only total number of votes recorded
- Do not record individual votes
- Abstain from voting if you miss part of the discussion

Review by convened IRB

OHRE SOP 11.0

- Studies involving greater than minimal risk, including:
  - Clinical trials with experimental drugs or devices
  - Behavioral interventions with vulnerable populations
  - Some studies involving sensitive information

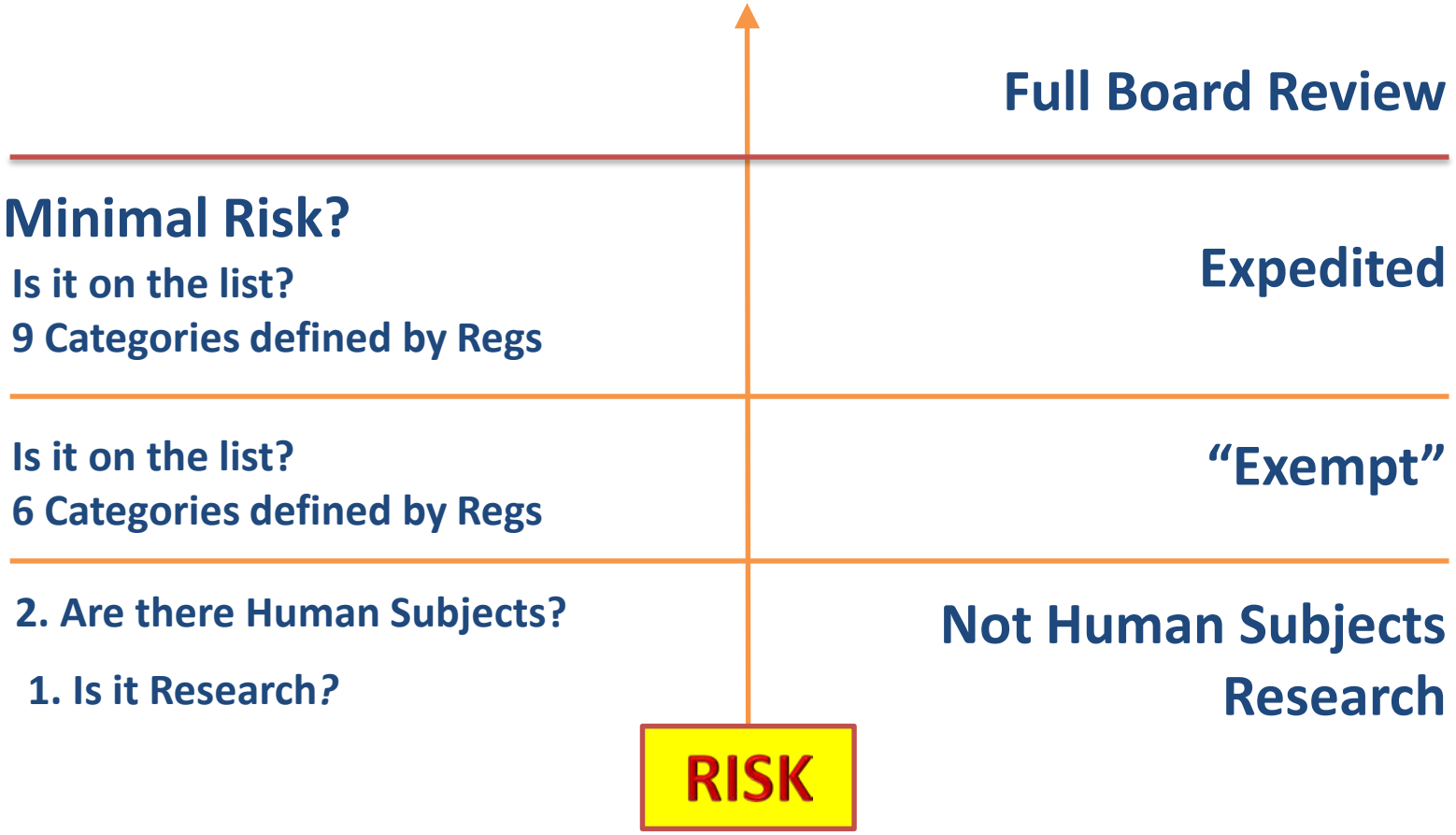
- Review the application and consent form(s) before the meeting

- Ensure the submission addresses the 111 criteria for approval

- Read the consent documents and confirm that they are consistent with the application / protocol

- Reading the consent for each study is a good way to begin your review

Level of Risk Generally Determines Level of IRB Review



Note: The level of review is determined by IRB, not by the investigator or by the client. The requirements for each level are given in the regulations.

Review by convened IRB

OHRE SOP 11.0

- UNC-CH uses a primary reviewer system in which two members are assigned (in advance) to present the submission for discussion
- The primary reviewers
  - Provide the IRB with a brief overview of the research
  - Identify any major concerns
- All IRB members should review the application and consent form(s) before the convened meeting.
- Ensure the submission addresses the approval criteria

Modifications to Previously Approved Studies-
OHRE SOP 16.0

- Assess if the modification changes the level of risk
- Determine if the subjects need to be made aware of the new information
- If a revised consent form is included, ensure it is accurate

Continuing Review - OHRE SOP 17.0

- Assess whether the study is proceeding as expected, using information in the progress report
  - Is the number of subjects enrolled ≤ the number approved?
  - Have there been unanticipated problems that suggest a change in risk:benefit?
  - Are there trends in protocol deviations that may need to be addressed?
  - Do monitoring reports or Data Safety Monitoring Committee reports suggest issues that may need to be addressed?
  - Is there new information that changes risk:benefit ratio?
  - Is the consent form adequate and up-to-date?
  - Are there changes requested for the upcoming approval period?

IRB Actions Following Convened Review

OHRE SOP 12.0

- Approval
  - In the case of an approval with no changes, the research may proceed once the PI receives written documentation of IRB approval.
- Approval with Stipulated Minor Change
  - IRB may determine that a study may be approved after minor stipulations are clarified or resolved
  - Chair and/or primary reviewer may be assigned responsibility for reviewing the changes to ensure that changes are appropriately addressed.
  - Application receives final approval when all required changes have been submitted and approved.
- Unless otherwise specified, the approval period is one year from the date of the last convened meeting at which the protocol was reviewed.

IRB Actions Following Convened Review-*OHRE SOP 12.0*

- **Deferral**
  - The IRB determines that substantive changes must be made before approval may be granted
  - The PI's response, including any amended materials, must be reviewed by the convened IRB, in general, the same IRB that deferred the approval.

- **Disapproval**
  - If the IRB determines that the research has substantive issues that cannot be readily addressed, the project, as proposed, is disapproved and may not go forward

Suspension of Research by the IRB

An IRB has the authority to ***suspend*** or ***terminate*** approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected or serious harm to subjects.

IRB Actions for Ongoing Studies

OHRE SOP 12.0

- **Suspension**
  - Refers to the IRB's temporary withdrawal of approval for some or all research activities.
  - Suspended research remains under continuing review.
  - Though the Chair may temporarily suspend a study, only the convened IRB can make that suspension permanent.

- **Termination**
  - Refers to permanent withdrawal of approval of all research activities.
  - Terminated research no longer undergoes continuing review.

Appeal of IRB decisions - OHRE SOP 12.0

- Investigators may appeal IRB requirements for stipulations or specific changes in the protocol and/or consent document(s) in writing

- At the Chair's discretion, the PI may be invited to the IRB meeting at which their appeal will be considered

Scientific Review

OHRE SOP 24.11

- Not the sole responsibility of the IRB
- Bad science = Bad ethics
- If not scientifically valid, how does one justify the risks?
- Regulations require IRBs to balance risk:benefit, which requires understanding of the science
- Consider clinical equipoise

Criteria for IRB Approval

45 CFR 46.111 & 21 CFR 56.111

OHRE SOP 24.0

1. Risks minimized
2. Favorable risk : benefit ratio
3. Equitable selection of subjects
4. Informed consent sought
5. Informed consent documented
6. Monitoring plan for safety
7. Privacy and confidentiality protected
8. Additional safeguards for vulnerable populations

Elements of IRB Review

The IRB examines research protocols to determine that:

1. Risks to subjects are minimized:
   - by using procedures which are consistent with ***sound research design*** and which do not unnecessarily expose subjects to risk, and,
   - if appropriate, by using procedures already being used for diagnostic or treatment purposes.

Elements of IRB Review

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

3. Selection of subjects is equitable
   - Consider issues related to inclusion of vulnerable populations

Elements of IRB Review

4. Ensure that informed consent is obtained
   - From each subject before study participation begins
   - And includes all required elements.
5. Ensure that informed consent is documented

Elements of IRB Review

6. The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects, if appropriate.

7. There are adequate provisions to protect the privacy of subjects and the confidentiality of the data, if applicable.

Elements of IRB Review

8. Ensure that additional safeguards are included in the study for vulnerable populations (children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.)

Minimal Risk

- 45 CFR 46.102(i) defines minimal risk as: "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."

- The IRB makes the determination of risk level.

- Minimal risk studies may qualify for exemption or expedited review.

Requirements in UNC's FWA (#4801)

- ***The institution*** bears full responsibility for ensuring that all human subject research is conducted in accordance with Federal regulations.

- ***The IRB*** must review and approve or disapprove research involving human subjects according to guidelines set forth in 45 CFR 46.

- ***The investigators*** acknowledge and accept their responsibility for protecting the rights and welfare of human subjects and for complying with the FWA.

Others may review protocols before the IRB, depending on area and focus of research

DEPT- OR SCHOOL-BASED REVIEWS

- Exercise & Sport Science
- Psychology
- Geography
- Urban & Regional Studies
- Anthropology
- Sociology
- Computer Science
- City & Regional Planning
- Ctr for Developmental Science
- Frank Porter Graham Child Development
- Kenan-Flagler Business School
- Sch of Information & Library Science
- Sch of Journalism & Mass Comm
- Sch of Social Work
- Sch of Government
- Sch of Education
- Office of the President

NIH-MANDATED CENTER REVIEWS

- Lineberger Comp Cancer Ctr (PRC)

UNIVERSITY OFFICES OR OFFICIALS

- Office of University Counsel
  - Research Compliance Officer
- Office of Sponsored Research
- Office of Clinical Trials

CONFLICT OF INTEREST COMMITTEES

- SOM
- Arts & Sciences
- Institutional COI

OTHER COMMITTEES OR GROUPS

- Institutional Biosafety
- Radiation Safety
- Investigational Drug Service
- Data and Safety Monitoring Board (SOM)
- HIPAA Privacy Officers, PHI Custodians

EXTERNAL TO UNC

- NC Dept. of Correction
- EPA

Privacy and Confidentiality

- **Privacy** pertains to a person's control over the extent, timing, and circumstances of sharing aspects of oneself (physically, behaviorally, or intellectually) with others.

- **Confidentiality** pertains to the treatment of information that a person has disclosed in a relationship of trust, with the expectation that it will not be disclosed to others without specific permission.

Special Populations

- The federal regulations require that IRBs give special consideration to protecting the welfare of particularly vulnerable populations, persons who may not be able to make decisions for themselves or who may be unduly influenced by others in their decisions.

- There are specific regulations that must be followed to include children, prisoners, pregnant women (because of the need to protect the unborn child) in research.

- Other populations, such as mentally disabled persons, the homeless, or those who are economically or educationally disadvantaged, may also need special protection.

Informed Consent

- Informed consent is a person's voluntary agreement, based on adequate knowledge and understanding of relevant information, to participate in research.
- In giving informed consent, persons do not waive any of rights or release those conducting the research from liability for negligence.
- Informed consent is an ongoing process, not just the paper.
- The IRB can waive all or some informed consent requirements for certain types of research.

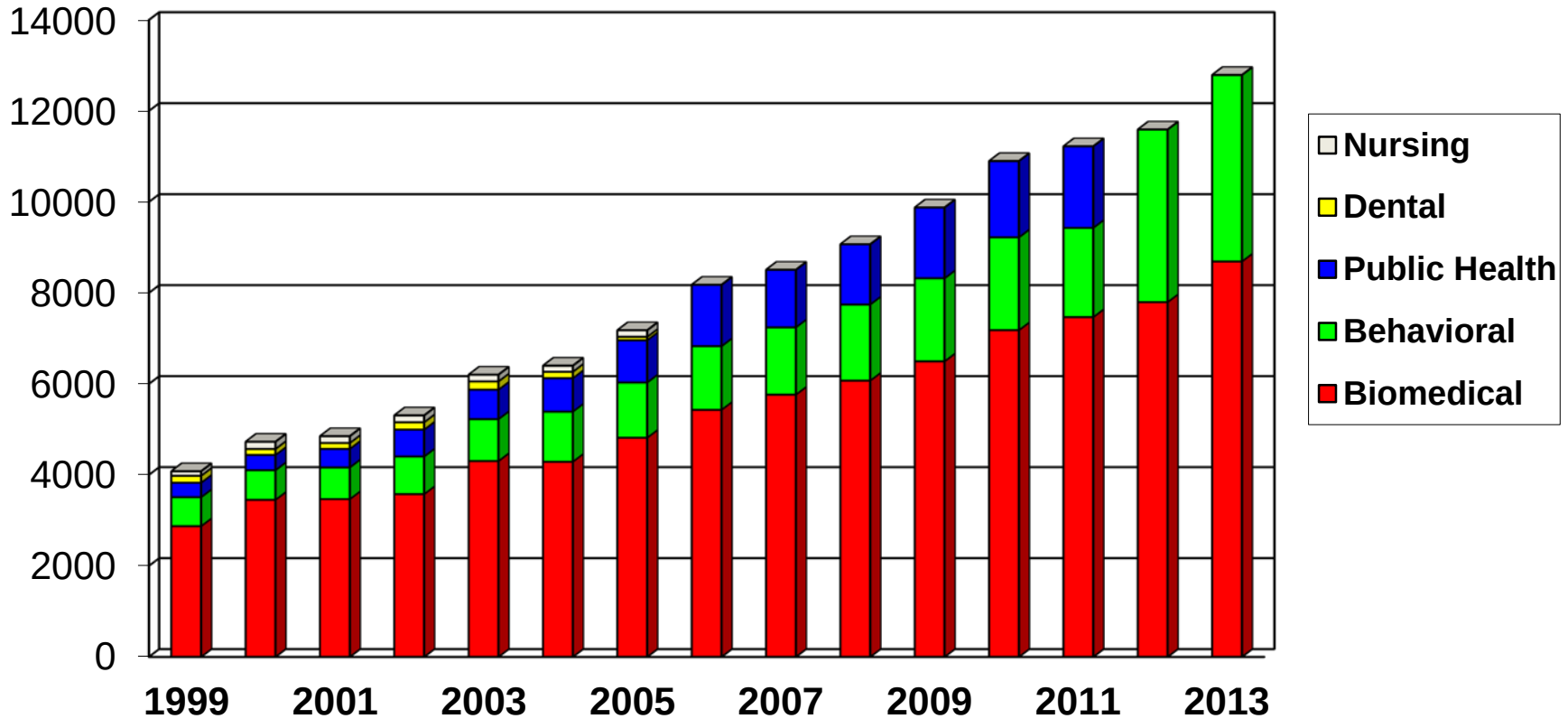
Principles of Informed Consent

- **Information** – Provide adequate information about the study, including purpose, procedures, risks, and benefits.
- **Comprehension** – Present the information in a way that is understandable to the person.
- **Voluntariness** – Convey that participation in any research study is always a free choice.

Translating The Belmont Report into Regulatory Requirements

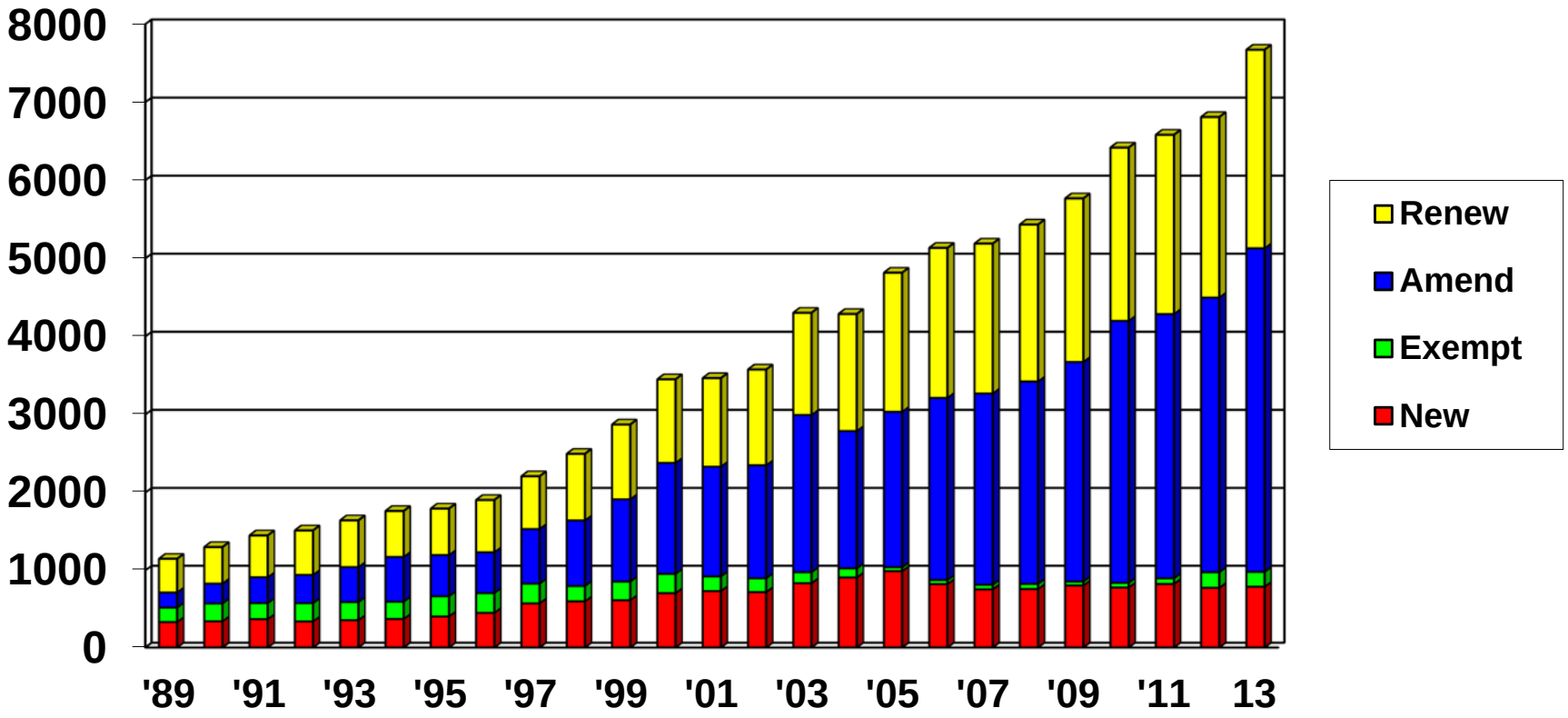
PRINCIPLE	PRACTICAL APPLICATION
Respect for persons	•informed/voluntary consent •protection of privacy •protection of vulnerable populations
Beneficence	•valid study design •favorable risk: benefit •competent investigators
Justice	•unbiased subject selection •fair recruitment

Total IRB Submissions at UNC-Chapel Hill 1999-2013



+10% last yr, +14% annualized over last 15 yrs

Total IRB Submissions
Biomedical IRB Only: 1989-2013



Primary Reviewer Assignments

- As a Primary or Secondary Reviewer you will be assigned agenda items to prepare & present.
- Assignments made 7-10 prior to the meeting,
- Will be notified by email

Primary Review Preparation

- Enter stipulations/comments in IRBIS & use the appropriate oral presentation outline for the type of review assigned to you,
- Email PI & Study Coordinator with any questions.
- Alert Chair to any controverted issues & potential deferrals
- Come prepared with your recommendations

IRB Member Responsibilities

1. Recuse yourself if you have a conflict of interest
2. Be prepared
3. Use the checklist (required for designated reviewers)
4. Make an organized presentation to the group
5. Allow for other perspectives and viewpoints
6. Maintain focus
7. Seek consultation, when needed
8. Honor the hair on the back of your neck
9. Don’t take yourself too seriously
10. Understand IRB’s power – IRB is a partner in the research process and we want to propose solutions when possible!

Resources

- IRB Website
  - Members' Website
- Educational presentations at each IRB meeting
- IRB Chairs & Staff