

# **Ways to Streamline the IRB Process: "15 Tips That Can Change Your Life!"**

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# Objectives

- **Identify mechanisms for IRB review that facilitate efficient and effective oversight of human subjects research**
- **Distinguish areas where regulations...**
  - **allow considerable flexibility for innovative practices**
  - **are more limiting**
    - **“Innovation” may create compliance problems**

# Disclaimers

- **Examples come from**
  - **Personal experience and observation**
  - **Federal and accreditation site visits**
  - **Regulations**
    - **45 CFR 46**
    - **21 CFR 50 & 56**
- **These are only suggestions**
- **May not work in all settings**

# **Tip #1: Make use of what the regulations give you!**

- **Federal regulations specifically and purposefully provide options for efficiency**
  - **Flexibility**
  - **Waivers or alterations**
  - **Levels of review**
    - **Exemption**
    - **Expedited review**
    - **Convened meeting review**

# Tip #2: Review guidance for what is allowed... and what is NOT

- **Office for Human Research Protections**
  - *OHRP Compliance Activities: Common Findings and Guidance, 2002 update*
  - <http://www.hhs.gov/ohrp/compliance/findings.pdf>
- **Food and Drug Administration**
  - *FDA Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators, 1998 update*
  - <http://www.fda.gov/oc/ohrt/irbs/default.htm>



**We've got a  
deadline... can you  
PLEASE  
expedite this  
review??**

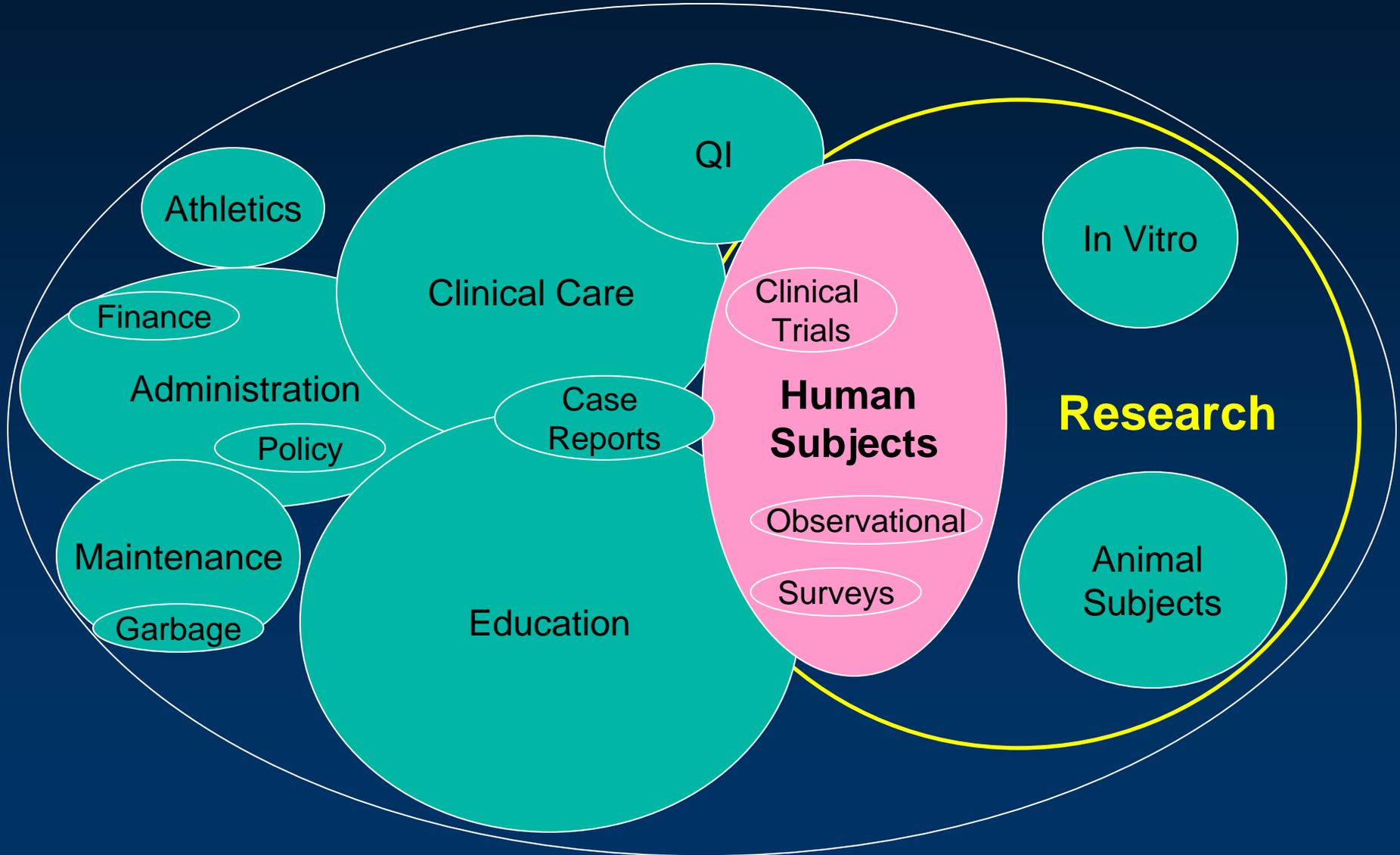
# Level of Risk Generally Determines Level of Review



# Tip #3: Understand the regulatory definitions and apply judiciously

- **“Research”** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge
- **“Human subject”** means a living individual about whom an investigator... conducting research obtains data through (1) intervention or interaction with the individual or (2) identifiable private information.

# What Requires IRB Review?



# Drawing the Lines

- Where should the lines be drawn, in separating “Human Subjects Research” from activities that do not require IRB review...
  - Quality improvement?
  - Case reports?
  - Classroom projects?
  - De-identified (or “tightly coded”) specimens or data?
  - Public health surveillance or interventions?
  - Innovative clinical care?
  - Key informant interviews about programmatic or organizational issues?
  - Training or center grants?
  - Other?

# Too Much of a Good Thing?

- If a little protection is good, shouldn't a lot of protection be better?
  - After all, the IRB has an important job, with a lot riding on it!
- What is the harm in erring on the side of reviewing things that might technically fall outside those (admittedly blurry) lines?

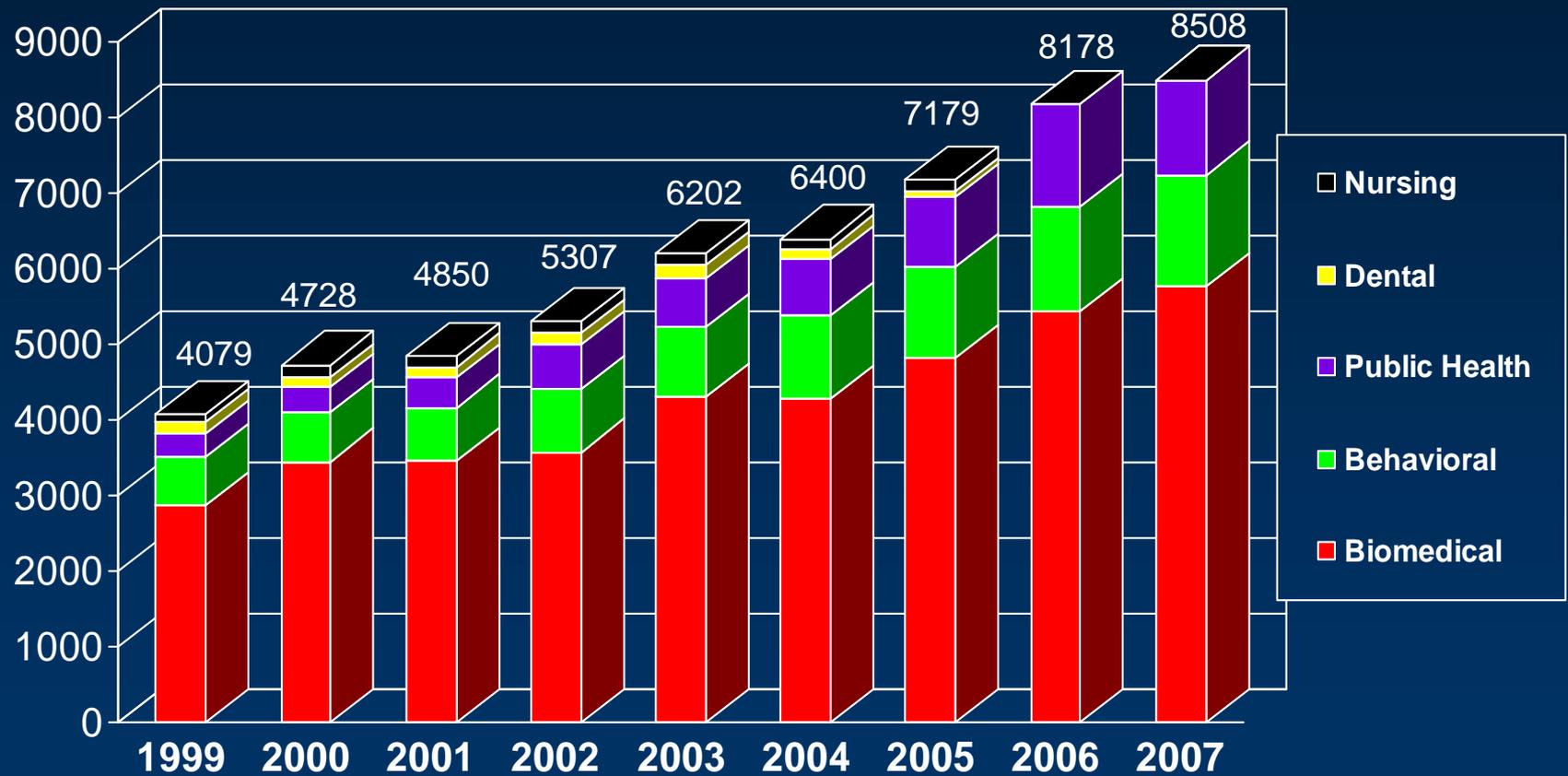
# What Can We Do About It?

- Empower institutions and their IRBs
  - Don't cower in fear of hypothetical or worst-case scenarios
- Use the flexibility inherent in the regulations
  - Understand and apply the definitions of “research” and “human subjects”
  - Give research an appropriate level of review → but don't exceed that level, as a matter of course
  - Save your Big Guns for studies that truly warrant
- Work “from the bottom up” in assigning level of review
  - Don't jump ahead in the decision algorithm

# Level of Risk Generally Determines Level of Review



# Total IRB Submissions at UNC-Chapel Hill 1999-2007



# Exemptions and “Not Human Subjects Research”



	1999	2000	2001	2002	2003	2004	2005	2006	2007
Not-HSR								404	510
Nursing	21	25	28	43	22	8	3		
Dental	6	6	3	5	8	1	2		
Public Health	67	80	109	102	44	2	1	20	32
Behavioral	187	205	150	126	65	14	0	7	7
Biomedical	242	250	190	180	143	119	50	57	64

# **A valid question, but not (necessarily) the IRB's to answer**

- Who should oversee activities that do not require IRB review, but still present some risk to
  - participants who are “not quite subjects?”
  - personnel who are “not quite researchers?”
  - university/institution/organization?

**OK... now that we've excluded  
activities that are NOT human  
subjects research...  
what do we do with those that are?**

Tip # 4: Keep working “from the  
bottom up” to assign an appropriate  
level of review

# **“Exempt” Research**

**45 CFR 46.101(b)\***

- **Six categories, defined by regulations**
- **IRB (or someone other than investigator) should make the determination**
- **Cannot be used for research involving prisoners, and some research involving children**

**\*HHS only. FDA provides exemption for emergency use of test article, but not for HHS categories**

# “Exempt” Research

45 CFR 46.101(b)

- Educational practices, curricula
- Surveys, interviews, public behavior\*
  - UNLESS identifiable responses could pose risk
    - Exception to the exception: elected officials or candidates for public office
- Existing data or specimens
- Studies of federal benefits programs
- Taste and food quality evaluation, consumer acceptance studies

*\*does not apply to research involving children if investigators interact*

# “Exempt” Research

45 CFR 46.101(b)(4)

Collection of study of *EXISTING*\* data, documents, records, specimens, if...

- publicly available, or
- information recorded so that subject cannot be identified, directly or through identifiers

\*on the shelf at time research proposed

## ...But don't over-apply exemptions

- *HHS regulations at 45 CFR 46.101(b) delineate six specific categories of exempt activities. OHRP finds that the institution has applied exempt status to research activities that exceed these categories. OHRP recommends that documentation for all exemptions include citation of the specific category justifying the exemption.*

# **Expedited Review**

**45 CFR 46.110, 21 CFR 56.110**

- **Chair or designated member**
- **Reviewer may not disapprove**
- **Meets criteria for expedited review**
  - **No more than minimal risk**
  - **On the list (Nov 9, 1998)**
  - **Not classified research**
  - **Minor changes in previously approved research**
- **Meets criteria for IRB approval**
  - **45 CFR 46.111, 21 CFR 56.111**
- **Members informed**

# Eligible for Expedited Review

- Clinical studies where IND/IDE *NOT* required
- Blood samples (routine methods, small amounts)
- Noninvasive prospective collection of biological samples
- Noninvasive collection of clinical data
- Data or specimens collected for non-research purposes
- Voice, video, digital recordings for research
- Individual or group behavior, surveys, interviews, oral histories
- Selected types of continuing review

# But don't over-apply expedited review...

*OHRP finds that:*

- *(a) The IRB inappropriately applies expedited review to research that involves minimal risk but does not appear in the categories of research published in the Federal Register.*
- *(b) The IRB inappropriately applies expedited review to research that involves greater than minimal risk.*

# But don't over-apply expedited review...

- *Inappropriate Use of Expedited Review Procedures for Review of Protocol Changes.* HHS regulations at 45 CFR 46.110(b)(2) permit use of expedited procedures for review of minor changes to previously approved research during the period for which approval is authorized. OHRP finds that the IRB has employed expedited procedures to review changes that exceed this limitation.

# But don't over-apply expedited review...

- *Failure to Advise IRB Members of Expedited Approvals.* OHRP finds that IRB members were not advised of (a) research protocols approved at time of initial or continuing review under an expedited review procedure, or (b) minor changes in research protocols approved under an expedited review procedure, as required by HHS regulations at 45 CFR 46.110(c).

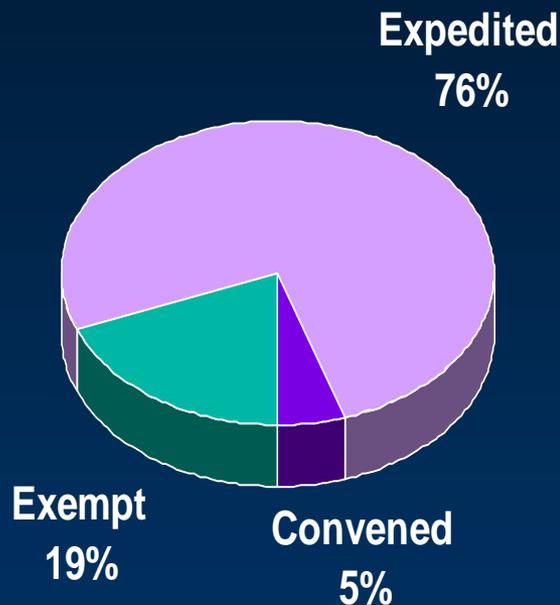
# **Whether Expedited or Convened Review...**

## **Criteria for IRB Approval**

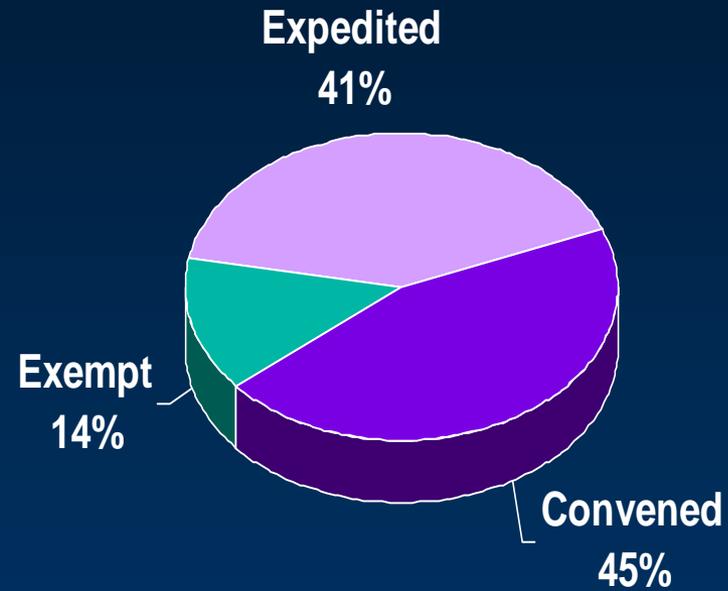
**45 CFR 46.111**

- Risks minimized**
- Acceptable risk:benefit ratio**
- Equitable selection of subjects**
- Informed consent process**
- Documentation of consent**
- Monitoring plan for safety**
- Privacy and confidentiality protected**
- Additional safeguards for vulnerable populations**

# Tip #5: Acknowledge and accommodate differences in areas of research



**Social and Behavioral**



**Biomedical**

*Disclaimer: These are not target percentages*

# **Tip #6: Consider IRB size and composition**

- **How many members is enough?**
  - **How many is too many?**
- **Some organizations form a small core committee of regular members**
  - **e.g., 5-7 members**
  - **Supplemented by ad hoc consultants**
  - **Variable combinations as required by research under review**

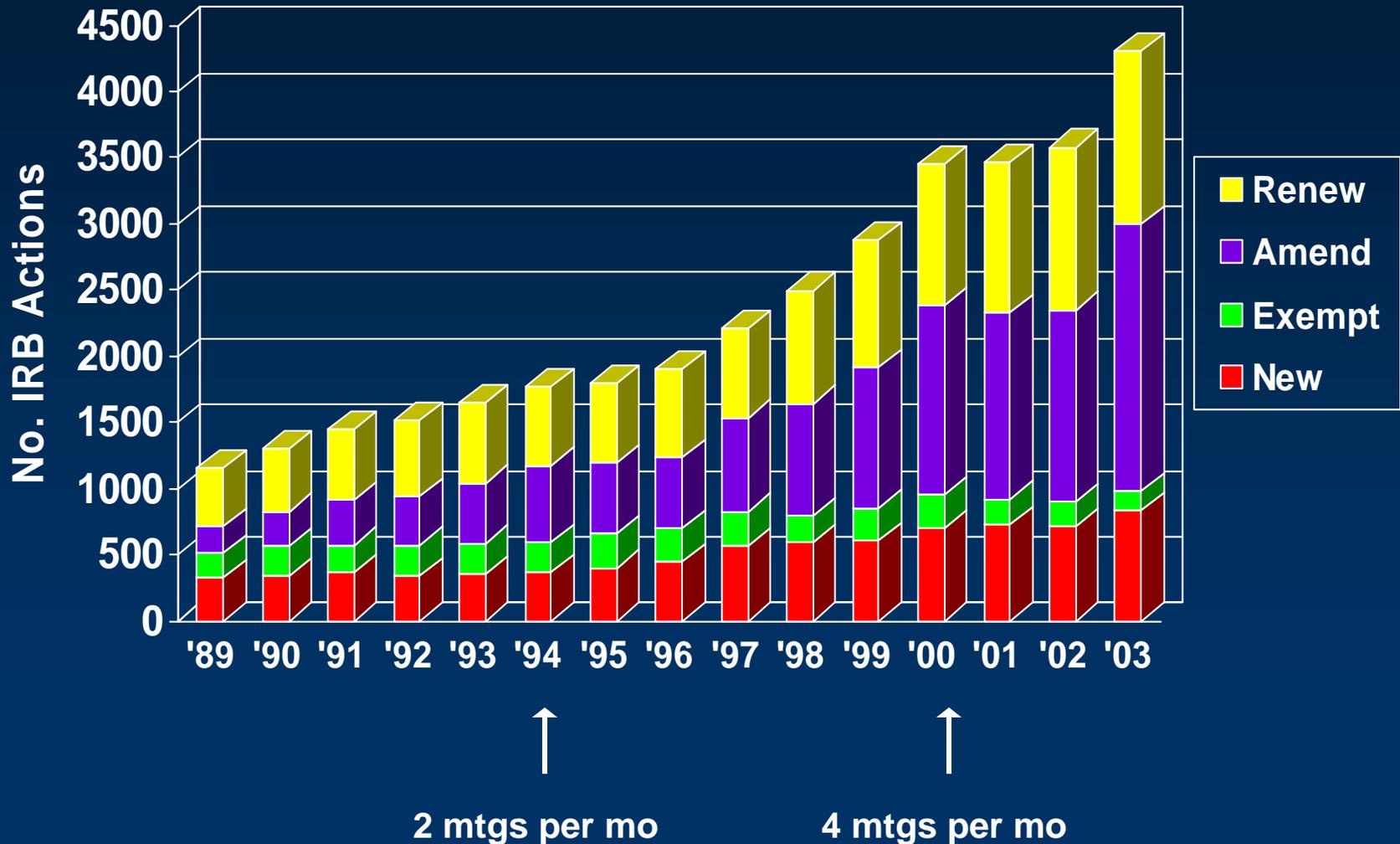
# Tip #7: Run an efficient and effective IRB meeting

- Thorough administrative review *prior to mtg*
  - OK to contact PI, if details can be clarified or resolved
- Everyone gets their say
  - Including “community members...”
- No one dominates discussion
- Don't waste committee time with discourse at the level of “The word ‘...the...’ is misspelled on page 6...”
  - Members can turn in written comments and marked consent forms
- To invite, or not to invite (the PI...)?
  - Investigators can often resolve and clarify on the spot
  - They are there to answer questions

## **Tip #8: Avoid canceling meetings or losing quorum**

- **Recruit IRB members who take seriously the commitment to attend**
- **Identify alternates to cover absences**
- **Reminders on the day of meetings**
- **Feed them!**

# Tip #9: Have an appropriate number of IRBs and/or meetings to handle the volume



# **Tip #10: Consider using primary reviewer systems**

- **One or more lead discussants for research reviewed at convened meeting**
- **Other members still get their chance!**
  - **Receive and REVIEW materials**
  - **Participate in discussion**
  - **Vote**
- **Allowed by the regulations**
- **Recognized by federal agencies**

# OHRP on Primary Reviewers

- *If the IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation.*
- *All other IRB members should at least receive and review a protocol summary (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111), the proposed informed consent document, and any recruitment materials, including advertisements intended to be seen or heard by potential subjects.*

# FDA on Primary Reviewers

- *Some institutions have developed a “primary reviewer” system to promote a thorough review.*
- *[This] is acceptable to the FDA if each member receives, at a minimum: a copy of consent documents and a summary of the protocol in sufficient detail to determine...*

# **Tip #11: Consider use of IRB Subcommittees**

- **Subcommittee approaches that work for some organizations**
  - **General policy decisions**
  - **Reports of Unanticipated Problems**
  - **Surveys and questionnaires**
  - **Pre-IRB scientific review**
  - **Informed consent**
  - **If no greater than minimal risk...**
    - **Amendments, modifications, revisions**
    - **Continuing review**

## **Tip #12: But just remember...**

**Neither Primary Reviewers nor  
Subcommittees take the place of  
the convened IRB committee**

# OHRP on Convened Meeting Review

- *Inadequate IRB Review at Convened Meetings.* *The minutes of IRB meetings, and our discussions with IRB members and administrators, indicate that little substantive review takes place at convened meetings. Most protocols undergoing [initial/continuing] review are neither individually presented nor discussed at a convened meeting by the IRB as a group. Furthermore, OHRP's inspection of available materials yielded scant evidence that IRB approval of research is consistently based on consideration of the determinations required under HHS regulations at 45 CFR 46.111.*

# OHRP on Convened Meeting Review

- *Inadequate Continuing Review.* *Continuing review of research must be **substantive and meaningful**. HHS regulations at 45 CFR 46.111 set forth the criteria that must be satisfied.... The minutes of IRB meetings should document **separate deliberations, actions, and votes** for each protocol undergoing continuing review by the convened IRB.*

# A case study in over-reliance on subcommittees...

- *(8) ...OHRP finds that the [IRBs] fail to review at convened meetings most research... not eligible for expedited review. As a result, the IRBs fail to ensure that all criteria required for IRB approval... are satisfied. [Our findings] indicate that **no review takes place at convened meetings for most protocols undergoing initial review. Most protocols are neither individually presented nor discussed at a convened meeting of any IRB.***

# A case study in over-reliance on subcommittees...

- (9) ... OHRP reiterates that **continuing IRB review of research must be substantive and meaningful**. In conducting continuing review of research not eligible for expedited review, **all IRB members should at least receive and review a protocol summary and a status report on the progress of the research**, including (a) the number of subjects accrued; (b) a description of any adverse events or unanticipated problems... (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document.

# A case study in over-reliance on subcommittees...

- *Your report stated that “[t]he review process undertaken before a convened meeting is designed to assure a triage process which assures that all issues relevant to the review process are identified and documented prior to the convened meeting.” OHRP’s site visit findings do not support this statement.*

# A case study in over-reliance on subcommittees...

- *While the OHRP site visit team **did not find the use of executive subcommittees to be objectionable** in and of itself, the site visit team unanimously found that the executive subcommittee review process, which does not represent substantive and meaningful IRB review, **was used to preempt review by the IRB at convened meetings** for most research projects.*

# Tip #13: Describe your processes and procedures

- *IRB Policies and Procedures– Operational Details.*  
*Written IRB policies and procedures should provide a step-by-step description with key operational details for each of the procedures required by HHS regulations...*
- *(c) Details of any process (e.g., a subcommittee procedure) that may be used to supplement the IRB's initial review, continuing review, review of protocol changes, and/or review of reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance.*

# Tip #14: Hire good staff and use them appropriately

- Triage of incoming protocols
  - Level of review?
  - Completeness of submission?
- Conduct pre-review
  - First pass for expedited review?
  - Prescreening for convened meeting review?
  - Consent documents?
    - e.g. some larger offices scan and rewrite → IRB
- Advise and educate investigators

**The Source of Many  
Inefficiencies and Much  
Ineffectiveness...**

***“Single Site Systems  
in a  
Multi-Site World”***

# **Tip #15: Consider options for Cooperative Review Arrangements**

- **IRB Authorization Agreement**
  - **Reliance on one IRB for ongoing review of shared protocol**
- **Standing agreement with central IRB**
  - **e.g., NCI Central IRBs for cooperative group oncology trials**
  - **e.g., Independent IRB for all or subset of projects**
- **Deferring institutions do not give up rights or responsibilities**

# **Closing Thoughts: Efficient IRB Review Mechanisms**

- **Federal regulations, accepted practice and AAHRPP accreditation standards allow considerable room for flexibility and innovation in IRB processes.**
- **Know your options... and your limits... and work within them.**
- **Find what works for you.**
- **It is possible to be creative and not get in trouble!**
- **Efficient IRB review mechanisms can both protect human subjects AND promote sound and ethical research.**