Keeping Your Eye on the Ball: How and Why to Keep the IRB Focused First and Foremost on the Regulatory Approval Criteria

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Objectives

- Describe examples of how rigorous application of the regulatory criteria for approval can improve IRB decisions.
- Outline a process of conducting IRB meetings that improves the consistency and quality of IRB review.

Survey Question

My IRB members struggle with their role in the scientific review of research

- ❑ Agree strongly
- ❑ Agree
- ❑ Neutral
- ❑ Disagree
- ❑ Disagree strongly

Survey Question

I worry that the decisions of my IRB members are too inconsistent

- ❑ Agree strongly
- ❑ Agree
- ❑ Neutral
- ❑ Disagree
- ❑ Disagree strongly

Survey Question

My IRB spends too much time editing consent forms

- ❑ Agree strongly
- ❑ Agree
- ❑ Neutral
- ❑ Disagree
- ❑ Disagree strongly

Review of ethical decision making

Ethical Decision Making

Principles

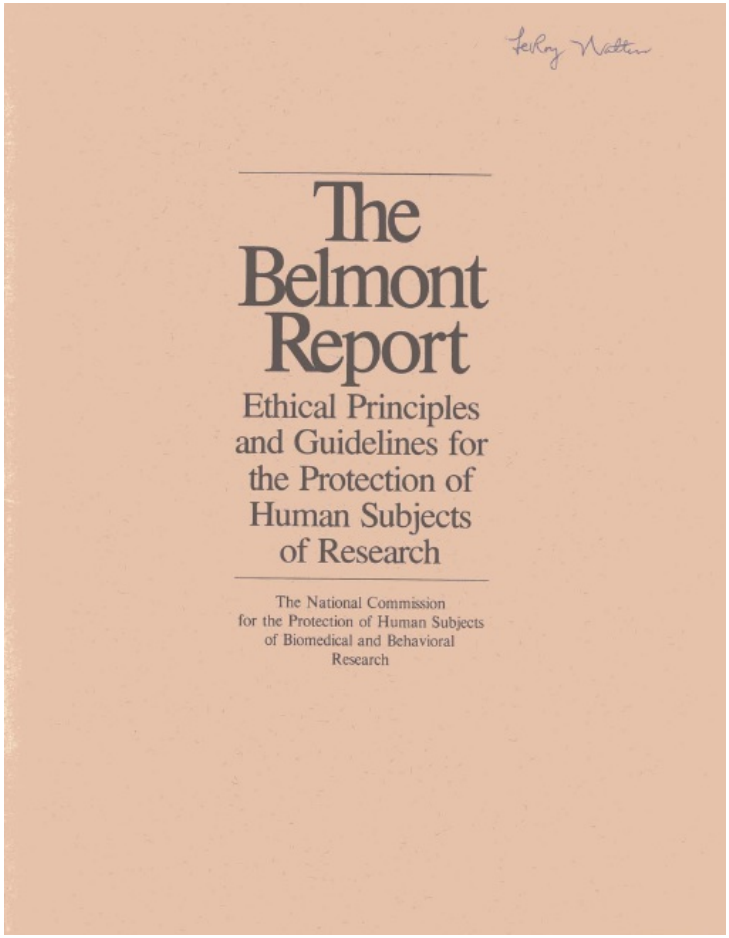
↓

Rules

↓

Decisions

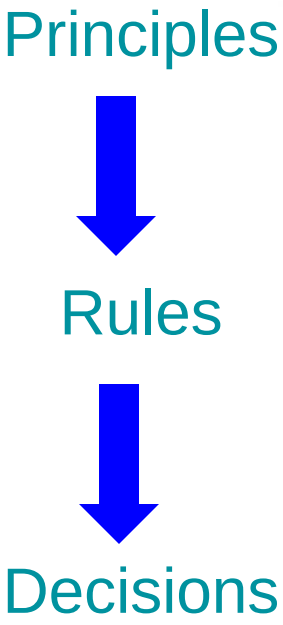
Ethical Principles Governing Human Research



- Respect for persons
- Beneficence
- Justice

Ethical Decision Making

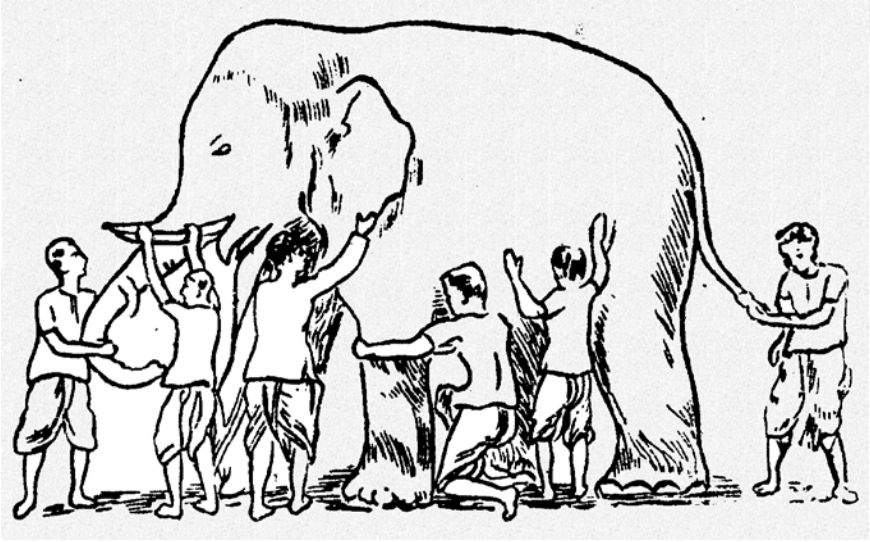
- The rules that derive from the Belmont Principles are the regulatory criteria for approval.
- The regulatory criteria for approval contain all rules necessary to protect human subjects



Ethics versus regulations

Applying the regulatory criteria for approval

- Consider each criterion one a time
- Resolve one criterion before moving on to another
- Use a checklist
  - There are too many criteria to memorize



Lidz CW, Appelbaum PS, Arnold R, Candilis P, Gardner W, Myers S, Simon L. How closely do institutional review boards follow the common rule? *Acad Med.* 2012 Jul;87(7):969-74.

Putting the pieces together

Questions that vex IRB managers and IRBs

- How much attention should the IRB place on science?
- What is the right level of attention to statistical analysis?
- Is my IRB too risk averse?
- How can I get my IRB to be more consistent?
- Why do we spend so much time editing consent forms?
- What is the right approach to studies involving drug washout or placebo?
- What is the appropriate degree of scrutiny needed for minimal risk student research?

How much attention should the IRB place on science?

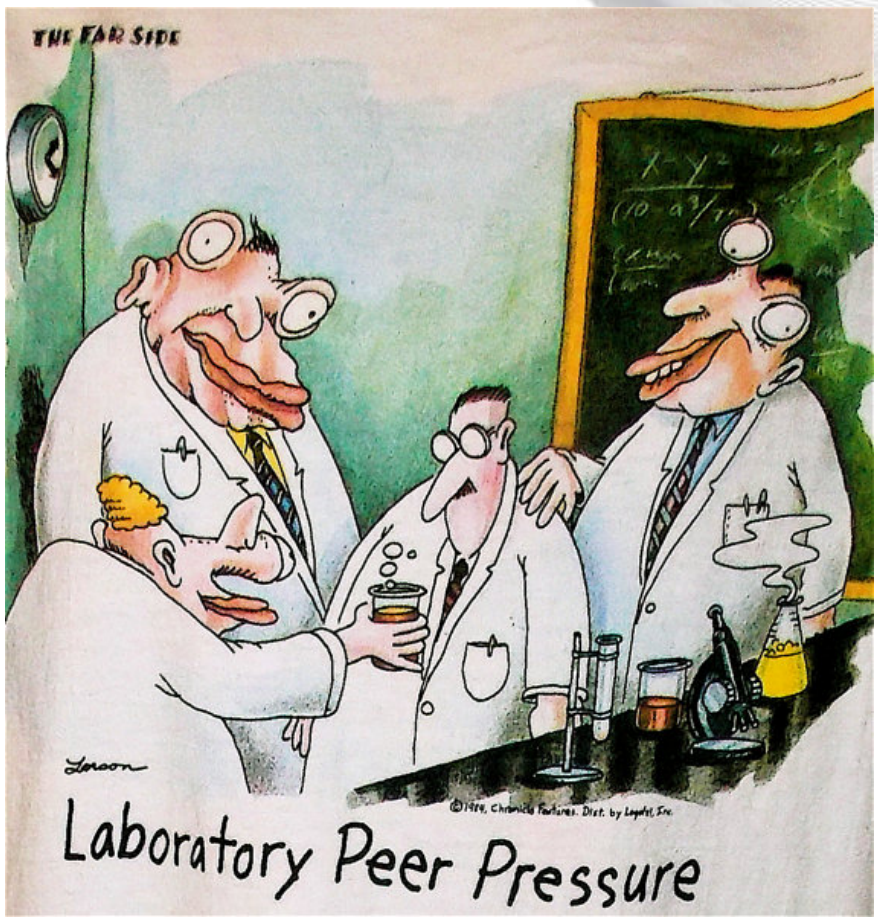
Survey Question

Under the regulations which one of the following are true?

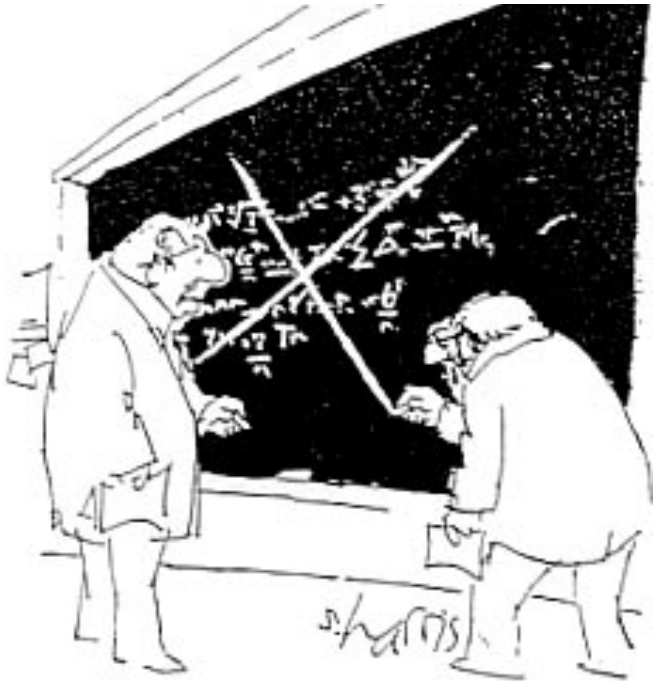
- ❑ Bad science is unethical
- ❑ Research procedures must be consistent with sound research design
- ❑ The IRB has to consider the likelihood that research will develop or contribute to generalizable knowledge
- ❑ All of the above
- ❑ None of the above

Types of “scientific review”?

- Peer review
- Merit review



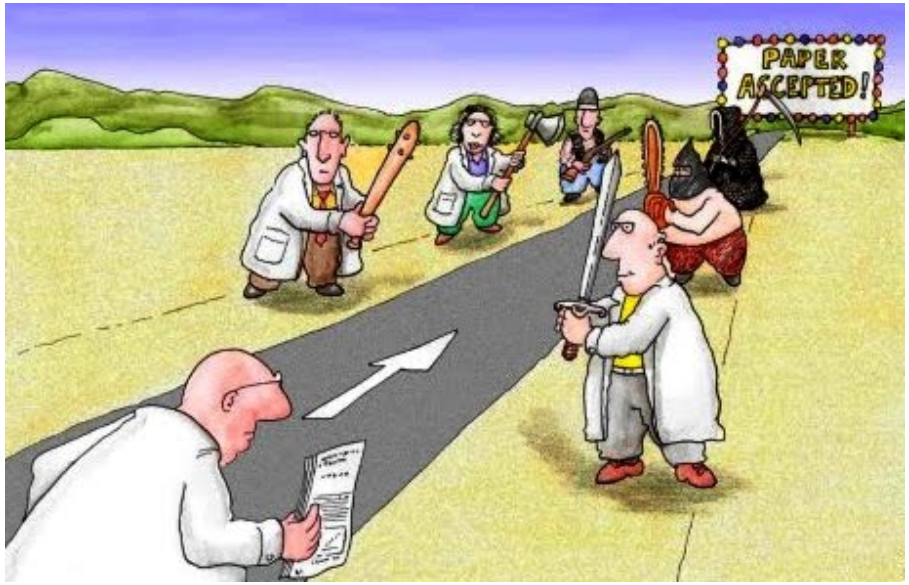
Peer review



"That's it? That's peer review?"

- Conducted by: Funding agencies, journals, and FDA
- Goal: Improve the quality of the science
- Process: Critique by peers
- Outcome: Criteria vary by people and time

Merit review



- Conducted by: Funding agencies, journals (not FDA)
- Goal: Allocate limited resources
- Process: Critique by peers follow by yes/no decision
- Outcome: Criteria vary by people, time, and resources

What is the role of the IRB when approving research?

Wrong

- Improve the quality of the science
- Decide which science should get limited resources

Right

- Determine whether the research meets the regulatory criteria for approval

Which criteria for approval intersect with science?

- Risks to subjects are minimized by using procedures consistent with sound research design that do not unnecessarily expose subjects to risk.
- Risks to subjects are reasonable in relationship to anticipated benefits to subjects, if any, and the importance of the knowledge expected to result.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

Criterion 1
What does this mean?

- Risks to subjects are minimized by using procedures consistent with sound research design that do not unnecessarily expose subjects to risk.

- Is there another way to do the research that allows its aims to be fulfilled ("… by using procedures consistent with sound research design …") that reduces risks to subjects ("Risks subjects are minimized…") but does not introduce unintended consequences ("…that do not unnecessarily expose subjects to risk")?

Criterion 1
What does this not mean?

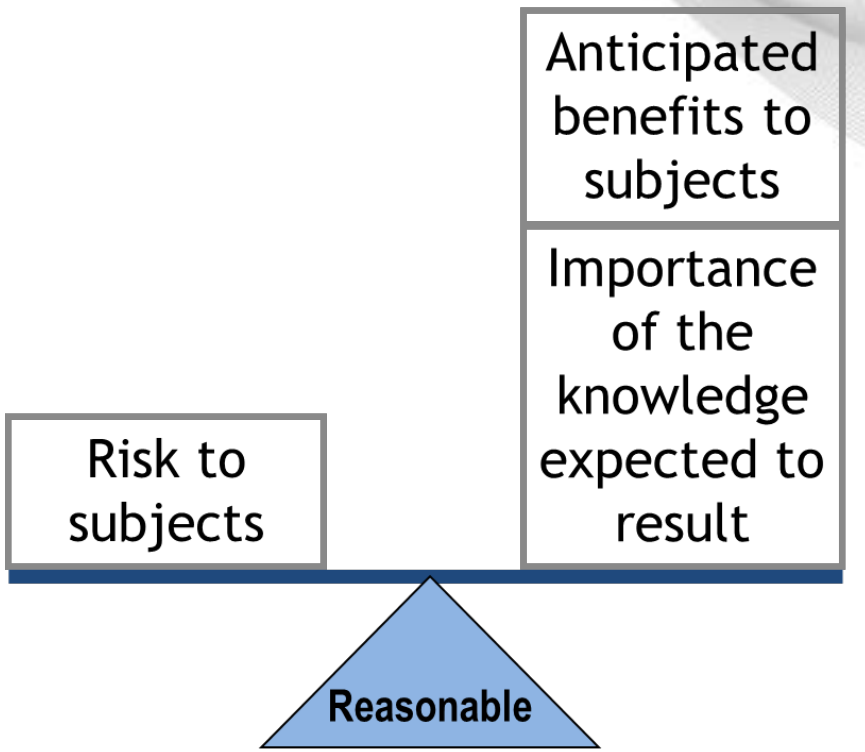
- Risks must be minimized.
- Procedures must be consistent with sound research design.
- If there is a way to reduce risk, it must be implemented.
- If the IRB thinks the research should be changed to reduce risk in a way that the research can no longer be done, the research must be disapproved.

Criterion 1
What scientific expertise does the IRB need?

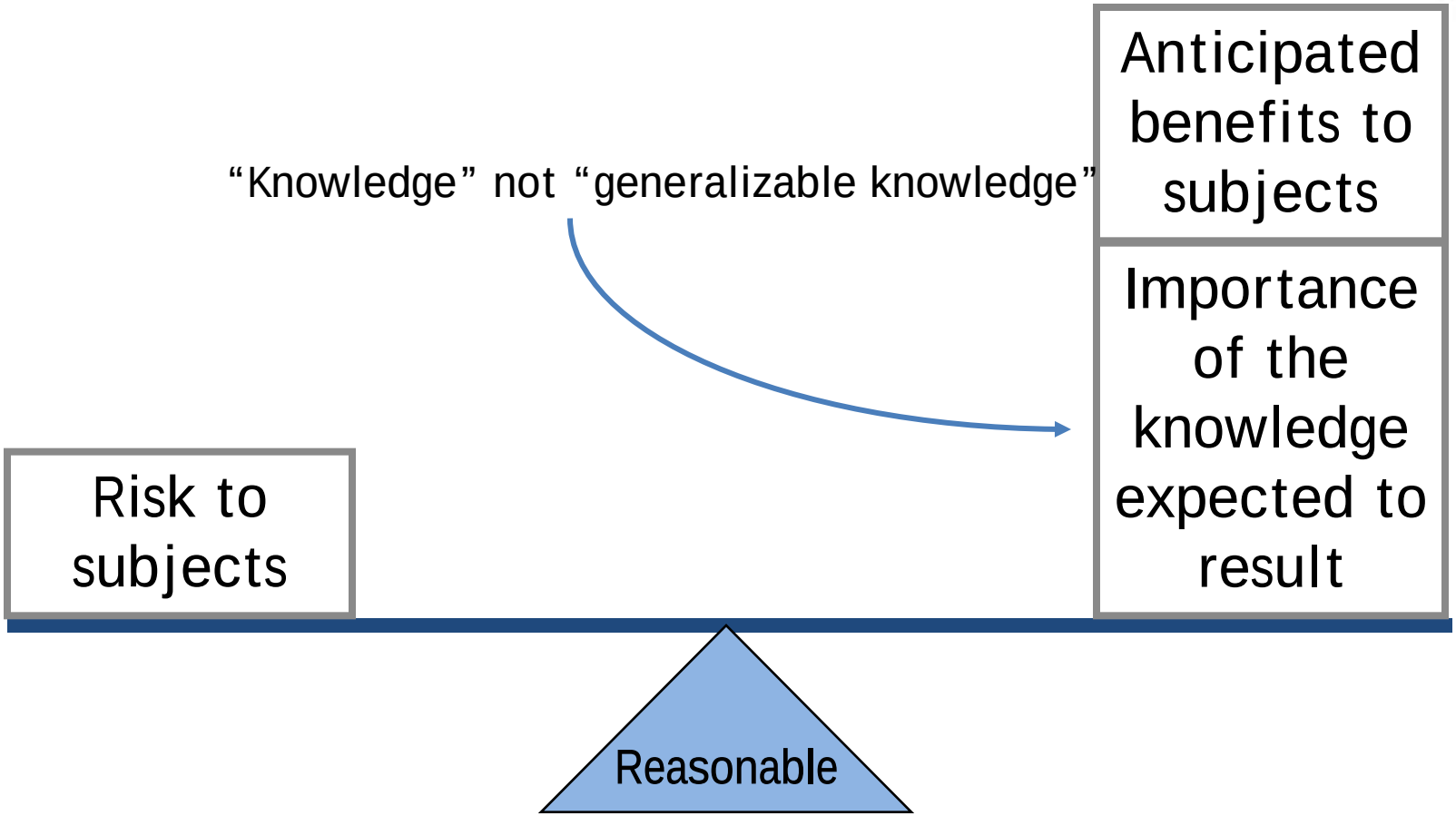
- **Criterion:** Risks subjects are minimized by using procedures consistent with sound research design that do not unnecessarily expose subjects to risk.
- **Knowledge needed:** Are there alternative ways of doing the research that still meet the scientific aims?

Criterion 2
What does this mean?

- Risks to subjects are reasonable in relationship to anticipated benefits to subjects, if any, and the importance of the knowledge expected to result.



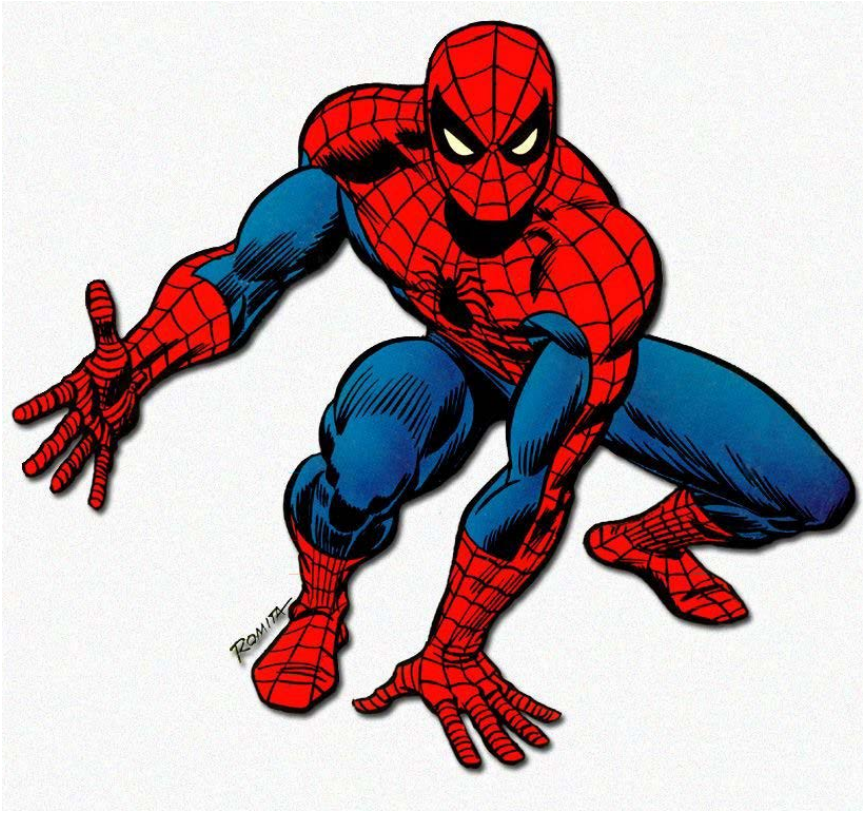
Key points


"Knowledge" not "generalizable knowledge"
Anticipated benefits to subjects
Importance of the knowledge expected to result
Risk to subjects
Reasonable

Is this knowledge? Important? Generalizable?

- More subjects should be studied
- This will have to be done internationally to work
- This is a promising approach
- This is not a promising approach

Criterion 2
The degree of scrutiny is based on level risk



- With great risks comes great responsibility
  - (to require greater amounts of anticipated benefit and
  - to require greater importance of the knowledge expected to result)

Is this knowledge?
Is it minimally important?

- This is not a good way to do research
- This is no longer an interesting idea
- I should not become a researcher

Criterion 2
What scientific expertise does the IRB need?

- Risks to subjects are reasonable in relationship to anticipated benefits to subjects, if any, and the importance of the knowledge expected to result.

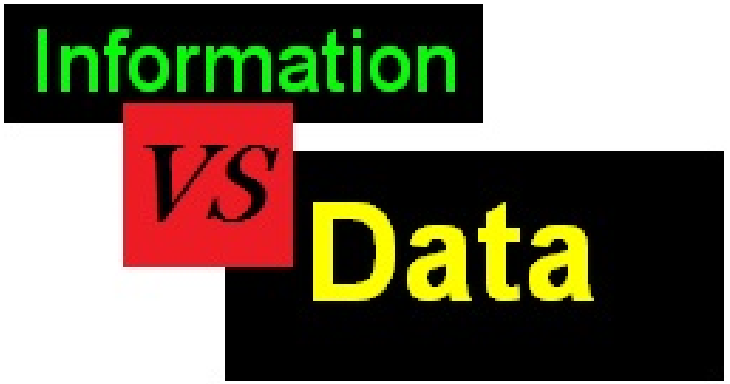
- What are the risks?
- What are the benefits?
- What is the knowledge expected to result?

Criterion 6
What does this mean?

- **Criterion:** When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- **Knowledge needed:** If unexpected bad things occur, is there a process in the protocol to detect this quickly enough so that subjects are kept safe?

Data safety monitoring plans

- The protocol reviews data and converts it into information
- The IRB reviews information NOT data



I am concerned about the science!

- What regulatory criterion is not met and why?
  - Must be a regulatory criterion
  - Other rules are off the table
- Does everyone else agree?
- What changes to the research would made the regulatory criterion be met?

How can I get my IRBs to be more consistent about their decisions?

Survey Question

My IRB makes too many inconsistent decisions

- ❑ Agree strongly
- ❑ Agree
- ❑ Neutral
- ❑ Disagree
- ❑ Disagree strongly

Scenarios

- After initial approval, the investigator submits a continuing review application. The research has been progressing well and there are no modifications. The IRB requires changes to the consent.
- At one meeting the IRB insists that a particular procedure be performed. At the next, the IRB does not insist on the procedure for essentially the same protocol.
- Whenever one statistician is present at the meeting changes are needed in the power analysis. Whenever another is present, changes are rarely needed.

Inconsistencies: *What's going on?*

Option A:

A. IRB 1 approved research that did not meet the regulatory criteria for approval
B. IRB 2 required changes to meet the regulatory criteria for approval missed by the first IRB

Option B:

A. IRB 1 approved research that met the regulatory criteria for approval
B. IRB 2 required changes that were not required to meet the regulatory criteria for approval

Option C:

Both reviews were wrong

Solution: Pre-meeting

- Policy: The regulatory criteria for approval are necessary and sufficient to approve research.
- Train IRB members on the regulatory criteria for approval.
- In advance of the meeting all members are to review all materials relevant to the regulatory criteria for approval
- In advance of the meeting all members are to determine which ones are met, and which are not met and why, or what additional information is needed.

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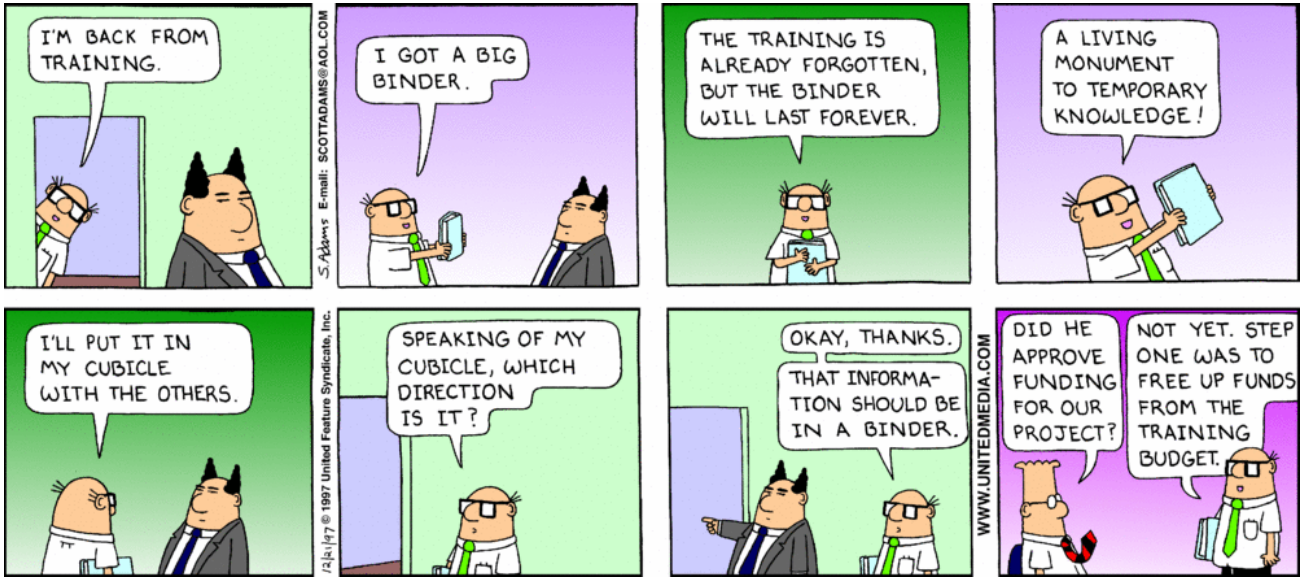
Training

- Rigorous training for all new members on the criteria for approval.
  - What they are
  - How to apply them
- Ongoing training at each meeting
  - Always relate back to the criteria



Solution: Meeting conduct

- Discuss one criterion at a time
- Require reviewers to justify changes on the basis of a regulatory criterion
- Changes not justified by the criteria are off the table
- IRB members who think that one or more criteria are not met cannot vote to approve research
- Minutes justify the basis of changes and recommendations using the criteria for approval

Committee Chair

- A strong committee chair is essential!

IRB Chair's Role

- What regulatory criterion is not met and why?
  - Must be a regulatory criterion
  - Other rules are off the table
- Does everyone else agree?
- What changes to the research would made the regulatory criterion be met?

Solution: Post meeting

- If the IRB requires changes that are not justified by the regulatory criteria for approval, the IO disapproves the IRB's approval, and makes the IRB do the review again, this time following IRB policy.
- On an annual basis, the IO reviews the IRB membership and does not reappoint IRB members who do not follow the IRB's policy (i.e., do not stick to the regulatory criteria for approval to make approval decisions.)

Other questions answered by the same process

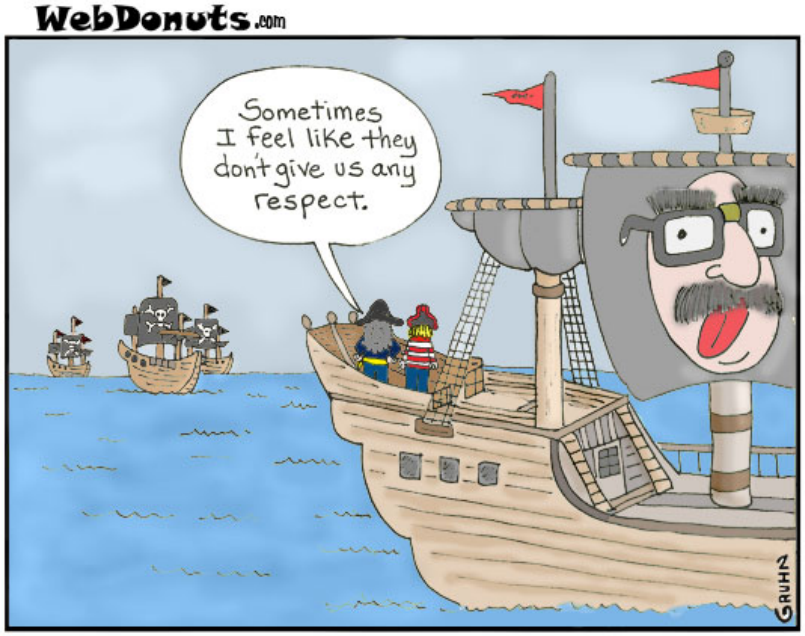
- What is the right level of attention to statistical analysis?
- Why do we spend so much time editing consent forms?
- What is the right approach to studies involving drug washout or placebo?
- What should the IRB do when there is an unanticipated problem involving risks to subjects or others?
- What is the proper response to low accrual?

Other considerations

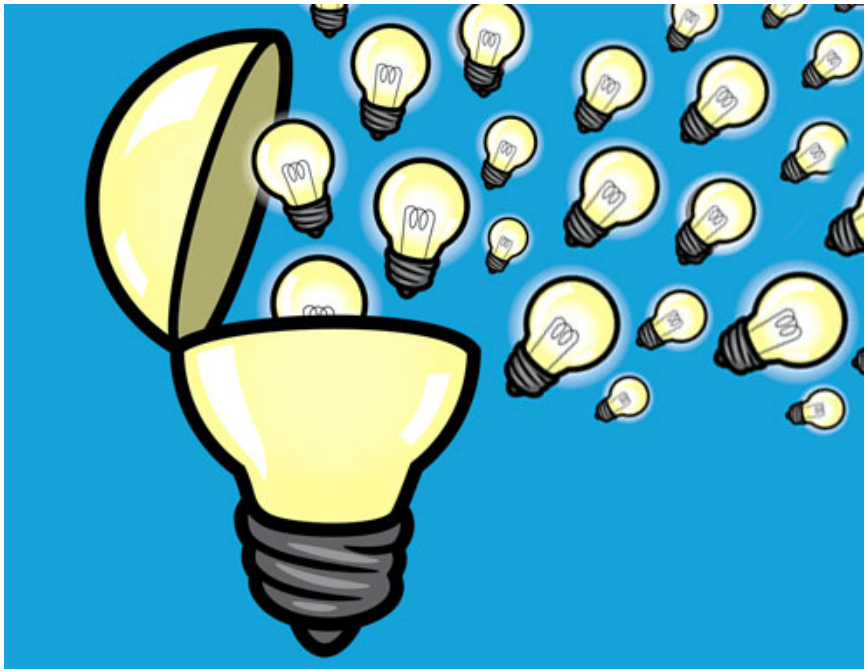
- How is your committee structured?
  - Is it too big?
  - Are your agendas too large?
  - Is the membership stagnant?

Why bother?

- Systematic assessment of the criteria assures that the research is both ethical and approvable.
- Consistent decisions based upon the criteria promote respect for the IRB among researchers



Summary: Key points



- Improves overall IRB review
- IRBs can adopt a process to ensure systematic application of the regulatory criteria for approval

Summary:
Key success factors

- Strong meeting leadership (IRB chair)
- Strong institutional leadership (Institutional or organizational official)

References

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