Translational Research Policies: Introduction to IRBs, Informed Decision-Making, and Consent

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What this Presentation will Cover

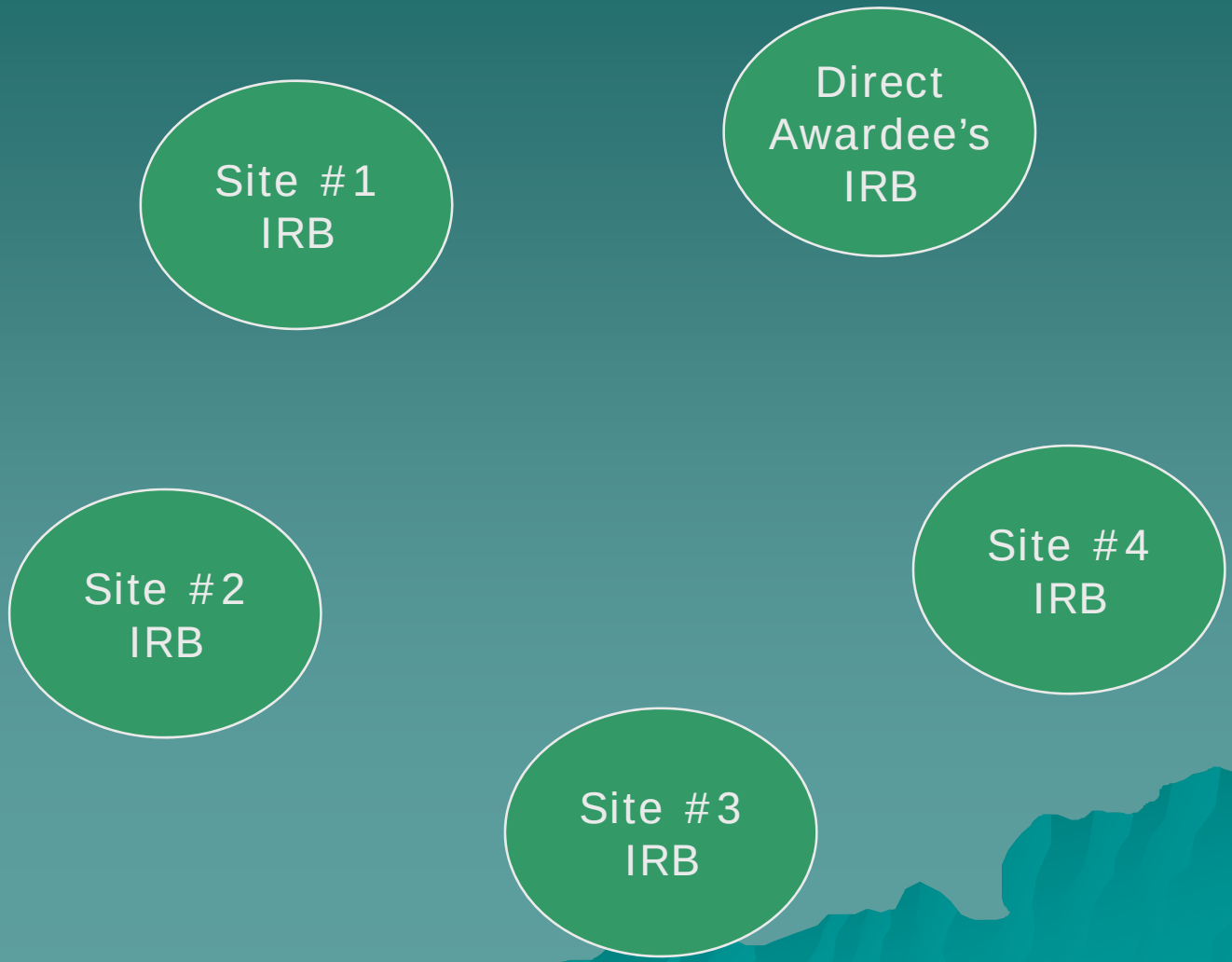
- Regulatory options for multi-center research
- Meetings on alternative IRB review models
- Proposal to hold IRBs directly accountable

IRB Review in a Multicenter World

- Clinical research is increasingly conducted at multiple centers
- Traditional model is for all local IRBs to review and approve protocol

Independent IRB Reviews

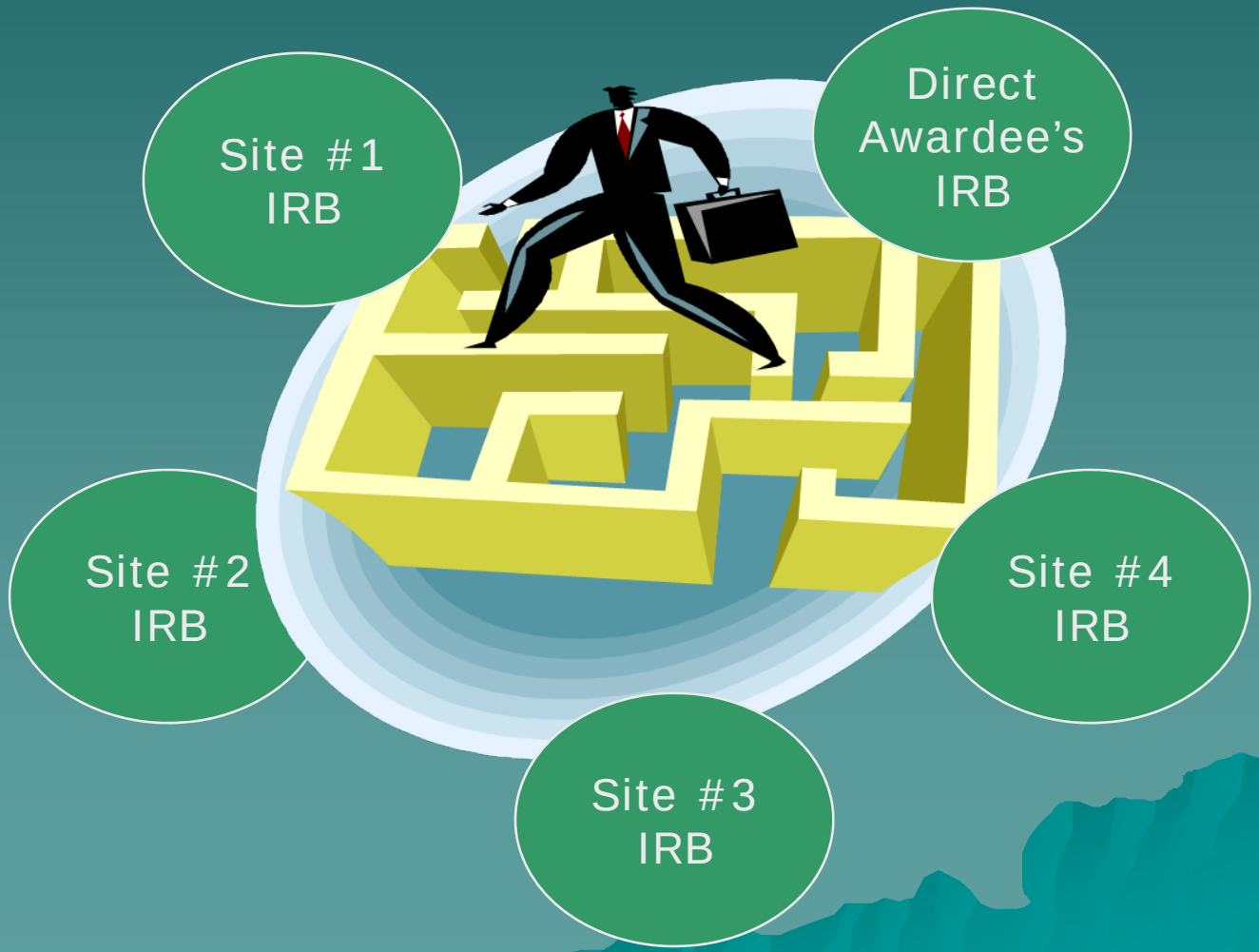
The 5 IRBs independently review the entire Protocol:



The Result

The PI bears the responsibility of communicating with the various IRBs to resolve differing IRB requirements.

In large multi-site studies, this process may consume 1-2 years.



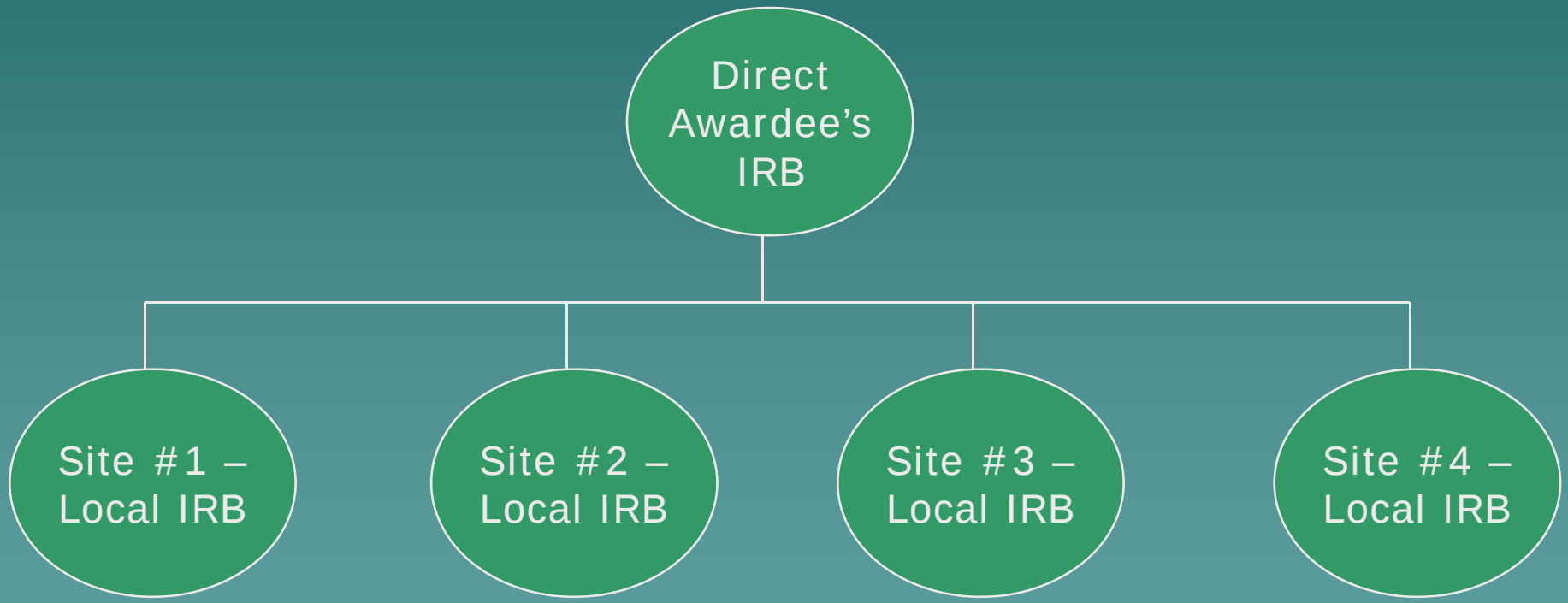
What are the alternatives to the traditional approach?

Structuring the Ethical Review: Regulatory Options

§46.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the Department or Agency head, an institution participating in a cooperative project may enter into a *joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.*

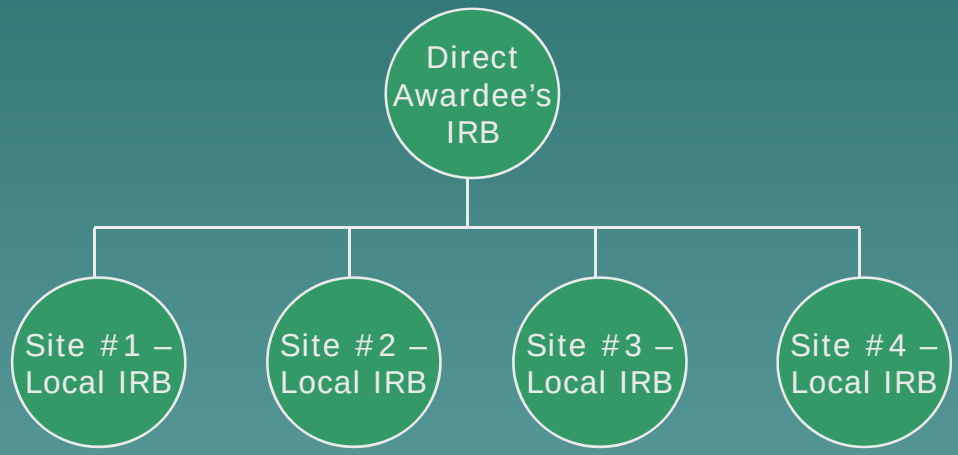
A. “Joint Review Arrangement”



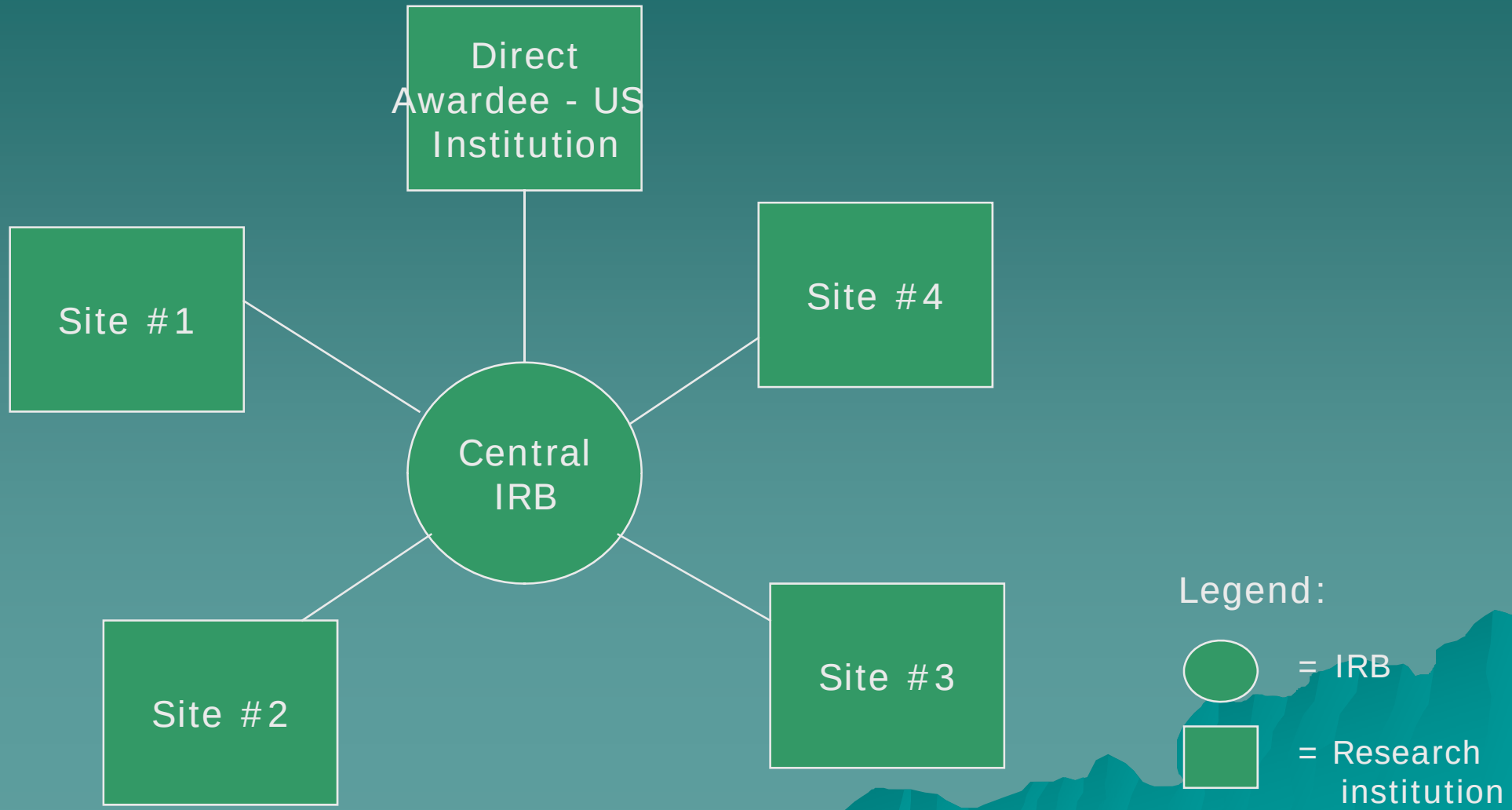
A. “Joint Review Arrangement”

1. The 5 IRBs develop an agreement about their respective areas of responsibility. The local IRBs might assume responsibility for issues such as:
- assure knowledge of local research context,
- review consent form,
- assure compliance with local laws.

2. The direct awardee lists each of the local IRBs on its FWA.



B. “Rely Upon the Review of Another Qualified IRB”

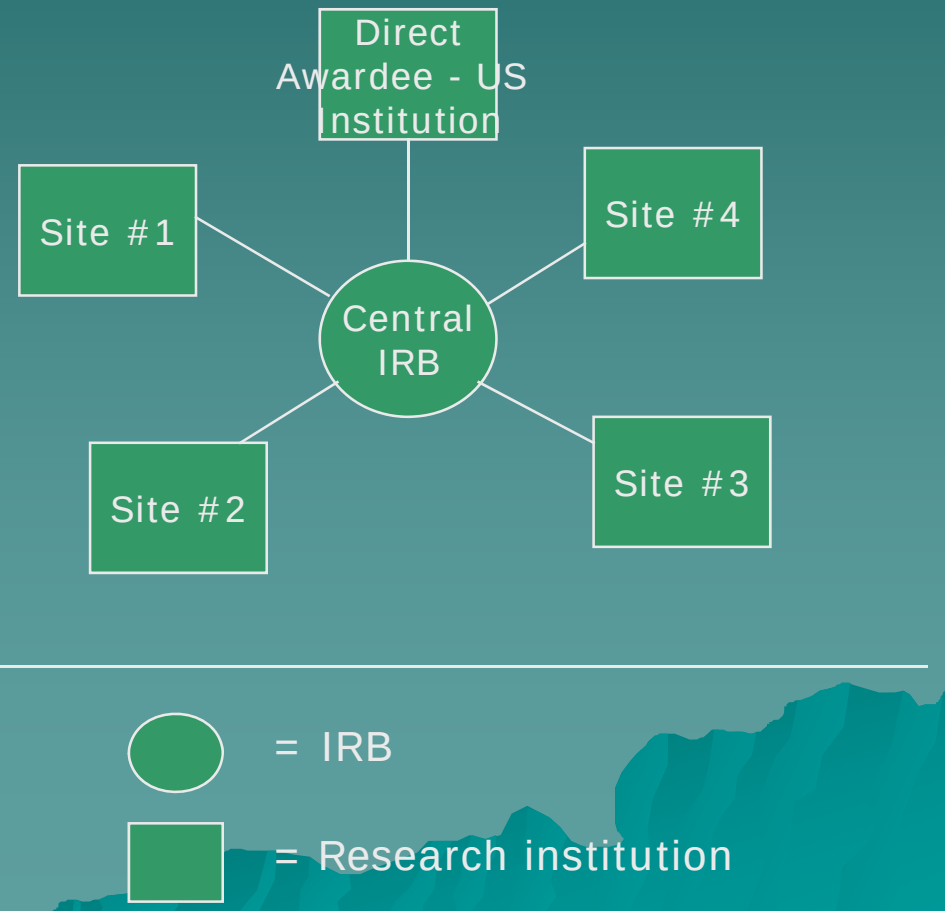


B. “Rely Upon the Review of Another Qualified IRB”

Caveats:

1. Each institution designates the Central IRB on its FWA.
2. The Central IRB performs all review functions.
3. The Central IRB may be:

a. one of the IRBs from the 5 institutions
b. a commercial IRB
c. an IRB created specifically for this study

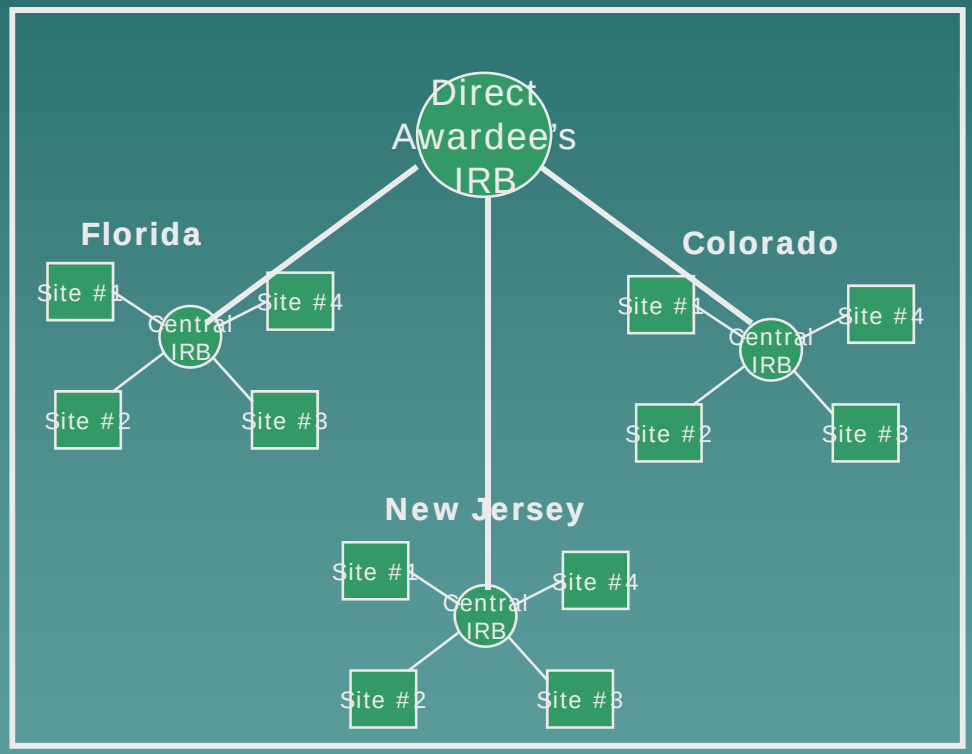


C. “Make Similar Arrangements for Avoiding Duplication of Effort”

Caveats:

1. Direct awardee designates both its own IRB and the Central IRB on its FWA.
2. Sites #1-4 designate the Central IRB on their FWAs.
3. The IRBs must clearly delineate areas of responsibility.

One possibility:



= IRB

= Research institution

Which Model is Best?

- All models are potentially workable approaches.
- Selection of the best model is based on such factors as:
  - specifics of the research protocol
  - expertise and resources available to the IRBs
  - prior working relationships among IRBs
  - requirement to comply with local laws and regulations
  - total number of performance sites

Meetings on Alternative IRB Models

- OHRP co-sponsored meetings on alternative IRB models in November 2005 and November 2006

- Other sponsors were NIH, the Association of American Medical Colleges, and the American Society of Clinical Oncology

Meetings on Alternative IRB Models

- *A key conclusion:*

  Despite existing regulatory flexibilities, some institutions remain reluctant to designate external IRBs.

- *A key factor:*

  OHRP currently holds an institution engaged in human subjects research study accountable for noncompliance on the part of an external IRB designated on FWA to review the research.

Proposal to Hold IRBs Accountable

- Should OHRP revise 45 CFR part 46 to enable HHS to hold IRBs directly accountable for compliance?
- A "Request for Information" is currently under development

Proposal to Hold IRBs Accountable

Regulatory requirements seem to fall into three categories of responsibilities:

1. Responsibilities unique to IRBs;
2. Responsibilities unique to the research institution;
3. Responsibilities that may be fulfilled by *either* IRBs or institutions engaged in human subjects research.

Responsibilities Unique to IRBs

1. Responsibilities that may be unique to IRBs:
   - Provision that except when an expedited review procedure is used, the IRB reviews proposed research at convened meetings
   - Provision that identifies criteria for IRB approval of research
   - Provision that permits IRB to alter or waive informed consent

Responsibilities Unique to Institutions

2. Responsibilities that may be unique to the research institution:
   - Requirement that investigator obtain IRB review and approval before beginning non-exempt human subjects research
   - Requirement that no investigator conduct non-exempt human subjects research without obtaining and documenting subjects' informed consent unless an IRB has waived these requirements as permitted by the regulations

Responsibilities of IRB *or* Institutions

3. Responsibilities that may be fulfilled by IRB *or* research institutions, eg:
   - Determining applicability of 45 CFR part 46 (e.g. exemptions)
   - Developing written IRB procedures which IRB will follow
   - Fulfilling documentation and recordkeeping requirements associated with IRB activities

Unanswered Question re: Shared Responsibilities

Are there responsibilities that are shared by the IRB *and* the research institution, eg:

- Provisions regarding IRB membership and qualifications to review type of human subjects research for which it is designated on an institution's assurance of compliance
- Provision that IRB conduct continuing review of research at intervals appropriate to degree of risk, but not less than once per year