Who Do You Call When the IRB is Significantly Delaying Approval of Your Research?

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OUTLINE

- A Case Study: Two Years and Ten Months For IRB Approval of a Multisite Observational Healthcare Research Study
- Me Too-Literature Review
- The model of IRB review for Single Study, Single Investigator Government Funded Grant: Why is it Problematic?
- Models of IRB Review Used by Physician Researchers
  - **Reciprocity Agreements** Between IRBs
  - **National Centralized IRBs**
    - National Cancer Center (NCC-IRB)
    - National Coordinating Center Cooperative Agreements (MACROS) (**multicenter academic clinical research organization)**
  - **Research Collaboratories**

OUTLINE

How can IRBs and Universities help Social Scientists Avoid Unwarranted Significant Delays?

Case Study

- The Study protocol was for a qualitative ethnography study aimed at describing in great detail the day to day practices of conducting gene therapy clinical trials at 3 clinical research sites in academic medical centers with a maximum of 12 interviews at each site for a total of 36 interviews with research staff, clinical staff, patients and relatives. There were 4 informed consents and 3 interview guides.
- NIH grant awarded in August, 2005 and two subcontracts at two clinical sites were finalized in February 2006 and March 2007, but the ethnography study protocol was not approved until July 2008.
- The study required oversight by four IRBs which are identified here as A, B, C, D in order to protect privacy and confidentiality of all IRBs involved.

Case Study

Amendments

1) one was to delete one co-investigator at one location/clinical site to replace that person with another co-investigator in the same department and institution.

2) two was initiated in October 2006 involving a second research data collection method. This method involved the PI of record recruiting Study Coordinators and PIs of gene therapy clinical trials from publicly available data bases and for collecting de-identified narrative interview data during private, confidential audio-recorded telephone conversations. submitted to IRBs A and B in February 2007 and to the third IRB C in March 2007 after the subcontract was approved. That amendment was not approved at all three IRBs until November 2007

3) three was initiated to include a fourth IRB because the PI of Record became employed by that institution;

Research Team Initiated Delays

- 1) slow research administrative process to negotiate financial subcontracts for two co-investigators; in one site the IRB application could not be submitted until the financial subcontracts was finalized which took 7 months;
- 2) Electronic e-file application required coordinated assistance by telephone with an IRB administrator at 3 out of 4 sites
- 3) Combined efile and paper documents (printing, collating, signing, and duplicating paper documents and waiting for fed ex delivery, or finding misplaced documents after Fed ex delivery)
- 4) not following the IRB directions correctly and having to redo the documents and resubmitting via efiles or paper files via Fed ex

IRB Initiated Significant Delays

1) Mixed messages and lack of consistency in treatment of the protocol and informed consents across multiple sites
2) Inefficiency in the combined systems of both paper and efiles
3) Duplication of administrative tasks at all sites
4) Negotiating between the IRB of record and two other IRBs about what counted as evidence of a complete and successful review
5) Poor communication and lack of availability of IRB staff in a timely manner
6) Linear IRB one step at a time process rather than seeing the whole project and planning ahead

Me Too-Literature Review

- More than 6,000 IRBs connected to universities, federal agencies, medical centers, foundations, or private contract research organizations in the US
- IRBs face heightened workloads due to an exponential growth of clinical trials worldwide, predominantly related to a major increase in pharmaceutical industry sponsorship of health related research.
- In the United States alone, the drug industry is a 1.3 trillion dollar business or, 13 % of the GNP (Icenogle & Dudek, 2002)
- IRBs are set up to process Industry Sponsored drug and devise studies

Me Too-Literature Review

Researchers have quantified and enumerated significant IRB delays by totalling the:

1) number of hours or days lost before data collection
2) number of protocol changes required
3) number and types of inconsistencies in and between local IRBs which make application processing across multisites unnecessarily difficult.
4) financial burden due to personnel costs for completing IRB applications and keeping up with annual renewals, modification, or amendments

Me Too-Literature Review

"Significant Delays" Criticisms:

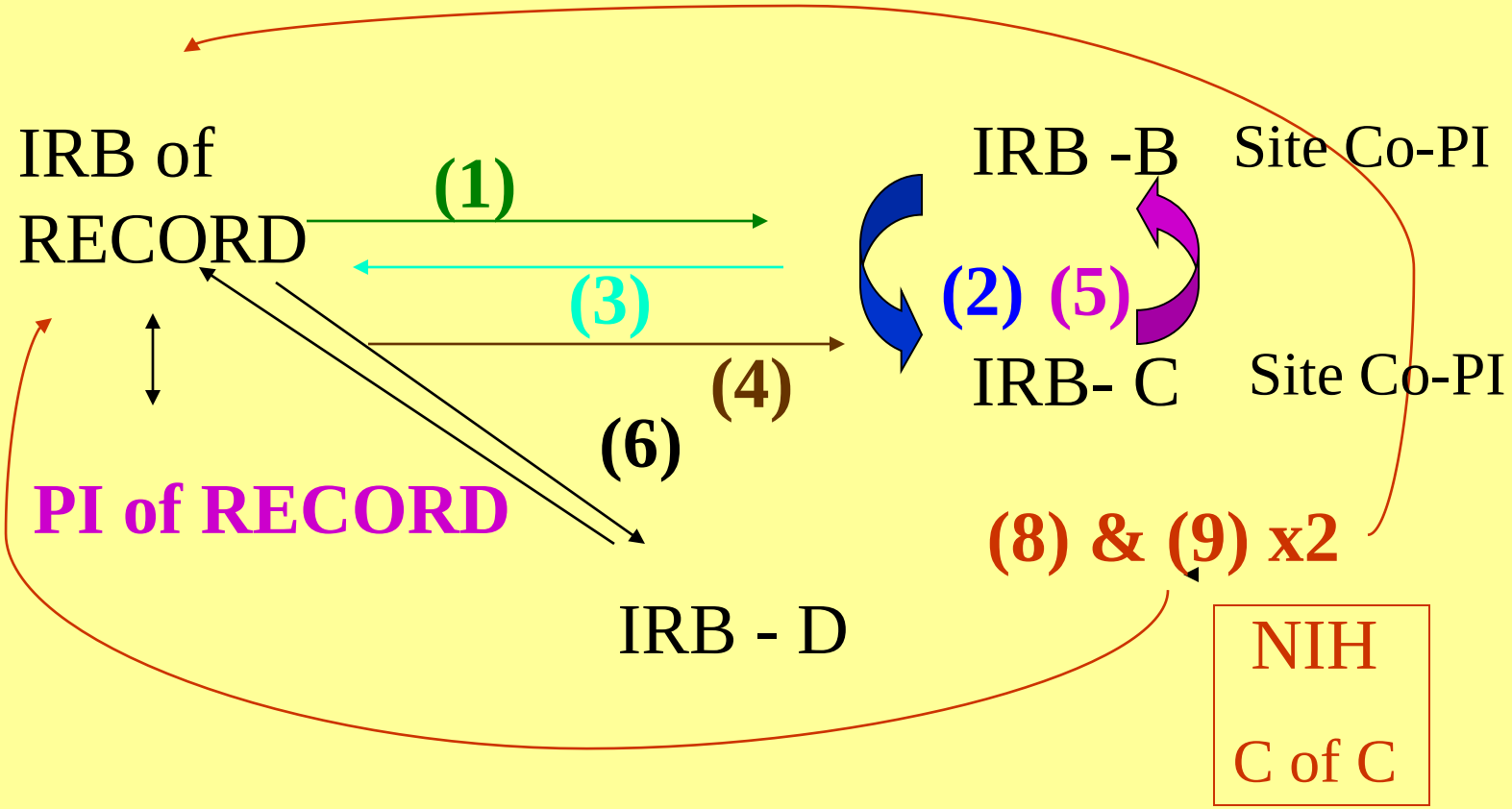
1) **Inefficiency and inconsistency across multiple sites** (Rogers et al., 1999; Green et al., 2006; Middle et al., **1995**; Redshaw et al., 1996; Silverman et al., 2001; Stair et al. 2001; Hirshon et al., 2002; Burman et al., 2001; Mc Williams et al., 2003; Dziak et al., 2005; Vick et al., 2005)
2) **Increasing demand for PIs to provide secretarial tasks to IRBs unrelated to protection of human subjects** (Burke, 2005, Wolf et al., 2005)
3) **Adversarial tension in relationships with social science PIs** (Kiskaddon, 2005)

Me Too-Literature Review

"Significant Delays" Criticisms:

4) **Poor communication** (Burke, 2005)
5) **Absence of standardized forms** (Gold & Dewa, 2005)
6) **Lack of IRB staff support** (Wolf et al., 2005; De Vries & Forsberg, 2002).
7) **Conflicting view points on templated versus non templated language and style of informed consents** (Dziak et al., 2005; Green et al., 2006; Hirshon et al., 2002; Middle et al., **1995**; Rogers et al., 1999; Silverman et al., 2001; 2003; Stair et al., 2001; Vick et al., 2005)

A Model IRB Review for this Single Investigator, Multi-site, Government Funded Grant



(1) IRB-A review before going to IRBs-B & -C

(2) IRB- C & -D review, if Changes, re-reviewed by IRBs –C & -D

(3) IRB-A re reviews, Changes already approved at IRBs –B & -C

(4) IRB- A approves, already approved protocols at IRBs –C & -D

(5) IRBs –C & -D have to re review and approve IRB-A protocols

(6) IRB-D completes an administrative review after all other IRBs Approve

(7) IRB-A approves after all other IRBs approve

(8) IRB-A letter of approval sent to NIH for a Certificate of Confidentiality

(9) NIH certificate of Confidentiality review request for edits, sent back to all IRBs for review and approval X 2

(10) IRB-A approves after NIH C of C approved

The protocol and the (4) informed consents were put through a revolving door of changes and resubmissions with as many as 9 versions of the consents over the 2 years & 10 months to complete the approval process

- Already approved informed consents had to be put onto new templates
- Changing from the PI of record to the Site PI name on all protocol documents and informed consents
- Annual reviews

Models of IRB Review Used by Physician Medical Researchers

- **Reciprocity Agreements** Between IRBs
- **National Centralized IRBs**
  - National Cancer Center (NCC-IRB)
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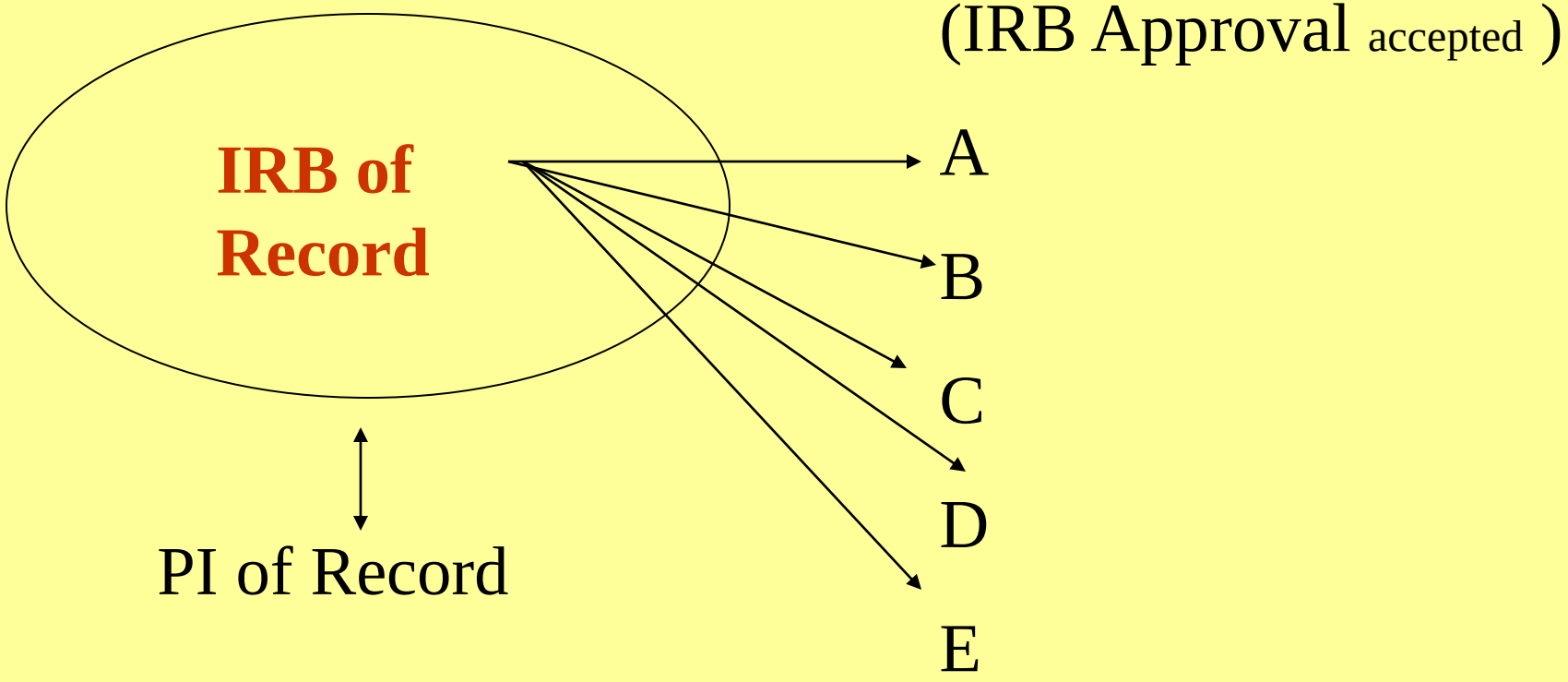
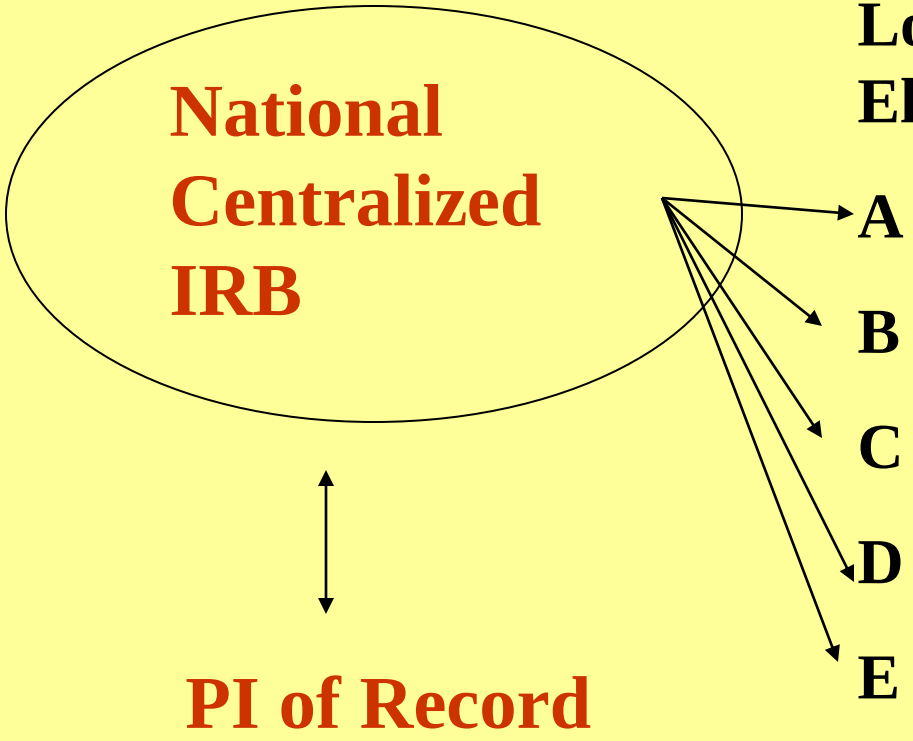
- **Research Collaboratories**

Reciprocity Agreements Between IRBs



National Centralized IRBs



Local IRB Review Not Eliminated but Limited

National Cancer Center

NC-IRB

Multicenter Academic Clinical Research Organization

MACRO

Cooperative Agreements

PI of Record ⟷ **National Research Coordinating Center**

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Coordinating Center Steering Committee Approval

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Coordinating Center Staff Obtain IRB applications and submit to other coordinating clinical centers

↓

IRBs at Coordinating Centers Review and Approve the same single study protocol

↓

A B C D E F G H I J K

Research Collaboratories

National Team Coordinating Center

National Collaborative Research Network

All Study Material provided

Supportive

Collaborative Engagement between PI, Site PIs and IRB members at each site

1-150 Sites &

Each Site Co-PI responsible for obtaining IRB approval

IRB approval Deadline

= In or Out of the Study

How can IRBs and Universities help Social Scientists Avoid Unwarranted Significant Delays?

1) Multisite study design as a way of making their research more efficient and generalizeable;
2) Risks associated with participation in social scientific studies are not as great as the risks associated with drug or devise randomized controlled trials
3) Less administrative support to navigate the complex waters of multiple IRB reviews, as compared to researchers conducting large multisite clinical trials launched by industry sponsors, private sponsors, or academic medical centers
4) Very modest budget compared with clinical trials
4) Unable to absorb the delays and unexpected expenses that can arise from multiple resubmissions and conflicting reviews”

Research Collaboratories

SINGLE Investigator Government Funded Social Science Observational Studies

All Study Material provided

Collaborative Engagement between PI, Site PIs & IRB representative at each site

A

B

C

D

IRB Support

Guidelines

Tools

Conference Calls

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