

# To document or not to document..?

## Flexible Multi-Site Reviews



The following options provide a framework to establish IRB review for non-federally funded multi-institutional research. If all institutions have an “unchecked box” the regulations do not apply.

Minimal documentation is nonetheless recommended to establish an appropriate framework for IRB review and ceding of review in these scenarios.

If participating partners have a checked box or if the projects are funded, a formal agreement must be established. Separating SOPs from any agreement allows changes to be made without review from legal counsel.

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### **Individual Investigator Agreement (IIA) (aka Unaffiliated Investigator Agreement)**

Used to document IRB oversight of an investigator who is not affiliated with an institution. Flexibility: IIA may be signed by the IRB Chair or Director instead of the Institutional Official OHRP IIA template (institutions may develop their own template):

<http://www.hhs.gov/ohrp/assurances/forms/iiabasicpage.html>

### **Collaborating Institution Agreements (CIA) – University of Michigan model**

Used to transfer responsibility from an IRB to a PI for verifying education/qualification, oversight, reportable events at the collaborating sites.

CIA template (University of Michigan):

<https://oprs.usc.edu/files/2013/07/CIA-Template-v-1-3-AAHRPP-version.docx>

### **IRB Authorization Agreement (IAA)**

Used to designate an “IRB of Record” for collaborative research among two or more institutions. Can cover one study or all studies an institution undertakes.

IAA is not a regulatory requirement for non-federally funded, non-FDA studies. An IRB may require an IAA at their discretion (eg. for documentation).

OHRP IAA template (institutions may develop their own template):

<http://www.hhs.gov/ohrp/assurances/forms/irbauthagree.html>

### **Memorandum of Understanding (MOU)\***

Typically, used between two institutions to designate the “IRB of Record” and the “Relying IRB” for an entire research program, designated class of studies or a specific study.

MOU Example (USC-Cedars):

[https://oprs.usc.edu/files/2013/05/FINAL-MOUnSOPs\\_USC-Cedars-3-27-13.pdf](https://oprs.usc.edu/files/2013/05/FINAL-MOUnSOPs_USC-Cedars-3-27-13.pdf)

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### **Master Reliance Agreement (MRA)\***

Used to designate “IRB of Record” for research where multiple institutions are engaged and provide agreement for the operating and legal framework.

*Example of MRA Elements (Harvard Catalyst):*

<http://catalyst.harvard.edu/programs/regulatory/reliance.html#aqr>

### **Cooperative Agreement (CA)**

Two institutions agree that either may serve as primary reviewer depending on which site gets funding or where accrual takes place.

*CA Example (USC-Rancho)*

[http://oprs.usc.edu/files/2013/01/Rancho\\_Agreement.pdf](http://oprs.usc.edu/files/2013/01/Rancho_Agreement.pdf)



# Creating Documentation for Multi-Site Review

*Below are ways to evaluate a) Lead IRB adequacy and b) Local responsibilities that remain under the purview of the Relying IRB.*

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## A) Lead IRB Considerations

The IRB must have appropriate expertise for research being reviewed, capacity and infrastructure to act as coordinator, receiver and dispenser of critical study related data.

- Adequate Infrastructure
  - Record Keeping Systems
    - Track each site independently
    - IRB electronic system access to collaborating sites
    - Written Standard Operating Procedures (SOPs) to manage:
      - Site-specific emergency care
      - Conflicts of Interest (COIs)
      - Sub-studies
      - Unique Consent Forms
      - Subject Complaints
      - Compliance Issues
      - Unanticipated Problems
  - Capacity to conduct site visits: Who conducts audits? Who incurs cost?
  - Evaluation of costs of single IRB Review: When deferring to Lead IRB, does Relying institution lose money?
- Process to obtain knowledge of state or international laws when compliance review involves out-of-state sites (unless local site will be responsible)
  - Written SOPs describing how local cultural and resource context info are gathered at initial and continuing review
- Single IRB coordination of issues such as unique institutional policies and review by other committees such as Institutional Biosafety Committee, Radiation Safety Committee, etc.
- Accreditation of Human Research Protection Program  
Collaboration with "Lead IRBs" that are AAHRPP-accredited: impose restriction or not?



# Creating Documentation for Multi-Site Review

## B) Relying IRB Considerations

The Relying IRB is responsible for local context issues, ancillary committees, and reportable events, if required. Local variations must be considered. Development of standardized worksheets may facilitate these issues.

- Significant COI Reviews
  - Investigator
  - Institutional
  - COI IRB Determination Results
    - Removal or restrictions imposed on Primary Investigator
    - Additional information in consent
    - Additional monitoring by DMC (Data Monitoring Committee) or DSMB (Data Safety Monitoring Board)
- Considerations of local and regional variations are critical to welfare of human subjects. Factors with significant variations:
  - State Laws governing human subjects/research data
    - HIPAA
    - Mental health Information
    - Cognitive Impairment
    - Developmental Disabilities Info
    - Surrogate Consent
    - Children in Research
    - Age of Majority
    - Age of Consent to certain medical treatments (e.g., substance abuse)
    - Investigator Licensing requirements
    - AIDS / HIV
    - Additional consent requirements (e.g., California law on Research Participants Bill of Rights)
    - State mandatory reporting laws for reporting of abuse/neglect
  - Emergency Research without subject consent (FDA local community consultation)
  - Disparate cultural norms for subject recruitment
  - Varying Investigator and Research Team Experience and Education
  - Translation of Consent Documents
  - Varying Institutional Policies such as compensation for Subject Injury
- Cost Incurred by relying IRB
  - Cost allocation cannot be a categorical decision to fund a single IRB