Regulatory and Financial Implications of Single IRB Review for Multi-Site Research

October 13, 2020

Welcome – Introductions

**Introduction:** Judy Birk, J.D.
Director, IRBMED

**Presenters:**

Nicole Duffy, MHA
sIRB Coordinator, IRBMED

Angela Faber, CIP, CCRC
sIRB Coordinator, IRBMED

Kevin Ferrell, MSPH, MBA
Administrative Manager Associate, IRBMED
# AGENDA

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<tr>
<th>Session</th>
<th>Presenter</th>
<th>Time</th>
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<td>Judith Birk, J.D.</td>
<td>10:00 – 10:05</td>
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<td>Director, IRB MED</td>
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<td>Accepting Oversight &amp; Workflows</td>
<td>Nicole Duffy, MHA</td>
<td>10:05 – 10:25</td>
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<td>siIRB Coordinator, IRB MED</td>
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<td>Budget Considerations</td>
<td>Kevin Ferrell, MSPH, MBA</td>
<td>10:25 – 10:40</td>
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<td>Ceding Oversight &amp; Workflows</td>
<td>Angela Faber, CIP, CCRC</td>
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<td>PI &amp; Study Team Responsibilities</td>
<td>Nicole Duffy, MHA</td>
<td>10:55 – 11:05</td>
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<td>Quality Assurance Efforts</td>
<td>Angela Faber, CIP, CCRC</td>
<td>11:05 – 11:20</td>
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**IRBMED:**

Accepting Oversight and Workflows

Nicole Duffy
Regulatory Requirement for sIRB in MSR

OHRP (Common Rule)

• Requirement became effective Jan. 20, 2020
• Federally funded/supported by agencies that have adopted/signed on to the new 2018 Common Rule
• Not limited to clinical research
• Domestic sites (U.S)

What does this mean?

• Two-step review process:
  • Regulatory review (one)
  • Local Context reviews (multiple)
• Single IRB budgets
• IRB agreements
• Participating site review/activation by single IRB

Outcome: Many different processes
**Defining Relationships**

**IRB of Record** (Reviewing IRB) (Central IRB)
- External IRB (An IRB external to U-M; not a University IRB)
- IRBMED

**Relying IRB** (Ceding IRB)
- External research sites/institutions
- IRBMED

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**Accepting Oversight**

**Before Grant Application**

- **8 weeks before deadline**
  - Request sIRB support from the IRB.

- **IRB Assessment**
  - The IRB will review the request.

- **IRB Agrees**
  - Reach out for letters of support from external sites.
  - IRB will draft a single IRB plan, PI reviews it.

- **Final plan & support**
  - IRB receives letters of support from external sites.
  - IRB finalizes single IRB plan and single IRB letter of support.
  - Provides plan and letter to PI for grant application.
Initial sIRB Request

- Important to discuss options with IRBMed early!
  - At least 8 weeks ahead of grant due date
- Completion of a single IRB request form is required
- IRBMed will determine if it is appropriate for IRBMed to serve as the sIRB for the proposed project

IRBMed’s Review of sIRB Requests

Evaluation criteria include:
- Risk level/complexity of study design
- Ability of study team and IRBMed to manage submission volume and communication
- Number of participating sites
- Location of participating sites
- Who holds any associated IND/IDE

IRBMed reserves the right to decline being the sIRB and will support research investigators to locate an external IRB to serve in that capacity.
Accepting Oversight
After Notice of Grant Award

IRB Application
• Type: Multi-site Research Application
• Be prepared to provide a list of participating sites, the site PIs and the PIs’ emails.

IRB Review
• Full Regulatory review
• Approval of the concept of these performance sites

Post approval
• Communication with external sites will begin
• Participating Site applications are created
• U-M Performance Site Application is created
• Remember external sites are not activated until U-M IRB has reviewed and approved the site individually.

eResearch Application
• Multi-site application type

• Participating site
  • Create
  • Post correspondence
  • Notify (IRB staff only)
Post MSR Approval: Participating Site Activation

- Information needed: PI name, PI email, Site name and FWA number.
- Friend accounts needed.

- After participating site applications are initiated they will be notified.
- Directions will be sent out.

- Local Context review is performed.
- Back and forth with study team as needed.

- Review is completed and site is activated.
- All site-specific documents are watermarked.

Participating Site Workspace

- Edit Project
- View Documents

Participating Site: Eastern Michigan University
Participating Site – Documents Tab (Pre-Activation)

<table>
<thead>
<tr>
<th>Main</th>
<th>IRB</th>
<th>Documents</th>
<th>History</th>
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<tbody>
<tr>
<td>Site Specific IRB Documents</td>
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<td>University of Michigan IRB Approved Consent Template Documents</td>
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Participating Site Application – Page 1

**General Information**

The following questions will collect information necessary for the University of Michigan IRB, as the Single IRB in a Multi-site study, to approve an individual performance site. For more information contact the Research Administration Office.

- **Site Name:** Eastern Michigan University
- **Year site Principal Investigator:** Nicole Duffy
- **2. Add site Co-investigators, Lead Study Coordinator, and additional Study Coordinator, and one IRB Staff Member point of contact from your institution:**
  - **Name:** [Enter Name]
  - **Role:** [Enter Role]
  - **E-Mail:** [Enter E-Mail]

  There are no items to display

- **3. Select all vulnerable populations your site intends to enroll in this study:**
  - **Population Type:**
    - [ ] Children

  There are no items to display

- **4. Informed Consent: Upload any completed University of Michigan IRB informed consent template documents with your site specific language (including site specific changes). To retrieve University of Michigan IRB informed consent template documents go to the Documents tab on the Participating Site workspace and click for Study Wide Document:**

  | Name | Version |
  | Test.doc | 0.01 |

- **5. Is it likely that non-English speaking subjects will be enrolled?**
  - [ ] Yes
  - [ ] No

- **6. Enter the estimated number of subjects to be enrolled at your local site:**
  - [ ] Adult
  - [ ] Children
  - [ ] Individuals age 18-19 or 18-20 not otherwise legally qualified as Adults

- **7. Do any of the study team members have a conflict of interest management plan?**
  - [ ] Yes
  - [ ] No

- **8. Upload any additional supporting documents related to your site, necessary for IRB review, that have not already been uploaded (e.g. local recruitment, HIPAA Authorization):**

  There are no items to display
Participating Site Application – Page 2

IRB Section

This section should be filled out or confirmed by your designated local IRB point of contact.

1. Is your site's Human Research Protection Program (HRPP) AAHRPP accredited?
   - Yes  No
2. Are the participant selection and recruitment procedures associated with this study protocol compliant with your local site's laws, policies, and are they in agreement with the study protocol?
   - Yes  No
3. Are the informed consent/assent procedures and documents associated with this study protocol compliant with your local laws and your site's policies?
   - Yes  No
4. Give the nature of this particular research study, are there any additional factors particular to the study site, study population, or the community (e.g., could contribute to the acceptability of this research study in the local area of your site)?
   - Yes  No
5. Which human subject educational program does your site utilize?
   - Site Specific
     - 5.1 Describe your site's educational requirements:

   - 5.2 How frequently is education refreshed after initial certification is complete?
     - Other

6. 5.1 Describe other
   - Text
7. Describe how your site gathers and evaluates financial conflicts of interest for the study team members (PI and other research team members)
   - Text

If there are any additional supporting documents related to your study that have not already been uploaded:

Name: Version:

There are no items to display.

The information provided in this application represents an accurate description of local context for the intended performance site.

Participating Site – Documents Tab (Post-Activation)

Main | IRB | Documents | Amendments | Continuing Reviews | Incident Reports | More...

Site Specific Documents:

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<th>Name</th>
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Site Specific IRB Documents:

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Study Wide Documents

University of Michigan IRB Approved Consent Template Documents:

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University of Michigan IRB Approved Protocol Documents:

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Post Approval: Other IRBMED Submissions
Accepting Oversight

Multi-site Research Application:
- Study-wide amendments
- Study-wide safety reports
- Study-wide continuing reviews
- Study-wide termination

Participating Site Application:
- Site-specific amendments
- Site-specific incident reports
- Site-specific continuing review data
- Site-specific termination

Budget Considerations
Kevin Ferrell
Direct and Indirect Costs for sIRB Review

Primary sIRB Activities
- Conducting the ethical review of the proposed research protocol and the informed consent template for the study

Secondary sIRB Activities
- Review of site-specific considerations and performing ongoing IRB oversight of each participating site

Changes in regulations for recovering review costs
- Institutions can recover the costs for Secondary sIRB activities since these are considered direct costs for review under the NIH policy.

How Rates are Determined

Recharge rate for Single IRB review
- A calculated cost per hour for review by IRBMED
- Allows for up-front budgeting for proposals
- Based upon the complexity of the project

Fees include:
- Study Level Start-up
- External Site-Level Start-up (Year 1)
- External Site-Level Recurring (Year 2+)
Rate Quote per Participating Site

Current Method

• Contact IRBMED to discuss options early
  
  At least 8 weeks ahead of grant due date

• Completion of a single IRB request form is required

Forthcoming Method

• Contact IRBMED to discuss options early
  
  At least 8 weeks ahead of grant due date

• Submit single IRB request form via MiCORES

• If it is determined that U-M will be the IRB of Record, a quote will be sent detailing the rate per participating site for review.

MiCORES

UMICH Single IRB Review

Overview of Institutional Review Board Services

University of Michigan’s Institutional Review Boards (IRBs) are designated to meet the needs of researchers conducting medical and non-medical related human research studies, regardless of sources of funding. The IRBs provide oversight for the University of Michigan Human Research Protection Program which is an institutional review board accredited by the University of Michigan Office of Research (UMOR). IRBMED or IRB Health Sciences and Behavioral Sciences (IRB HSSB) may provide oversight services for your human research study depending on the responsibilities you provide for this survey.

IRBMED is supported by the U-M Medical School. IRBMED is devoted to reviewing research conducted at the U-M Medical School. IRBMED’s mission is to ensure that all research conducted at the University of Michigan complies with all applicable laws, regulations, and University policies that are designed to protect the rights and welfare of human subjects. IRBMED’s mission is to ensure that all research conducted at the University of Michigan complies with all applicable laws, regulations, and University policies that are designed to protect the rights and welfare of human subjects.

IRBMED is also responsible for reviewing IRB-IRB regulated research, clinical investigations conducted by the U-M School of Dentistry, some research using the Functional MRI (fMRI) Laboratory and for research that uses Michigan Medicine’s clinical health information. IRBMED research activities are reviewed by one of six (6) different IRBs depending on the type of research and medical expertise required to review the human research and medical interventions involved.

IRB Health Sciences and Behavioral Sciences (IRB HSSB) is supported by UMOR. IRB HSSB provides oversight for research involving health, behavioral, educational and social science research conducted at U-M’s Ann Arbor, Dearborn and Flint educational campuses and at other collaborating institutions or organizations by U-M faculty, staff, students and others. IRB HSSB does not include research conducted at Michigan Medicine with limited exceptions. IRB HSSB human research activities are reviewed by one of two (2) IRBs depending on the specialty area of the researchers, location of the researchers and/or human subjects involved in the research.

This survey is designed to collect information necessary for your U-M IRB (IRBMED or IRB HSSB) to determine the appropriate IRB oversight for your multi site or other collaborating human research project. U-M IRBs typically provide three (3) types of services to the human subjects research community related to single IRB oversight. You will be asked to identify if you are requesting a U-M IRB to:

1. Serve as the reviewing IRB (IRB-of-Record) for an individual collaborator or for an organization that may or may not have an IRB or FWA (Federal Wide Assurance).

   An Exempt Collaborator is defined as an individual or entity not affiliated with the University of Michigan who is collaborating with University of Michigan researchers. This includes performing research on behalf of the University of Michigan or participating sites.

   The University of Michigan does not enter into agreements for Exempt research. If you are a Collaborator on research, you should seek an exempt study determination at your own institution.
MiCORES Billing

MiCORES Billing Management

Price Breakdown
- Study Level Start-up Rate (one-time standard fee charge)
- External Site-level Start-up = $X/external site
- External Site-level Recurring = $X/external site/year

- Invoices will be sent from MiCORES via email directly to the Responsible Investigator for the project.
- Individual invoices are not sent to each participating site investigator.
- It is expected that the Responsible Investigator will coordinate payment of the fees, whether the fee is paid as a direct cost on the primary award or from a subcontract.
- Billing is done on a monthly basis for any invoices sent out.
IRBMED: Ceding Oversight and Workflows

Angela Faber

Ceding IRB Oversight Discussion

IRBMED process for initiating a ceded study
- Commercial IRB
- Academic IRB

Post Approval Activities
- Upload Non-UM IRB Approval Documents
- Amendments
- Continuing Reviews/Terminations
- Adverse Events and ORIOs
Regulatory Requirement for sIRB in MSR

OHRP (Common Rule)

• Requirement became effective Jan. 20, 2020
• Federally funded/supported by agencies that have adopted/signed on to the new 2018 Common Rule
• Not limited to clinical research
• Domestic sites (U.S)

What is ceding?

• Because of regulation changes, only one IRB reviews and approves research studies.

• Ceding oversight means IRBMED will rely on the review and approval of another IRB.

• IRBMED does not approve ceded research studies; instead IRBMED acknowledge the review by another IRB.

• U-M is still responsible for local context issues and ancillary reviews.
Use of Independent (Commercial) IRBs

Finalized Master Services Agreements
• Permits ceding to several independent IRBs:
  • Advarra (formerly Shulman, Chesapeake, Quorum)
  • Western IRB (WIRB) (formerly Copernicus)
  • NCI CIRB
  • Ethical and Independent Review Services (E&I)
• An eResearch application is always required when requesting to cede to an external IRB.
• The "Request Review by a Non-UM IRB" (Ceding) Application within eResearch is required for an Acknowledgement letter from IRBMED.

Ceding to Commercial IRBs
- **Type**: Requesting review by non-UM IRB (Section 1-1.1 of the eResearch application)
- **You will need**: Finalized protocol, informed consent templates, and overall study approval.
- **Submit Application**
- **All local ancillary reviews are still required as part of this process.**
- **This is a limited type of review.**
- **Acknowledgement**
- **Submit an application to the commercial IRB.**
- **Remember U-M is not activated as a performance site until IRB of record and/or sponsor indicates so.**
Independent IRB Review

Documents required when submitting:

- IRBMED acknowledgment letter
- Section 25-1 from IRBMED application (HIPAA)
- ICF with U-M boilerplate language inserted

Initial sIRB Request - Ceding

To request IRBMED’s support to cede oversight to an external:

Contact IRBMED prior to grant applications

1. Contact IRBMED at least 3 weeks prior to grant application due date
2. Request is discussed with leadership and a letter of support is drafted.

Email the sIRB team for request: irbmedreliance@umich.edu
Academic IRBs

• U-M does not have any master services agreement with external academic IRBs.
• These requests will be made on a study-specific basis.

SMART IRB

• IRBMED has signed on to be a participating institution with the SMART IRB agreement and prefers to use that route for agreements if the academic IRB participates in it as well.

Ceding to External Institutions

After Notice of Grant Award

• Type: Requesting review by non-UM IRB (Section 1-1.1 of the eResearch application)
  • You will need: Finalized protocol, informed consent templates, overall study approval and any agreement document and/or local context forms.
  • Submit Application

• All local ancillary reviews are still required as part of this process.

• This is a limited type of review.
  • Local context, agreement processing and approval.

• Depends on site processes
  • Remember U-M is not activated as a performance site until IRB of record and/or sponsor indicates so.
Academic IRB Review

• Additional Required Documents
  • Local Context Form
    • State law and U-M requirements
  • Study Specific Reliance Agreement
    • Initiated by the lead site
  • ICF with U-M boilerplate language inserted (prior to IRBMED acknowledgment)

After U-M Activation

Upload Non-UM IRB Approval Documents Activity

• Click box stating U-M received approval from external IRB
• Upload external IRB approval letter for U-M as performance site
• Upload external IRB approved ICF

This communicates to IRBMED that U-M is now a performance site. Also, funding will be released.
Post Approval: Other IRBMED Submissions
(Ceding Oversight)

- Amendments that affect Study team or Ancillary Committee(s)
- UM-specific Adverse Events
- UM-specific ORIOs
- UM-specific continuing reviews
- UM-specific termination

Ceding Application

Amendments

Submit amendments that impact U-M ancillary committees:
- Research Pharmacy (aka IDS): changes in dosing, addition of medication prescribers;
- RDRC/SHUR: changes in radiation dosing;
- CRAO: billing calendar updates, changes that would impact subject injury language in consent;
- COI: addition/removal of study team members

What to submit:
- Upload any documents that prompted submitting the amendment
- External IRB approval letter
Reportable Events

Submit the following events involving local subjects to IRBMED:

- **Serious Adverse Events** that are related to the research per IRBMED guidance
- **Unanticipated Problems**
- **Protocol deviations** that may represent a systematic problem requiring local evaluation by IRBMED to determine that sufficient local resources are available for safe conduct of the study
- Reports of Continuing and/or Serious **Non-Compliance**
- **Study holds or suspensions** that are not built into the study design from External IRB or Sponsor (e.g.: interim analysis or enrollment complete need not be reported)

**May require dual reporting – IRBMED and External IRB**

Continuing Review Approval

**Continuing Review**
- Submit prior to expiration
- Include the external IRB letter

**Study Termination**
- Include the external IRB letter
More Information

- External IRB specific information
- Reporting requirements
- Boilerplate ICF Language

https://umich.app.box.com/v/MultisiteResearchDocuments

PI & Study Team Responsibilities
Nicole Duffy
Responsibilities when Accepting

• Adequate training
• Have a communication plan
• Obtain documented approval to cede review from relying site(s)
• Promptly respond to questions/inquiries from relying site(s)
• Provide the relying site with the applicable IRBMED policies
• Initiate participating site applications

Responsibilities when Accepting Continued...

The Principal Investigator must:

• Be aware of all reportable events, amendments & continuing review data
• Submit study-wide amendments, reportable events & continuing review reports
• Promptly report to relying site(s) any problems involving risks to subjects or significant subject complaints, when needed
• Provide access, upon request, to study records for audit purposes
Responsibilities when Ceding

- Adequate training
- Comply with the communication plan
- Obtain documented approval to cede review from IRBMED
- Promptly respond to questions/inquiries from lead site
- Follow the single IRB reporting policies
- Continue reporting locally as outlined by IRBMED procedural documents
- Provide access, upon request, to study records for audit purposes

Quality Assurance Efforts
Angela Faber
Quality Assurance Discussion

U-M obligations when:
- A study is ceded to another IRB
- IRBMED is the IRB of record for other institutions

Expectations when a study is chosen for review:
- What will be reviewed
- Timeframe
- Possible next steps

What do the regulations say?

45 CRF 46.103(e)
"...the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy..."

45 CFR 46.155(9)
Documentation specifying the responsibilities that an institution and an organization operating an IRB each will undertake to ensure compliance with the requirements of this policy, as described in §46.103(e))

U-M Operations Manual Part 12
AAHRPP Standards – Element I-5
"The Organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program"
How does this apply to a ceded study?

Although the IRB review and approval has been ceded to another IRB, local context issues and ancillary reviews are still a U-M responsibility.

...and to a study when IRB MED is the reviewing IRB?

- IRB MED is responsible for the conduct at all performance sites
- Need to have a mechanism for assessing what is happening
- IRB MED can partner with the PI and the PI may request review of a performance site
How are studies chosen?

1. Random
2. Past areas of concern
3. Targeted reviews
   • Informed Consent Form review during UMOR mandated pause

What is reviewed?

• Version Control
  • Informed consent
  • Protocol amendments
• Eligibility Criteria
• Data Management
• Conflict of Interest Management Plans
• Other as needed

IRBMED may review some or all of these areas during one review.
Quality Review Process

- All multi-site studies will be evaluated
  - Scheduled reviews based on complexity and frequency
- Reviews will be conducted electronically, not in person
- May request de-identified documents as confirmation
- May request further information or clarification
- Final report

Possible Outcomes

- No further action necessary
- Refer to ORCR for additional review
- Board review and determination
- Notification of other involved IRBs
  - IRB of record for a ceded study
  - Performance site PI and IRB for a relying site
Thank you.

Single IRB and Multi-Site Research Guidance on Research A-Z