SMART TALK

A Community Forum to Explore Issues Surrounding Single IRB Review

Funded by the NIH National Center for Advancing Translational Sciences through its Clinical and Translational Science Awards Program, grant number 3UL1TR002541-01S1.

What Is SMART Talk?

An approximately monthly forum with:

- Presentations on topics relevant for single IRB review
- Q&A on topic presented as well as questions submitted when participants register

Open and free to anyone with interest

Upcoming sessions

May: No SMART Talk – AAHRPP virtual conference

June: Reviewing IRBs: Working with Relying Institutions and Study Teams

FYIs

Please provide feedback by completing the survey. A link will be posted in chat and emailed. This helps us identify topics of interest to the community.

A recording of this talk will be posted on the SMART IRB website

A link to the talk will be sent to those who registered for the talk when it is posted

If you have any questions for the panelists, please use the chat function or Q&A function to submit them

SMART IRB Harmonization Working Group: Recommendations for Harmonization of Conflict of Interest Management and Review

Other Harmonization Steering Committee Recommendations

- **Ancillary Reviews** Posted for comment
- **Single IRB Continuing Review Process**
- **Single IRB Review: Responsibilities Associated with the Review of Study Personnel**
- **Reportable Events**
- **Institutional Profile**
- **Protocol-specific Document**
- **Fees and Costing Models under NIH sIRB Policy**
- **Institution v. IRB Responsibilities Guidance**
- **In progress:**
  - **Post-Approval Auditing for Studies Subject to Single IRB Review**

Conflicts of Interest HSC Working Group

SMART Talk

Wednesday, April 21, 2021

Stacey C. Goretzka, CIP
IRB Manager, Medical University of South Carolina
SMART IRB Ambassador

Monika S. Markowitz, Ph.D
Director, Research Integrity and Ethics
Office of the Vice President for Research and Innovation
Virginia Commonwealth University

Conflicts of Interest Working Group Membership

- Lindsay Abraham (WCG)
- Holly Bante (University of Cincinnati)
- Barbara Bierer (Harvard Catalyst/Brigham & Women's Hospital)
- Tiffany Coleman (Augusta)
- Valery Gordon (NCATS)
- Stacey Goretzka (Med Univ of SC) – *Co-Leader*
- Jonathan Green (NIH)
- Karen Jeans (VA)
- Martha Jones (MGB)
- Monika Markowitz (VCU) – *Co-Leader*
- Julia Slutsman (NIH)

Started and Finished

- First Meeting: August 24, 2020
- Last Meeting: March 29, 2021
- Met approximately twice a month

CHARGE!

Conflicts of Interest HSC Working Group

- Charge: Identify, propose and harmonize best practices for conflict of interest reviews of studies being reviewed under a reliance agreement.
- For Committee Consideration:
  - What materials should be collected from investigators for COI reviews?
  - Can we identify a threshold for reporting conflicts of interest and for requiring a management plan?
  - Can we develop guidance on consent document disclosures?
  - Guidance for how reviewing IRBs should handle COI reviews for investigators at relying institutions.
  - Consider differences in how COIs are handled by federal agencies.
  - Recommendations on how to handle institutional conflicts of interest by either the reviewing IRB or the relying institution.

Committee Discussion

Top issues for committee to focus on:

1. Agreement on what is a COI – institutional, individual.
2. How should a reviewing IRB handle institutional COI identified at the relying institution.
3. How is the reviewing IRB apprised of a COI at a relying institution.
4. Management of COI by the reviewing IRB when identified by relying institution – possible management scenarios.
5. Trusting the COI review of the relying institution.
6. How much info about the COI identified by the relying institution should be shared with reviewing institution – the management plan, details about the SFI?.
7. Role of the reviewing IRB in assessing and managing COI for conformity and consistency across institutions and studies.
8. Non-financial COI
9. Different COI regulations among different federal agencies - relying and reviewing IRB responsibilities.
10. Other issues?

Additional considerations:

- IRB "mission creep" for evaluating investigator COI:
  - IRBs often assume institutional role in evaluation of investigator COI
- IRB threshold for determining when a financial COI exists:
  - IRBs are highly variable on determinations of financial COI, especially when (1) an Investigator is a member of the board or consultant for the collaborator or (2) holds a patent.
  - IRBs variable in reference to the IRB review of the involved research, including informed consent issues.
- IRB determinations of mitigation when an investigator COI has been determined to have a financial conflict of interest as reported to the IRB
  - IRBs often move into institutional territory when determining mitigation of financial conflict of interest from a human subjects protections position
- Strategies for determining changes in financial COI after a study has been initiated:
  - What seems to be a very simple situation is not – how does an IRB ensure that any change in financial COI that would impact the IRB's on-going approval of the protocol is reported. [to it.]

SMART IRB Master Reliance Agreement (v2)
Responsibilities of the Reviewing IRB(s) & Reviewing IRB Institution(s)

5.8 Conflicts of Interest. Consider any applicable conflict of interest assurances received from federal Relying Institutions or conflict of interest determinations and associated management plans provided by non-federal Relying Institutions pursuant to Section 6.6 hereof with respect to the Overall PI, Site Investigator(s), and other Research Personnel in connection with the Research. The Reviewing IRB will ensure that any management plan is incorporated into its initial or continuing review or other deliberations, as applicable, and without limiting the foregoing, that any disclosures to subjects required by the plan and that are approvable by the Reviewing IRB are included in the approved informed consent form(s) for the relevant Relying Institution. The Reviewing IRB retains the authority to impose additional prohibitions or conflict management requirements more stringent or restrictive than proposed by a non- federal Relying Institution if necessary to approve the Research, provided, however, the Reviewing IRB will not modify or change any management plan or mandated disclosure to subjects without discussion with and acceptance by the Relying Institution.

SMART IRB Master Reliance Agreement (v2)
Responsibilities of the Reviewing IRB(s) & Reviewing IRB Institution(s)

- In the extraordinary circumstance that the Reviewing IRB is unable to implement/approve a non-federal Relying Institution's prohibitions or management plans, the Reviewing IRB will so inform such Relying Institution or, if the non-federal Relying Institution fails to accept any additional prohibitions or requirements, the non-federal Relying Institution will so inform the Reviewing IRB. If the institutions are not able to identify a mutually agreeable approach, the Research will be withdrawn from Ceded Review (without an IRB approval or disapproval) with respect to that non-federal Relying Institution.
- If the Reviewing IRB concludes that it cannot rely upon the assurances from a federal Relying Institution, the Reviewing IRB will so inform the federal Relying Institution, and the Research will be withdrawn from Ceded Review (without an IRB approval or disapproval) with respect to that federal Relying Institution.

SMART IRB Master Reliance Agreement (v2) Responsibilities of the Relying Institution(s)

6.6 Conflicts of Interest. Maintain policies regarding the disclosure and management of Research Personnel conflicts of interest related to Research and to share those policies with the Reviewing IRB, as requested.

Unless the Reviewing IRB and the Relying Institution agree to an alternate approach in advance, the non-federal Relying Institution(s) will perform its own conflict of interest analysis under its relevant policies and provide to the Reviewing IRB any resulting conflict of interest determinations, prohibitions, and management plans as well as any updates to such prohibitions, determinations, or plans, that the Relying Institution has determined to be necessary for the conduct and approval of the Research at the Relying Institution under such policies. The non-federal Relying Institution will abide by and will require its Research Personnel to abide by its institutionally required prohibitions or management plans related to the Research, as well as any additional prohibitions or conflict management requirements required by the

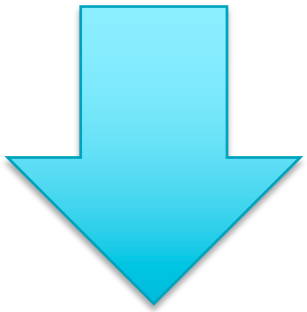
SMART IRB Master Reliance Agreement (v2) Responsibilities of the Relying Institution(s)

Reviewing IRB. As provided in Section 5.8, in the extraordinary circumstance that the Reviewing IRB is unable to implement/approve the non-federal Relying Institution's prohibitions or management plans, the Reviewing IRB will so inform the non-federal Relying Institution. If the non-federal Relying Institution fails to accept any additional prohibitions or requirements of the Reviewing IRB, the non-federal Relying Institution will so inform the Reviewing IRB. If the institutions are not able to identify a mutually agreeable approach, the Research will be withdrawn from Ceded Review (without an IRB approval or disapproval) with respect to that non-federal Relying Institution.

Federal Relying Institution(s) will provide assurance to the Reviewing IRB that they have completed conflict of interest analyses under existing relevant federal policies and that the participation of agency Research Personnel is permissible and consistent with federal law. Federal Relying Institutions will abide by and will require their Research Personnel to abide by institutionally and legally required prohibitions or management plans related to the Research. If the Reviewing IRB concludes that it cannot rely upon the assurances from a federal Relying Institution, the Reviewing IRB will so inform the federal Relying Institution, and the Research will be withdrawn from Ceded Review (without an IRB approval or disapproval) with respect to that federal Relying Institution.

Began by developing 3 separate documents

- Parent – "SMART IRB: Guidance for Harmonizing COI Considerations for Reviewing and Relying Institutions"
- Child – "Specific guidance: Identifying whether there is a COI and Management Strategies"
- FAQs – started with 14 questions >>>> ended with 5



Combined into one continuous document

Recommendations

Guidance

SMART IRB: COI Review Processes for Single IRB Review

Contents:

A. Regulatory and ethical justification for IRBs reviewing COI

B. Who is responsible for determining if an investigator COI exists?

- **B. 1 The relying institution has a COI policy compliant with 42 CFR 50 Subpart F for PHS funded research**
- **B. 2 The relying IRB's institution indicates that it does not have a COI policy compliant with 42 CFR 50 Subpart F for PHS funded research and/or no COI policy at all**

C. Identifying whether there is a COI and Management Strategies

D. FAQs

A. Regulatory and ethical justification for IRBs reviewing COI

- For this guidance document, COI refers to an individual's financial COI. Institutional COI if briefly addressed in an FAQ.
- NIH definition of a financial COI adopted
- Conflicts of interest directly impact the IRB's ability to approve research.
- IRBs must be aware of any investigator COI and determine that adequate measures are in place to manage the conflict.
- Challenges emerge with the single IRB review process.

B. Who is responsible for determining if an investigator COI exists?

- SMART IRB Master reliance agreement
  - Requires relying institutions to "Maintain policies regarding the disclosure and management of Research Personnel conflicts of interest related to Research and to share those policies with the Reviewing IRB, as requested."
- Default position: Relying institutions are responsible for performing a COI review of their investigators under their own policies.
- Alternate approach
- Guidance document describes two scenarios

B.1. The relying institution has a COI policy compliant with 42 CFR 50 Subpart F for PHS funded research; it will review for COI and develop management plan when COI is identified.

Roles and Responsibilities

Relying Institution

- Have polices that define what interests require disclosure and which are considered a significant financial interest (SFI)
- Have a process in which any identified COI is resolved
- Communicate the presence of any COI and associated management plan to the Reviewing IRB
- Non-federal institutions will provide information about the managed conflict of interest as well as the management plan to the reviewing institution's IRB upon request.
  - A Federal Relying Institution(s) will provide assurance
- Monitor the relying institution's investigators' adherence to the management plan

Reviewing IRB/Institution

- Have a process to receive information about COI and associated management plans from relying institutions
- Determine if the management plan is sufficient or if additional management strategies are needed
- If additional changes or strategies are needed, communicate with relying institution
- Accept the assurance from the federal agency that all federal investigator COI policies have been met and that participation of federal investigators in the research is permitted.

B.2. The relying institution indicates that it does not have a COI policy compliant with 42 CFR 50 Subpart F for PHS funded research and/or no COI policy at all and is thereby relying on the reviewing institution or the primary recipient of federal funds (if applicable) to review for COI and manage COI for conflicted investigators.

Roles and Responsibilities

Relying Institution

- Makes it clear in the Reliance Agreement that it does not have a COI policy and process and/or does not have a COI policy that is adherent to 42 CFR 50 Subpart F when the research is PHS funded.
- Ensures that its investigator(s) understand that they will be working with the reviewing IRB's COI review entity for disclosure and review of their financial interests according to the policy of the reviewing IRB's institution.
- Point of contact will disseminate the management plan to its investigators and institutional officials.
- Responsible for monitoring and ensuring adherence of the conflicted investigator with the COI management plan.

Reviewing IRB/Institution

- Have a process for investigators associated with the relying institution to confidentially disclose financial interests to the reviewing IRB or institution.
- Review the disclosed financial interests of investigators from the relying institution according to its own policy.
- Determine whether investigators at the relying institution have a conflict of interest.
- If determined that a COI exists for investigators from the relying institution, the COI will be mitigated or managed according to the reviewing IRB's institutions' policy and process.
- the conflicted investigator at the relying institution will be asked to agree to or accept the management plan.
- Implement aspects of the management plan within its purview.

C. Identifying whether there is a COI and Management Strategies

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1. Financial interests that may constitute conflicts of interest within a study context

- Consulting for a company* (payment > $5,000 over the past 12 months) associated with the study, includes Scientific Advisory Board membership.
- Paid speaking (> $5,000 over the past 12 months) for a company associated with study.
- Paid or reimbursed travel (> $5,000 over the past 12 months) by a company.
- Serving in a paid or unpaid fiduciary role for an entity, i.e. Board of Directors, Chief Scientific Officer, associated with the study.
- The conflicted investigator's investigational product being evaluated in the study is licensed to the company sponsoring the research or providing the investigational product.
- The conflicted investigator's investigational product utilized in the study is patented, but not licensed.
- Founder and/or equity owner of a non-public company associated with the study.
- Holding a > $5,000 equity interest over the past 12 months in a public company associated with the study.

C. Identifying whether there is a COI and Management Strategies

2. Consider the impact of the conflict of interest

- Is the nature of the conflict something that a participant would want to, or should, know about in order to make an informed decision?
- Could the conflict result in decisions that adversely affect subject safety and welfare?
- Could the conflict bias the conflicted investigator's judgement so that decision making about eligibility, adverse event reporting, clinical care, etc. is not objective?
- Could the conflict impact the data collection?
- Could the conflict impact analysis of data?
- Is the conflicted investigator's participation essential for the conduct of the research? (unique knowledge, skill, access to patient population?)
- Could the outcome of the research impact the financial interest?

C. Identifying whether there is a COI and Management Strategies

Consider COI management strategies

COI Management Strategies – implement one or more
1) Disclosure (if legally permissible) of the conflict in the informed consent form and in any publications or presentations related to the research.
2) Restricted access to identifiable data (communicate with relying IRB)
3) Restrictions on the conflicted investigator from determining eligibility status of prospective subjects (communicate with relying IRB).
4) Conflicted investigator cannot obtain informed consent (communicate with relying IRB).
5) Restrictions on the conflicted investigator from adjudicating AEs/SAEs/UPs (communicate with relying IRB).
6) Restrictions on the conflicted investigator participating in data analysis and interpretation (communicate with relying IRB).
7) Removal of conflicted investigator as PI but retain a co-investigator role. (Requires significant dialogue with the relying IRB).
8) Removal of conflicted investigator from involvement in the conduct of the study. (A last resort consideration. Requires significant dialogue with the relying IRB).

The strategies are organized from minimal management to more restrictive management. Because management strategies beyond #1 may impact the relying institution's ability to conduct the study, unilateral application of COI management by the reviewing IRB without communication with the relying institution is discouraged.

D. Frequently Asked Questions

- How should a reviewing IRB handle a situation where COI management plans for similar COIs differ greatly among other institutions involved in the same study?
- For PHS funded research, who is responsible for ensuring that an institution's COI policy adheres to the PHS regulation on Promoting Objectivity at 42 CFR 50 Subpart F?
- If the reviewing IRB has follow-up questions regarding an investigator's COI, whom should they contact?
- What kind of information about COI and its management should be conveyed to the reviewing IRB?
- How is organizational or institutional COI dealt with for both the relying and reviewing institutions?

Did we address the charge?

For Committee Consideration:

1. What materials should be collected from investigators for COI reviews.
2. Can we identify a threshold for reporting conflicts of interest and for requiring a management plan.
3. Can we develop guidance on consent document disclosures.
4. Guidance for how reviewing IRBs should handle COI reviews for investigators at relying institutions.
5. Consider differences in how COIs are handled by federal agencies.
6. Recommendations on how to handle institutional conflicts of interest by either the reviewing IRB or the relying institution.

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1. Yes - in terms of COI disposition and management plan.
2. No threshold, all COI needs to be reported.
3. No – most reviewing IRBs will already have established ICF disclosure language.
4. Yes
5. Yes – cases where federal agency is the relying institution are infrequent.
6. Maybe? ICOI is a 'can of worms' also not addressed by the PHS regulations.

Discussion & Questions

Save the date for the next SMART Talk
June 16, 2021
2:00-3:30 pm ET

Reviewing IRBs: Working with Relying Institutions and Study Teams

Questions?
Contact
help@smartirb.org

Register at smartirb.org

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