AIM AHEAD

Regulatory Compliance Office

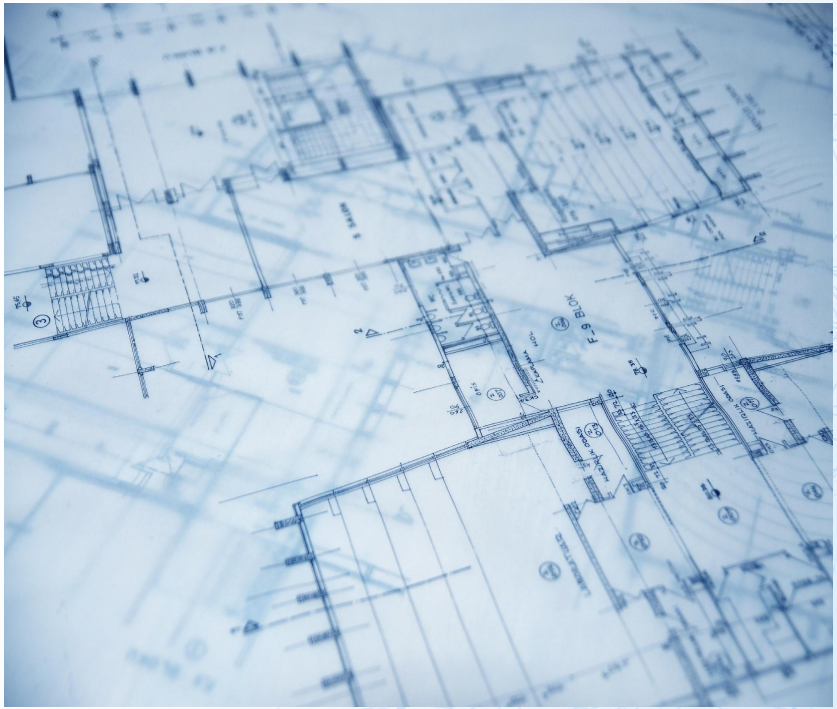
Maintaining Compliance After Approval

Modifications, Continuing Reviews, and Other Important Practices

AIM-AHEAD Coordinating Center is funded by NIH, Agreement No.: 1OT2OD032581

Today's Discussion

- Modifications and Continuing Reviews
  - IRB Oversight Refresher
  - What are mods/CRs?
  - When they may apply to your research
  - Why are they useful?
  - How to complete a mod/CR
  - Best practices



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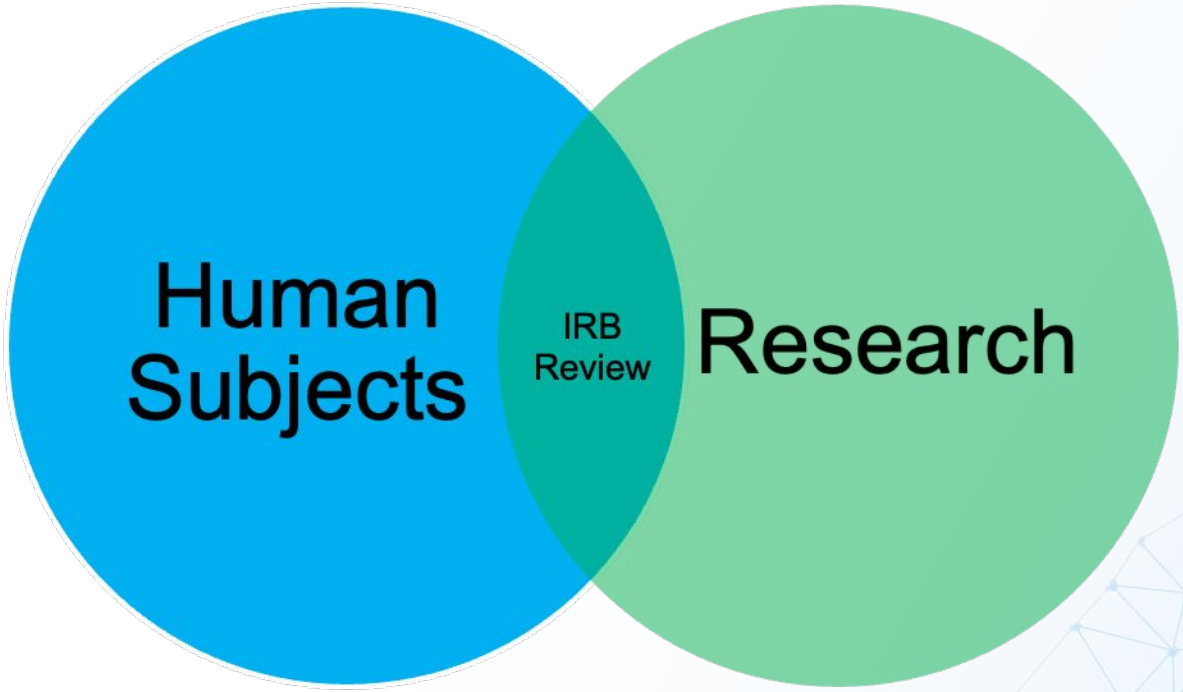
When is IRB oversight required?



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Adapting to a Changing Research Landscape

- A range of events and circumstances can influence the progress of your research study
  - Local, State, Federal Policies
  - Life events
  - Career events
  - Unforeseen outcomes
- Adapting your research study and maintaining compliance through anticipated and/or unforeseen changes is possible through modifications and the Continuing Review process

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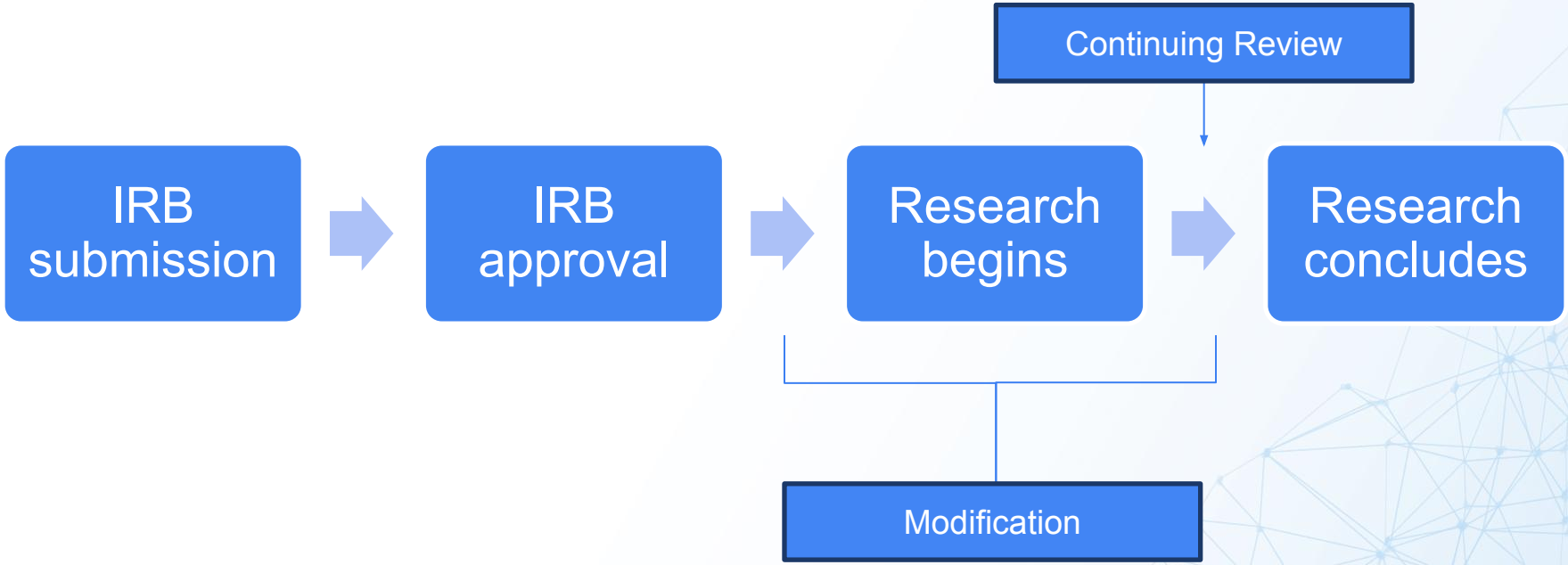
Research Study Timeline



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Modifications and Continuing Reviews (CRs)

Overview

- Modifications: formal requests to make changes to a research protocol that has already been reviewed and approved by an IRB
  - Modifications are submitted to the IRB that originally reviewed and approved your research

- Continuing Reviews: periodic re-evaluation of ongoing research studies to ensure risk has remained minimized and compliance is maintained
  - The frequency for CRs is determined by your IRB
  - Required at least annually for research studies approved as expedited or full board

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Modifications Overview

- When can you make a modification?
  - Any time after original approval
    - Can be made before official study implementation
- Why modify your study?
  - Operational feedback
    - Study design, methodology, or procedures
    - Study personnel or site changes
    - Data collection tools
  - Study Documents
    - Consent forms
    - Recruitment materials

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Modifications Example Scenarios

Scenarios that may require a modification

- Change of PI
- Addition of new federal funding source
  - AIM-AHEAD funding is federal funding
- Obtaining or recording identifiable data from a new source
- Active recruitment of new target population
- Change of data collection methodology
- Consent form revisions
- Addition of new study site
- Addition of study team members involved in subject engagement or analysis of identifiable data
- Additional data elements/variables added to dataset

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Modifications Example Scenarios

Scenarios that may not require a modification

- Wording changes that do not affect the meaning of text on research documents
- Changes in contact information for study personnel
- Target enrollment total change
- Changes to data analysis plans
- Adding questions to a survey or interview script that do not increase risk
  - No ‘sensitive’ data changes
- Increasing data security standards

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Modifications Process Overview

1. Identification of change to be made
2. Contact your IRB representative to confirm if a modification is necessary to implement the change(s) you aim to make
3. If a modification is required, you will use the same online portal you initially used to submit your protocol for IRB review and approval
4. IRB's will have different policies as to what changes warrant submission of a modification.
    - Note that as the PI, it is your responsibility to ensure that all applicable policies are followed.
    - RCO is here to help you adhere to any policies that may impact the changes you aim to make through modifying your research study

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Modifications Best Practices

- Plan ahead
  - Allow time for IRB review before implementing changes
  - Provide clear rationale for each proposed change
- Track your changes
  - In your research records, include tracked changes versions of revised documents. Your IRB will likely also require submission of a tracked changes version in your mod
  - Highlight how changes affect risks, benefits, or the consent process
- Do not implement study modifications until approved by IRB
- Ensure training and COI disclosures are updated for new personnel

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Continuing Reviews Overview

§ 46.109 IRB review of research.

- An IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year, except as described in §46.109(f).
    - Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:
        - (i) Research eligible for expedited review in accordance with § 46.110;
        - (ii) Research reviewed by the IRB in accordance with the limited IRB review described in §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);
        - (iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
            - (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
            - (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Source: https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.109#p-46.109(f)

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Continuing Reviews Overview

Components of a continuing review may include:

- Study progress report (enrollment numbers, adverse events, protocol deviations)
- Summary of any new findings that may affect risk/benefit ratio for subjects
- Updated consent document(s) if applicable
- Confirmation of data security and privacy protections
- Updates to research timeline or milestones
    - Recruitment updates, shifting to data analysis only, study closure, etc.

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Continuing Reviews Overview

- Do you need to complete a CR?
  - Your IRB approval letter/memo will have this information available
  - IRBs can define these differently, but CRs are typically needed when either of these dates are listed on your documentation:
    - Study Renewal Date, or
    - Study Expiration Date
- When does a CR need to be completed?
  - Check your original IRB approval document for a date
  - These dates are typically one year after initial approval was given by an IRB, but may vary depending on your IRB's policies

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Continuing Reviews Best Practices

- Take note of when your study is up for renewal and allocate time for CR processes in your research timeline
  - When you receive a determination from your IRB, a CR date will be indicated on your determination letter
  - Start the CR process at least a month in advance (preferably two months) to avoid a last-minute rush or possible lapses in compliance
    - An IRB's turnaround times can fluctuate throughout the year, and starting this process early can avoid timing complications
- Maintain thorough research records throughout the course of your study
  - This will put you in the best position to complete your CR in a timely and accurate manner
    - Make sure to track:
      - Subject enrollment
      - Adverse event and deviation tracking
      - Staff training updates
- If your CR date passes without renewal
  - Pause **ALL** enrollment processes, research activities, and data analysis until CR is completed

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Modification or CR Completion – What Next?

- When you receive an approval notice from your IRB about your modification or renewal of your study through CR completion:
  - You will receive an official document from the IRB indicating the approved changes and/or renewal of your study
  - When a CR is completed, a new renewal/expiration date will be provided. Make note of this new date and prepare accordingly in your research records
- Take actions as needed resulting from the changes made through the modification process
  - Inform subjects if required by your IRB
  - Issue new study materials to subjects if applicable
- Remember you can submit modifications as needed throughout the course of your research
  - Just because you modified your study once does not mean this cannot be done additional times

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Reportable New Information(RNI)

- An event is reportable if it meets criteria for being unanticipated, serious, and related to your research activities
- When such an event is recorded, researchers must promptly report it to the IRB
- Reporting procedures:
  - Researchers must submit an RNI to the IRB using the organizations designated submission system
    - Most organizations will have a template for reporting
  - The specific deadlines for reporting vary depending on the nature and severity of the RNI, with some events requiring reporting within 24 hours, others within 5 or 10 business days.
  - The RNI submission typically involves completing a form or supplement and attaching relevant supporting documents, such as a DSMB report.

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Reportable New Information(RNI)

- Examples of events that warrant reporting as an RNI include
  - Unanticipated problems involving risks to subjects or others.
  - Non-compliance with the IRB-approved protocol.
  - New risk or safety information related to the research.
  - Audit findings that raise concerns about participant safety or data integrity.
  - Allegations of non-compliance or research misconduct.
  - Complaints from participants that cannot be resolved by the research staff indicating an unanticipated risk.

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Protocol Deviations (PD's)

- For studies requiring continuing review, you will typically include a summary of any deviations that required reporting since the previous review
- Protocol deviations vary in their impact related to potential risk to subjects by conducting research outside of your approved protocol:
  - Major deviations:
    - those that impact participant safety, affect the integrity of study data, or significantly alter the risks to participants, generally require prompt reporting to the IRB (e.g., within five or seven days of discovery, depending on the organization's policies).
  - Minor deviations:
    - those that do not significantly impact participant safety or the integrity of study data, may not require prompt reporting.
      - However, organizations may recommend keeping a log of these minor deviations and summarizing them at the time of continuing review.

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Adverse Events (AE's)

- **What to Include in the Continuing Review Report**
  - A summary of all AEs that have occurred during the study period
  - An analysis of the relevance and significance of these events
  - The investigator's assessment of the relationship of the events to the research
- **What to Report Promptly**
  - A serious AE that was unexpected and related to the research
  - An unexpected problem involving risks to subjects or others that requires changes to the protocol or consent form

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Thank you!

- The RCO is here to help!
  - Reach out to us via the RCO Inbox
    - rco@aim-ahead.net
    - AIM-AHEAD Connect RCO Help Desk
  - Consultations, one-on-one support, regulatory resources and expertise

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A customized subset from **OCHIN**

Data Bridge from **MedStar Health**

60+ studies from **NHLBI BioData Catalyst**

NCATS N3C Data Enclave

NIH All of Us

SCHARE

AWS Public datasets

https://docs.google.com/presentation/d/1XE5wZDVEWlmm9ehCgsQgaS8Xk0hmYcq4/edit?slide=id.g2bc4684dfea_1_0#slide=id.g2bc4684dfea_1_0

https://docs.google.com/spreadsheets/d/14yZzqUAABtSJC3tXSEI_t4wFCPWw8UyybP9ZaGgh2NI/edit?gid=0#gid=0

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