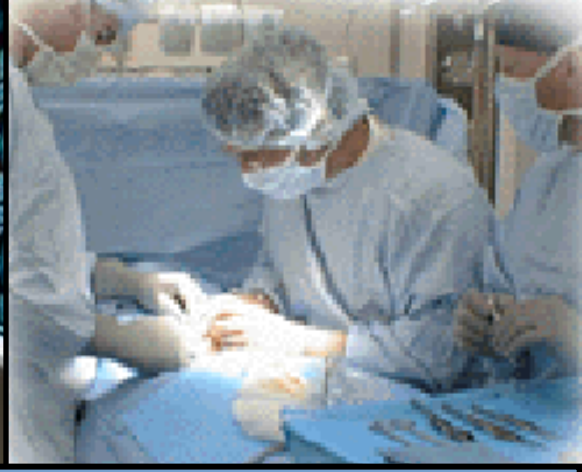
National Cancer Institute



NCI CIRB Initiative

Alliance Spring Group Meeting
Chicago, IL
May 8, 2014

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CIRB Operations Office

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

National Cancer Institute

Agenda

- Overview of the CIRB
- Key definitions
- Steps for enrolling in the CIRB
- Opening a study
- After opening a study
- Benefits of the CIRB

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Overview of the CIRB

- **Goal**
  - ***Reduce the significant local administrative burdens of multi-site trials while maintaining a high level of human subjects protection***
- **Three CIRBs**
  - ***Adult CIRB – Late Phase Emphasis***
    - **Began reviews of Cooperative Group Phase 3 treatment trials in 2001**
  - ***Adult CIRB – Early Phase Emphasis***
    - **Began reviews of phase 0, 1, 2 trials late 2013**
  - ***Pediatric CIRB***
    - **Began reviews of COG phase 2, 3 and pilot trials in 2004**

Overview of the Use of the CIRB

- **All studies on the CIRB menu can be opened by PIs at institutions enrolled in the CIRB.**
- **There is no requirement to specify which CIRBs an institution will be using.**
  - ***Institutions can only open studies that they have access to based on Network Group affiliations.***
- **Timelines for enrollment by institutions in the NTCN and ETCTN will be announced by NCI. The CIRB encourages institutions to enroll on an ongoing basis.**
- **The CIRB menu will not be expanded to include Group studies that were not previously reviewed by the CIRB.**
- **There is no fee to use the CIRB.**

Overview of the CIRB Model

- **As of January 1, 2013 the CIRB operates under an independent model for review of NCI-sponsored research**
- **What is the "independent model"?**
  - ***CIRB continues to review studies as before***
  - ***CIRB becomes IRB of Record for investigators***
    - **Local IRB has no review responsibilities**
  - ***CIRB reviews institution's local context considerations before approving new study at institution***
  - ***CIRB reviews locally-developed recruitment/educational materials; locally-occurring unanticipated problems or serious or continuing non-compliance; responds to investigator/institution questions***
  - ***Institution is responsible for monitoring conduct of research***
    - **Includes reporting concerns to CIRB**

Signatory Institution

- The Signatory Institution in the CIRB Initiative is the institution whose Signatory Official signs the Authorization Agreement and Division of Responsibilities document
- The Signatory Institution's responsibilities are outlined in the Division of Responsibilities
- The Signatory Institution must have a Federalwide Assurance (FWA)
- The Signatory Institution must have independent oversight of the research

Signatory Institution's Component Institution(s)

- **The Signatory Institution's Component Institution operates under a different name than the Signatory Institution but the Signatory Institution has legal authority for the Component Institution**
- **The following information for a Component Institution must be the same as the Signatory Institution:**
  - ***FWA number***
  - ***Local context considerations***
    - **If the local context considerations are not the same, the institution cannot be a Component Institution**
  - ***Boilerplate language and institutional requirements***
  - ***The office that monitors the conduct of research***

Signatory Institution's Affiliate Institution(s)

- **The following information for an Affiliate Institution must be the same as the Signatory Institution:**
  - ***Local context considerations***
    - **If the local context considerations are not the same, the institution cannot be an Affiliate Institution**
  - ***Boilerplate language and institutional requirements***
  - ***The office that monitors the conduct of research***

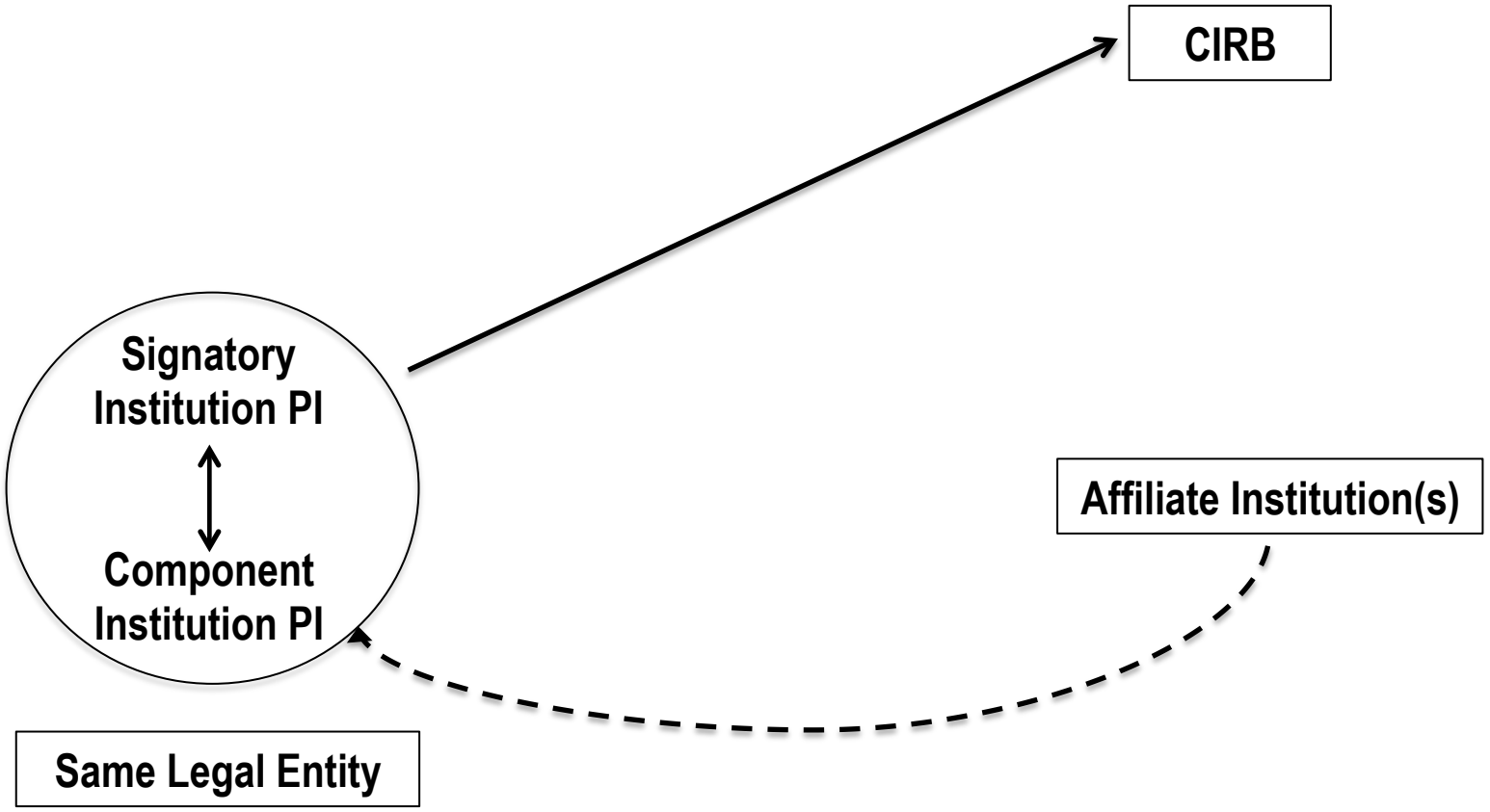
Institutional Relationships

- In the CIRB Initiatives, any Network institution can be Signatory Institutions. They can also be a Component or an Affiliate Institution of a Signatory Institution.
- All institutions involved in a grant funded arrangement should determine how using the CIRB is appropriate for each institution.

Signatory Institution's Principal Investigators

- **The Signatory Institution's Principal Investigators (SIPI) must have a working relationship with the the Signatory Institution.**
- **An SIPI may be located at a Component Institution because the Component Institution is part of the same legal entity as the Signatory Institution.**
- **An SIPI may not be from a Signatory Institution's Affiliate Institution.**

Principal Investigator Relationships to CIRB



Local Context Considerations

- **What constitutes the CIRB's review of local context?**
  - ***Consideration of local population for any unique requirements***
  - ***Confirmation that any institutional requirements, local and state laws are appropriately addressed***
  - ***Consideration if investigator has sufficient time to conduct research safely***
  - ***Consideration if investigator has an adequate number of qualified supporting research staff***
  - ***Consideration if facilities are adequate to conduct research and protect study participants***
  - ***Confirmation that boilerplate language for the consent form complies with Federal regulations***

Consent Form Review

- **CIRB Review of the Consent Form**
  - ***CIRB reviews and approves the model consent form as supplied by the Study Chair for each study***
  - ***CIRB reviews and approves the institution's boilerplate language as supplied in the Annual Signatory Institution Worksheet***
  - ***Principal Investigators have the responsibility to insert the CIRB-approved boilerplate language into the CIRB-approved model consent form***

Division of Responsibilities under CIRB Model

CIRB

- *Initial Review*
- *Continuing Review*
- *Amendment Review*
- *Conducts reviews for institutional local context considerations*
- *Reviews/determines Unanticipated Problems both locally-occurring and trial-wide impact*

Signatory Institution

- *Ensures safe and appropriate conduct of research at the institution*
- *Maintains records for CIRB-approved studies per network/program guidelines*

Institutional Considerations Prior to Enrollment

- Identify the Signatory Institution
- Verify that any institutions relying on the Signatory Institution's IRB meet the CIRB's definition of a Component Institution or an Affiliate Institution
- Identify the individual(s) who will be the Signatory Institution Primary Contact(s)
- Review the information required by the CIRB to assess your institution's local context considerations
- If you have any questions, contact the CIRB Helpdesk before you begin the steps for Enrollment

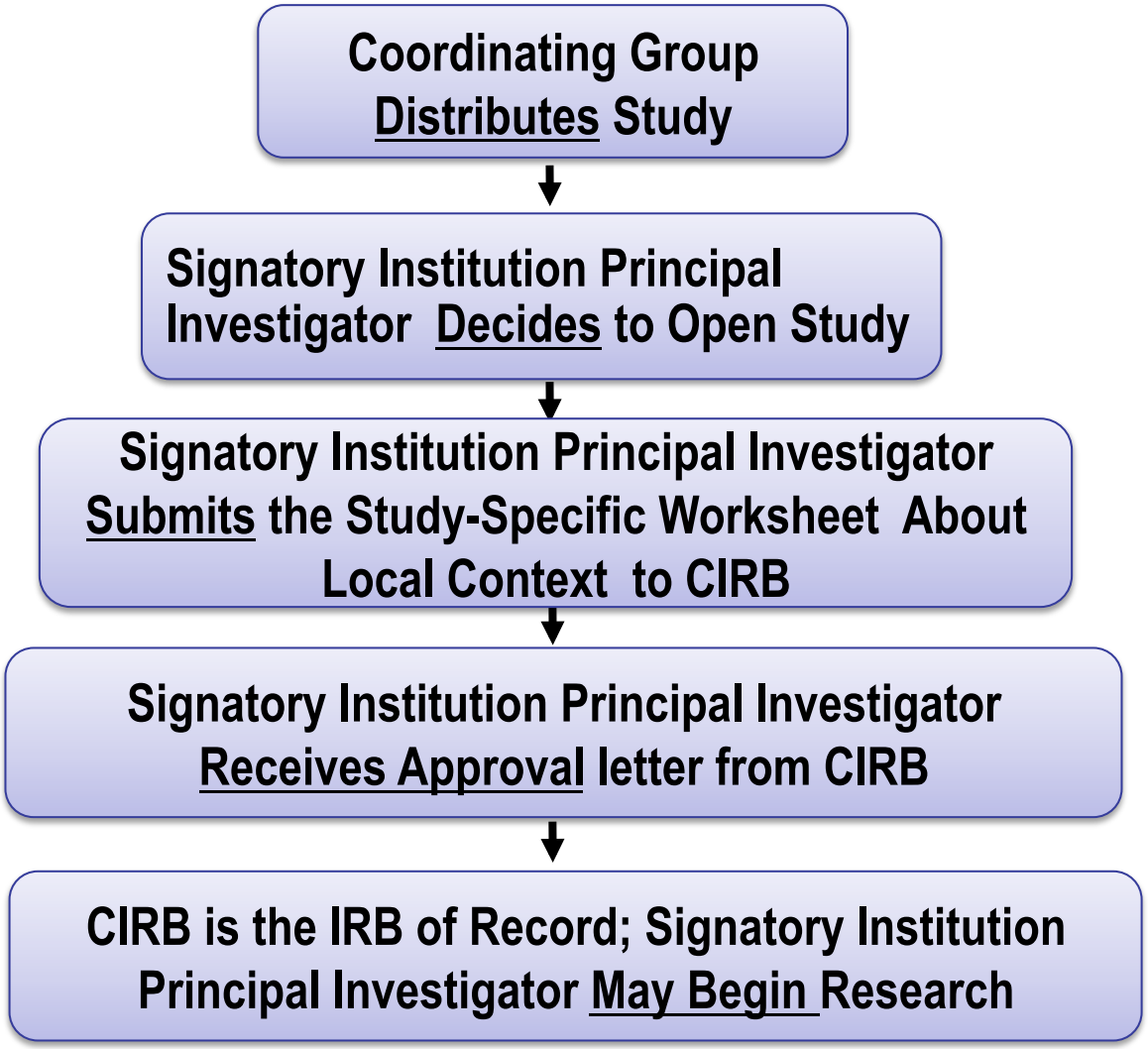
6 Easy Steps – Summary of Enrollment

1. **Complete and submit the NCI CIRB Signatory Institution Enrollment Form**
   - *Located on the CIRB website (https://www.ncicirb.org) using the "Enrollment Packet" link under the heading "How to Join"*
   - *Provides general information about your Signatory Institution and any Component or Affiliate Institution as well as contact information for key personnel*
   - *Submit via email to the CIRB Helpdesk at ncicirbcontact@emmes.com*
2. **Complete and submit signed Authorization Agreement and Division of Responsibilities document (requires signature of Signatory Official)**
   - *Located on the CIRB website (https://www.ncicirb.org) using the "Enrollment Packet" link under the heading "How to Join"*
   - *Submit hardcopy signatures via mail to the CIRB Operations Office*

6 Easy Steps – Summary of Enrollment (cont.)

3. **Modify your Institution's Federalwide Assurance (FWA), if applicable**
4. **Complete and submit the Annual Signatory Institution Worksheet About Local Context via IRBManager**
   - *Contains descriptions of state and local laws, including required boilerplate language*
5. **Complete and submit the Annual Principal Investigator Worksheet About Local Context via IRBManager**
   - *Provides research activity descriptions*
6. **Receive letter from the CIRB confirming that enrollment is complete and may begin to open studies**

After Enrollment: Opening a New Study



After Opening a Study

- Information the CIRB needs after a study is open
  - Reports of potential unanticipated problems
  - Reports of potential serious or continuing noncompliance
  - Notification of a Change of PI for CIRB review and approval
  - Submission of locally-developed materials and translations for CIRB review and approval prior to use
  - Notification of study closure

Unanticipated Problems - Definition

- **Federal regulations do not define Unanticipated Problems**
  - **FDA and OHRP have issued guidance documents that define Unanticipated Problems as:**
    - **Unexpected (in nature, frequency, severity)**
    - **Related or possibly related to participation in the research, and**
    - **Suggests greater risk to subjects or others than previously known**

OHRP: "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" (January 15, 2007). http://www.hhs.gov/ohrp/policy/AdvEvntGuid.htm

FDA: "Adverse Event Reporting to IRBs – Improving Human Subject Protection" (January 2009). http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf

Potential Local Unanticipated Problems

- Occur at or are limited to a particular institution and do not impact the trial nationally
- Are identified by the PI, institution, or local compliance offices usually directly from the participant or from information received about a particular participant or research activity
- Are reported to the CIRB by the PI, including a management plan
- Are reviewed by the Local Context Subcommittee or forwarded for review by the convened CIRB
- If determined to be an unanticipated problem, are reported to OHRP, and when applicable, FDA, and institutional officials at CTEP and the local institution

Hypothetical Situation 1

- A PI from Big Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg
  - The participant experienced a severe allergic reaction immediately after the administration of the investigational agent
- Is the incident/experience unexpected given the research procedures?
- Is the incident/experience related/possibly related to participation in the research?
- Does the incident/experience suggest a greater risk of harm to participants or others?

Hypothetical Situation 1

- A PI from Big Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg
  - The participant experienced a severe allergic reaction immediately after the administration of the investigational agent

- Is the incident/experience unexpected given the research procedures? – No, consent form lists the risk of the potential serious allergic reaction
- Is the incident/experience related/possibly related to participation in the research? – Yes, the experience of the allergic reaction was possibly related to the increased dosage of the investigational agent
- Does the incident/experience suggest a greater risk of harm to participants or others? – No, because the harm was already known and provided to the study participants as part of the consent form
- Since the event is not unexpected and does not suggest greater risk of harm, this should not be reported as an unanticipated problem

Potential Local Noncompliance

- Occurs at or are limited to a particular institution and do not impact the trial nationally
- Includes complaints, protocol deviations, and audit findings
- Is reported to the CIRB by the PI, including a management plan
- If determined to be serious or continuing noncompliance, is reported to OHRP, and when applicable, FDA, as well as institutional officials at CTEP and the local institution

Hypothetical Situation 2

- A PI from Big Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg, but due to an error in calculation was given a dose of 10mg/kg
  - There was no noticeable impact on the participant

- Is the incident/experience noncompliance?
- Is it serious noncompliance?
- Is it continuing noncompliance?

Hypothetical Situation 2

- A PI from Big Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg, but due to an error in calculation was given a dose of 10mg/kg
  - There was no noticeable impact on the study participant

- Is the incident/experience noncompliance? – Yes, the PI failed to follow the CIRB-approved protocol
- Is it serious noncompliance? – No, there was no result that meets the definition of serious
- Is it continuing noncompliance? – No, there is no indication that there is a pattern of noncompliance or a systematic and habitual disregard of the requirements or decisions of the CIRB or of Federal regulations
- This does not require reporting as serious or continuing noncompliance

Hypothetical Situation 3

- A PI from Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg, but due to an error in calculation was given a dose of 15mg/kg
  - The participant experienced more severe nausea than is typically observed, requiring administration of an antiemetic and an additional day's stay in the hospital

- Is the incident/experience noncompliance?
- Is it serious noncompliance?
- Is it continuing noncompliance?

Hypothetical Situation 3

- A PI from Big Medical Center A reports the following
  - Per the protocol, the participant was to be given a dose of Drug X, the investigational agent, at 5mg/kg, but due to an error in calculation was given a dose of 15mg/kg
  - The participant experienced more severe nausea than is typically observed, requiring administration of an antiemetic and an additional day's stay in the hospital
- Is the incident/experience noncompliance? – Yes, the PI failed to follow the CIRB-approved protocol
- Is it serious noncompliance? – Yes, the participant experienced more severe adverse events requiring a prolonged hospital stay
- Is it continuing noncompliance? – No, there is no indication that there is a pattern of noncompliance or a systematic and habitual disregard of the requirements or decisions of the CIRB or of Federal regulations
- This should be reported to the CIRB to make a determination based on the potential serious noncompliance

Reporting Change of PI

- Change of PI is reported to the CIRB using the Study-Specific Worksheet About Local Context
- The new PI submits a Study-Specific Worksheet and indicates that the submission is a Change of PI
- The CIRB provides an approval letter to the new PI noting the change from the previous PI

Submission of Locally-Developed Material and Translations

- **Locally-developed material and translations are submitted using the Locally-Developed Materials Submission Form found on the CIRB website as a Word document**
- **Review of translations require the following documents be submitted:**
  - ***CIRB-approved version of the English document***
  - ***Translated document***
  - ***Copy of translator's certificate of accuracy***
- **CIRB provides an approval letter for the submitted material.**

Study Closures

- **Study closures should be submitted to the CIRB in IRBManager when the following criteria are met:**
  - ***The study is closed to accrual at the Signatory Institution and all Component and/or Affiliate Institutions relying on the Signatory Institution for this study.***
  - ***All study participants on this study have completed study intervention(s) and follow-up activities OR no study participants were enrolled.***
  - ***There will be no further research activities for this study (this includes recruitment, enrollment, data collection, data analysis, data submission, etc.).***
- **CIRB provides a letter approving the closure.**

Benefits of Using the CIRB

- **Benefits patients and research participants**
  - ***Oncology-specific, multidisciplinary Boards***
  - ***Dedicated review for study participant protections***
  - ***Opens trials faster, supports completing trials faster***
  - ***Easier to open trials for rare diseases***
- **Benefits for investigators and research staff**
  - ***Eliminates back-and-forth with IRB to gain study approval***
  - ***Eliminates frequent submissions to IRB for amendments, continuing reviews, adverse events, etc.***
  - ***Eliminates completing IRB application and duplicating IRB submission packets***
- **Benefits for IRB members**
  - ***Saves IRB members' time and effort by eliminating full board review of network/program trials***

Contacting the CIRB

Helpdesk Email: ncicirbcontact@emmes.com

Helpdesk Toll-free Number: 1-888-657-3711

(May request a specific staff member when calling)

Fax Number: 1-301-560-6538

CIRB Website: http://www.ncicirb.org