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THE SITUATION OF MULTICENTER
CLINICAL RESEARCH IN INDONESIA AND THE CENTRALIZATION OF ETHICS APPROVAL

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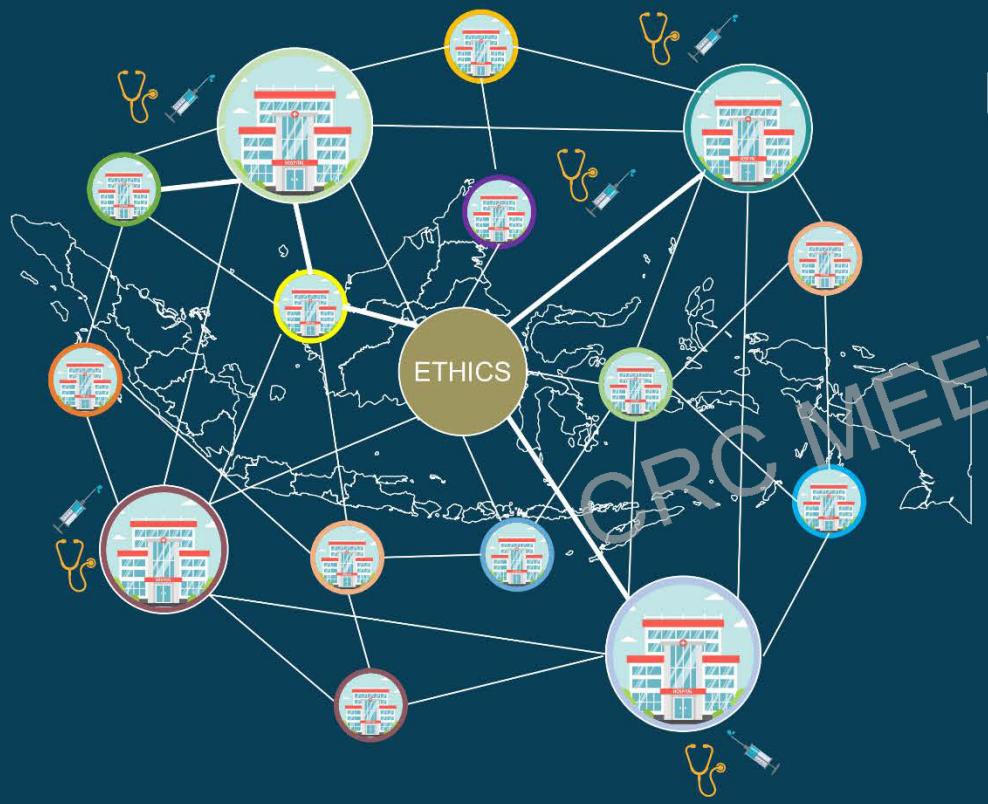

USE OF A CENTRAL IRB FOR MULTI-SITE RESEARCH IN THE UNITED STATES

Overview of single/Central IRBs, NIH sIRB Policy, Goals, Challenges

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Use of a Central IRB for Multi-Site Research in the United States

Overview of Single/Central IRBs, NIH sIRB Policy, Goals, Challenges

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IRB Experience

- 2011-2013: Study coordinator on pediatric headache research (non-NIH)
  - Used eIRB submission system, but prior to sIRB requirement
- 2013-2020: NIAID intramural IRB office staff member
  - Reviewed submissions of NIAID IRP research, participated in AAHRPP accreditation, assisted in developing institute policies and guidance
- 2020-present:
  - NIAID liaison for NIH IRB and HSR issues, coordination of central IRB activities for US sites participating in DCR/INSIGHT COVID research

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US Institutional Review Boards

- Review research involving human subjects, power to decide outcomes, ensure HSR protection in documents
- Convened group must have expertise to review research, relevant expertise if vulnerable group included
- Member conflicts of interest managed appropriately
- Each IRB is comprised of members of varying backgrounds, one must be lay person
- IRBs can be in medical or academic institution, health department, government agency, commercial
- *IRB can be independent of US government, all required to follow US FDA regulations*

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Centralized IRB Overview

- Referred to as single IRB (sIRB), central IRB, IRB of record, or reviewing IRB
- One IRB reviews/oversees study conduct; accountable party for regulatory compliance
- Can manage ancillary reviews and serve as Privacy Board
- Group responsibilities include:
  - Central IRB: All IRB oversight responsibilities for the study are delegated to this group, local IRB review/approval not needed (does not supervise the local IRB)
  - Study sponsor/lead group: Initiate IRB process, any regulatory pre-review (FDA, etc), submit protocol documents, send safety-related findings to IRB on behalf of sites, notify IRB of relevant findings, ensure study is monitored appropriately
  - Sites: Communicating local context information and site changes to IRB, delegating tasks and conducting informed consent appropriately, handling site study conduct, event reporting to sponsor, meeting requirements of local HRPP

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Centralized IRB Overview - continued

- Local IRB cedes review through an institutional reliance agreement (e.g. SMART IRB platform) – this is to occur prior to site IRB submission
- How is the sIRB selected?
  - Any registered IRB can serve as sIRB (e.g. academic institution, federal agency, commercial not affiliated with a site)
  - Selected sIRB often IRB of the main protocol team, but can be chosen based on Sponsor choice, the number of sites, established relationship with an IRB. Some local IRBs have site number limits for this model

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NIH IRB Overview

- Reviewing Board for the NIH Intramural Research Program (IRP) – intramural research includes both domestic and international
- Housed within the NIH Office of Human Subjects Research Protection (OHSRP)
- NIH funding for research does not mean NIH IRB approval needed – NIH IRB only involved with intramural research
- Can serve as IRB of record, or NIH IRP site (US) can rely on an external US IRB, as appropriate
- Full *Association for the Accreditation of Human Research Protection Programs, Inc.* (AAHRPP) Accreditation since 2014

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NIH sIRB Requirement & Revised Common Rule

- Terms *multi-site* versus *cooperative*
- January 25, 2018 – *NIH sIRB policy* took effect
  - All multi-site research "supported by" NIH required to abide
  - Limited to US sites, non-exempt HSR, other limited exceptions
- July 19, 2018 – *OHRP Revised Common Rule* took effect (fully in effect January 20, 2019)
  - Aimed to reduce administrative burdens while maintaining high quality HSR protective of participants
- January 20, 2020 – *Cooperative Research Provision* (45 CFR 46.114(b)) of Revised Common Rule took effect
  - Cooperative research at US institutions must use sIRB for domestic site research
  - NIH research excluded, does not apply to cooperative research initially approved before January 20, 2020
  - Exception to *some* cooperative COVID-19 research approved before May 11, 2023

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Goals of sIRB Requirement

- Reduce administrative burdens, duplicated efforts, and delays
  - *IRB oversight* ceded, sites still follow local requirements as applicable
  - Streamlined processes - one group submitting documents, centralized reviews
  - Key: More efficient/use of resources, for central oversight and sites; not compromising HSR protections
- Consistency across sites
  - Keeping to one IRB's requirements and schedule
  - Reduces differences among approved documents
  - Changes, annual reviews, reporting can be handled centrally
  - Local Context reviews may be needed, not regulatory requirement

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Multiple IRB Review vs. sIRB Model

- Multiple IRBs can equal multiple opinions, multiple document versions
  - Often same general IRB outcome (approve with mod, approve, defer, etc), but different requested edits
  - Study document changes are harder to track centrally
- Inefficient use of site resources: Non-reviewing IRBs of participating sites can focus resources on their single site research
- Hesitancy to conduct first review: Can add delays to study start
- Registered IRBs have the same required structure and responsibility, so one group taking this on benefits everyone

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Challenges in sIRB Implementation

- Not always less work for sites and local IRBs
  - Sites can still require own IRB and other reviews, though not required by regulations
  - Different needs among states or sites (e.g. document retention, documentation of consent, privacy language, birth control language, special participant population)
  - Hesitancy of some local IRBs to give up full control of documents used at that site
- Not always faster
  - Local IRB processes can delay adding a site to an approved study (e.g. ancillary reviews that are required at site prior to applying to central IRB)
  - Site review timelines not aligning with sIRB and sponsor timelines
- Not all eIRB systems (and staff structure) are equipped to handle multi-site research – improvements as sites learn

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Addressing Challenges of sIRB Model

- Use of broader reliance agreements; use of SMART IRB
- Simultaneous or central reviews where possible
- Start preliminary steps at sites as soon as possible
- Local context documentation: encourage only necessary site-specific ICF edits
- Open communication among sites, sponsor, sIRB
- Improvements to electronic IRB systems
- Experience with this model will naturally improve efficiencies over time

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Other Groups Referenced

- OHRP's 2018 **Revised Common Rule**
  - https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html
- **AAHRPP** - Association for the Accreditation of Human Research Protection Programs
  https://www.aahrpp.org/accreditation/why-accreditation-matters/overview
- **SMART IRB** - Streamlined, Multisite, Accelerated Resources for Trials IRB Reliance platform
  - https://smartirb.org/about-us/

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Questions?

Please feel free to contact me with any questions or comments:

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