



Overview of Federated Model for IRB Review of the National Children's Study (NCS) Vanguard Study

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Aims of Presentation



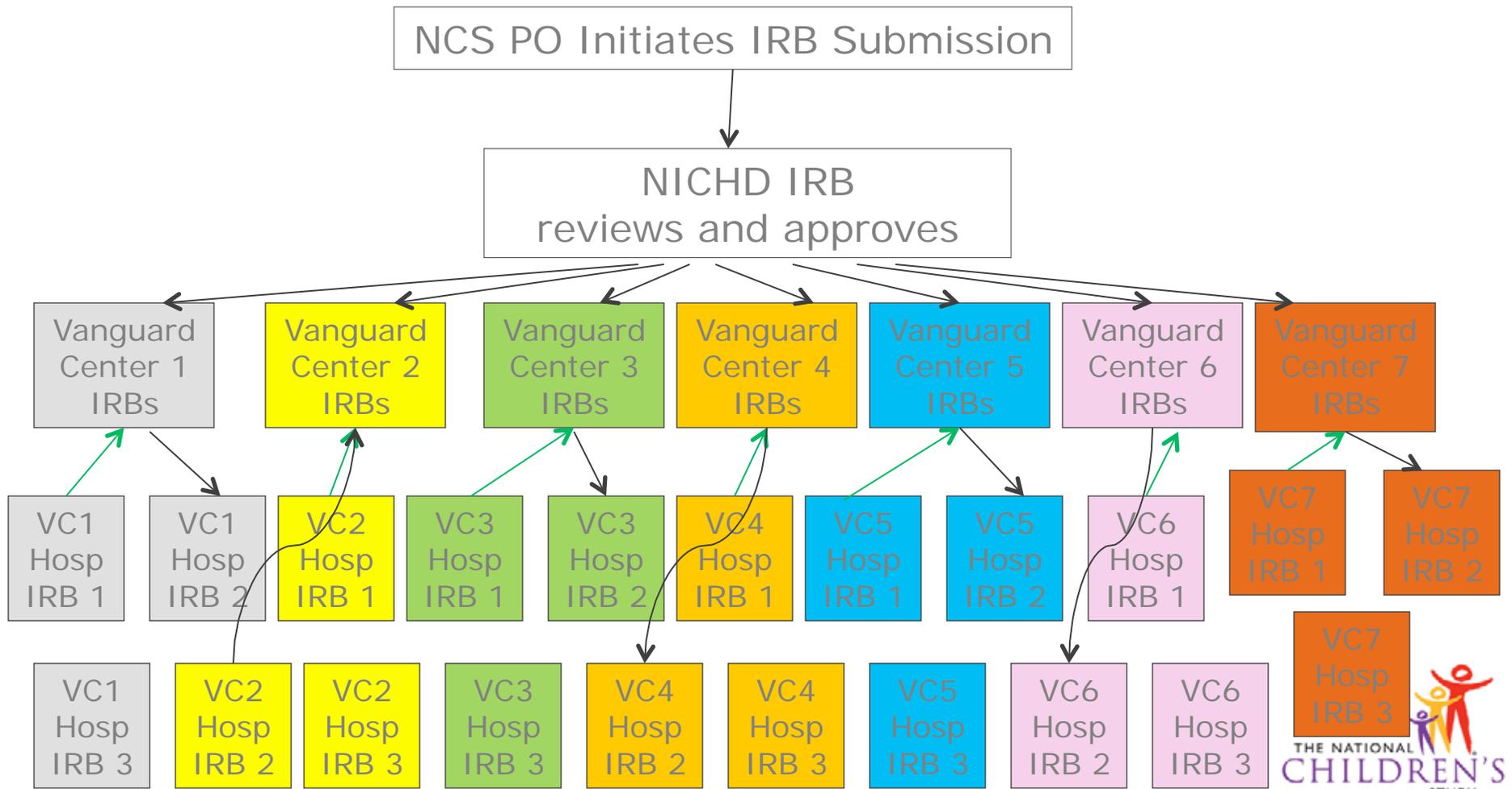
- Discuss current approach to IRB review of NCS protocol
- Explain new approach: Federated Model
- Discussion of Federated Model

Current Approach to IRB Review of NCS Vanguard Study



- NCS Program Office (PO) submits protocol, amendments, and other supporting material to NICHD IRB
- NICHD IRB reviews and approves
- NCS PO submits NICHD submission to local principal investigators /IRBs at Vanguard Center site IRBs for review and approval
- Vanguard Center IRBs send protocol to sub-contractor IRBs, hospital and birthing center IRBs for review, determination of engagement

Current System for IRB review of NCS Protocol



How is the current approach working?



- All IRBs have approved the initial protocol and subsequent amendments though with great variability in the time required
- All IRBs have made the determination that the Study is minimal risk
- Multiple Vanguard Study PIs have voiced concerns about the amount of time, effort and money spent on multiple IRB submissions and communications with local IRB(s).

How is the current approach working?



- The majority of submissions have been protocol amendments describing minor changes to approved research, changes with no impact on risk/benefit ratio and welfare of participants
 - Variation in local IRB practices with respect to review of minor changes to approved research
- Some delays in implementation of Study Visits due to time involved in IRB review
- NCS fatigue among some local IRBs due to the number of amendments and submissions (about 26 during the past year)
- Interest among some Vanguard Center institution relying on NICHD IRB

What is the mission of the Federation of NCS IRBs?



The mission of the Federation IRB is to maintain the highest ethical and regulatory standards in the review and oversight of the National Children's Study while minimizing duplicative effort among IRBs across multiple Study sites.

What is the Federated Model of IRB Review?



- The Federated model is a mechanism for:
 - establishing a shared set of principles, process and performance for the review of the NCS protocols;
 - sharing information across all Institutional Review Boards (IRBs)
 - providing the opportunity to facilitate local IRB review by allowing a reliance on the NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) intramural IRB.
- All IRBs required to review the NCS protocol are potential participants in the Federation of NCS IRBs.
- Local IRBs at NCS Study locations may select from various tiers of participation and may choose to rely on the NICHD IRB.
- The Federation is administratively supported and coordinated by the NCS Federation IRB Operations Center.

What is the Federated Model of IRB Review?



- The Federation of NCS IRBs is modeled after an approach to centralize review for multi-site studies first articulated by institutions receiving Clinical and Translational Science Awards (CTSA).
- The Federated model was presented to the Secretary's Advisory Committee on Human Research Protections (SACHRP) during its July 21, 2009 meeting.
- This model of IRB review of multi-site studies will be implemented as a pilot effort with institutions participating in the NCS as well as the possibility of additional institutions with CTSA awards participating in pediatric clinical trials.

Compact for Federation of NCS IRBs



- Statement of commitment to shared principles, operational process, and measurement of performance (of Federation model) in the human subject protections review of the NCS Vanguard Study protocol

Compact - Principles



- Compliance with pertinent regulations
- Commitment to protection of human subjects
- Commitment to focus review on issues most pertinent to the protection of human subjects
- Commitment to ensure that the most up to date information and study documents have IRB approval
- Require procedures describing the withdrawal of individual participants and for closure of the Study, regardless of the risk profile of the Study
- Recognition that outcome measures and assessments should be population specific
- Recognition that assessment schedules should accommodate families and should be age appropriate

Compact - Principles



- Recognition that local experience should be an important factor in risk determinations made by scientific review groups and IRBs
- Recognition that data sharing is a goal and that the permission, assent, and consent processes should anticipate future uses of data and specimens
- Recognition that variations are possible when determining under what circumstances permission, assent, and consent are required and when they can be waived
- Recognition that demonstrating respect for participating communities by sharing relevant Study results is a goal of the Study
- Recognition that monitoring is context dependent
- Recognition of a hierarchy of evidence in making inferences, extrapolations and interpreting data
- Commitment to protection of community

Compact - Performance



- Logistics of protocol distribution from protocol development team will be handled by a Protocol Coordinator at a Protocol Operations Center
- IRB review will follow Scientific Review
- For initial review of a study, first IRB will review in one cycle based on regularly scheduled meetings
- IRB summary review of the initial IRB review will be attached to protocol package for delivery to subsequent IRBs
- Subsequent IRB review of a study already approved by a recognized IRB within the Federation will occur in one cycle based on regularly scheduled meeting. Review may be abbreviated
- Each subsequent IRB summary review will be attached to protocol package for delivery to Protocol Coordinator to maintain a composite file of all comments
- Any changes in perception of risk category or approvability will be communicated to all IRBs by Operations Center Coordinator upon receipt of assessment
- Protocol amendments will follow the same process of initial IRB review and subsequent distribution to other IRBs
- Tracking of time from submission to distribution to action will be warehoused by Protocol Operations Center

Compact - Process



- Affirmation of Federation IRB Compact and for those institutions interested in a reliance of facilitated review option the creation of an MOU
- Local experience should be an important determinant of risk so data regarding local experience with assessments and interventions should be available. Absent adequate local data, literature should be used to guide risk determination
- Criteria for supplemental monitoring such as a recommendation for an Independent Data Monitoring Committee should be proactively developed
- Common plan between relevant parties such as investigators, institutional offices, sponsors, funding organizations and regulatory authorities should be proactively developed
- Information regarding other competent assessments of a proposed study, for example other IRBs or review groups, should be shared
- Definitions of responsibilities among review parties such as Scientific Review Group, Independent Study Monitoring Oversight Committee (iSMOC) and IRB are clarified

How will the Federated model operate?



- Trust: Shared commitment to protection of NCS participants codified in Federation Compact
- Flexibility: Level of participation in Federation IRBs is determined by each local FWA holding institution at a given Study Location.
 - Tiers of participation specified in Memorandum of Understanding (MOU)
- Coordination: The Federation is managed by the NCS Federation IRB Operations Center within the NCS Program Office.
- Communication: Determinations and documentation are shared across all reviewing IRBs

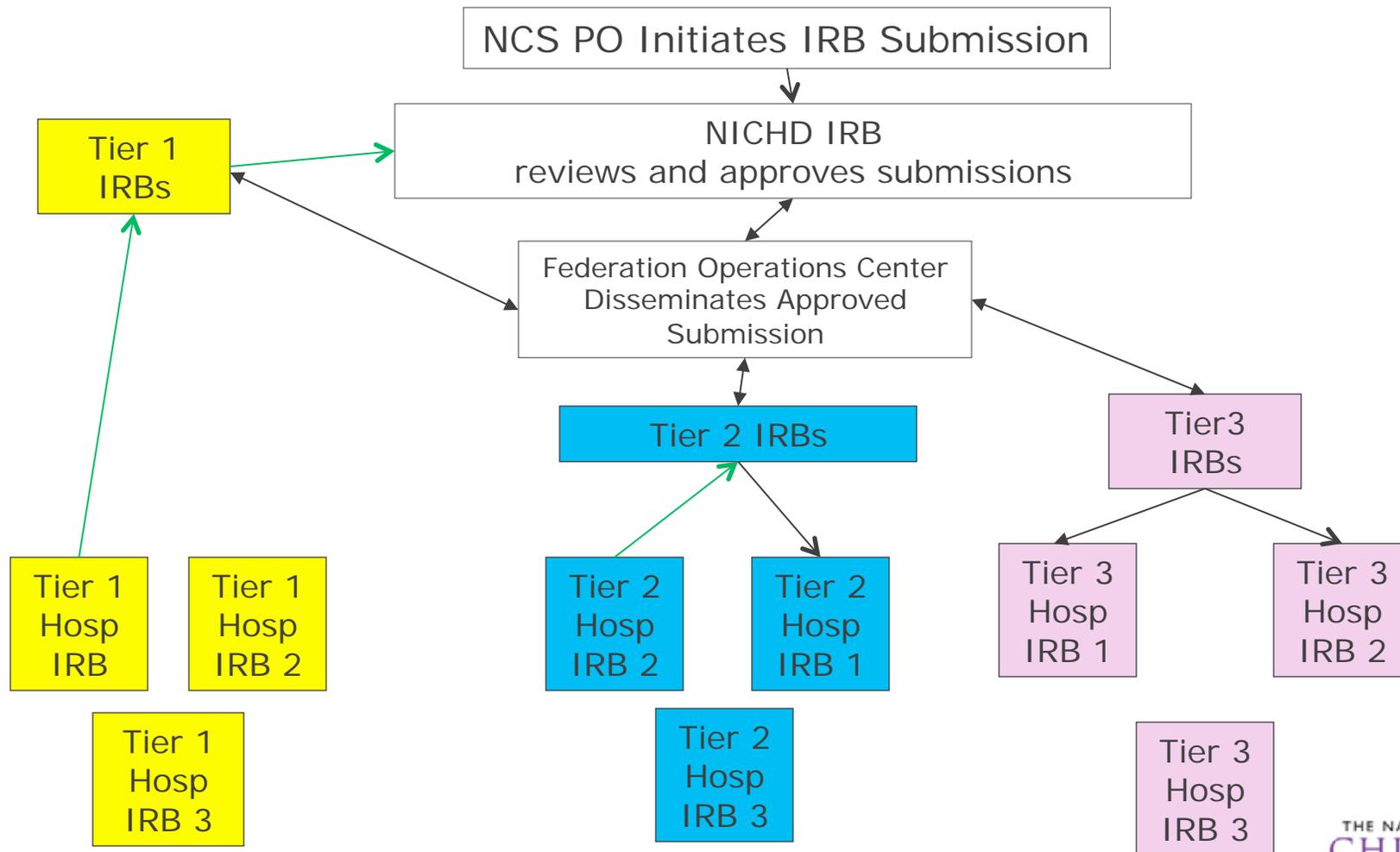
Tiers of Participation in Federation of NCS IRBs



Tier*	Review Responsibilities of Local IRB	Review Responsibilities of NICHD IRB	IRB of Record (NICHD or Local IRB)	MOU Required (Y or N)
1 Reliance on NICHD IRB as IRB of Record with option for local review	<ul style="list-style-type: none"> Local context issues review Communication of local context issues to NICHD IRB via NCS IRB Operations Center 	<ul style="list-style-type: none"> Initial reviews Continuing reviews Protocol amendments initiated by NCS Program Office 	NICHD	Y
2 Routine local review and option to designate NICHD IRB as IRB of Record	<ul style="list-style-type: none"> Routine review of materials approved by NICHD IRB Local context issues review Communication of local context issues to NICHD IRB via NCS IRB Operations Center Local implementation review and oversight Protocol amendments initiated by local Principal Investigator (if local IRB is IRB of record) Unanticipated event reporting to OHRP Serious Adverse Events iSMOC reports 	<ul style="list-style-type: none"> Protocol amendments initiated by local Principal Investigator Unanticipated event reporting to OHRP Serious Adverse Events iSMOC (Independent Study Monitoring and Oversight Committee) reports All other documents submitted 	NICHD or Local IRB as designated by local institution	Y
3 Reliance on local review	<ul style="list-style-type: none"> Initial reviews Continuing reviews Protocol amendments Serious Adverse Events iSMOC reports All other documents submitted Local context issues review Local implementation review and oversight 		Local IRB	N highly recommended

*Adherence to principles in Compact required for all tiers

Federated System for IRB Review of NCS Protocol



What are the advantages to an institution/IRB/investigator?



- The advantages of the Federation vary depending on the level of participation an institution accepts.
- As a central goal of the Federation of IRBs, there will be a reduction in duplication of review and a reduction of administrative burden at the local level while maintaining the highest standard of human subject protections review and oversight.
- Attention to local context is maintained and becomes the priority of the IRB. Mechanism to provide local context is set up between local institution/IRB and Operations Center.
- With less responsibility to provide a duplicative review at the local level, approval turnaround is anticipated to improve.
- Establishment of a culture of information sharing and trust.

Next Steps:



- Request feedback
 - Input from NCS Stakeholders
 - Input from OHRP
 - Input from NIH leadership
- Coordination with Clinical and Translational Science Awards Federated IRB Pilot Project