Harmonization and streamlining of research oversight for pragmatic clinical trials

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Comments on the Title

• Note that the title is NOT:
  – “The use of central/single IRBs for streamlining and harmonizing research oversight”

• Harmonization and streamlining are related but distinct goals
  – Harmonization suggests consistency of approach
  – Streamlining suggests efficiency and reduction of duplicative effort
Basic Assumptions

• Oversight of human research is complex
• Oversight of multi-site human research is ‘complexer’
• Harmonization and streamlining are worthy goals...
  – BUT...only if human subject protections are not eroded in the process
Agenda

• Understanding the Human Research Protection Program (HRPP)
  – IRB Responsibilities
  – Non-IRB Institutional Responsibilities

• Central/Single IRBs
  – What are they
  – How they may help

• Other opportunities for harmonization and streamlining
Elements of the HRPP

• Process for IRB review *(can be local or external)*
  – Initial review
  – Continuing review
  – Review of amendments, unanticipated problems, deviations

• Non-IRB institutional responsibilities
  – Ancillary committee review/s (E.g., pharmacy, rad’n safety)
  – HIPAA
    • Although often assumed by the IRB working as Privacy Board
  – Conflict of interest
  – Research billing
  – Investigator training and education
  – Reporting requirements per the FWA (Federal Wide Assurance)
Institutional Responsibility

– Per Federal Wide Assurance (FWA):

• “All of the Institution’s human subjects research activities, regardless of whether the research is subject to the U.S. Federal Policy for the Protection of Human Subjects (also known as the Common Rule), will be guided by a statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution.”

http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html
Human Research Protection Program
IRB vs Institution

Institutional Oversight Responsibilities

IRB Office Responsibilities*

IRB Regulatory Review

* IRB Office responsibilities ≠ IRB regulatory responsibility
Human Research Protection Program
IRB vs Institution

Institutional Oversight Responsibilities

IRB Office Responsibilities
- IRB Regulatory Review

Grants and contracts
- Sponsored research
- COI
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Helpful terms

• Reviewing IRB
• Relying institution
  – Remember it is the *institution* that relies

http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html
Central/Single IRB oversight

• A CIRB is used for regulatory review
  – Of some or all regulatory requirements
• The relying institution retains responsibility for non-regulatory review
• Process:
  – Reliance Agreement signed by all parties
    • Delineates respective roles and responsibilities
  – SOPs
The only ‘stuff’ that is ceded
Hence the institution...

- Must retain/develop a system for fulfilling all institutional responsibilities
- Must develop a mechanism for reporting relevant institutional review information to the reviewing (Central) IRB
Hence the institution...

• Must retain/develop a system for fulfilling all institutional responsibilities
• Must develop a mechanism for reporting relevant institutional review information to the reviewing (Central) IRB

Unfortunately this is a surprise to many institutions and investigators!
I thought that I had ceded review!
CIRB Arrangements

• Type of IRB
• Scope
• Voluntariness
• Designation of reviewing IRB
• Share versus non-share models
CIRB Arrangements: Type of IRB

• Independent/commercial
  – This is their business

• Academic Medical Center
  – This is becoming their business
  – Pretty-much an add-on to regular business
  – Paucity of metrics re: resources needed
CIRB Arrangements: Scope

– Single protocol review
  • One-by-each protocol determination

– Category of research; e.g.,
  • Cancer
  • Pediatrics
  • Defined network

– All research
  • Perhaps the local institution does not have an IRB!
CIRB Arrangements: Voluntariness

– Protocol-by-protocol decision
– Mandated
  • By funding agency
  • Network ‘business’ rules
CIRB Arrangements: Designation of reviewing IRB

– Single IRB designated for all relevant reviews
  • NCI
  • NeuroNEXT
  • Commercial/Independent IRB

– Protocol-by-protocol decision
  • One-by-each
  • Reciprocal reliance agreement
Reciprocal Reliance Agreement

– Multiple institutions sign the same reliance agreement
  • Allows any of the signatories to be the reviewing IRB
  • Allows each institution to decide on a protocol-by-protocol basis whether or not to rely
Share and non-Share Models

• Based on who does what regulatory review

• Share
  – Multiple IRBs may be involved
  – Local and Central IRBs have some regulatory responsibility

• Non-Share
  – Only one (reviewing) IRB has regulatory responsibility
# CIRB Models: non-share and share

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<th>Non-share Model</th>
<th>Share Model</th>
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<td>CIRB</td>
<td>CIRB</td>
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<td>CIRB</td>
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<td>CIRB</td>
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Comments on the models

• Share models
  – Potential confusion re: assignation of regulatory responsibility for specific actions
  – Local familiarity with protocol may be difficult if initial review done centrally
  – Confusion re: IRB regulatory vs institutional tasks

• Non-share model
  – Local IRB discomfort with NO regulatory authority
    • May spawn shadow reviews
  – Confusion re: IRB regulatory vs institutional tasks
Institutional Process Responsibilities

• Determination of eligibility for cede review
• As outlined in the reliance agreement:
  – Process for identifying and completing all institutional reviews
  – Process for communicating review results to the reviewing IRB
  – Process for handling non-compliance and reporting to federal and funding agencies
• Development of workflow
  – Sequential review
  – Parallel review
Remember

• Everyone needs clear understanding of who is responsible for what
• The Reliance Agreement matters
• There are myriad logistics that must be considered by:
  – The reviewing IRB
  – The relying sites
  – The investigators
• And there is the matter of cost
Robust communication between CIRB and relying sites is critical
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Challenges and Opportunities for harmonization and/or streamlining

• Comparative effectiveness research
  – Understanding risk which informs oversight

• Social Media
  – Heterogeneity of sites; participant expectations and privacy

• Software applications
  – Accuracy, authenticity, validity, MR-worthiness

• Sponsor requirements
  – One-by-each negotiations

• Patients and patient advocates as research team members
  – Poor definition of role; questions re: required training and oversight
Challenges and Opportunities for harmonization and/or streamlining

- **Privacy**
  - Including patients as study team members

- **Cluster randomization**
  - Questions of informed consent, institutional sign-off

- **Local context**
  - How best to identify, communicate and consider

- **Conflict of interest**
  - Heterogeneity of institutions

- **Payment**
  - Lack of coverage standards – affect the protocol and ICF

- **Federal Wide Insurance (FWA)**
  - How to handle non-traditional settings
Summary

• Streamlining and harmonizing oversight of multi-site research is a laudable goal
• Solutions must address the multi-faceted inter-dependent processes of research and research oversight
All we need is a single IRB!
All we need is a single IRB!