Working with the VA Central IRB: A Dialogue with the IRB

Moderated by
Soundia A. Duché, MA, MS, PRIDE

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Outline

- Introductions
- What is the VA CIRB and why was it formed?
- What is required to use the VA CIRB?
- The VA CIRB Review Model
- Post-Approval Monitoring
- VA CIRB Portfolio
- The Good, The Bad, and the Heartburn-Inducing
- What the Future Looks Like
- Resources
Introductions

- VA CIRB Co-Chairs:
  - Stephen D. Bartlett, RPh, MSPH, VA Eastern Colorado HCS, CO
  - Fred J. Hendler, MD, PhD, Robley Rex VAMC, Louisville, KY

- VA CIRB Administrator
  - Annette Anderson, MS, VA Central Office, DC
Polls 1 and 2
Poll 1: Today’s Audience

What is your primary role in research?

a) Investigator or Study Team Member
b) Study Coordinator or equivalent
c) IRB/R&D Committee Member (non-voting members included)
d) Research Office Staff (VA or Affiliate)
e) Other
Poll 2: Experience with the VA CIRB

How many years have you worked with the VA CIRB?

a) None so far
b) 1-2
c) 3-5
d) 6-8
e) >8
What is the VA CIRB and Why was it Formed?
VA CIRB Composition

• 16 voting members from across the country comprised of:
  • 2 VA Central IRB Co-Chairs (1 MD and 1 Research Pharmacist)
  • 11 additional scientists (7 MDs and 4 PhDs)
  • 1 non-affiliated non-scientist
  • 2 affiliated non-scientist
• 4 nonvoting members
  • VHA National Center for Ethics in Health Care
  • VHA Office of General Counsel
  • VHA Privacy Office (with 1 alternate)
  • Information Security Office (with 1 alternate)
VA CIRB HRPP

• Institutional Official
  • Carolyn Clancy, MD, Executive in Charge

• Human Protections Administrator (HPA)
  • Marisue Cody, PhD, Director of Operations, ORD

• VA CIRB Administrative Office
  • 1 IRB Administrator
  • 6 IRB Managers and 1 Support Specialist
  • 2 Database Managers
  • 1 Part-time Regulatory Advisor
  • 1 Part-time Administrative Officer
Why was the VA CIRB Formed

• Improve human research protection in ORD multi-site studies by ensuring
  • Expert ethical and scientific review
  • Local issues are addressed
• Enhance efficiency of IRB reviews
VA Central IRB Implementation

- Established as part of the VHA Central Office Human Research Protection Program (HRPP) in 2008
- Institutional Official (IO) is a senior member of VHA Leadership
- First study reviewed in **August 2008** and approved in **October 2008**
- As of June 15, 2018, the VA Central IRB is overseeing or is in the process of reviewing a total of 211 multi-site studies involving a little over 1,371 sites
- The VA Central IRB also approves Requests for Exemptions
Original Mandate

• ORD funded studies only (with one exception)
  • ORD Service (e.g., CSP, RR&D, HSR&D, Queri)
• More than one VA facility engaged in human subjects research or
• Single site pilot studies that will eventually have multiple VA sites engaged in human subjects research
Current Policy Includes

- Non-ORD funded multisite studies from other federal agencies, VHA Central Office, research networks, and industry
  - Currently overseeing or in the process of reviewing
    - 17 commercially sponsored studies involving approximately 117 VA sites
    - 5 NIH-funded studies
    - 7 DoD-funded studies
    - 5 research network studies
VA CIRB Advantages

• Consistency
  • Reduces local site variations in implementation
  • Uniform application of regulations and policy

• Quality
  • Expertise and experience of the members

• Early Identification of Safety trends

• Efficiency
  • Ease of adding local sites
  • Continuing review and amendment implementation done simultaneously across entire study
VA CIRB Advantages (continued)

• Allow for large, multisite precision medicine studies that need to screen a large number of patients to identify a small number with specific markers to more efficiently open local sites, even if they have only one subject.

• Ability to focus on the Veteran community, its needs, and characteristics by ensuring a culture throughout VA that has the highest regard for Veteran volunteer safety and privacy.
Oversight of the VA CIRB

- Local Research and Development Committees at each site with an MOU
  - Review of minutes and approval letters
  - Annual HRPP Report
  - Local site comment period and Local Site Liaisons
- Local Research Compliance Officers
- VHA Office of Research Oversight
What’s Required to use the VA CIRB?
Requirements to Use the VA CIRB

Facilities must:

• Amend their Federalwide Assurance to include the VA CIRB as an IRB of record

• Enter into an Memorandum of Understanding (MOU) with VHA Central Office (and affiliated NPC if applicable)

• Develop standard operating procedures (SOPs) for using the VA CIRB as an IRB of record

• Modify affiliate MOU as necessary
Memorandum of Understanding (MOU)

• Spells out the respective authorities, roles, and responsibilities of the VHA Central Office HRPP, the VA CIRB, the local VA facility, and the affiliated NPC if applicable

• VA facilities that do not use the VA CIRB will not be able to participate in studies reviewed by the VA CIRB

• As of June 5, 2018, the VHA Central Office HRPP has MOUs with 104 VA facilities with FWAs; 93 VA Non-profits; 8 Department of Energy Laboratories; the University of Cincinnati Strokenet; Baltimore Research and Education Foundation; and Johns Hopkins School of Medicine (COVET)
Local Accountability for Research

• The MOU requires the VA Facility Medical Center Director to appoint local site representatives to:
  • Provide local comments to the VA Central IRB regarding the VA Central IRB’s review of the Principal Investigator New Project Application
  • Serve as the Local Site Liaison with the VA Central IRB
Polls 3 and 4
Poll 3: Local Facility Responsibilities

The local facility is responsible for the following activities when projects are overseen by the VA CIRB:

a) Receiving copies of VA CIRB approved documents
b) Providing comments on newly approved projects
c) Ensuring review and approval by other local subcommittees
d) All of the above
e) None of the above
The local facility IRB is responsible for the following activities when projects are overseen by the VA CIRB:

a) Receiving copies of VA CIRB Approved Documents
b) Reviewing VA CIRB Approved Documents
c) Both A and B
d) None of the above
e) I’m really not sure
VA CIRB Model
Types of Reviews

• Prior to submission of a new project for review by the VA CIRB, the PI may request the following reviews as applicable:
  • A Human Subjects Research Determination
  • An Exemption Determination
  • A multisite Engagement Determination
  • A Regulatory Pre-review

• New Projects are reviewed using a unique 2-stage application process
Two Stage Application Process

- **PI/Study Chair (PI/SC) Application**
  - PI/SC has overall responsibility for the study
  - Subjects may or may not be recruited at the PI/SC site
  - If known, PI lists participating local sites
  - PI/SC Application is reviewed by either convened board or expedited review and approval letter is signed by an IRB Co-Chair

- **Local Site Investigator (LSI) Application**
  - Each participating site submits an LSI application
  - LSI application is typically reviewed by expedited review
Principal Investigator (PI)/Study Coordinator (SC) Application

PI/SC Application is comprised of:

- Co-PI and Coordinating Center Supplements
- Protocol and other documents (e.g. surveys, scripts, investigator drug brochures)
- Waiver requests
- Vulnerable population supplements
- Model Documents (i.e., informed consent forms, recruitment materials, HIPAA Authorization Forms)
- COI statements from personnel in investigator roles only
- CVs of investigators only
- Local ACOS/R&D certification
Local Site Investigator (LSI) Application

LSI Application is based on and mirrors PI/SC Application and focuses on the following:

• Local study team information
• Local resources
• Local recruitment practices
• Local participant compensation practices
• Customized model documents
• All differences from the PI/SC Application must be justified
• Signed by LSI
• Local ACOS/R&D certification
VA CIRB Review Process – 7 Steps

1. PI/SC completes and submits PI/SC application
2. VA CIRB (including ISO/PO) reviews and approves PI/SC Application via expedited or convened board review
3. Local site comments requested (15 day comment period) and submission of local site investigator applications
4. Review of local site comments and local site investigator applications
5. PI and LSI submit revisions as applicable
6. VA CIRB makes final approval decision on LSI application
7. Local site final approval issued (note, R&D Committee approval required prior to initiation of study at each facility)
Post Approval Monitoring
Amendments and Updates

- **PI Amendments**
  - Made available to all sites through SharePoint
- **Local Site Investigator Amendments/Updates**
  - LSI Amendments: Site-specific changes
  - Updates: based on approved PI Amendments or change in model document field (e.g., room or phone numbers)
- **Addition of a Site**
  - Sites added after approval of PI/SC application will not get 15-day comment period but still may make comments through local R&D process
Continuing Review

• Continuing Review date is set for overall study, not for each site

• Two step application and submission process:
  • LSI submits a report to PI by PI established deadline
  • PI/SC submits summary report, along with copies of all LSI reports

• Local Site Applications cannot be approved, even if no further modifications, until PI Application is approved
Reportable Events

- VA CIRB Table of Reporting Requirements
- Specific reporting forms available on VA CIRB website (https://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm)
- Reports are sent to the VA CIRB, not local IRB
- Separate SharePoint folder for uploading reports
RCO Audits and Other Local Site Audits or Reports

• Submitted at Continuing Review:
  • Routine Research Compliance Officer (RCO) audits (informed consent and triennial) if no findings require review by the IRB
  • MVP exception – Quarterly summary from ORO Central Office
• Submitted immediately (by RCO, PI, LSI):
  • Any reports of apparent serious noncompliance
  • Any other issues identified that require IRB review
VA CIRB Portfolio
### VA CIRB: 2017 Workload

<table>
<thead>
<tr>
<th>Workload Factor</th>
<th>Volume Q1</th>
<th>Volume Q2</th>
<th>Volume Q3</th>
<th>Volume Q4</th>
<th>Total Volume</th>
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<tbody>
<tr>
<td><strong>Total Continuing Approval Reviews Performed</strong></td>
<td>212</td>
<td>212</td>
<td>210</td>
<td>190</td>
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<td>PI Continuing Reviews</td>
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<td>38</td>
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<td>Local Site Continuing Reviews</td>
<td>169</td>
<td>202</td>
<td>163</td>
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<td><strong>Total Amendments Processed</strong></td>
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<td>117</td>
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<td>PI Amendments</td>
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<td>75</td>
<td>59</td>
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<td>Local Site Amendments</td>
<td>30</td>
<td>37</td>
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<tr>
<td><strong>Study Administrative Updates Processed</strong></td>
<td>103</td>
<td>63</td>
<td>146</td>
<td>165</td>
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<td><strong>Local Site Applications Approved</strong></td>
<td>37</td>
<td>48</td>
<td>49</td>
<td>61</td>
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<td><strong>Local Site Applications Closed/Withdrawn</strong></td>
<td>32</td>
<td>27</td>
<td>47</td>
<td>31</td>
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<td><strong>Serious Adverse Events/Unanticipated Problem Reports Reviewed</strong></td>
<td>29</td>
<td>23</td>
<td>19</td>
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<td><strong>Protocol Deviation Reports Reviewed</strong></td>
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<td>66</td>
<td>70</td>
<td>58</td>
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<td><strong>Study Administrative Pre-reviews Completed</strong></td>
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<td>8</td>
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<td><strong>800 Line Phone Calls Logged</strong></td>
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<td>70</td>
<td>81</td>
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<td><strong>MOU Addenda Received and Processed</strong></td>
<td>14</td>
<td>52</td>
<td>25</td>
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<td><strong>FWA Updates Processed</strong></td>
<td>16</td>
<td>15</td>
<td>21</td>
<td>15</td>
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Select VA CIRB Approved Projects
The Good, The Bad, and the Heartburn-Inducing
What keeps us (and you) up at night...

• Things we do really well
• Things we are continuously improving
• Areas where study teams can help out
The Future
2018 and Beyond...

• New Fee Structure for Industry-Sponsored Studies
• Single IRB Mandates: The revised Common Rule and NIH policy
• New Initiatives
  • Strategic Planning
  • Industry/NAVREF
  • Increasing Availability of Clinical Trials to Veterans
Resources
### VA CIRB Website

<table>
<thead>
<tr>
<th>Meeting Dates</th>
<th>Information for Investigators and Local Sites: FWA and MOU Information</th>
</tr>
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<tbody>
<tr>
<td>- Typically meets twice a month</td>
<td></td>
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<tr>
<td>Forms</td>
<td>Submitting applications to the VA CIRB</td>
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<tr>
<td>SOPs</td>
<td>Table of Reporting Requirements</td>
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<tr>
<td>IRB Roster</td>
<td>Information for RCOs and Local Site Liaisons</td>
</tr>
<tr>
<td>FAQs</td>
<td>List of VA Facilities that have an MOU with the VA CIRB to serve as an IRB of record</td>
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https://www.research.va.gov/vacentralirb/default.cfm
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Questions?
# Upcoming Cyberseminars: Tentative Schedule

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<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Lead Office</th>
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<tr>
<td>30-Jan-18</td>
<td>Records Management</td>
<td>ORD</td>
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<tr>
<td>20-Feb-18</td>
<td>Engagement in Human Subjects Research</td>
<td>ORD</td>
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<tr>
<td>20-Mar-18</td>
<td>MyhealtheVet and Secure Messaging</td>
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<td>24-Apr-18</td>
<td>Continuing Review</td>
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<td>15-May-18</td>
<td>Expedited Review</td>
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<td>16-May-18</td>
<td>Overview of the Revised Common Rule</td>
<td>ORO</td>
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<td>19-Jun-18</td>
<td>Working with the VA CIRB</td>
<td>ORD</td>
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<tr>
<td>17-Jul-18</td>
<td>Waivers: Common Rule, Privacy Rule, and FDA Regulations</td>
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<tr>
<td>18-Jul-18</td>
<td>Informed Consent: ICFs; Broad Consent; and Posting of ICFs</td>
<td>ORO</td>
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<tr>
<td>18-Sep-18</td>
<td>Myth Busters: Common Misperceptions re. VA Research</td>
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<tr>
<td>19-Sep-18</td>
<td>Exempt Review and Limited IRB Review</td>
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<tr>
<td>16-Oct-18</td>
<td>Transition Provisions and Overview of the revised VHA Handbook 1200.05</td>
<td>ORD</td>
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<tr>
<td>20-Nov-18</td>
<td>In-depth Focus on the revised VHA Handbook 1200.05</td>
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<tr>
<td>21-Nov-18</td>
<td>External IRBs and FWAs</td>
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<tr>
<td>18-Dec-18</td>
<td>In-depth Focus on the revised VHA Handbook 1200.05</td>
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