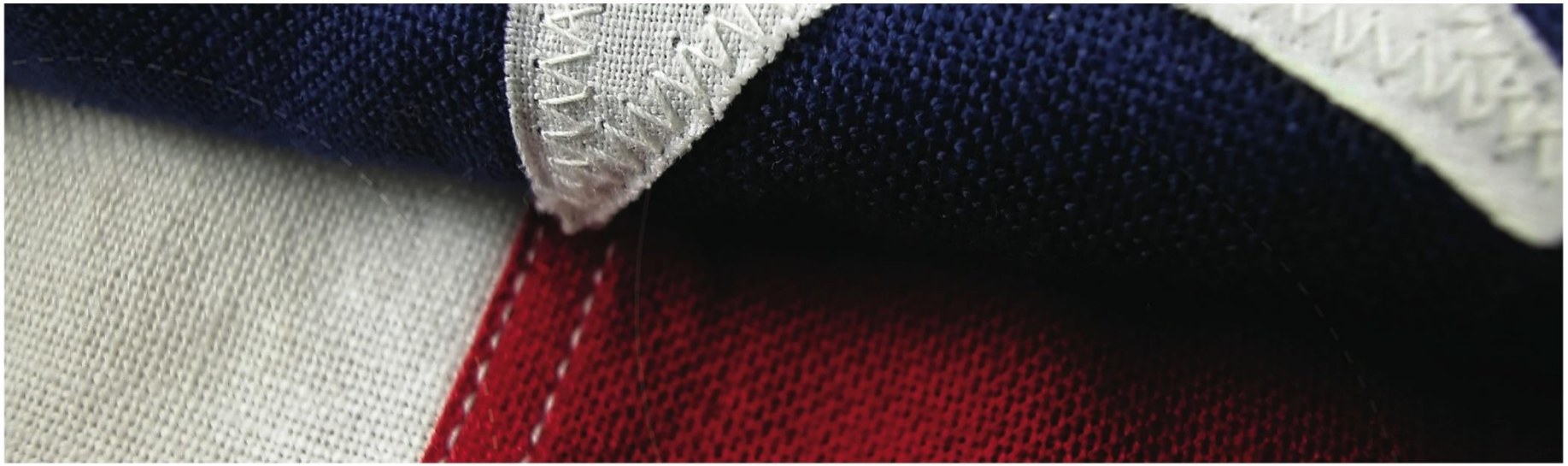

Working with the VA Central IRB: A Dialogue with the IRB

Moderated by
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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

VA Central IRB
VA Institutional Review Board for Multisite Studies

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

Poll 4: Local Facility IRB Responsibilities

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

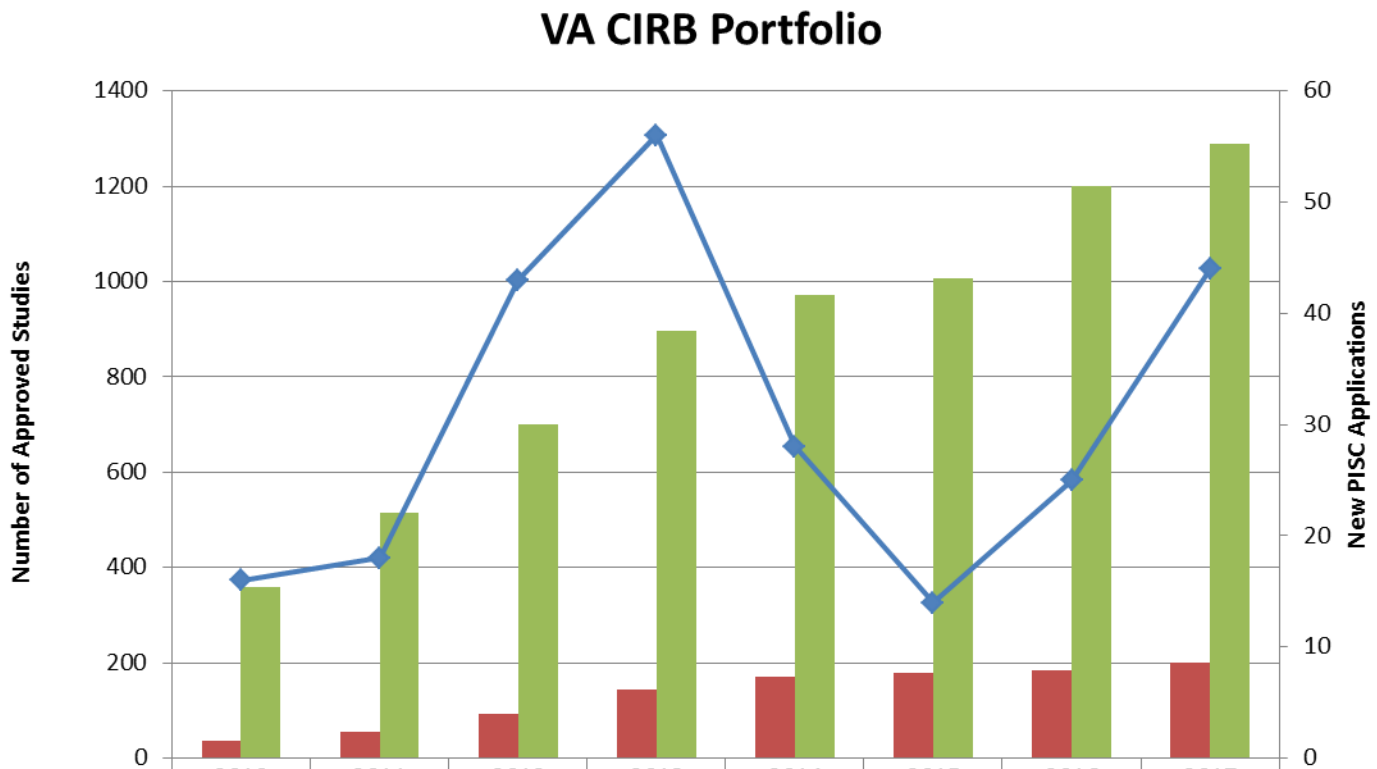
- VA CIRB Table of Reporting Requirements
- Specific reporting forms available on VA CIRB website (https://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm)
- Reports are sent to the VA CIRB, not local IRB
- Separate SharePoint folder for uploading reports

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 Central IRB Portfolio



	2010	2011	2012	2013	2014	2015	2016	2017
Approved PISC Studies	36	55	94	144	171	178	185	200
Approved LSI Studies	359	514	700	897	973	1006	1201	1290
New PISC Applications	16	18	43	56	28	14	25	44

VA PRIDE Program for Research Integrity Development & Education

VA CIRB: 2017 Workload

Workload Factor	Volume Q1	Volume Q2	Volume Q3	Volume Q4	Total Volume
Total Continuing Approval Reviews Performed	**212**	**212**	**210**	**190**	**824**
PI Continuing Reviews	43	38	47	44	**172**
Local Site Continuing Reviews	169	202	163	146	**680**
Total Amendments Processed	**108**	**117**	**87**	**117**	**429**
PI Amendments	78	75	59	71	**283**
Local Site Amendments	30	37	28	46	**141**
Study Administrative Updates Processed	103	63	146	165	**477**
Local Site Applications Approved	37	48	49	61	**195**
Local Site Applications Closed/Withdrawn	32	27	47	31	**137**
Serious Adverse Events/Unanticipated Problem Reports Reviewed	29	23	19	16	**87**
Protocol Deviation Reports Reviewed	75	66	70	58	**269**
Study Administrative Pre-reviews Completed	5	8	3	1	**17**
800 Line Phone Calls Logged	78	70	81	93	**322**
MOU Addenda Received and Processed	14	52	25	20	**111**
FWA Updates Processed	16	15	21	15	**67**

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

Meeting Dates - Typically meets twice a month	Information for Investigators and Local Sites: FWA and MOU Information
Forms	Submitting applications to the VA CIRB
SOPs	Table of Reporting Requirements
IRB Roster	Information for RCOs and Local Site Liaisons
FAQs	List of VA Facilities that have an MOU with the VA CIRB to serve as an IRB of record

https://www.research.va.gov/vacentralirb/default.cfm

Contact Information

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Questions?

Upcoming Cyberseminars: Tentative Schedule

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