Fourth Annual Medical Research Summit

Compliance Issues for Research at VA Medical Centers

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Baltimore, MD

"…to care for him who shall have borne the battle and for his widow and his orphan…" --Abraham Lincoln

Agenda

- ✓ Congressional Legislation
- ✓ ORO Mission
- ✓ Oversight Responsibility
- ✓ Regional Offices
- ✓ Compliance Issues 2003-2004

ORCA → ?? → OHRO → **ORO**

(1999 → → → 2004)

- Few changes in mission and responsibilities
- Legislated mandate
- Preserves the principle of external review and accountability
- We oversee, conservatively, $400 million in appropriated VA-conducted research.
- Approximately, conservatively, 3,000 investigators.
- Add about another $740 million for NIH, other federal, academic, pharmacy, biomedical, and smaller outside organizations.

¶ 7307. Office of Research Oversight

"**(a) Requirement for Office.**-(1) There is in the Veterans Health Administration an Office of Research Oversight (hereinafter in this section referred to as the 'Office'). The Office shall advise the Under Secretary for Health on matters of compliance and assurance in human subjects protection,…"

ORO Mission

Advise the Under Secretary for Health on matters of compliance and assurance related to human subjects, animal welfare, research safety, and research misconduct.

ORO Actions

Office monitors, reviews, and investigates regulatory compliance and assurance with respect to human subjects protections, animal welfare, research safety, and provides oversight management of research misconduct in medical research.

Hierarchy of Flexibility for Solutions to Problems

1. Law
2. Regulations
3. Policy
4. Standard Operating Procedures
5. Accreditation Standards
6. Guidance/Best Practices
7. Philosophy
8. Historical Practice

ORO Oversight Responsibility

Human Subjects Protections

- Oversee compliance with protections established by Common Rule following 38 CFR Part 16, other VHA policies, and federal regulations.
- Manage VAMCs Assurances and MOUs

Federalwide Assurances

- Commitment of each VA facility engaged in research
- IRBs of record
- Protections for patients and employees involved as subjects of research

ORO Oversight Responsibility

- Review accreditation survey reports for regulatory compliance
- Oversee and guide investigators into allegations of research misconduct (FFP in proposing and performing, or reviewing research, or in reporting results).

  (M-3, Part 1, Chapter 15 (HB 1200.14))

ORO On-Site Reviews

Types of Reviews

- For-Cause
- Routine

Reviews Focus on Regulatory Compliance

- Identify deficiencies

For-Cause On-Site Reviews

- Investigate reported or alleged instances of noncompliance with the laws, regulations, policies, and/or procedures governing research
  - Teams of 2-5 members, 2-4 days
  - Site visit report
  - Facility develops action plan
  - Continuous follow-up until actions complete
  - (Assurance restricted/suspended)

Routine On-Site Reviews

- To assess compliance and assurance with the laws, regulations, policies, and procedures governing research
  - Rotate thru VHA facilities with research programs
  - Site visit report may require action plan
  - Follow-up if action plan required

What is ORO's Organizational Structure?

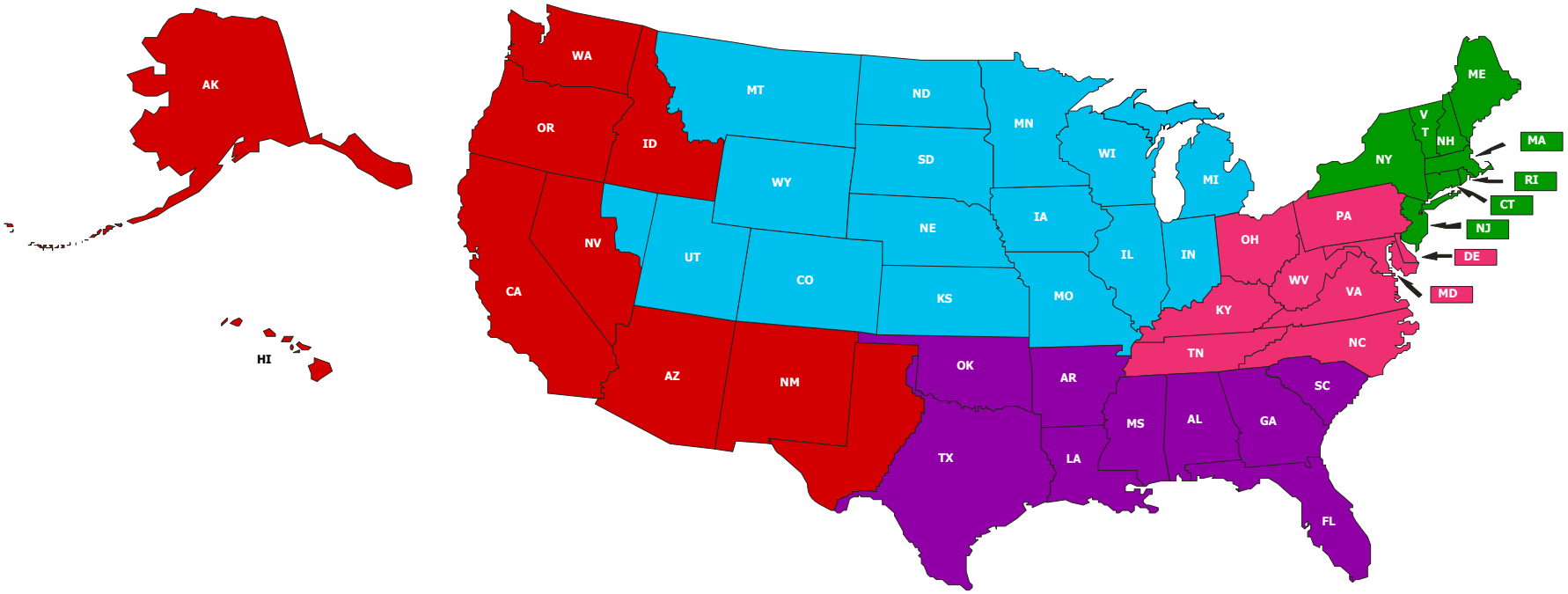
Central Office Component:

- Manage ORO
- Strategic guidance, coordination, and oversight

Regional Offices:

- Field operational units
- Geographically distributed
- 5 locations across the country
- Oversee research compliance and assurance for 21 VISNs
- Oversee research compliance and assurance for research in c.115 VA facilities

ORO Regional Offices



ORO Regional Office Directors

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ORO Regional Office

- Answers questions about regulations, policies, directives, and best practices
- Assists with concerns about incidents that may pose compliance problems
- Helps locate information and resources
- Conducts routine and for-cause reviews

Reporting AEs in Research to ORO

- Identifies AEs to be reported to ORO
- Provides timeliness for reporting
- Indicates information to be reported
- SACHRP reforms?

In Progress

- Research Misconduct Handbook
- Assurance Handbook

Compliance Review Findings
2003-2004

Core Regulations and Policies

- **38 CFR 16** Protection of Human Subjects
- **21 CFR 50** Protection of Human Subjects
- **21 CFR 56** Institutional Review Boards
- **21 CFR 312** Investigational New Drug Application
- **21 CFR 812** Investigational Device Exemptions

Core Regulations and Policies

- Handbook 1200.5, Requirements for the Protection of Human Subjects in Research (July 15, 2003)
- What to Report to ORO (November 11, 2003)
- Manual M-3, Part I
  - Chapter 2: Organizational Structure
  - Chapter 3: Functions of the Research and Development Committee

What to Report to ORO Memorandum

Date: November 12, 2003

From: Acting Chief Officer, Office of Research Oversight (ORO) (10R)

To: Institutional Officials of VHA Facilities Conducting or Supporting Research

What to Report to ORO Memorandum

Identifies issues VHA facilities must report to ORO as required by various Federal regulations and VHA policies.

http://www.va.gov/oro/

OHRP Compliance Activities

http://ohrp.osophs.dhhs.gov/compovr.htm

Common Findings and Guidance (77)

Major Categories:

- Initial and Continuing Review
- Expedited Review Procedures
- Reporting Unanticipated Problems & IRB Review of Protocol Changes
- Applications of Exemptions
- Informed Consent
- IRB Membership, Expertise, Staff, Support, and Workload
- Documentation of IRB Activities, Findings, and Procedures
- Miscellaneous OHRP Guidance

Compliance Findings 2003-2004

- Failure to obtain written informed consent
  - 38 CFR 16.116 and 117a; VHA 1200.5, Appendix C; CFG 31, 32
- Failure to follow IRB approved protocol
  - 38 CFR 16.103.b.4.iii; VHA 1200.5, 7 c. 1; CFG 23

Compliance Findings 2003-2004

- Failure to obtain R&D Committee approval prior to conducting research
  - M-3, Part 1, Chapter 3.01.e; VHA HB 1200.5, 7.b
- Resources inadequate for HRPP program; Inadequate HRPP staff to support HRPP; Inadequate protocol/records tracking system
  - 38 CFR 16.103.b.2; CFG 52

Compliance Findings 2003-2004

- Lack of understanding and adherence to VHA and other HRPP regulations
- IRB approval stamps on signed informed consent forms exceed 365 days
  - 38 CFR 16.109(e); VHA HB 1200.5

Compliance Findings 2003-2004

- **Failure to maintain records for at least 3 years after completion of the study**
  - 3 years in 38 CFR 115(b); 5 years in VHA HB 1200.5.8.j
- **Inconsistent documentation in IRB minutes and IRB files**
  - 38 CFR 16.115.a.1,3,4,7, and 116d; CFG 55-57, 69, 70
- **Reviews of SAE by R&D and IRB not documented**
  - 21 CFR 56.101(a), 21 CFR 56.108, and 21 CFR 56.111

Other Findings 2003-2004

- Inappropriate use of expedited review and contingent approvals
- Failure to report unanticipated problems posing risks to subjects or others to federal agencies
- Failure to distribute continuing review materials to IRB members

Other Findings 2003-2004

- IRB SOP incomplete and contains regulatory inaccuracies
- R&D do not annually review IRB performance
- R&D does not receive adequate and timely information to review applications

Other Findings 2003-2004

- IRB operates with incomplete SOPs
- HRPP policy requires revision
- Expedited review inappropriately used to prevent expiration of approval when IRB could not complete review on time

Other Findings 2003-2004

- Appointment/removal of chairs and members inconsistently performed by Medical Center Director as required in M-3, Part 1, Chapter 2.02(b) and 3.01e
- Major delays in completing minutes. To be completed within 3 weeks per VHA HB 1200.5(7)(i)(2)

Other Findings 2003-2004

- Incomplete IRB study files
- Poor communications and relations among research pharmacy, R&D Committee, and Research Service
- +++++ more

National Committee for Quality Assurance (NCQA)

About 23 facilities accredited so far in VA

- Accredited for 3 years
- Accredited for 1 year
- Not accredited

ORO Take Home Message (1)

- **ORO** advises the USH on regulatory compliance and assurance
- **ORO** is responsible for regulatory compliance in research
- **ORO** is receptive to questions (hypothetical or real) on research compliance
- **ORO** requires reporting: What to Report to ORO?

ORO Take Home Message (2)

- **ORO** facilitates/maintains assurances with VA facilities
- **ORO** supports accreditation
- **ORO** Handbooks -- watch for new releases
- **ORO** requests your assistance to improve/support compliance

http://www.va.gov/oro/

The End