Managing Compliance Related to Human Subjects Research Review

Fourth Annual Research Summit

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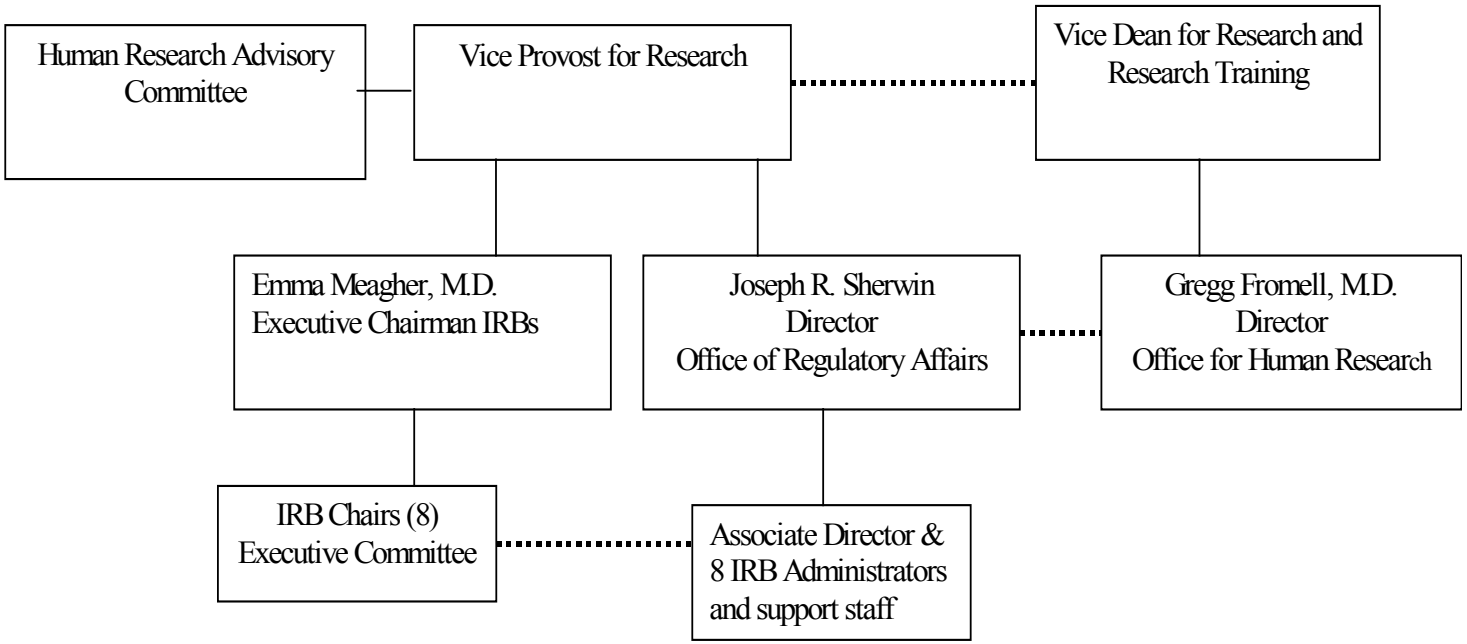
Presentation Goals

- To review the findings of a detailed (and ongoing) assessment of clinical research at U Penn
- To discuss the process of quality assurance in academic research programs involving human subjects as implemented at U Penn
- To discuss the role of quality assurance versus quality improvement in the conduct of clinical research and the IRB's role
- To discuss the pros and cons of the U Penn approach
- I will not discuss QA/QI of the IRB process due to time constraints

Current Practice and Organization University of Pennsylvania

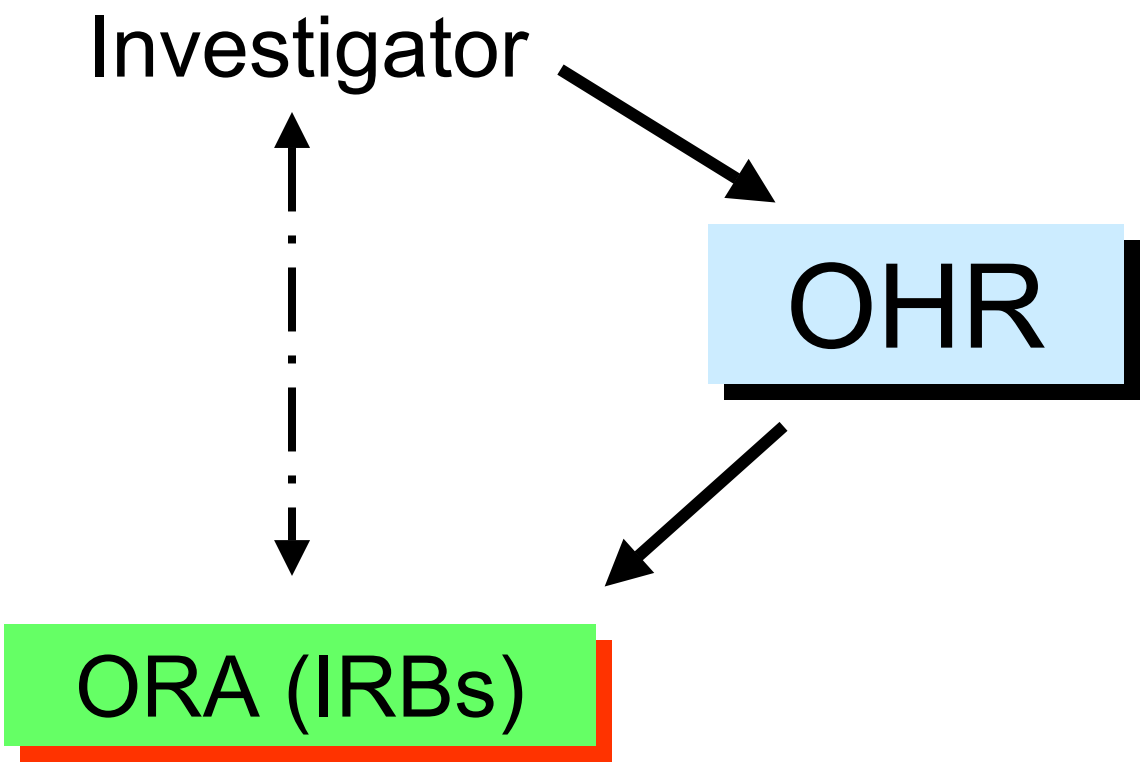
- **Created a Human Research Protections Program (HRPP), supported by two offices:**
  - Office of Regulatory Affairs
    - Supports the 8 IRBs with a staff of 20 FTEs
    - Level of background and research experience has risen
  - Office for Human Research (OHR)
    - Responsible for development and implementation of training programs
    - Responsible for assessment of investigator compliance with UPenn HRPP policies and procedures, including monitoring
    - Clinical research operations support, process improvement, and technology solutions
    - OHR supports a separate faculty advisory committee (Office for Human Research Faculty Advisory Committee)
    - Reviews proposed research management tools, monitoring guidelines and educational programs
- **And co-ordinated by a central steering committee**

Human Research Protections Program



CLINICAL RESEARCH AT PENN

Office of Human Research (OHR) and Office of Regulatory Affairs (ORA)



HUMAN RESEARCH AT PENN

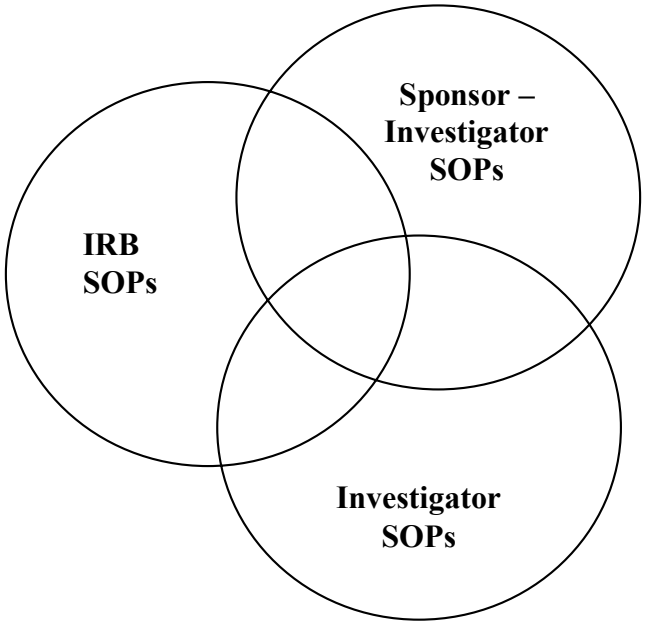
OFFICE OF HUMAN RESEARCH (established Fall, 2001)

Formed Spring 2001
Director: Dr. G. Fromell

Relationship Between ORA and OHR Basic responsibilities (not complete!)

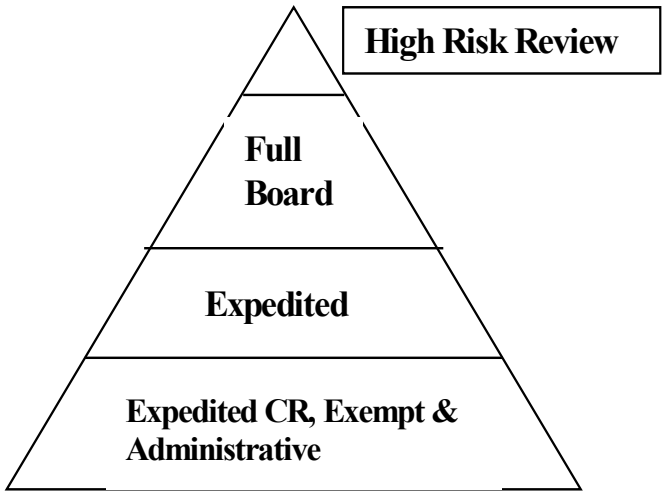
- **ORA - IRB**
  - **Review all human subjects research**
  - **Monitors ongoing studies through correspondence as part of continuing review**
  - **Refers issues of possible non-compliance to OHR**
  - **Coordinates correspondence and or audits by OHRP**
  - **Implements SOM and other school policies on training and HIPAA**
  - **Educates non-SOM faculty (Social behavioral sciences)**
  - **QAs own activity**
- **OHR**
  - **Reviews new IND, or high risk protocols**
  - **Conducts quality assurance review of "customer complaints"**
  - **Provides quality improvement oversight for clinical sites**
  - **Assist in development of new protocols or revising inadequate protocols**
  - **Conducts regular data monitoring visits of high risk studies**
  - **Coordinates other monitoring**
  - **Provides training on trial activity (GCP)**

Relationship Among Policies Proposed by Implementation Committee (HRAC)

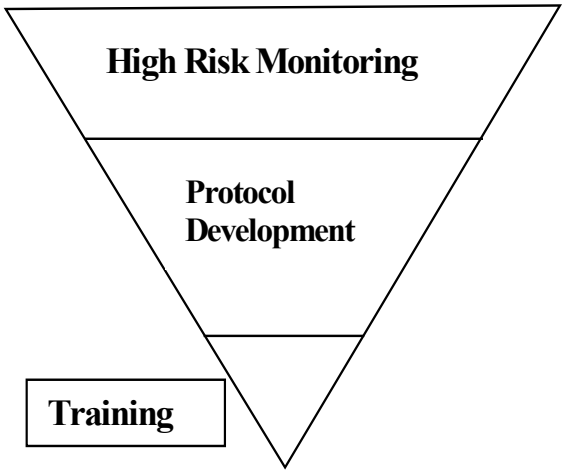


Relationship Between ORA and OHR

IRB- ORA



OHR



Calls for Quality Assurance (cont'd.)

- Who is auditing (or even monitoring or assessing) the sponsor-investigators in FDA-regulated trials?
- Who is auditing (or monitoring or assessing) investigator compliance in noncommercial studies ?
- Do we see the same level of quality assurance or a comparable focus on quality improvement when industry is not involved ?
- Is academia embracing quality assurance and quality improvement in oversight of its own research programs ?

Definitions - The U Penn Versions

- Assessment of compliance (QA)
  - Routine
  - Complaint driven (Subjects, sponsors, IRB)
- Monitoring
  - data integrity monitoring
  - safety monitoring (medical monitoring, DSMB)
- Auditing
- Remediation (QI)

Current Practice and Organization University of Pennsylvania

- **Conducted QA assessments of clinical trials**
  - Found a major gap between standards for clinical research compliance documentation in academic setting compared to pharmaceutical industry
  - Documentation lacked format for good QA review
  - Incorporated the assessment findings into training modules and SOPs
  - Develop and implemented quality improvement activity
- **Evaluating risk of a research project**
  - Involved an independent risk assessment of protocol by the IRB
    - Subject safety – Used regulatory definition of minimal risk as a base then added categories of **low**, **moderate**, and **high**
    - Other considerations including IND status and conflicts of interest
    - Frequency of IRB Re-approval and monitoring dependent on risk
      - High risk studies must have monitoring plan
      - IRB may require additional protections (ie DSMB)
      - IRB needs to address alternate methods for low risk and social behavioral sciences

Quality Assurance Unit - OHR Division

- Assures management (the IRB, institutional officials (through HRAC) and external agencies) that the facilities, equipment, personnel, methods, practices, records and controls are in conformance with the regulations.
- For any given study, the quality assurance/assessment unit shall be entirely separate and independent of the personnel engaged in the direction and conduct of the study.
  - How this principle is implemented has major impact in academic centers
  - At U Penn the QA unit is funded by and reports through the Vice Dean of the School of Medicine

QA Assessment Reports

- Written QA report includes
  - Scope and objectives of the audit/assessment - complaint or routine
  - Methodology; name of reviewers, dates; and adherence to assessment plan
  - Observations
  - Recommendations for corrective and/or preventive actions (Quality improvement!) - Management plan
  - Audit report distribution list - Department chairs, Deans etc as well as IRB.
  - IRB review, endorsement or modification and notification of Institutional Official via regular reporting or HRAC if necessary.

Follow-Up

- Investigator Responsibility
  - Determining, initiating, and completing corrective action plan
  - Communication thereof to the OHR and IRB
    - Usually as a request to IRB for re-approval of protocol
- Follow-Up
  - Corrective action plan and any follow-up visits must be completed within an agreed time
    - OHR and IRB have procedures for dealing with issues related to investigator willingness to comply with corrective action plan
    - At Penn continuing noncompliance reported to IRB for consideration of investigator suspension
      - Such suspensions trigger OHRP/FDA notification and fund restrictions

Trial QA/QI: Looking Ahead

- Quality assurance and quality improvement should become the prevailing themes in clinical and non-clinical research
- This may include new venues for QA
  - Academic institutions and their IRBs
  - Research hospitals and clinics
- The U Penn model may not be the best model for all academic centers
  - Strengths
  - Weaknesses

Questions