# Lessons Learned

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# Objectives

- Procedures
- Recurrent Problems
- Lessons Learned

# OHRP Authority/Responsibility

- Assurances
- Education
- Oversight (Audit)

# OHRP

## Human Subjects
## Compliance Oversight Procedures

# Compliance Oversight Jurisdiction

- 45 CFR 46
- OHRP Approved Assurance

# How An Investigation Gets Started

- Complaint(s)
  - PI, IRB Member, Subject, Private Citizen, etc.
- Self Reporting
  - Institution, PI
- Media
- Other Incident Report *
  - FDA Inspection
  - NIH Project Specific Violation (PSV) Report
  - Cooperative Group Audit

* **Most Incident Reports Do Not Become A Compliance Case**

# Compliance Procedures

- Written Compliant(s)
- OHRP Initiates Inquiries
- OHRP Evaluation

# Compliance Site Visit

Site Visiting

- OHRP Staff
- Consultants
- Specific Complaint
- Systemic Protections

# Action

- Ensure subjects are protected
- Require corrective actions
- Recommend institution - Wide education effort

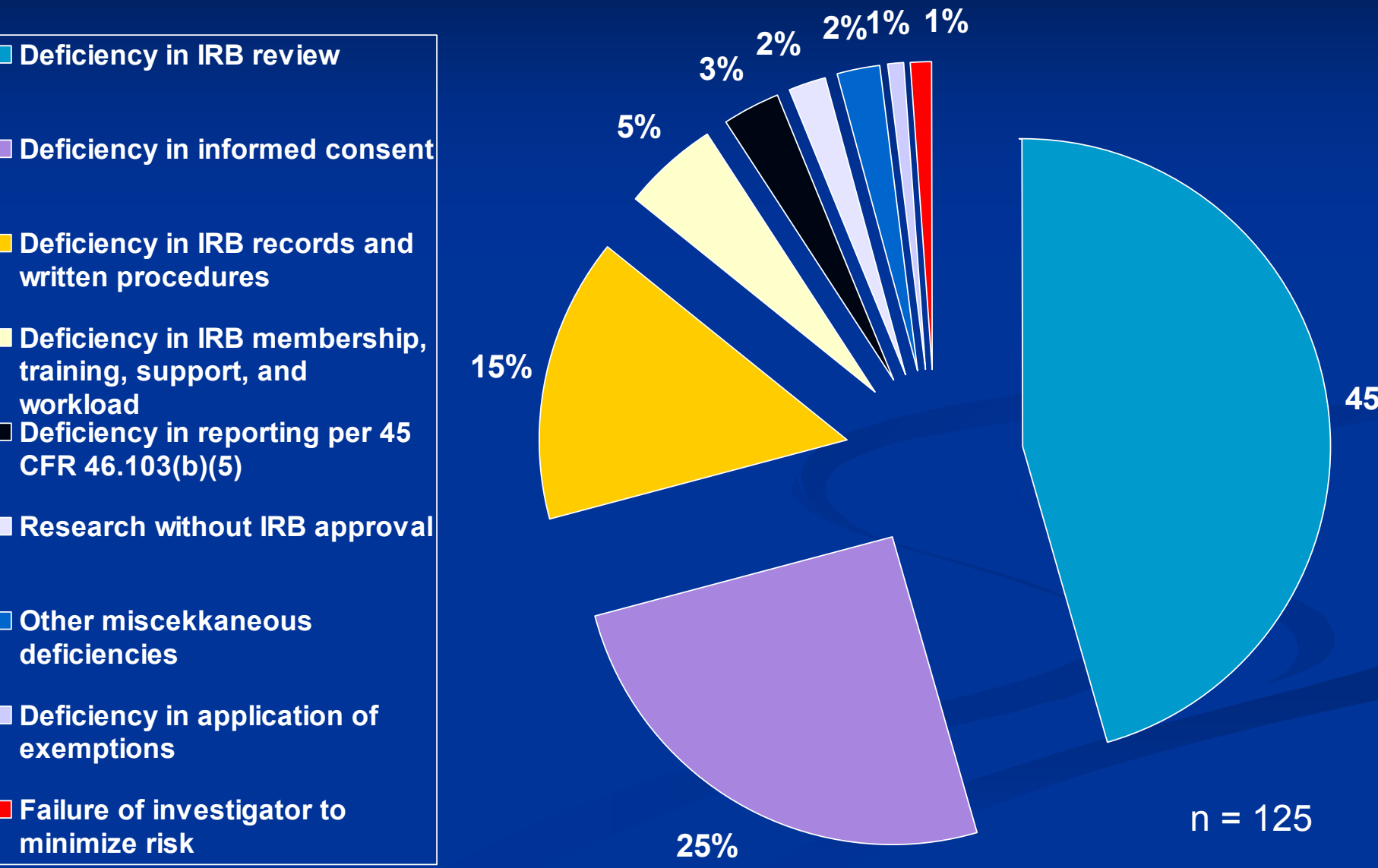
# Action

- Recommend Additional IRB Resources
- Restrict Assurance (Multiple Project Assurance-MPA)
- Postpone MPA Renewal
- Recommend Additional Action by Other HHS Offices

# Annual Statistics

- 100 Cases
- 6 - 8 Project Specific Violations (PSV)
- 2 - 3 Multiple Project Assurance (MPA) Restrictions or Suspensions

# OHRP Compliance Oversight Data



# Recurrent Compliance Problems (1)

- IRB lacks sufficient information to make determinations
- Inadequate continuing review, or longer than 1 year
- Inadequate IRB review at convened meetings

# Recurrent Compliance Problems (2)

- Contingent approval without subsequent re-review
- IRB meetings without a quorum
- IRB members with conflicts of interest
- Inadequate records, minutes, files, documentation, policies and procedures

# Recurrent Compliance Problems (3)

- Inappropriate use of expedited review for new, continuing, and changes
- Failure to report unanticipated problems to IRB, IO, OHRP
- Failure or inadequate review of protocol changes
- Inappropriate use of exempt categories

# Recurrent Compliance Problems (4)

- Deficient or inadequate informed consent documents
- Lack of diversity, expertise of IRB membership
- Overburdened IRB
- Inadequate IRB resources

# JHU
# Research Suspension

Ellen Roche
24 years old

- Healthy volunteer in a asthma study
- Died on July 2, 2001 inhalation of a non-approved drug
- Lungs were destroyed
- Employed at Johns Hopkins University

# OHRP Site Visit Plan

July 16 & 17, 2001

# OHRP Site Visit

July 16 - 18, 2001

# Site Visit Team

- 5 OHRP Staff
- 3 Consultants
- 1 FDA Representative

# Suspension of Assurance

July 19, 2001

# OHRP Findings

- IRB not given published toxicity information on the product
- The drug was not approved for human use, no IND
- Quality of the drug uncertain
- IRB inappropriately used expedited review

# OHRP Findings

- IRB did not approve protocol changes
- Informed consent:
  - procedures inadequately described
  - failed to disclose drug status
  - inadequately disclose risks

# OHRP Findings

- Inadequate IRB information for continuing review
- Inappropriate IRB minutes and backlog
- Some IRB members had conflicts of interest

# OHRP Findings

- IRB overloaded, lacking staff
- IRB members in need of education

# Actions Taken OHRP

- Suspended assurance, suspending all federally-sponsored research
- Required re-evaluation of protocols
- Requested a plan to restructure the system for protecting human subjects
- Required plan to educate IRB members, staff and researchers

# Univ. of Michigan

# Research Suspension

# Univ. of Michigan

News Release

August 30, 2001

# Internal Investigation

- Suspend Research Privileges
  - leading cancer surgeon
- Extensive Investigation
  - numerous regulatory infractions
  - five human clinical trials

# Researcher

- Not allow to conduct human research
  - three years
  - retroactive to October 20, 2000
  - all human research suspended by IRB

# Findings

- Breaches of IRB Rule
  - 5 trials
  - 94 research volunteers
  - frequent and pervasive
  - not adhere to federal and university rules

# IRB Breaches

- Informed consent
  - obtain after study begin
  - inadequate documentation
- Deviation from the IRB approved protocol
- Patients enrolled after the study was closed
- Adverse events
  - not reported
  - not reported in a timely manner

# Lessons Learned

- Strengthen Continuing Review
- SAE Reporting
- DSMB

# Internal Investigations

# vs.

# OHRP/FDA Investigations

# Lessons Learned

- Roles & Responsibilities
- Polices & Procedures
- Staff Training & Education
- System Adequacy

# Lessons Learned

- Leadership
- Institutional Commitment

# Proactive Prevention

# vs.

# Reactive Enforcement

# Effective Monitoring

- Quality Improvement
- Continuing Education
- Commitment

# Quality ⟷ Compliance

- Quality Programs Enhance Compliance
- Compliance Programs Enhance Quality


Compliance
Quality

# Shared Goals

Protecting Human Subjects

Promoting Ethical Research

# Shared Responsibilities

- Investigators
- IRB (chair, members, administrator)
- Institutional CEO