Overall Goal: Create an ideal clinical support and oversight structure for the NIH intramural research program

1. Assure compliance with existing regulatory requirements (established Office of Research Support and Compliance)
2. Improve support of clinical investigators and clinical research at the NIH (working group),
3. Reorganize IRBs (subcommittee of IC Directors), and
4. Use more uniform IT systems to support these functions.
Delayed SAE
and UP Reporting Events

• Reported to CCHRB in January 2017: *Late reporting is not an isolated event within the NIH intramural clinical research program*

• Short term and longer term actions planned.

• CCHRB requested a Root Cause Analysis.
Root Cause Analysis (RCA)

- A structured method used to analyze serious events
- A central tenet of RCA is to identify underlying problems that increase the likelihood of errors while avoiding focus on mistakes by individuals
- Uses a systems approach to identify both active errors (errors occurring at the point of interface between humans and a complex system) and latent errors (the hidden problems within organizations/systems that contribute to adverse events)

From: The Agency for Healthcare Research and Quality, Patient Safety Network
Objective

• To query research staff in an effort to understand the root causes and/or contributing factors that influence timely and accurate research event reporting.

• The NIH Clinical Center Office of Patient Safety and Clinical Quality facilitated the analyses.
Process

• 8 teams participated in RCA meetings:
  • 7 teams with one or more delayed event to IRB, Sponsor, or both
    • Late events ranged across spectrum, up to Grade 5
    • 1 team with no late reporting served as a “positive control.”

• 8 research protocols examined:
  • 6 Institutes
  • 1 Natural History Studies
  • 7 Clinical Trials
Participants

- Participants included:
  - Principal Investigators
  - Research Nurses
  - Study Coordinators
  - Protocol Navigators
  - Fellows
  - Nurse Practitioners
  - Quality Assurance/Improvement Specialists/CRO Representatives
  - Regulatory Affairs Staff
Domains Explored

- Human Factors
- Policies & Procedures
- Communication & Information
- Leadership & Culture
- Human Resources & Training
- Environment & Equipment
Human Factors - 1

- Very high acuity patients*
- Complex disease processes*
- Complex protocol design (dose escalations, multiple arms)*
- Limited staff resources*
- Consolidation of patient care units resulted in patients being housed on units with nurses not as familiar with specific research study requirements

*Identified multiple times
Human Factors - 2

• Tension between patient care responsibilities and research requirements*

• Sense of urgency for reporting lower for events identified during retrospective audits

• Reporting responsibilities vary and not always clear for IRB/Sponsor and among different team members.*
  • Variable use of checklists/task triggers*

• Email fatigue: “Information overload” from large number of emails to PIs and team members results in flawed communication*
Policies and Procedures

• Unclear/inconsistent understanding of what events to report*
  • Reporting requirements are complex and sometimes difficult to interpret consistently/properly*

• Confusion about when the “clock starts ticking” for reporting (e.g., when the event occurred versus when the PI is made aware of the event)*

• Rules/processes for determining “seriousness” of an event seem ambiguous*

• One IC required three signatures (PI, Branch Chief, Clinical Director) before an event can be submitted to the IRB

• Reporting requirements vary among sponsors (e.g., timing, forms) and may be different than NIH requirements*

• Protocols designed with exceedingly rigorous reporting requirements creating unnecessary workload and increased deviations/unanticipated problem findings
Communication & Information

• IRB reporting tools (PTMS and IRIS) are not “user-friendly*:
  • Do not provide effective alerts/triggers for users
  • Information in the systems are not easy to access

• Some research teams do not have redundant communication processes (feedback loops) in place with the PIs regarding event reporting*

• Many teams did not have regularly scheduled forums to review events and the status of reporting*
Human Resources & Training

Human Resources/Staffing:
- Study management staffing is under-resourced (e.g., patient care/coordination, regulatory/compliance activities)*
- No clear and objective processes in place for allocating research resources*
- Staff caring for patients and implementing the protocol are also responsible for reporting

Training:
- Training regarding reporting requirements should be more interactive and include case studies
- Study nurses and coordinators receive inconsistent orientation and training about reporting requirements *
Leadership and Culture

• Clinical research requirements are taken seriously; however, patient care requirements are equally important – trade-offs sometimes occur*

• Some ICs’ “culture” is to wait to report until all the details of the event are available*

• “Customer service”/ Relationship with the IRBs is variable

• Processes for delegating investigator responsibilities when PIs depart can be overwhelming for the PIs who must assume the added caseload
Findings

Lapses are not the “FAULT” of an individual or team...

Lapses occur because of sub-optimally designed processes and policies, local and organizational management decisions, and complex regulatory requirements.
Update: Steps to monitor and assure timely reporting of problems in NIH intramural clinical research protocols

1. Routine rounds for prompt recognition and discussion of reportable events
2. Standard operating procedures (SOPs) to monitor and assure timely event reporting
3. Ensure that problems reported to one entity are reported to other applicable entities
4. Refresher training on event reporting for all members of all teams for all studies
5. Education campaign for event detection and timely reporting
6. Modify PMAP elements for all team members for tracking and timely reporting
Routine rounds for prompt recognition and discussion of reportable events

**Goal:** team discussion to identify events requiring reporting to IRB, sponsor, or FDA in a timely fashion

- Every clinical research protocol/team has a plan
- Occur on at least a weekly basis
- More frequent meetings for busy services, teams or programs
- Can combine with safety rounds, inpatient rounds, or patient care/research conferences, etc.
- Flexible and risk-based

**Timeline:** March 30, 2017 ✔
Standard operating procedures (SOPs) to monitor and assure timely event reporting

**Goal:** routinely review timeliness of reporting and to detect and address late reporting

- All clinical research activities, including non-interventional protocols
- Review and monitor for timely reporting
- Include plans for remediation of late reporting
- Flexible and risk-based
- “Placeholder” plans accepted until IC has access to infrastructure to revise SOPs

**Timeline:** April 24, 2017  ✔️
Ensure that problems reported to one entity are reported to other applicable entities

**Goal:** cross-check event reporting to IRB, study sponsor, and FDA (if applicable)

- Described in an SOP
- “Placeholder” plans accepted until IC has access to infrastructure to revise SOPs

**Timeline:** April 24, 2017 ✓
Refresher training on event reporting for all members of all teams for ALL studies

- Applies to all studies, including non-interventional studies
- In-person basic refresher training
- Team training encouraged when feasible

Timeline: April 24, 2017 ✓
Education campaign for team approach to event detection and timely reporting

- Trans-NIH campaign including posters, etc.
- Working with NIH Office of Communications and Public Liaison to communicate a positive message

Timeline: May, 2017
Modify PMAP elements for all team members for tracking and timely reporting

- Principal and associate investigators, research nurses and other team members
- Will include a minimal benchmark for tracking and timely reporting of reportable events
- Will incorporate into current plans for inclusion in mid-year review

Timeline: June or July, 2017
Trans-NIH independent audit

- Outside auditor selected: April 2017
- Audit begins: May 2017

**Protocols being audited:**
- Conducted on NIH intramural research program site(s)
- Open for enrollment as of 05/01/2017
- Intervention or data gathering through interaction with subject(s) in preceding 6 months.
- Excluding repository, training, and screening protocols
- Excluding protocols audited by the FDA within the last 5 years

**Items being audited:**
- Expedited event reporting, e.g., UPs and SAEs
- Informed consent
- Compliance with eligibility and exclusion criteria
Questions?

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Our Research Changes Lives

one program
many people
infinite possibilities

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