



Delayed Reporting Root Cause Analysis for Clinical Research at the NIH

Clinical Center Research Hospital Board
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Intramural Research Program
Our Research Changes Lives

one program
many people
infinite possibilities



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)

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 - 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

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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