Corrective Action Plans for Research Non-Compliance

Sarah Mumford, IRB Administrator
Ann Johnson, IRB Associate Director
John Stillman, IRB Director
Jerry Treiman, MD, IRB Chair
Non-Compliance Review Process

1. Report Form Submitted
2. Administrative Review
3. Subcommittee Review
4. Board Review
5. Determination
6. Notifications
7. Response
8. Completion
Initiation of Review

How is a non-compliance review initiated?

1. PI reports deviation(s) to the IRB via a Report Form
2. IRB receives a complaint/concern indicating that there may be non-compliance
   - PI submits a Report Form, regardless of merit of complaint
   - Inquiry is conducted to determine if there is evidence of non-compliance
3. Audit (IRB or other) finds instances of non-compliance
   - Audit report requires reporting of any deviations/non-compliance via Report Form
Report Review Process

There are 3 levels of review that may occur:

1. **Administrative review** – Sarah Mumford
   - Starting point for all report forms EXCEPT adverse events
   - Not non-compliance – Review ends
   - Non-compliance but not serious or continuing – Review ends
   - Possible continuing or serious non-compliance – Review continues

2. **Subcommittee review** – conducted by Ingrid Nygaard, Chris Stock, or Dennis O’Rourke
   - Starting point for adverse events
   - Non-compliance but not serious or continuing – Review ends
   - Possible continuing or serious non-compliance – Review continues

3. **Convened board review**
   - Depending on severity, non-compliance may go directly from administrative review to board review
   - Final Determination – Non-compliance but not serious or continuing, Serious non-compliance and/or Continuing non-compliance
Board Review

• Report Form Review
  • Primary Reviewer
  • Secondary Reviewer (Possible Serious)
• Determination
  • Non-compliance, not serious or continuing
  • Serious non-compliance
  • Continuing non-compliance
• Corrective Actions
• Suspension/Termination
Follow-up

- Notifications
  - Letter to PI
    - Includes determination, justification, corrective actions
  - Copies sent to:
    - VP for Research, AVP for Research Integrity, IRB Director
    - Sponsor
    - Division Head, Department Chair
    - FDA
    - OHRP
- Corrective Actions
  - Completion Letters
CORRECTIVE ACTIONS “CASE STUDIES”
Case 1

• Various issues led to an IRB audit of several studies of same PI. Multiple deviations uncovered.
• Concerns: Significant amount of missing data and deviations raising concern over ability to analyze data, DSMB consisted of PI’s junior partner and other subordinates
• Corrective Actions Required
  • *Independent* Audit of ALL data
  • *Independent* DSMB including statistician to review all data as compiled from audit
  • Standard Operating Procedures
  • One year improvement plan to include quarterly internal monitoring, ongoing independent audits on ALL studies
Additional Actions

- One study terminated due to a complete lack of ability to evaluate data as per recommendation of DSMB/statistician
- Two other studies suspended due to issues discovered during review of all studies as part of improvement plan due to insufficient information provided to participants in consent forms
- Corrective actions should always take into consideration currently enrolled participants, how should they be handled in order to prevent further risk, based upon specific situation
Case 2

- Department audit uncovered significant deviations during a review of 2 of 12 participants.
- Concerns: Deviations included enrolling patients who were ineligible for various reasons, patients on prohibited medications, missed labs. Based on large number of deviations, can data be analyzed? Investigator-initiated IND
- Corrective Actions Required
  - *Independent* Audit of ALL data (other 10 participants)
  - DSMC to review audit and provide recommendations to IRB
  - Good Clinical Practices training
  - One year improvement plan to include quarterly internal monitoring, ongoing independent audits on ALL studies
  - No investigator-initiated IND studies until satisfactory completion of one year improvement plan
Case 3

• Prior continuing non-compliance determination. IRB received staff complaint.
• Issues included in complaint had been previously reported and received continuing non-compliance determination. Majority involved documentation errors and timing of discovery and timing of IRB submissions
• Non-compliance not serious or continuing – Corrective Actions still required
  • One year improvement plan to include quarterly internal monitoring, ongoing independent audits on ALL studies
  • Design and implement training plan to train team on monitoring
  • Formal plan for prompt submission of IRB requirements