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Non-compliance, Misconduct and Fraud

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Clinical Research Conference 2015
Orlando - FL
Horror Stories in Scientific Research do not always start and end with Fraud but includes mishaps and misconducts at the level of the Sponsor, Investigators and IRB/IEC

*Clinical Quest*
Fraud Associated Characters

- Incompetence
- Arrogance
- Greed
- Ambition
- Laziness
- Dishonesty

- Bad Science
- Poor Ethics
- Contempt for Patients
- Contempt for Rules
- Contempt for sponsor
- Poor team spirit
COMPLIANCE IN CLINICAL TRIALS

Key to a successful Clinical Trial - Compliance!

Protocol

Regulations

SOPs

ICH

Compliance!
Fraudulent research has more serious consequences than other forms of deception or misconduct.
DRIVERS OF NON COMPLIANCE

Non-compliance: GCP demands that you say NO!

Honest Error

Compliance Noncompliance

Failure to see the “experiment”
- Complicated study procedures
- Poor infrastructure
- Miscalculation/ misjudgment

Study protocol ambiguous
- Rationale of study unclear
- Patient inconvenience
- Overrated techniques/ equip.
MISCONDUCT

Pre-conceived notions

“I WONDER HOW MY GENETICS EXPERIMENT IS COMING ALONG...?"

“Noooooo!!! THAT’S NOT THE RESULT I WANTED TO SEE !!!"

“BLAM! BLAM! BLAM!"

“WELL, GEE ERIC...! THERE WAS NO NEED TO SHOOT THE KNA..."

“To a physician, the patient’s welfare is more important than scientific truth”
MAJOR DRIVERS OF MISCONDUCT

- Under-qualified study staff
- Unrealistic expectations
- Poor statistical plan
- Low recruitment

Systematic
- Time Constraints
- Lack of Involvement
- Inappropriate Delegation
- Continuing non-compliance

Noncompliance

Significant
EXAMPLES OF SCIENTIFIC MISCONDUCT

- Under reporting Adverse Events
- Unexplained handwritten changes to CRF and Source Data
- Patients not dating their own ICF's
- Source data as uncertified photocopies
- Direct CRF entry
- Source Data withheld
“Scientists aren’t saints. The field is so competitive that many misbehave in many ways; few falsify results.”

-David Goodstein

"There now...WE get our wish of continuing our work unimpeded, and THEY get their wish of being in a position of direct oversight at all times..."
Drivers of Fraud

Financial gain

Pressure to publish

Power, Arrogance & Prestige

Misconduct

Psychiatric illness

"The most difficult crime to track is the one which is purposeless" - Sherlock Holmes
INCIDENCE OF FRAUD

Believed to be uncommon

Estimated to be 4-5% annually

No systematic registration (except UK, Denmark & USA)

“We believe probabilities and choose the most likely. This is very scientific use of imagination”
"I am going to enter you as three patients, in your name, nee name and pseudonym."
The incidence of reporting fraud is on the increase.
Falsification of Data

- Falsification of data includes
  - creating, altering, recording, or omitting data in such a way that the data do not represent what actually occurred
Examples of falsification of data include but are not limited to

• creating data that were never obtained;
• altering data that were obtained by substituting different data;
• recording or obtaining data from a specimen, sample or test whose origin is not accurately described or in a way that does not accurately reflect the data
• omitting data that were obtained and ordinarily would be recorded
EXAMPLES OF FRAUD

• Tampering with eligibility criteria for inclusion/continuation
• Pt. disguised & entered several times
• Pts. enrolled in other concurrent studies
• Investigator enrolling himself in study
• Forged Consent Forms
• Falsifying EC approval
• Fabricating lab results
• Charging for test article
• Plagiarizing Publications

“As to the (forged) signatures of 4 out of 80 patients...we are talking of a margin of error of 5%—this is within recognized statistical limits.” - Dr. Robert Fiddes
"I don't think this is an SAE, after all you did not need that appendix, did you?"
THE BLAME GAME - WHO GETS THE BLAME?

- Study Coordinator: 39%
- Nurse: 17%
- Hospital: 9%
- Sponsor: 9%
- Investigator: 9%
- Office Staff: 9%
- Sub-investigator: 4%
- Monitor: 4%

Any player in clinical research can potentially commit fraud.
IMPACT OF FRAUD

- Patient abuse & exploitation
- Integrity of submitted/published data – questionable
- Rejection of data/reanalysis without suspect data
- Licenses issued based on unreliable data - Public health endangered
- Waste of public finances
MANAGEMENT STRATEGIES

Prevention

- Identify and eliminate/ minimize risk factors

Detection

- Monitor and recognize signs

Correction

- Promptly investigate and report findings

One should be able to Prevent, Recognize and Report
PREVENTIVE MODALITIES

- Simplify workflow
- Clear Communications
- Train, share uncertainties
- Equip teams with money, machines & men
- Motivate workers

- Careful Selection of Investigators
- Minimize use of enrollment incentives
- Close Monitoring
- Strict Auditing

Interim Data Review
GATHERING PROOF

• Remain discreet – do not accuse!
• Look for:
  ➢ Perfect documentation
  ➢ Patterns across patients
  ➢ Spurious data
  ➢ Tampering of documents
  ➢ Deviation from other centers
  ➢ Suspicious behavior

“There is nothing like first-hand evidence”
DETECTION TOOLS

- Get Technical - Read ECGs, lab results, don’t just inventory
- Fill in the Blanks - Question missing dates & time
- Don’t be intimidated - tell the emperor he has no clothes
- Don’t shoot the messenger - believe the monitor, put the burden of proof on the person suspected
- Beware of blame shifting
- Cultivate whistleblowers - establish rapport with study staff, be approachable and available, listen to grievances

“There is nothing more deceptive than an obvious fact”
"When you have eliminated all of which is impossible, then whatever remains, however improbable, must be the truth"

- Sherlock Holmes
WHEN FIRST DETECTED

- Do not suppress suspicions
- Handle discretely
- Do not reveal suspicions at site
- Do not immediately start using terms such as “fraud”
- Seek advice and help
- Confirm suspicions with objective evidence
- Collect circumstantial evidence and data
ACTION AGAINST MISCONDUCT

- Warning letter to investigator; demand improvement
- Increasing monitoring activity and training
- Act to save data at the site – where feasible
  - Correct the documentation
  - Reconsent all patients
  - Validate all data → modify the database
- Justify exclusion of data from final report
- Worst case: close centre and avoid using again

Principal steps on detecting misconduct: saving the data and ensuring patient safety
RESPONDING TO FRAUD

- Vital to have a company **SOP** to follow
- Initiated by suspicion by any member of staff
- Suspicion **reported** to line manager
- Suspicion relayed to operational manager and/or QA
- Evidence **reviewed** to substantiate or remove suspicion
- If substantiated, promptly notify senior management (& sponsor)
- Undertake for cause **audit** and statistical data review/analysis
- If confirmed, determine course of **action** as per SOP

Data probably compromised beyond recovery
ACTION AGAINST FRAUD

- Close errant centre and prevent future use
- Inform the relevant regulatory agency
- Inform the errant investigator’s institution/professional body
- Inform the Ethics Committee

Understand that fraud cannot be fully eliminated and work towards minimizing it
SANCTIONS

- Indemnification withdrawn
- Initiate disciplinary action
  - Professional
  - Institutional
  - EC
- Potential for civil or criminal prosecution
  - Breach of contract (e.g. Inv. Agreement)
  - Deception
  - Compensation (e.g. recover financial losses)
WHO BELLS THE CAT?

• UK
  – ABPI (medical director networking)
  – GMC statutory declaration
• USA
  – FDA maintain a list of restricted or debarred clinicians
    (www.fda.gov/oc/oha/list2)
• Nordic Countries
  – Denmark : Committee in Scientific Dishonesty (health & medical
    science)
  – Finland : National Research Ethics Council
  – Norway : National Committee for evaluation of Dishonesty in Health
    Res.
  – Sweden : Committee for Research Ethics, Expert Committee
• Germany
  – “Golden memory” of the Deutsche Gesellschaft fur Pharmazeutische
    Medizin
THE NON COMPLIANCE CONTINUUM

Anybody can commit it, Somebody should detect it, Everybody should minimize it
Most of Physicians

Inquiry for Study  Signing CTA  IM & Training

Site Initiation  Beginning of Recruitment  Ongoing Activities

Towards the End  NO MORE STUDY
THANK YOU
Let Us Meet Again

We welcome you all to our future conferences of OMICS International

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