Noncompliance and Corrective Action Plans

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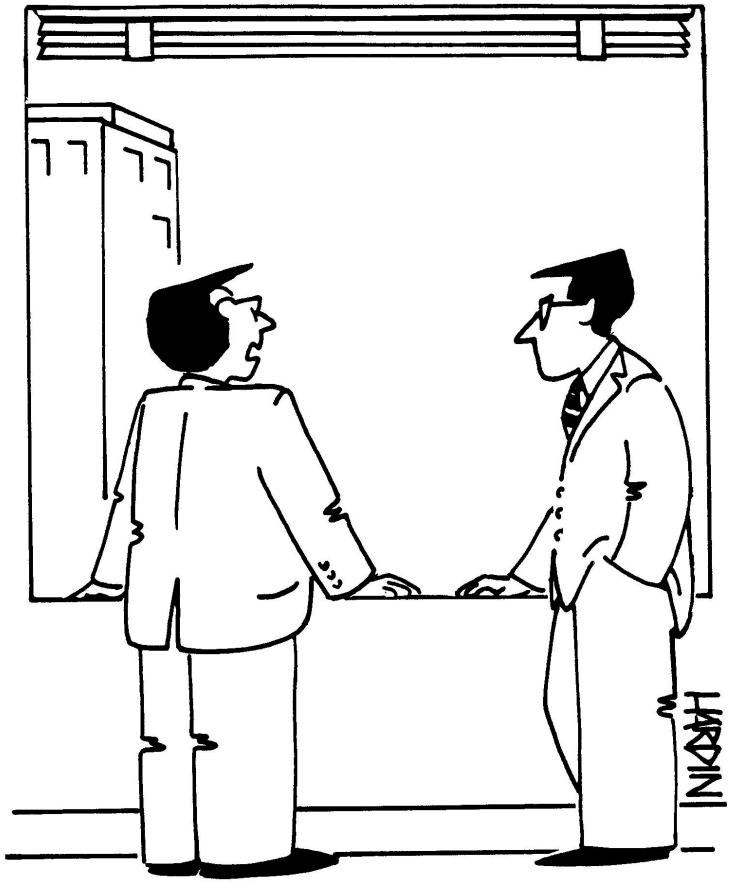
Case study

- Audit shows several patients did not get mandatory safety labs prior to receiving doses of chemotherapy
- Investigator's corrective action plan:
  - "We will re-educate coordinators on the importance of ordering safety labs"

  - Doesn't discover the cause(s) of the problem
  - Doesn't address the cause(s) of the problem
  - Doesn't prevent the problem from happening again

Analysis of incident

- Why did it happen?
- What needs to be done now to reduce risks to current subjects?
- What needs to be done now, and in the future, to keep it from happening again?



"The fault lies not in our stars, but in ourselves – If we move fast, though, we can pin it on Rendleman in Accounting."

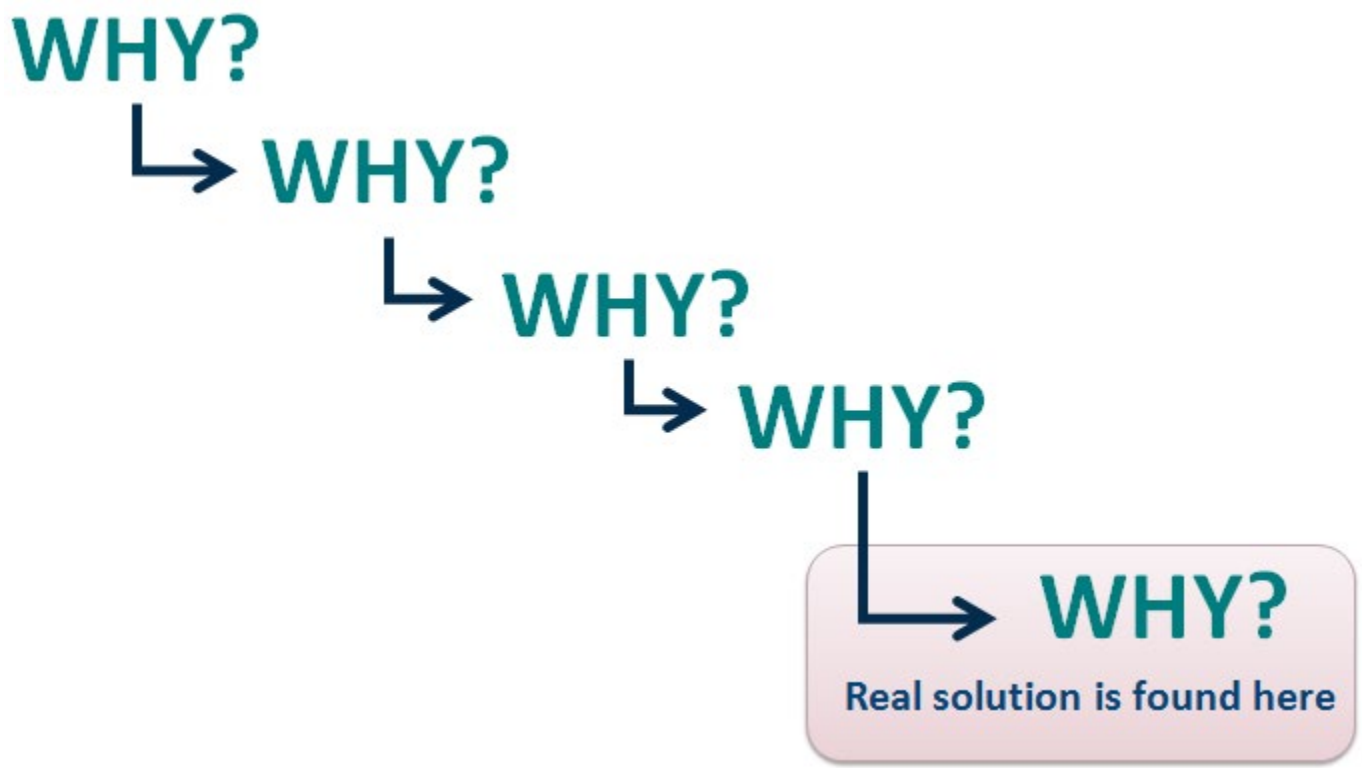
- Why did it happen?
  - Analysis needs to be performed primarily by the investigator
    - Investigator is familiar with the research, with the conditions surrounding the research, and with the event
  - Process-driven
    - Root cause analysis
  - IRB may need to perform its own investigation

"To address this mistake we need to utilise our thorough system of root cause analysis. I will begin, if I may, by pointing out that it's not my fault"

Root cause analysis

- 5 Whys
- Event / causal factor trees
- Fishbone diagram

Root cause analysis



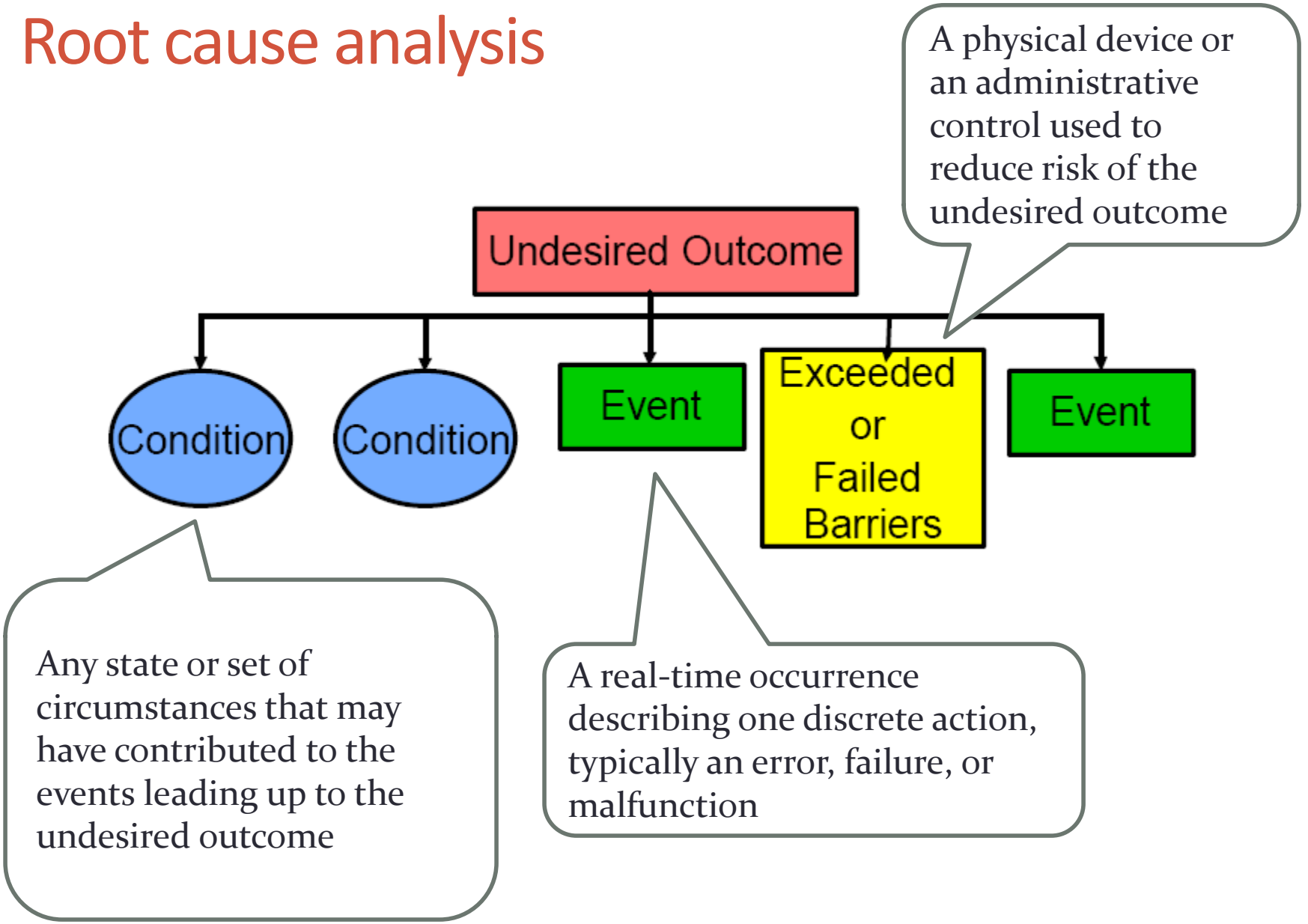
Root cause analysis

- Safety labs not ordered
  - Why?
    - Clinical coordinator didn’t add them to the routine order set
  - Why?
    - She wasn’t informed that there were new required orders based on most recent amendment
  - Why?
    - Protocol office submitted changes to the IRB and modified the "master protocol" but didn’t realize coordinator didn’t get a copy of the amendment and didn't tell her the protocol was updated
  - Why?
    - SOP not established to communicate amendments with clinical coordinator

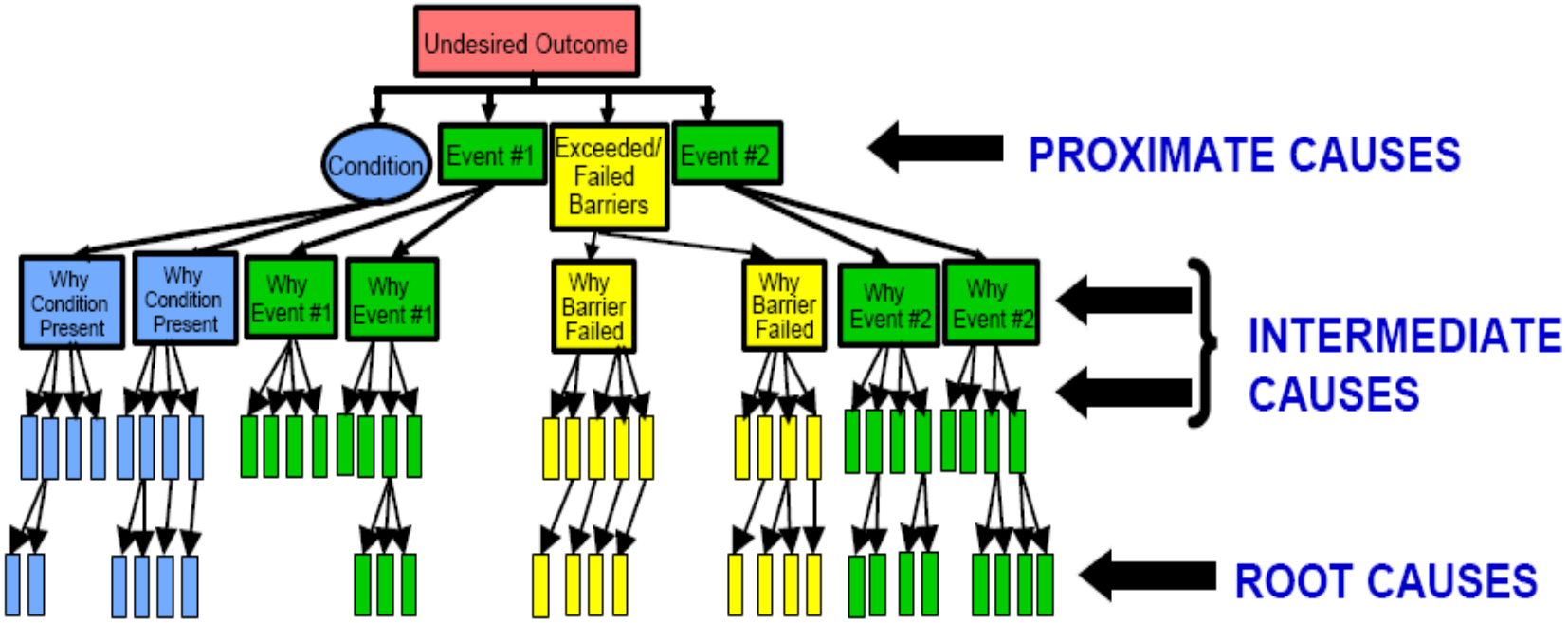
Root cause analysis

- But other events occurred …
  - PI did not communicate study progress report which alerted investigators to new toxicity (and generated change in protocol for new safety labs)
    - Why didn't he?
- Other barriers failed …
  - Data managers should have collected lab results for CRFs in real time and noted absence of safety labs
    - Why didn't they?
- Other predisposing conditions existed …
  - Clinical coordinator, managing multiple research studies, didn't have time to regularly review "master protocols" for changes
    - Why didn't she?

Root cause analysis



Root cause analysis



MS Herald of Free Enterprise

- Roll-on roll-off car and passenger ferry, commissioned in 1980
- Regularly serviced Calais to Dover route

MS Herald of Free Enterprise

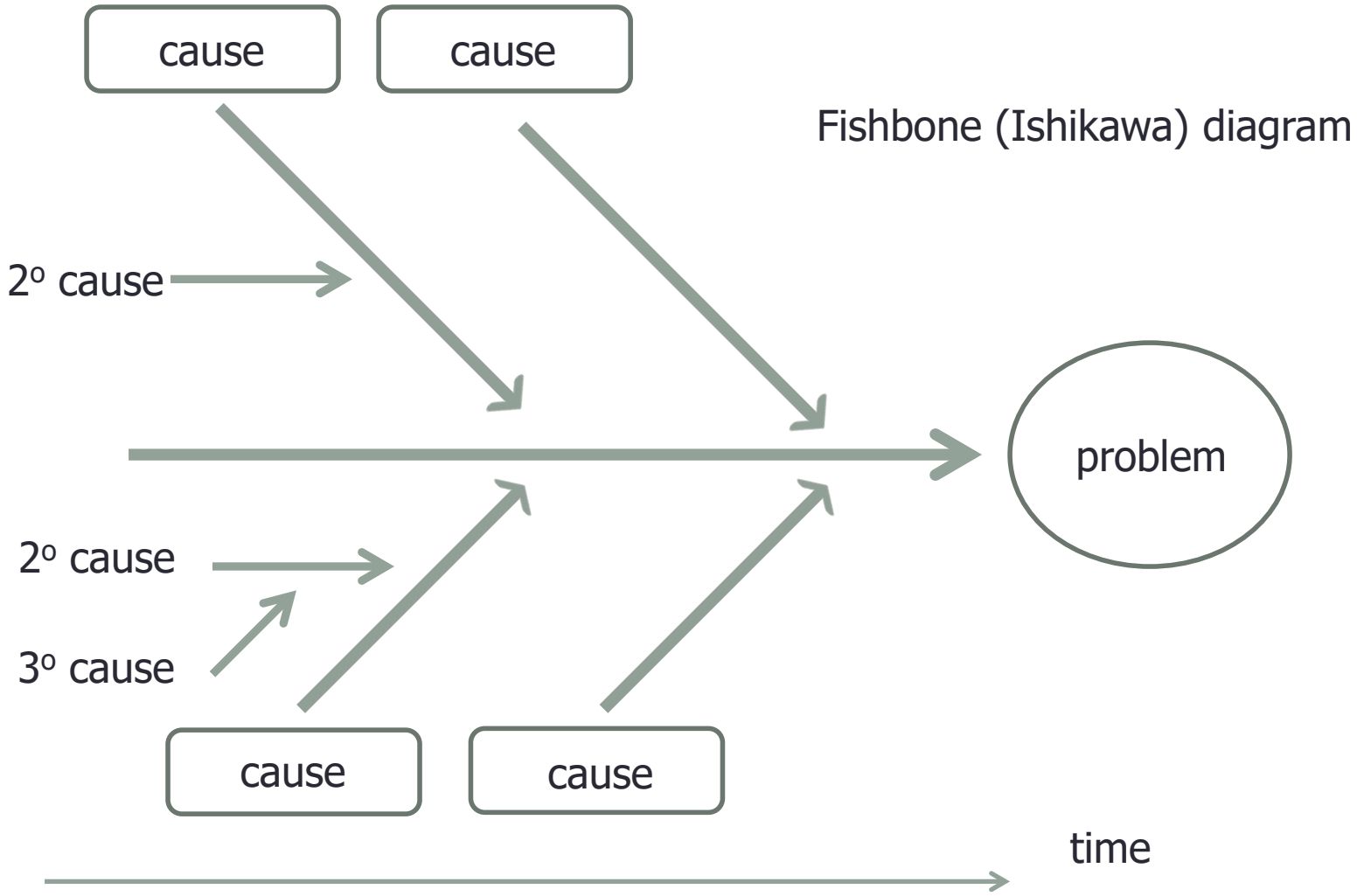
- Capsized shortly after leaving Zeebrugge (Belgium) harbor on the night of March 6, 1987
- 193 people died

MS Herald of Free Enterprise

- Assistant bosun failed to close bow doors
- First Officer failed to make sure bow doors were closed
- Captain left port without confirming bow doors were closed

- Standing orders did not require captain to ask if bow doors were closed
- Ferry lacked indicator on bridge that bow doors were open
- Ferry lacked high-capacity pump to empty ballast tanks

Root cause analysis



"What do you mean 'it just happened'?
Didn't we discuss cause and effect?"

Analysis of incident

- Why did it happen?
- What needs to be done now to reduce risks to current subjects?
- What needs to be done now, and in the future, to keep it from happening again?

- Modifications to reduce risk to current subjects
  - Protocol changes
    - Additional monitoring for AEs
    - Modification of subsequent dosing
  - Inform subject / re-consent

Analysis of incident

- Why did it happen?
- What needs to be done now to reduce risks to current subjects?
- What needs to be done now, and in the future, to keep it from happening again?

- Modification to reduce likelihood of noncompliance in the future
  - Plan of action must be
    - realistic (achievable)
      - "hire three new coordinators" might not be achievable
    - meaningful (address the problem)
      - "make coordinator take CITI course again" doesn't really address the problem
    - measurable

- Modification to reduce likelihood of noncompliance in the future
  - Protocol changes
  - Process modification
  - Investigator modification

Modification to reduce likelihood of noncompliance in the future

- Protocol changes
  - If the problem was due to an unrealistic expectation in the protocol, revise the protocol
    - Vital signs every 5 minutes may not be necessary for patient safety, and is likely to be too burdensome to be achievable
    - Fifty-page questionnaire may be too burdensome, leading to subjects not completing

Modification to reduce likelihood of noncompliance in the future

- Process modification
  - Provide education regarding current (adequate) processes
    - If the process is realistic and achievable, but not being followed because it is not understood by research team, then education is appropriate
    - However …
      - perhaps the initial process of education is defective and needs correction

Modification to reduce likelihood of noncompliance in the future

- Process modification
  - Revise process so that it fits within the limitations of the system
    - Blood drawing for pharmacokinetics is being missed at the end of a long drug infusion because there is less nursing staff at the end of the day
      - you can't make the day longer – but you can start things earlier

Modification to reduce likelihood of noncompliance in the future

- Process modification
  - Revise the process by providing more support (minimizing or removing limitations)
    - personnel
    - hardware

Modification to reduce likelihood of noncompliance in the future

- Investigator modification
  - Education
    - General vs process-based
  - Restrictions
    - Different from punishment
    - Appropriate if noncompliance was due to manpower issues or time constraints
  - Punishment
    - "Let the punishment fit the crime"

"I really can't explain it too much except to say that it's part of a court order."