CDER Perspective: Good Clinical Practice

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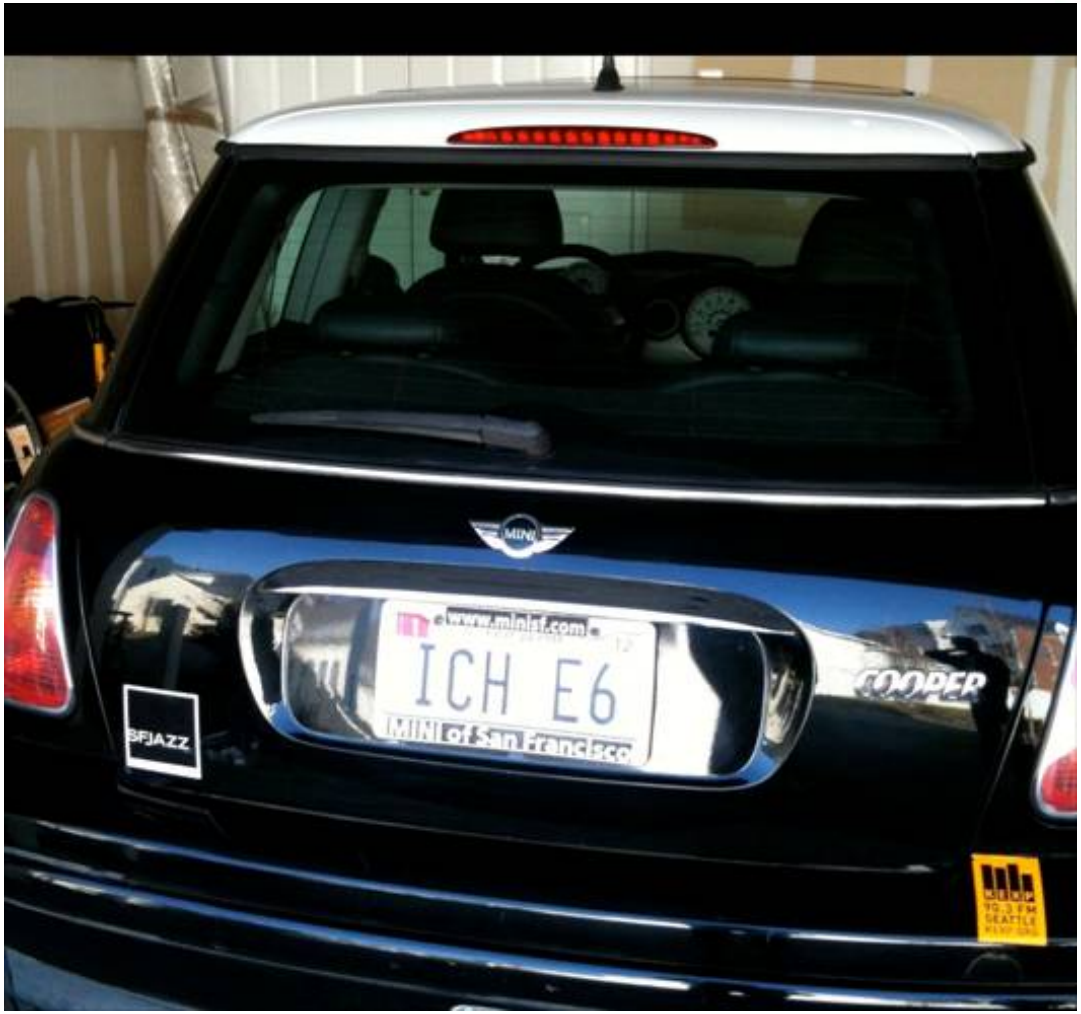
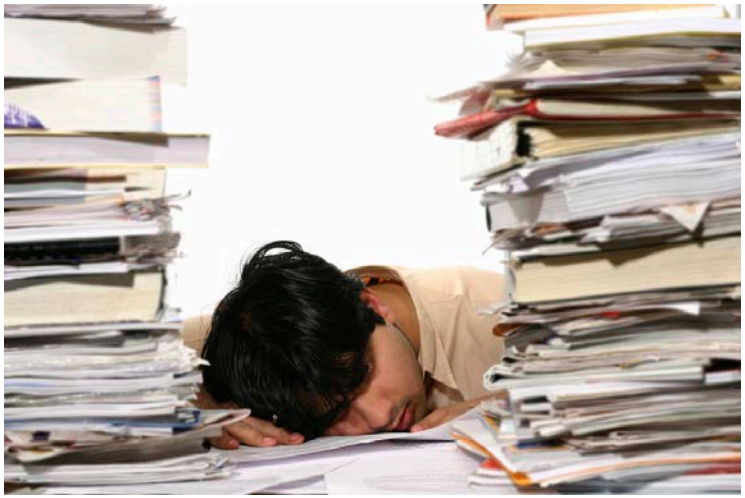
A Confession . . .



Difference interpretations of ICH E6 may lead to different approaches



Critical points in

Quality control should be applied to **each stage of data handling** to ensure that **all data** are reliable and have been **processed correctly**.

important

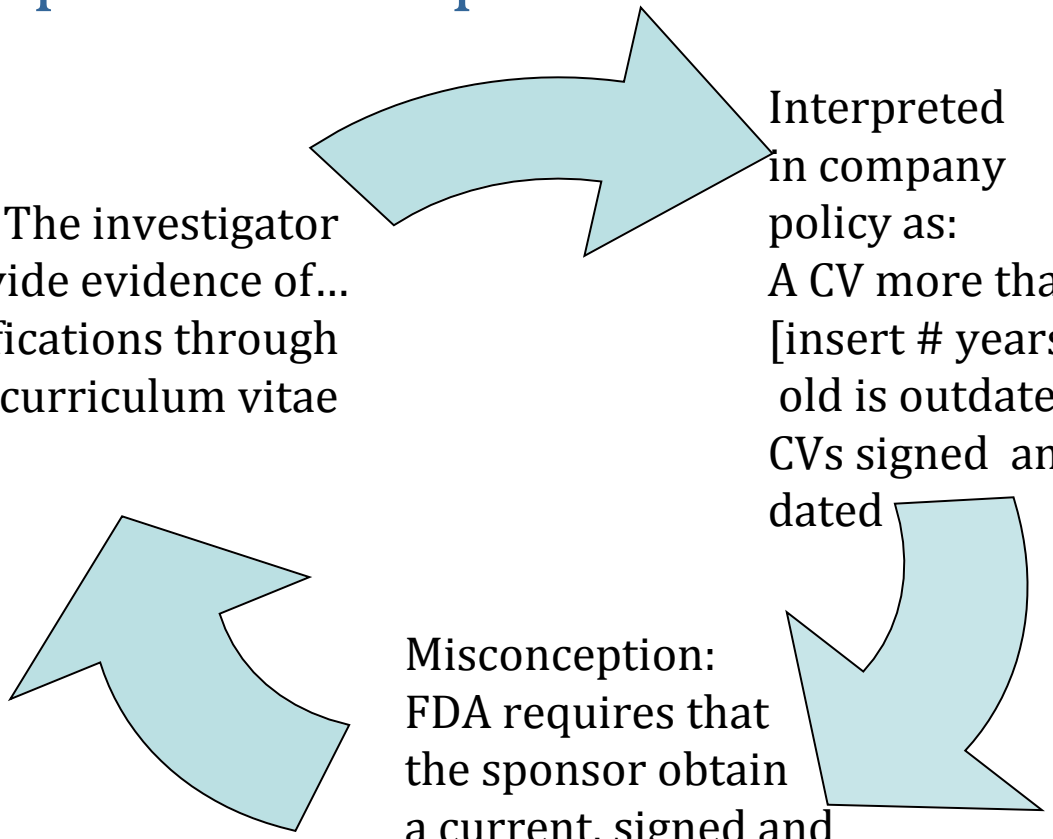
Misconceptions about what GCP requires may become perceived requirements

- FDA regulations are legally enforceable requirements
- FDA adopted ICH E6 as official guidance

ICH E6: The investigator should provide evidence of… qualifications through up-to-date curriculum vitae

Interpreted in company policy as:
A CV more than [insert # years] old is outdated.
CVs signed and dated

Misconception:
FDA requires that the sponsor obtain a current, signed and dated CV that is less than [x years] old.



Challenges Cause Uncertainty for Both Drug Developers and Regulators

How do we find a clear path forward?

1. Greater dialogue with all stakeholders
2. Identify and address areas where regulatory framework may:
   - Inadequately reflect evolving models of trial conduct
   - Unintentionally introduce inefficiency
3. Standardize / harmonize where feasible
4. Return to first principles: focus on "what matters"
5. Build quality into trials

Desired State for Clinical Development

"Maximally efficient, agile clinical development programs that reliably produce high quality data* and protect trial participants without extensive regulatory oversight"

*Data that are fit for purpose

- Janet Woodcock, MD CTTI Monitoring Workstream #3 Workshop

Another perspective

- ***If everything is under control, you are moving too slow***
  - Mario Andretti

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Building Quality into Clinical Trials

- Quality cannot be audited or inspected in retrospectively
- "The most important tool for ensuring human subject protection and high-quality data is a well-designed and articulated protocol."

  FDA Draft Clinical Monitoring Guidance (published 29 August 2011)

- At the trial level, the protocol is the blueprint for quality

Systematic, proportionate approach to clinical development

- Emphasis on process control
- What if, at the time of protocol development:
  - Clearly define objectives for the study
  - Prospectively identify the risks to these objectives
  - Analyze risks and determine which are important
  - Tailor the protocol and its implementation to eliminate or mitigate the **important** risks.
- Risk Management is NOT about risk adversity… it is all about being ready for the future

What is FDA doing?
Draft Monitoring Guidance

- Effective monitoring is critical to
  - Human subject protection
  - Conduct of high-quality studies
- FDA IND and IDE Regulations
  - Obligate sponsors to oversee their clinical trials
  - Are not specific about how sponsors are to conduct monitoring

Existing Oversight Practices

- Clinical Trials Transformation Initiative Monitoring Project Survey (Workstream 1) [1]
  - Wide range of monitoring practices
  - Industry sponsor:
    - Frequent visits with 100% source data verification (80%)
    - Use of centralized monitoring methods (33%)
- Oversight efforts not commensurate with risks
  - "The flexibility in the GCP guidelines is not often utilized" [2]
- Resource intensive
- May not optimally address significant risks

1. *Monitoring the Quality of Clinical Trials: A Survey of Current Practices. Clin Trials 2011. 8: 342-349 .*
2. *Sensible guidelines for the conduct of large randomized trials. Clin Trials 2008 5: 38*

Overview: FDA Monitoring Draft Guidance

- Makes clear that sponsors can use a variety of approaches to fulfill monitoring responsibilities
  - "No single approach to monitoring is appropriate or necessary for every clinical trial"

- Encourages sponsors to develop risk-based monitoring strategies and plans that are:
  - Tailored to the specific human subject protection and data integrity risks of the trial
  - Use a combination of monitoring activities
  - Incorporate greater reliance on centralized monitoring practices

What is FDA doing?

- Collaboration with other stakeholders to improve clinical trial efficiencies and promote best practices
  - Clinical Trial Transformation Initiative (CTTI) projects
    - Monitoring
    - Safety Reporting
  - IOM Forum on Drug Discovery, Development and Translation
  - OECD Working Group

- Collaboration with international regulatory authorities: FDA-European Medicine Agency GCP Initiative

- Encouraging a proactive, risk-adapted approach to design, conduct, monitoring, data management and reporting of clinical trials, e.g.
  - Clinical Trial Transformation Initiative (CTTI) project
  - DIA Special Interest Area Community on QRM
  - CDER pilot prospective review of sponsor's IQMP

What is FDA doing? (cont.)

- Risk-based inspection planning
  - Taking a compliance intelligence approach
    - Data used to inform inspection prioritization and scope
    - Real-time vs. retrospective inspections
  - Application based tool in pilot
  - Tools under development for
    - Generic drug,
    - IRB
    - Sponsor inspections

Thank you!

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