U.S. FOOD & DRUG ADMINISTRATION

Building Quality into Clinical Research

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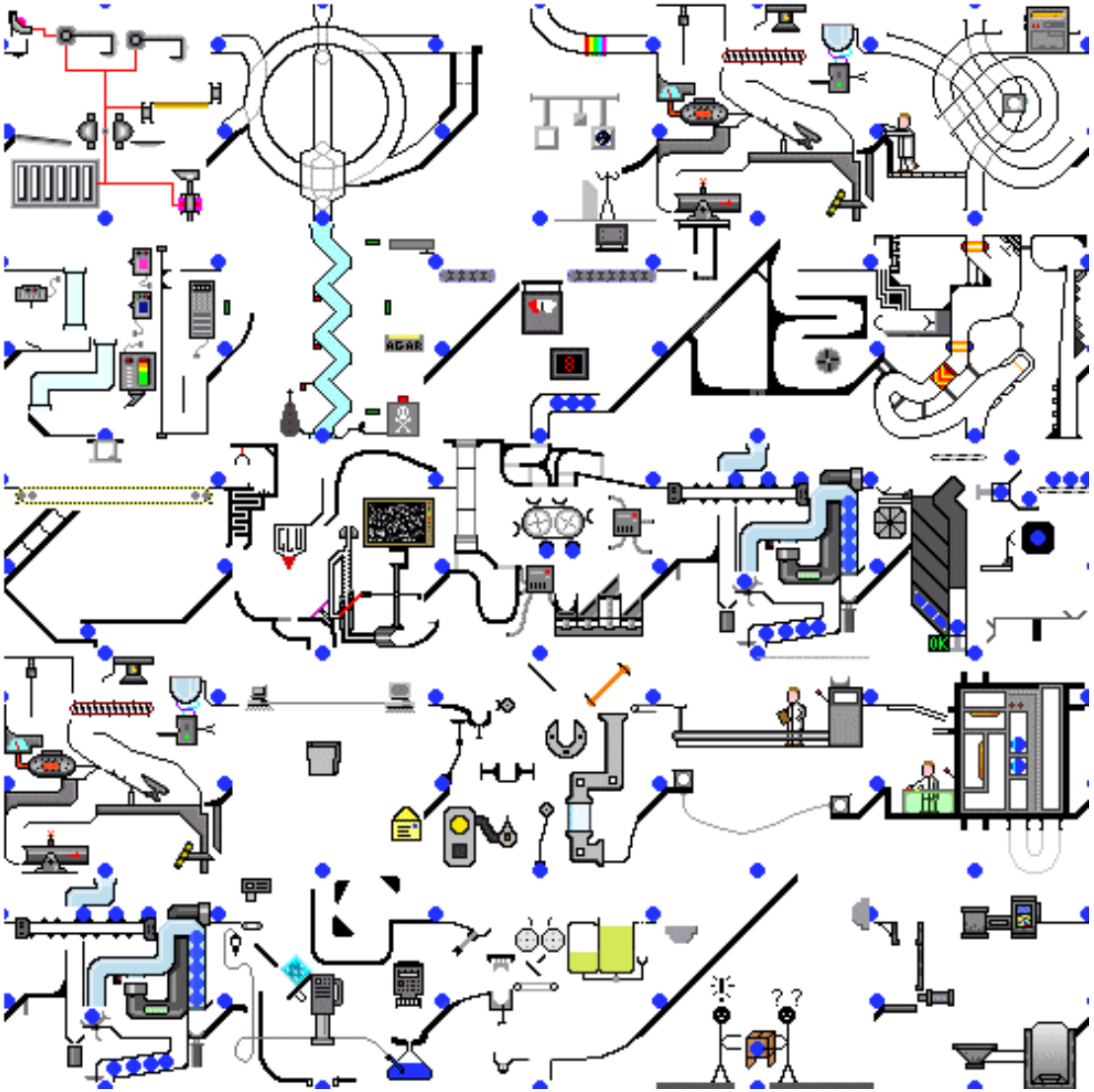
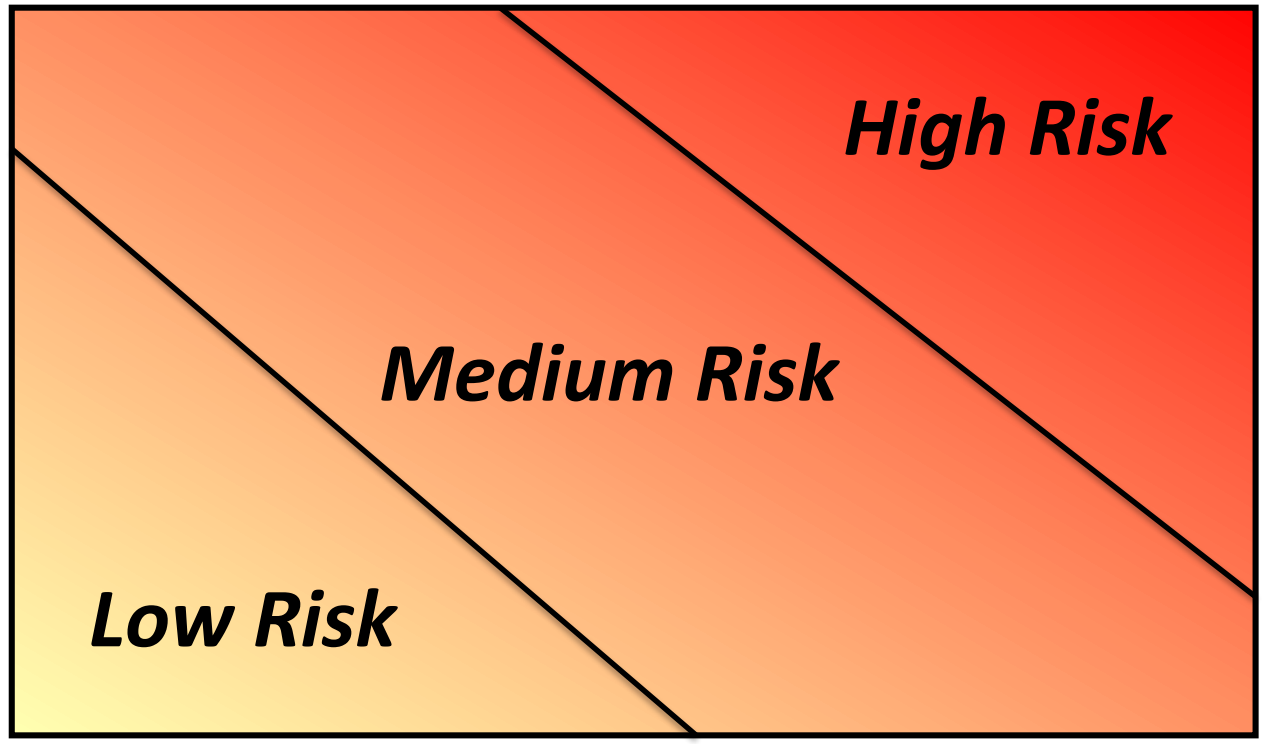
A Quality System



Severity and Probability → Risk



↑ Increasing Probability of Occurrence

Increasing Severity of Harm/Consequence →

Building Quality Into Clinical Trials

- **"The most important tool for ensuring human subject protection and high-quality data is a well-designed and articulated protocol."**

  FDA Risk-Based Approach to Monitoring Guidance (published August 2013)

- At the trial level, **the protocol is the blueprint for quality.**
  - ***Prospectively identify*** **the important risks to subject safety and data reliability**
  - Tailor the protocol and its delivery to ***eliminate*** or ***mitigate*** these important risks

How Sites Can Build Quality

1. **Create a system designed to support quality research**
   - ❖ Create systems that limit opportunities for errors
   - ❖ Create systems that increase the visibility of errors
   - ❖ Simplify protocol and outcomes assessments
   - ❖ Standardize systems and formats where possible; use validated instruments and standard definitions
   - ❖ Keep protocol amendments to a minimum; check CRFs and consent forms against each change
   - ❖ Insist on training, and then test it

How Sites Can Build Quality

2. Select qualified staff and ensure that they receive adequate training and supervision

- Ensure that staff are qualified to performing assigned tasks
- Ensure proper oversight of sub-investigators and study staff
- Adequate time, staff, and equipment
- Knowledge of applicable regulations
- Understanding of the “clinician vs. clinical investigator”
- Adequate training and re-training

How Sites Can Build Quality

3. Fully understand the scope of your responsibilities

- Ensure that protocol is consistent with best interests of patients and allows adequate monitoring for subject safety
- Assess your ability to comply with protocol visits; laboratory testing; electronic systems for data capture, archiving, and transmission to sponsor; maintaining records; drug/device accountability; and inspections by FDA

4. Implement system to detect and correct errors in real time

- Pay attention to monitoring queries, and respond promptly
- Evaluate need for system wide corrections
- Ensure that audit trail of changes makes clear **what** was changed, **who** changed it, and **why** it was changed

Common Pitfalls

1 – Clinical Investigator v. Physician

- Change in mindset
- Follow a protocol v. full treatment flexibility
- Hippocratic Oath – Do no harm
- Team member v. absolute authority

Common Pitfalls

2 – Time

- If you “spend money to make money”
- And you believe “time = money”
- Then you must – spend time to make time
- Change in perspective

Common Pitfalls

3 – Christmas Tree Protocols

- Start with a basic protocol
- Add provisions, tests, forms, reports

- Next study, you add more
- And more…
- And more…

- But when do you remove them?

Common Pitfalls

4 – Awareness and Understanding

"Everyone has a plan until they get punched in the face" – Mike Tyson

- Perfection v. resilience
- Aware of rules/regulations
- Aware of process, and responsibilities
- System and relationships supporting success

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Preparing for Inspections

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Director
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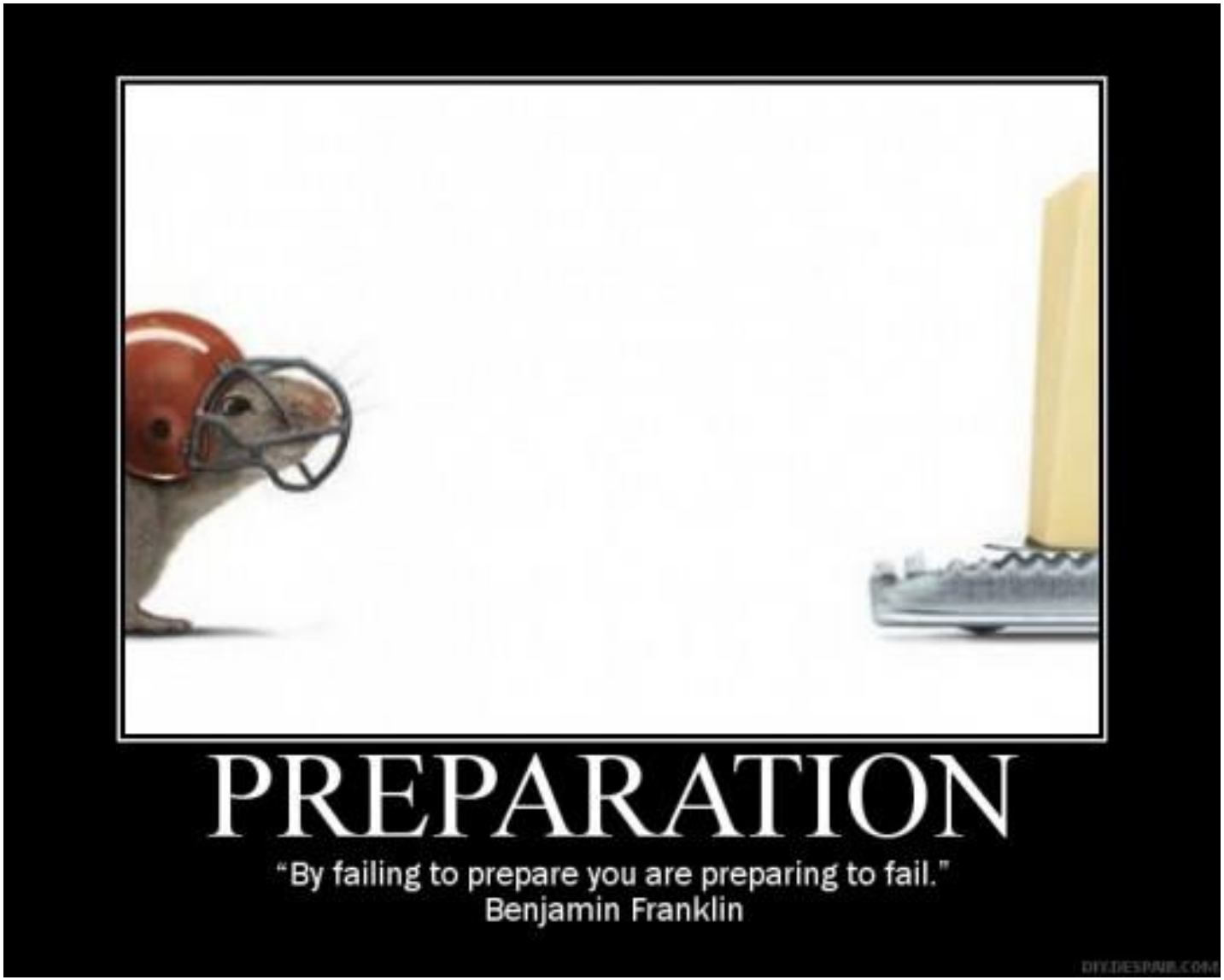

PREPARATION
"By failing to prepare you are preparing to fail."
Benjamin Franklin

Why Me?


Application filed
Prior inspection history
Inspection
Data outliers
Complaint

Trust but Verify

Data Integrity

- Can the data be relied upon?
- Support safety and effectiveness profiles?
- Fraud, recordkeeping issues?
- Failure to follow investigational plan

Human Subject Protection

- Were subjects informed?
- Were subjects protected?

Scope

Facilities & Equipment

Subject Files

Communications

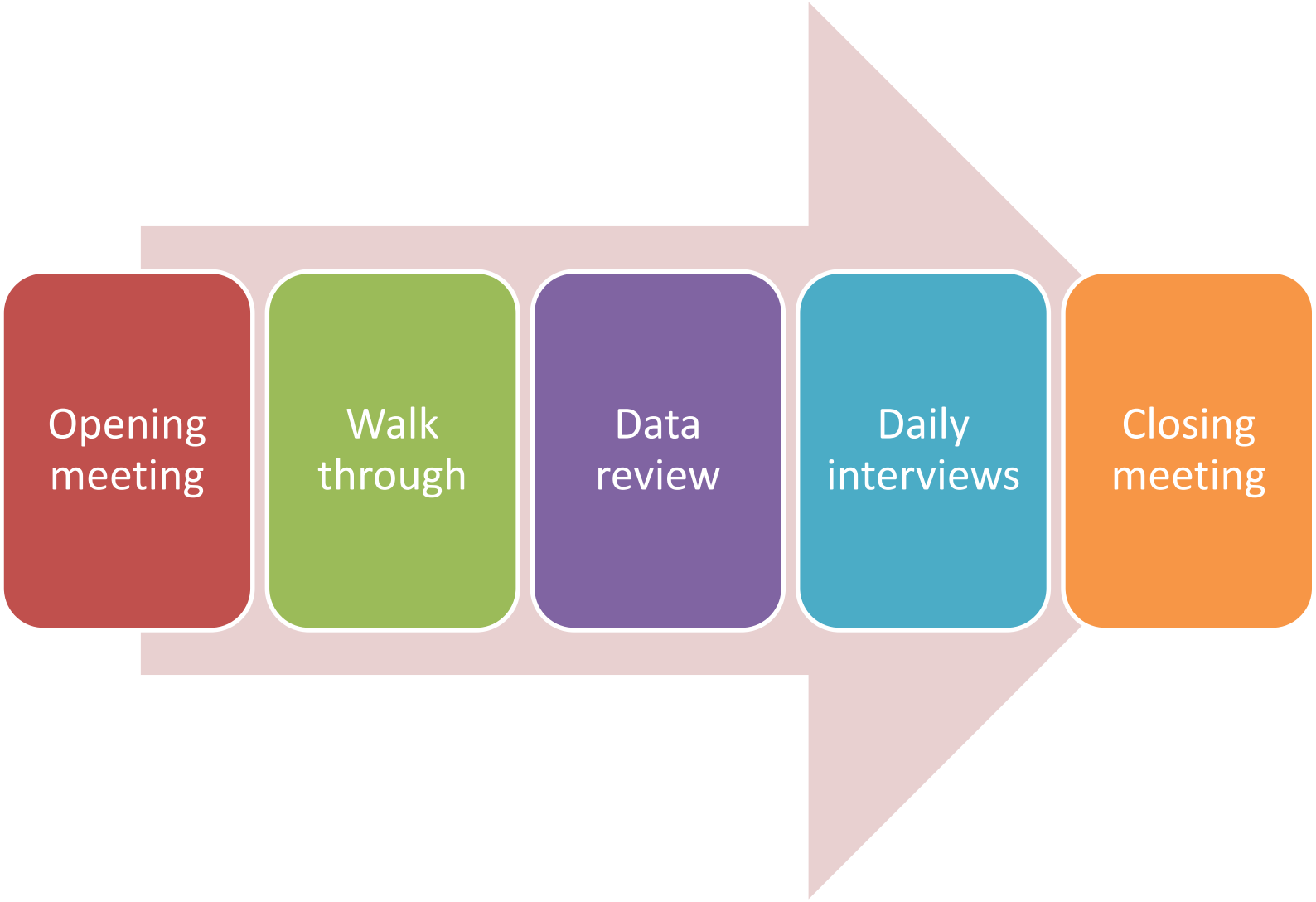
Test Article Accountability

Delegation of Authority

What to do when FDA calls…

- Identify any commitments which cannot be changed (annual conferences, surgery, etc.)
- Mark your calendar
- Gather your records
- Allocate time and workspace

Inspection Flow



Records on the Ready

- Protocol with amendments
- Investigator's Brochure
- IRB, sponsor, site correspondence
- Informed Consent Forms
- FDA-1572 / Statement of Investigator
- Financial Disclosure Forms
- Case Report Forms
- Medical records
- Shadow charts
- Test article accountability
- Curriculum Vitaes
- List of studies
- Publications referencing audited study
- Recruiting materials (TV/newspaper/radio advertisements)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