CTTI REGISTRY TRIALS PROJECT

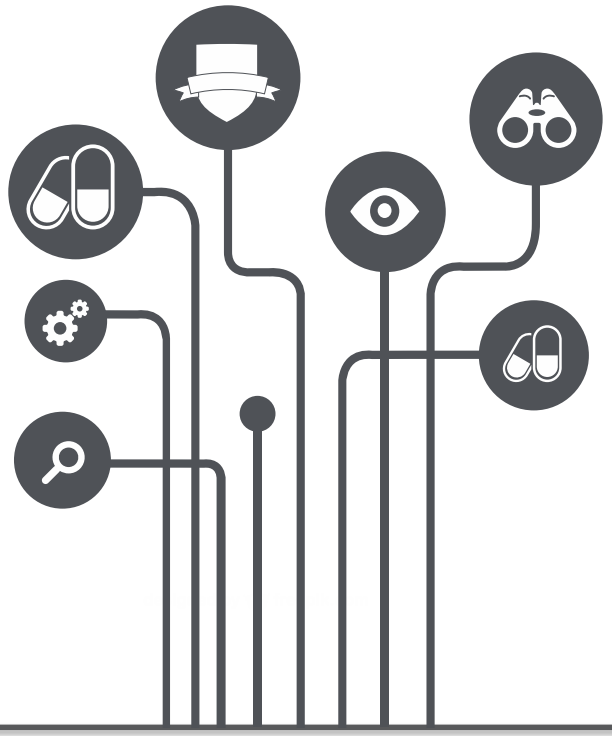
A Brave New World: Registry-Based Clinical Trials

Breakout Session Report-Outs

Data Quality
Registry Design
Regulatory
Governance

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

MARCH 30, 2016



DATA QUALITY

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DATA QUALITY (1)

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First, define “data quality”:

- “absence of errors that matter” – includes completeness of data
- Fit for purpose
- Reflects clinical reality
- What is the information upon which decisions are made?
- Data quality assessment recommendations for pragmatic trials – NIH group – reference this document…

DATA QUALITY (2)

- ***Should the standards for registry-based trials' quality be the same as pre-market trials?***
  - If yes, how would registries need to change to meet higher standards?
    - Software development:
      - Software: should it need to follow FDA clinical trial requirements? E.g. CFR-21 Part 11 compliant and CDRH quidance on software validation
      - Risk assessment based on what we need and don't need
    - Data itself – should the data quality "rules" be different than clinical trials?
      - Depends on the question to answer or the purpose of the registry
      - Industry requirements for safety reporting from registry is similar to for clinical trials, however, more limited collection of AEs than in trials
      - Risks that lower quality data reported to FDA would delay approvals
  - If no, what should the standards be? Or what trade-offs could be made?
    - Is this perception of FDA's expectations misconceived? Red herring?
    - Do we need more guidance from FDA on data quality standards? Is it quality, or is it too much data collection? Any latitude for embedded RCTs in registries?
    - Define sensitivity analyses and key variables for analyses in initial SAP.

Data Quality (3)

- ***Who assesses data quality? Those conducting the trial? Regulators? Other?***
  - We do – registry study designer and analysts (statisticians) – but we could use guidance from customers, e.g., regulators, reviewers (journals) and payers, especially if it is for submission or publications
  - Put quality report in the submission…
- ***When are monitoring and adjudication important?***
  - *"It depends" on risk assessment*
  - *Consider any risk to patient and to study*

DATA QUALITY

- Data Quality recommendations
  - Clearly define data quality
  - Risk assessment based on what we need and don't need
  - Depends on the question to answer or the purpose of the registry
  - Data quality section in the SAP discusses degree and/or randomness of missingness, sensitivity analyses; Data Management Plans too?
  - Data quality is responsibility of registry study designer and analysts (statisticians) – but we could use guidance from our customers, e.g., regulators, reviewers (journals) and payers, especially if it is for submission or publications

Thank you.

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REGISTRY DESIGN

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What best practices/solutions do you recommend in Registry Design to increase value, acceptance, and success of registry-based clinical trials?

- **Can existing registries be adapted to conduct trials? For example, role of modular add-ons for trial specific data?**
- **Are we more likely to have success in therapy-based vs. disease-based registries?**
  - If therapy, can multiple therapeutic options be tested within the registry?
  - How can a registry successfully incorporate both therapy and disease?

REGISTRY DESIGN

- Make it easier to look for existing data sources, such as by encouraging participation in AHRQ's registry of registries.
- Disease-specific registries are more sustainable and valuable than therapy-specific registries.
- Partner with stakeholders from the start—not just doctors, but end users, patients, etc.
  - Stakeholders have different motivations for developing registries; need to develop collaborations and gather multi-stakeholder input to influence registry design.
- To have sustainable registries, need a business model framework; registries should not be designed for a single, narrow purpose.

REGISTRY DESIGN

- Keep registry design simple and add on as needed.
- Have the capacity to add adjudication but only when needed based on the research question.
- Need greater data standards.
- Need an overall culture change to incorporate learning into healthcare systems: physicians do experiments on patients everyday.
  - Demonstrate the value of using registries.
  - Stop doing pilots and move forward with doing registries. This will help develop the business model.
- Rethink how to do clinical trials through registries. Don’t try to apply the old ways of thinking.
- The real question is: how can trialists and registry owners collaborate?

Thank you.

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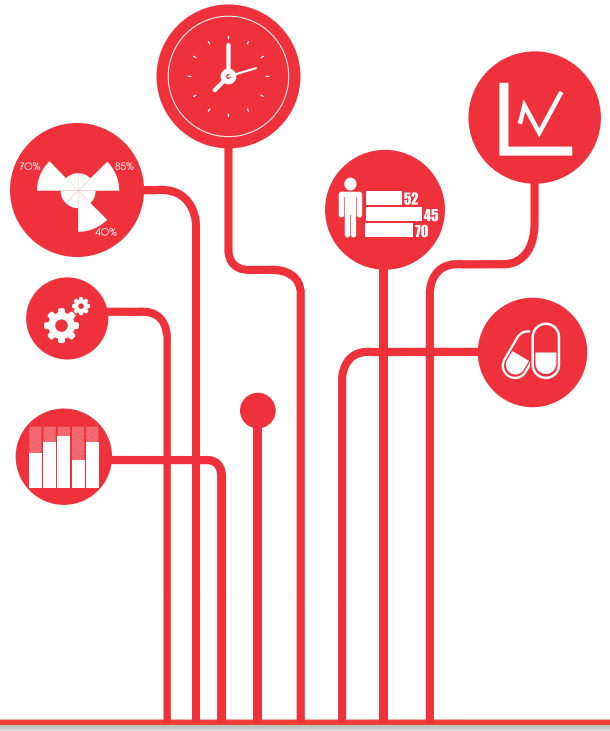

REGULATORY

Recommend best practices/solutions concerning regulatory factors

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- **What are the regulatory issues around informed consent?**
- **What type and level of quality of data are necessary for regulatory purposes?**
  - What would be reviewed during an inspection?
  - What is required to make regulators comfortable about data quality?

Informed Consent

- Issue – Common Rule allows waiver of consent, FDA part 50 does not
- If data being used for regulatory purposes need informed consent
- Regulatory recommendation #1 – Obtain informed consent if intent is regulatory submission
- Hope – harmonization of Common Rule and FDA regulation in progress

Data Quality

- CDRH – 3Rs – Reliable, Robust, Relevant
- Data is being audited for internal or external validity
- If following standards for well conducted RCTs - this data ok
- Monitor internal validity through data monitoring
  - Should be risked-based
  - Data audit same as RCTs
    - Automatic queries for out of range values
- External Validity through site audits – select % of sites participating in registry based on certain criteria
  - For example - audit poor performing sites

Best practices

- Pre-planning better than retrofitting
- If regulatory submission intended, set up registry
  - to obtain informed consent and/or obtain permission to contact patients
  - As part 11 compliant (electronic standards)
- Ability to add modular add-ons to existing registries
- Combine registry workflow with study work flow
- Ability to link to data registries

Thank you.

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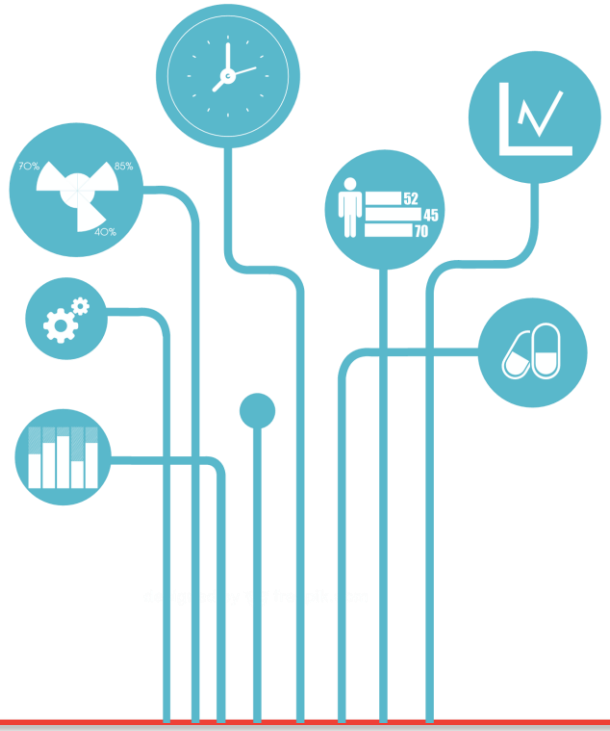

GOVERNANCE

Recommend best practices/solutions around registry governance

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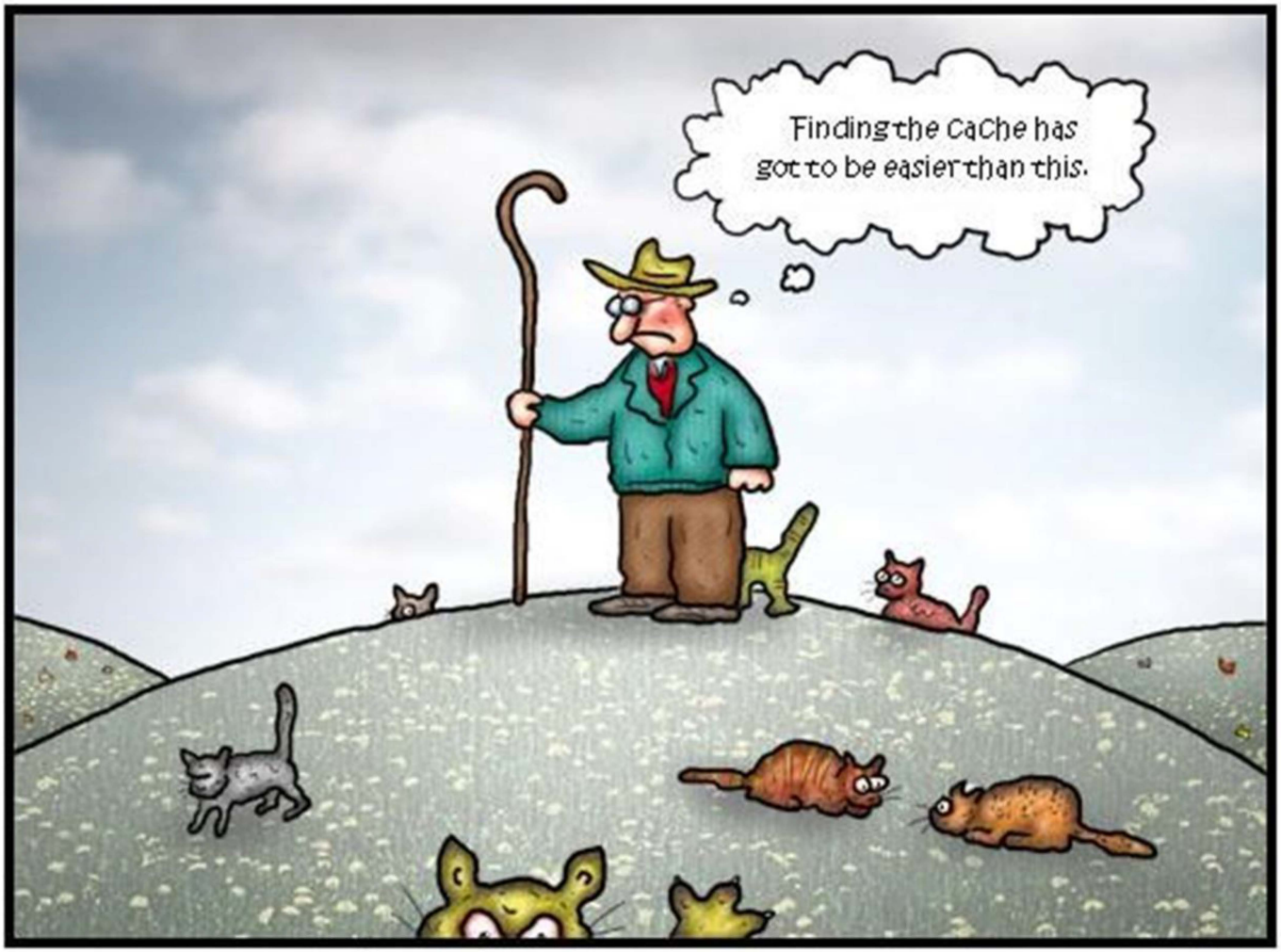
- What are the governance issues around ownership and informed consent?
- What is the process for gaining access to the data? (Application, Advisory Committee, etc.)
- How can the need for immediate access to the data be addressed, if data ownership is shared?



The daydreams of cat herders

GOVERNANCE

- Governance recommendation #1:
  - Establishing the registry intent
- Governance recommendation #2:
  - Need a very prescribed process and structure
- Governance recommendation #3:
  - Develop a decision tree to decide if ICF is needed

Thank you.

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