Essential Practical Aspects of Conducting Clinical Trials

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Introduction

- **Perspective**
  - Human use trials
  - Regulated / non-regulated
  - Interventional / epidemiology
  - US and SE Asia
  - Sponsor
  - Investigator (AI or PI)
  - Audit recipient

- **Aspects**
  - Protocol
  - Team selection
  - Site selection
  - Regulatory climate
  - Quality support
  - Sample management
  - Product management
  - Medical infrastructure
  - Training
  - Communication
  - Publications

- Will NOT review in detail published guidelines, guidance documents, policy.

- Primary reference document during study execution
  - Always the first place to look when a question arises

- Single or multi-center (core + site specific documents)

- Clear, complete, and concisely written
  - Ensure readability for IRB / EC and investigators

- Detailed description of key clinical / lab processes
  - Information may be captured in SOPs / SSPs

- Maintain a copy at every study site (correct version)
2. Choose the right team.

- Principal Investigator
  - Responsibilities
    - Overall conduct of the trial
    - Study subject safety
    - IRB / EC interface
    - Team leader
  - Desired characteristics
    - Leadership traits
    - Clear communicator
    - Capable of completing risk assessments
    - Experienced with the study type (i.e. regulated)
2. Choose the right team.

- Research physicians
  - Responsibilities
    - Trial execution
    - Study subject safety
    - Interfacing with subjects / parents
    - Data collection

  - Desired characteristics
    - Appropriate medical specialty (ideal but not necessary)
    - Astute “research” clinicians (different from practice)
    - Detail oriented (strictly following protocol)
    - Understands & appreciates quality/regulatory principals
    - Detailed knowledge of protocol/supporting documents
2. Choose the right team.

• Clinical Research Coordinators**
  – Adequate number

  – Responsibilities
    • Study process and procedure management
    • Interfacing clinical with logistic/administrative duties
    • Often the first line of contact with subjects/parents

  – Desired characteristics
    • May function in duties autonomously
    • Organized
    • Detail oriented
    • Understands & appreciates/practices quality control
3. Choose the right study site.

- Community and political support for trial
- Disease incidence well established
- Population demographics match study design
- Adequate physical infrastructure to support trial activities
  - Reliable internet access
- Reliable utilities (electricity source and back-up)
- Adequate medical care infrastructure and support for trial
4. Supportive regulatory climate.

- Human subjects protection committees
  - Compliant with IRB / EC guidelines
  - Regularly scheduled meetings
  - Timely reviews and feedback of protocols/amendments
  - Experience reviewing trial type (regulated, interventional)

- Licensing / marketing authorization application review
  - Sponsor access to agency
    - Consultation
    - At key milestones throughout clinical development
  - Capability to review/make decision on packet
    - Host nation
    - Partnerships
5. Quality support systems.

- **Good clinical practices (GCP)**
  - A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

- **Application**
  - Strictly follow protocol/SOPs/SSPs
  - Use internal clinical QC/QA monitoring capabilities
    - Study chart QC
    - Identifying/correcting deviations
    - Periodic review of trial master file
5. Quality support systems.

- Good documentation practices (GDP)
  - Result: concise, legible, accurate and traceable records
  - Application
    - Internal clinical QC/QA monitoring capabilities
      - Complete entries (electronic data capture)
      - Clear entries (dates, descriptive, signatures, dates)
      - Proper technique correcting errors

- SOPs/SSPs (Study specific procedures)
  - Standardize common clinical activities
  - Harmonize activities across investigators/sites
  - Improve data quality
  - Reduce deviations
5. Quality support systems.

- Good clinical laboratory practices (GCLP)
  - A quality system for laboratories which undertake the analyses of samples from clinical trials

- Organization
- Personnel, Facilities
- Equipment
- Materials and Reagents
- SOPs
- Work Planning
- Sub-contracting

- Trial materials
- Work conduct
- Reporting results
- QC/QA
- Storage / retention of records
- Confidentiality

- Key to safety, immunogenicity, efficacy, licensure

- Proper management required for regulatory compliance
  - Future use, specimen banks, shipments abroad

- Components
  - Labeling
    - No personal identifiers
    - Samples/aliquots receive unique identifier
  - Accountability/Inventory management
    - Track samples in, out, and residuals
    - Auditable database
  - Storage
    - Continuous temperature monitoring, Back up power
7. Product (drug / vax.) management.

- **Mismanagement places development timelines at risk**

- **Components**
  - Accountability/Inventory management
    - Track product in, out, used, destroyed
    - Auditable database
  - Storage
    - Continuous temperature monitoring
    - Back up power
    - Data required for investigating temperature deviations
  - Shipping
    - Reliable vendor
    - Retrieveable temperature data
    - Customs / Permits
8. Medical care infrastructure.

- Medical professionals
  - Supportive of study / objectives
  - Manage disease process under study
  - Manage adverse events

- Adequately resourced health care facilities
  - Personnel
  - Equipment and materials
  - Financial (resourced to manage study related events)

- “Fast track” access to medical care for study subjects

- Accredited clinical/biochemistry laboratory

• Ensures consistency, standardization, quality, safety

• Components
  – Protocol
  – Supporting documents (information sheet, ICF, AF)
  – SOPs/SSPs
  – Operating guidelines
  – Study laboratory manual

• Training files
  – Document training activities
  – Supports study staff roles and responsibilities
10. Communication.

• Study team
  – Efficient dissemination of important information
  – Ensure common understanding (events, facts)

• Regulatory agencies (IRB/EC/Sponsor)
  – Meet reporting timelines/requirements (i.e. SAE, AE, etc.)
  – Consultation when issues arise

• Study subjects/parents/families
  – Clear and timely dissemination of important information
  – Listen
10. Communication.

• Community
  – Begin communication process early (before study start)
  – Utilize existing community organization / personnel
  – Continuously evolving and improving process
  – Listen

• Press/Media
  – May threaten successful completion of study
  – Designate primary spokespeople
  – Prepare
    • Known (frequently asked questions about study)
    • Unknown (combating misinformation, rumors)
    • Bad news (related or unrelated to study)
  – Train study staff to speak with/not speak with media
11. Publications.

- Quality studies lead to quality publications

- Ethical obligation to publish
  - Subjects/volunteers assume risk to advance science
  - Results (positive or negative) should be shared
  - Scientific literature a component of ethical review

- Publish results in timely manner when results are relevant*
Conclusions

- Executing safe and high quality clinical trials is difficult / risky

- Evolving regulatory and quality requirements
  - Increase difficulty of study planning and execution
  - Increase cost (personnel, paperwork)
  - Increase timelines…BUT…
  - Often increase safety and quality

- Selecting the right team and appropriate study site are key

- Early and frequent community engagement is important

Global disease threats worsen, we need countermeasures, we develop countermeasure through clinical trials.