Clinical Trial Training

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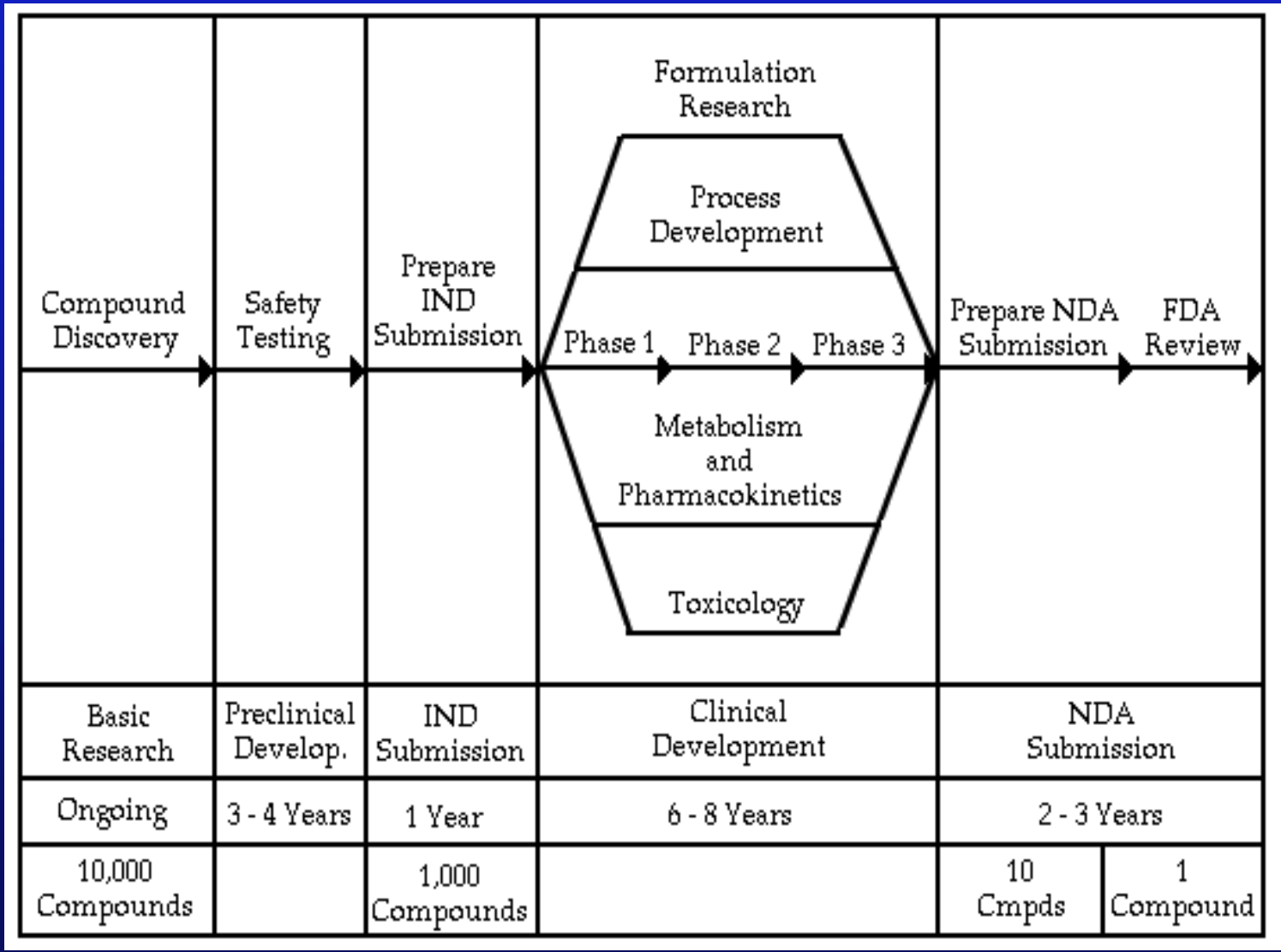
OPTI WEST 4th Annual Research Conference

August 24, 2010

Goals for Today

- To gain a broad overview of the terminology and processes utilized in the planning and execution of a clinical trial
- A look at clinical trial sites focusing on site selection criteria
- To optimize communication with Pharma partners

Drug Development Process



Drug Development and Approval Process

1. Early research and preclinical testing
2. IND application filed with FDA
3. Clinical trials (phases I, II, and IIIa/b)
4. NDA/BLA filed with FDA
5. FDA validates and approves drug
6. Labeling
7. Continued monitoring and Phase IV
8. Post marketing requirements

Protocol Development is a Complex Process

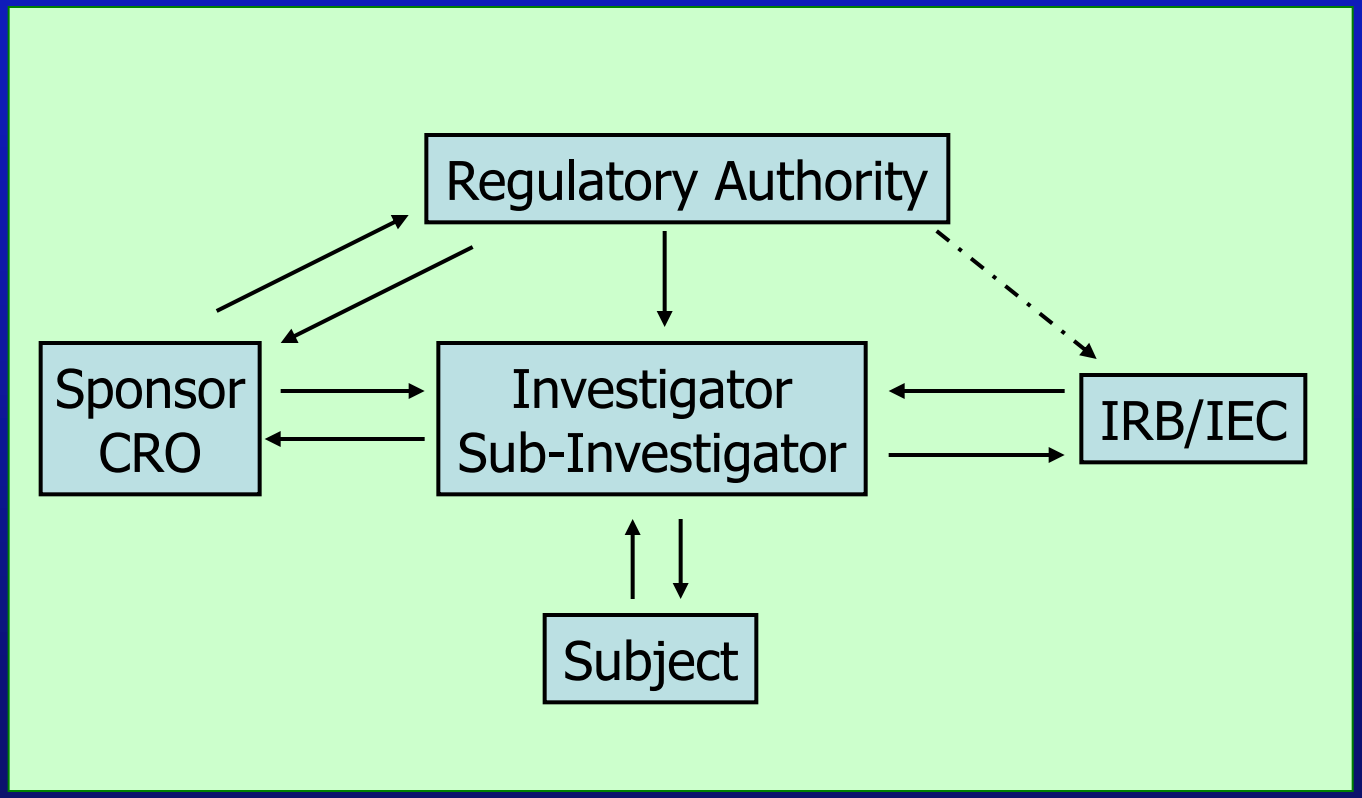
- Cross functional team approach

- Several internal review cycles to assess:
  - Scientific integrity
  - Study feasibility
  - Regulatory requirements
  - Costs
  - Risk
  - Business and marketing plan compatibility

Key Players in Clinical Research

- Sponsor
- Investigator
- Clinical Research Organization (CRO)
- Monitors or Clinical Research Associate (CRA)/ Clinical Site Manager (CSM)
- Clinical Research Coordinator (CRC,CCRS,SC,CCRP)
- Institutional Review Board (IRB)
- Study subjects

Relationship Between the Players



Sponsor

An individual, company, institution or organization which takes responsibility for initiation, management, and/or financing a clinical trial.

ICH Glossary

Sponsor Responsibilities

- IND/BLA submission (protocol included)
- Scientific quality and integrity of the study
- Protecting the rights of the participants involved in the study
- Federal and GCP guidelines
- CRO, Investigators, and supporting staff
- Safety and AE reporting
- Budget and contracts

Contract Research Organization (CRO)

A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

ICH Glossary

Monitor, Clinical Research Associate (CRA), Clinical Site Manager (CSM)

Representative of the sponsor or CRO who oversee the progress of the clinical trial and ensure that it is conducted, recorded and reported in accordance with the protocol, standard operating procedures (SOP), Good Clinical Practice (GCP) guidelines, and applicable federal and state regulations.

ICH Glossary

CRA Responsibilities

- Site evaluation and initiation
- Assure regulatory requirements met
- Assure site personnel are trained and informed
- Assure site is provided with all materials required to conduct trial
- Assure site personnel are qualified and aware of obligations
- Monitor data and verify source records
- Oversee the progress of the study at site level

Investigator

An individual who actually conducts a clinical investigation (i.e.under whose immediate direction the drug is administered or dispensed to a subject).

In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team.

Title 21 CFR part 312 investigational new drug applications Section 3 Definitions

Investigator Responsibilities

Responsible for all aspects of a clinical trial

- Ensures regulatory, GCP, and fiscal compliance
- Determines a recruitment plan, evaluation and treatment of research subjects
- Supervises the medical staff participating in the study
- Provides timely review of all clinical and laboratory data
- Ensures proper adverse event reporting and assess causality of all adverse events
- Performs physical exams and other required procedures
- Meets with study monitor, verify subject data
- Ensures proper retention of study documents

Institutional Review Board (IRB)

Definition

An independent body constituted of at least five medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial.

Function

Reviews, approves, and provides continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

ICH Glossary

IRB Responsibilities

- First and foremost-protect the rights, safety, and welfare of human subjects engaged in research
- Initial review of the protocol with emphasis on the consenting process and related paperwork .
- Meet annually and address safety issues as they arise
- Must approve amendments before they are implemented
- Right to observe study conduct and Informed consent process and take corrective action if needed

Clinical Research Coordinator (CRC)

- Works directly with the PI, sub I, CRA, labs, IVRS, and staff
- May function as the study nurse
- Coordinates all aspects of the trial at the site and serves as a liaison for the team
- Can have a huge impact on the success or failure of a study

Medical Monitor

MD usually from the CRO who:

- Answers questions about safety and protocol
- Protocol Inquiry Forms
- Available 24/7
- First line of communication is with the CRA who will triage the problem to the Medical Monitor

Data and Safety Monitoring Board

- DSMBs/DMCs are typically made up of individuals who have expertise in the field, experience in the conduct of clinical trials, and/or statistical knowledge, and who do not have any serious conflicts of interest

- Meet at least annually to ensure the accrual, quality, management, and data outcomes to assure the safety of participants and the integrity of the clinical trial.

Study Personnel

Clinical Project Manager (CTM) – responsible for overall implementation of trial; oversee progress of trial; global trial communications; reporting to FDA, budget and cost control.

Data Manager - generate data queries to ensure quality of data; maintain ongoing data entry; monitor data analysis and provide reports.

Statistician – analysis of data – provide reports for data safety monitoring board (DSMB) or Endpoint committee

Most Common at sites: Investigational pharmacist, clinical research manager, technicians, phlebotomist, research assistants, regulatory specialist, recruiters, data coordinators

Site Selection

Site/PI Qualifications

- Knows the rules of conducting a study (GxP, AE reporting, local regulations, recall, etc.)
- Understands basic trial design/statistics, sample size calculations
- Documented experience as Sponsor or as Investigator with training in Sponsor's obligations
- Planned timelines and budget are realistic
- Site is equipped and able to manage all aspects of the study (e.g. medication storage, data capture)
- Investigator's history acceptable ➔ not on FDA 'Black List'; no unsatisfactory performance (audits, past poor experience in trials)

Appropriate Site Selection

Goal is to identify and select qualified investigators to properly and safely conduct the trial within the time specified

Considerations:

- Compliance with government and local regulations, GCP guidelines, and study protocol
- Meet study milestones within timeframe and budget
- Provide quality data
- Good communication and site project management

Qualities of a good research site

- Appropriate trial infrastructure
  - Central IRB vs Local IRB
  - Academic non-academic
- Able and interested staff
  - Study coordinator vital to the success of the study
  - PI who has the patient population and time to conduct the study
  - Sub investigators who can assist in study recruitment if needed
- Other considerations
  - Competing studies
  - Experience of the staff
  - Local standards of care mimic study design

Conclusions