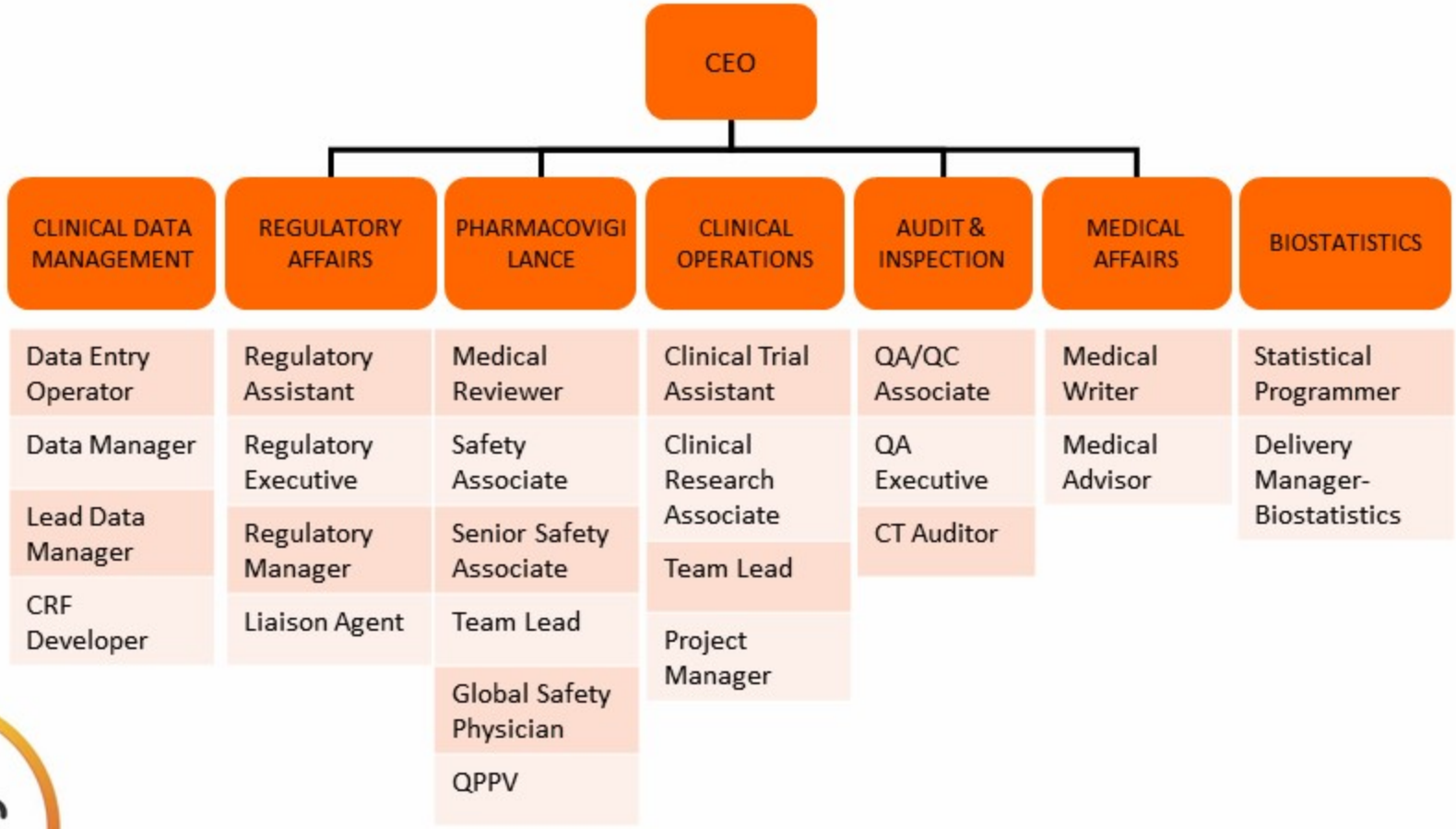
Site Personnel

Investigator, CRA & CRC Responsibilities

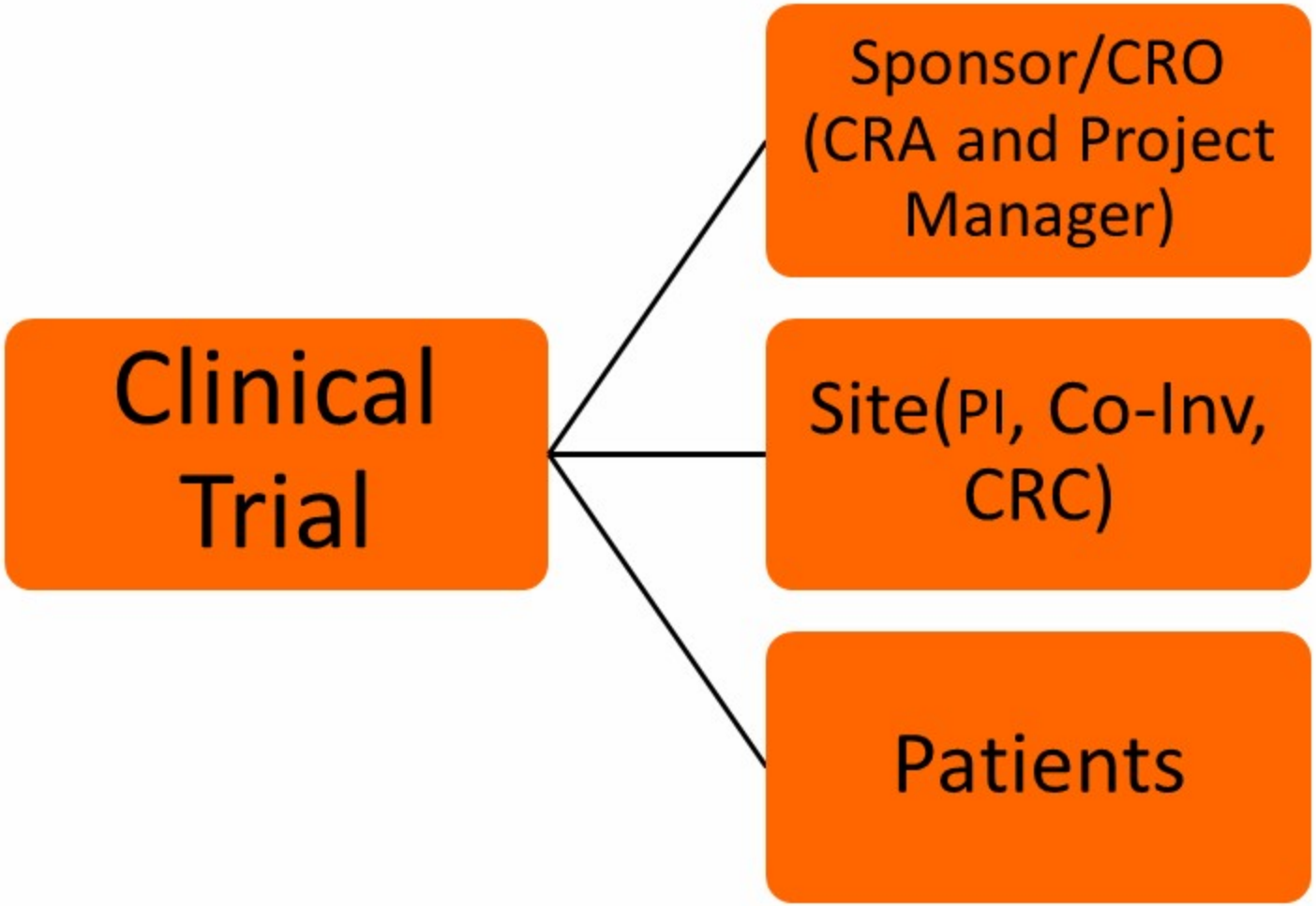
Module 6 Topic 2

A typical CRO Structure

Key Department Personnel



Clinical Operations-Key Stakeholders



Principal Investigator- Key Roles

- Qualifications & agreements
- Resources
- Responsibilities to the subject
- Ethics
- The protocol
- The IMP & randomisation
- Informed consent
- Reports & records
- Safety reporting

Responsibilities

The following principles are from ICH GCP Topic E6 and apply to clinical trials of Investigational Medicinal Products

Qualifications & Agreements

The Investigator should be:

- Qualified by education, training & experience
- CV's, training records, other relevant documentation
- Thoroughly familiar with the protocol & medicinal products
- Comply with GCP and applicable regulations

Qualifications & Agreements

- Permit monitoring and audit by the sponsor inspection by regulatory authorities
- Maintain a delegation list
- Ensure that all persons assisting with the trial are adequately informed about the
  - Protocol
  - IMP
  - Their duties and functions

Resources

The Investigator should be able to demonstrate potential for:

- Recruiting the required number of subjects
- Have sufficient time to properly conduct and complete the trial within the agreed period
- Have available adequate facilities and qualified staff to conduct the trial properly and safely

Medical Care of Trial Subjects

- A qualified physician who is an investigator (or sub-investigator) should be responsible for all trial related medical decisions
- During and following participation the Investigator should ensure adequate medical care for any Adverse Events (AEs)
- The Investigator should make a reasonable effort to ascertain reasons for withdrawal from the trial (although a subject is not obliged to give reasons)

Ethical Approval

Before initiating the trial there should be:

- Written and dated approval/favourable
- Opinion from the Ethics Committee for the protocol, consent form, amendments

Compliance with Protocol

- The Investigator should
  - Conduct the trial in compliance with the approved protocol
  - Sign to confirm their agreement
  - Not implement any deviation from the protocol without prior approval/favourable opinion of the IEC and the sponsor

CRA

- A Clinical Research Associate (CRA) is a professional who oversees all aspects of clinical trial conduct
- They oversee clinical trials to test drugs/medical devices/biologics/or in vitro diagnostics for their effectiveness, risks and benefits to ensure they are safe to allow on to the market

CRA (contd)

- CRAs are also known as Clinical Trial Monitor or Clinical Monitor
- They oversee clinical trials to test drugs/medical devices/biologics/or in vitro diagnostics for their effectiveness, risks and benefits to ensure they are safe to allow on to the market
- Designs study documents such as, study designs, synopsis, site specific protocols, informed consent forms, case report forms, site study procedure manuals and project tools, monitoring plans, and tracking tools, clinical study reports, budget and contract negotiation

CRA (contd)

- Performs independent monitoring of sites including: conducting site pre-qualification, initiation, monitoring visits, and close-out visits
- Maintain frequent contact with and work effectively with investigators and coordinators
- Coordinate with the ethics committee, which safeguards the rights, safety and wellbeing of all trial subjects
- Review and resolve discrepancies in clinical data with clinical sites or through a contract research organization (CRO)
- Low amount of travel may be required (e.g. up to 25-30%)

Education and Skills Needed

- Although there are no exact rules, general educational requirements for a CRA role is typically a bachelor of science (BS) or a bachelor of art (BA) degree in life sciences, medical sciences, or healthcare related field such as nursing

Type of CRA

- **In-House CRAs -** CRAs who work for a sponsor company are called in-house CRAs. An in-house CRA may be overseeing all aspect of clinical trial conduct, from planning to clinical study report (CSR) generation for submission to regulatory bodies

- **Regional CRAs/Home-Based CRAs -** who work independently from home are called regional CRAs or home-based CRAs. Regional or home-based usually don't handle planning and preparation of clinical trials. They generally handle the monitoring function and oversee trial conduct. Thus, they can work from home and they usually travel quite a bit more than their in- house CRA colleagues

Types of Monitoring

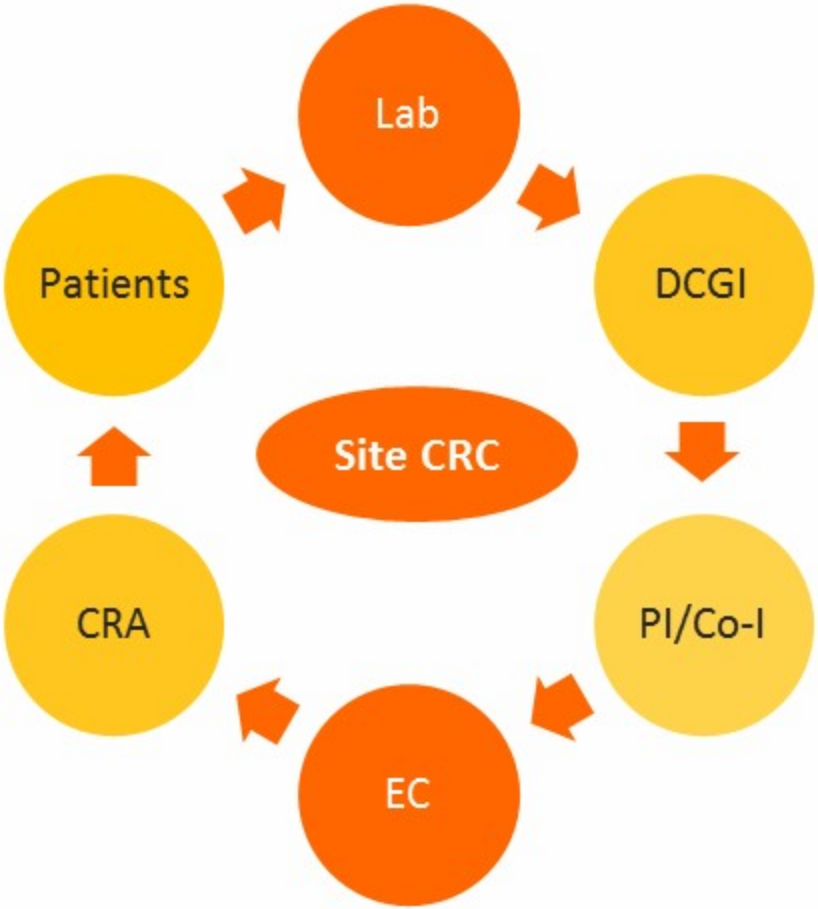
Centralized Monitoring	On-Site Monitoring	Off-Site Monitoring
• Monitoring data quality, critical data reporting, AE/SAE trending, unusual distribution of data, etc. • Proactive and early identification of quality/safety/operational risk/issue (s) based on continuous monitoring of data and key risk indicators • Tracking site performance metrics • Planning/triggering site contacts/visits based on the risk/issue(s) identified	• Critical risk/issue(s) management • Shifting from 100 percent SDV to a risk-based approach for SDV with more focus on critical data related to eligibility criteria, primary / secondary efficacy and safety end points, and key protocol procedures • Percentage of SDV & SDR • In-person engagement, co-ordination with site staff, drug accountability, verification of facility/equipment and overall quality conduct	• Coordinating with the sites for managing risk/issue(s) identified during centralized monitoring • Following-up with the sites as a part of site management activities and to support inquiry management.

CRC Responsibility

- A Clinical Research Coordinator (CRC) or the study coordinator is responsible for conducting clinical trials at clinical trial sites according to the protocol, ICH-GCP and other regulatory requirements, under the auspices of the Principal Investigator (PI)

- Vital link between all the other players involved in the clinical trial

CRC Network



Key Responsibilities

- Complete Feasibility Questionnaires
- Participating in Investigator meetings
- Preparation and Submission of EC Dossier to EC of site for approval
- Cost analysis and budget negotiations
- Contracting with pharmaceutical companies before the start of the clinical trial
- Subject recruitment and Retention related activities
- Participating with PI in AV & informed consent process
- Preparing and Maintaining all the types of documents

Key Responsibilities (contd)

- Storage and Study drug accountability
- Maintaining IVRS and IWRS Record
- Report Adverse Event / Serious adverse event within timelines and their follow ups
- Filling up-to date Electronic Case report forms
- Check all Central lab reports Reviewed and signed by PI
- Patient Safety & Care and appropriate visit conduct for the patient

Key Responsibilities (contd)

- After close out of the trial In accordance with the local IRB, the CRC will complete IRB study close documentation and make any appropriate notifications to the study subjects, research team, and pharmacies
- CRA will verify all documents
- After verification of all documents by the CRA, CRC will assist in archiving the documents at site
- As per ICH GCP, Site has to maintain all study related records for 15 to 20 years

References

- ICH GCP R2 Section 4 and 5
- https://www.fda.gov/downloads/training/clinicalinvestigatortrainingcourse/ucm378565.pdf
- http://www.med.wmich.edu/sites/default/files/Investigator%20Responsibilities%20Clinical%20Trials%20Research