2.2 – Roles and Responsibilities in the Conduct and Assessment of Clinical Trials

Presentation to APEC Preliminary Workshop on Review of Drug Development in Clinical Trials

Celia Lourenco, PhD, Manager, Clinical Group I Office of Clinical Trials Therapeutic Products Directorate
Disclaimer: the information within this presentation is based on the presenter's expertise and experience, and represents the views of the presenter for the purposes of a training workshop.
Objectives

Who are the players?

What are their roles & responsibilities (R&Rs) in assessment and conduct of clinical trials?
Players in CTs

- Regulator
- Sponsor
- Institutions/Clinical Trial Sites
- Qualified Investigators (QI) & Staff
- Research Ethics Boards
- Clinical trial subjects or legal guardians
- Data safety Monitoring Board (DSMB)
- Contract Research Organization (CRO)
- Site Management Organization (SMO)
**R&Rs of the Regulator (1)**

- **Implement** regulations, guidelines, systems and procedures to:
  - Protect clinical trial subjects
  - Ensure scientific research has merit
  - Ensure consistency in the assessment of CTs
  - Maintain sponsor, stakeholder, and public trust

- **Process and review** CT applications in accordance with the regulations
R&Rs of the Regulator (2)

- **Review** CT applications to determine whether:
  - There is sufficient data to support the safety of the drug in the trial
  - The trial has scientific merit
  - The safety assessments and risk management measures adequately mitigate the potential risks to trial subjects
  - All the information provided, including the safety and efficacy variables, suggest the objectives of the trial will be achieved
  - The potential risks and anticipated benefits are adequately communicated in the informed consent form
  - The quality, chemistry & manufacturing information is acceptable
  - Overall, the anticipated benefits outweigh the potential risks to trial subjects
R&Rs of the Regulator (3)

- **Provide** opportunities for dialogue with the sponsor during review of CT applications
- **Issue the decision**
  - Letter of authorization
  - Letter of rejection: clearly communicate all deficiencies to the sponsor
- **Assess** safety information on the drug through analysis of ADRs, lot-release information, and other information as the trial is ongoing
- **Communicate** with the sponsor if concerns arise while the trial is ongoing
R&Rs of the Regulator (4)

- **Conduct** inspections of CTs to:
  - Ensure protection of CT subjects
  - Verify and ensure data integrity
  - Ensure that the responsibilities of the sponsor, QI, REB, and other players, are maintained
  - Ensure the trial is conducted in accordance with the regulations and GCP

- **Maintain** accurate and confidential records for all regulatory functions in the review and inspection of CTs
R&Rs of the Sponsor (1)

- **Submit an application** for authorization of a CT in accordance with the regulations and guidelines
- **Attest** that:
  - Information and material contained in, or referenced by, the application for a CT are complete and accurate and are not false or misleading
  - Will conduct the CT in accordance with the applicable regulations and Good Clinical Practices
  - Trial will not commence until the authorization is received or 30 calendar days have elapsed from time of receipt of complete application
  - Provide information during review of the CT in accordance with the regulations (2 day turnaround)
  - Maintain accurate records for specified period, accessible to inspection
R&Rs of the Sponsor (2)

- **Provide** information to the regulator:
  - As requested during review
  - After authorization of the trial
    - Name of Qualified Investigator & trial site
    - Approval at each site by a properly constituted REB
    - REB refusals, if any
    - Lot release fax-back form for biologics
    - Report all serious, unexpected, adverse drug reactions
    - Protocol and/or chemistry & manufacturing amendments
    - Premature discontinuation of the CT
    - Other information as requested by the regulator
    - Comply with the regulator before, during, and after CT inspections
R&Rs of the Sponsor (3)

• **Ongoing** assessment of the trial & drug:
  – Implement systems and procedures for the monitoring and assessment of safety in CTs
  – Monitor and evaluate all safety and efficacy information as it becomes available and to the extent possible with a view to assessing impact on the safety of CT subjects and the merit of the CT
  – Periodically review the investigator’s brochure
  – Ensure that any DSMB, set-up to review the data in the trial, is independent and constituted by individuals with appropriate knowledge and experience
  – Keep all players informed of new information that impacts on the CT as required by local regulations and guidelines
R&Rs of the Sponsor (4)

- **In conduct of the CT, ensure:**
  - Applicable regulations and GCPs are followed
  - Sufficient supply of the drug
  - Trial supplies are labelled in accordance with the regulations
  - QIs and sites have the required infrastructure, equipment, expertise, and trained staff to conduct the CT
  - Roles and responsibilities are clear to the QIs
  - Appropriate forms are developed and used consistently for recording all trial data
  - Updated safety information, including the IB, is provided to the QIs in a timely manner
R&Rs of the Sponsor (5)

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- Protocol amendments are authorized by the regulator and the REB prior to implementation
- Quality of the drug is maintained throughout the CT
- Serious, unexpected, adverse drug reactions are reported to the regulator and the REB
- Information is provided to the regulator when requested
- Sites are monitored and audited as appropriate, to ensure conduct of the trial continues to meet GCP, the protocol, and regulations
- All players are informed and all unused drug is retrieved where a trial is discontinued prematurely
- Accurate records are maintained for all aspects of the trial, in accordance with regulations or guidelines, as applicable
R&Rs of Institution/QI (1)

- **Conduct** the clinical trial in accordance with the applicable regulations and GCPs, including:
  - Implement systems and procedures for the monitoring and assessment of safety in CTs
  - Obtain approval by an appropriately constituted REB and communicate this approval to the sponsor
  - Ensure staff conducting the trial have the required training and experience
  - Ensure that the objectives of the trial, procedures and tests involved, potential risks, and anticipated benefits are explained to clinical trial subjects
  - Inform subjects of their rights and provide sufficient time for the informed consent discussion
  - Supply a copy of the signed informed consent form to subjects
  - Provide support to research subjects, including the contact name & telephone number of the investigator and research ethics board chair
R&Rs of Institution/QI (2)

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– Provide for trial-related medical care of trial subjects
– Communicate concerns to the sponsor in a timely manner
– Support the function of the REB, inspectors, and sponsor
– Communicate serious, unexpected, ADRs to the REB, sponsor, and regulator
– Follow the protocol as written and respect the design of the trial including randomization and blinding
– Label, use, and store the drug in accordance with the regulations and the protocol or investigator’s brochure
– Maintain accurate records, including source records, REB attestation of approval of all versions of the protocol and informed consent form, and all original signed informed consent forms for each subject for all versions of the protocol, as applicable
R&Rs of the REB

- **Implement** systems and procedures for assessment of clinical trials, including safety
- **Review** the protocol, informed consent form, investigator’s brochure, advertising material, compensation of trial subjects, and any other pertinent information with due regard to the current regulations, guidelines, and highest ethical standards
- **Ensure** the REB reviewing the trial is constituted in accordance with the regulations
- **Communicate** concerns to the QI in a timely manner
- **Provide** for annual review and approval of the clinical trial
- **Maintain** accurate records of all trial reviews
Role of Clinical trial subjects or legal guardians

• By signing the informed consent form, the subject does not forfeit his/her legal rights
• Subject has the following roles:
  – **Read** the informed consent form and seek understanding of the CT
  – **Ask** questions and understand his/her rights
  – **Follow** carefully all directions pertaining to drug dosing, tests and procedures, and appear for CT visits as scheduled
  – **Report** any apparent/potential adverse drug reaction to the investigator
Responsibilities of the DSMB

• **Abide** by rules of conduct (e.g., terms of reference describing frequency of meetings, how data will be analyzed, how records of proceedings will be generated, etc.)
• **Implement** systems and procedures for assessment of safety in clinical trials
• **Conduct** objective and independent review of the safety and efficacy of the drug in the trial
• **Communicate** concerns to the sponsor in a timely manner
• **Maintain** accurate records of all reviews
Responsibilities of CROs & SMOs

- **Implement** systems and procedures for conduct of, and assessment of safety in, clinical trials
- **Conduct** CTs in accordance with the applicable regulations and guidelines
- **Abide** by contract signed with the sponsor
- **Communicate** concerns to the sponsor in a timely manner
- **Maintain** accurate records
Summary

- Regulator has the legal authority, therefore, has responsibility and accountability
- Sponsor, REB, QI/Institution, and CROs/SMOs all have legal and ethical responsibilities and accountabilities
- By signing the consent form, subjects do not forfeit their legal rights
## References

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