Regulator's Role in GCP

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APEC GCP Inspection Workshop

May 27, 2008

Objectives of this Talk

- Review the roles and responsibilities of the regulatory authority under GCP
- Identify within our respective countries:
  - Which functions are already well-established within the national authority
  - Which functions have yet to be established
  - Which functions could be strengthened --- and how

ICH GCP: The Role of the Regulator

- ICH GCP does not contain a separate chapter on the roles and responsibilities of the regulator or regulatory authority
  - But does mention “applicable regulatory requirements” and “regulatory authority” in Definitions, in Principles, and in sections on the IRB/IEC, the Investigator, the Sponsor, and the Essential Documents

International GCP: The Role of the Regulator

- The WHO (World Health Organization) “Guidelines for GCP” (1995) and Handbook for Implementation (2005) does include separate sections on the role of the Drug Regulatory Authority
- And the PAHO (Pan American Health Organization) “GCP Document of the Americas” includes a chapter on “GCP Compliance Monitoring by Regulatory Authorities” and an Annex: “Guide to Clinical Investigator Inspections”

An Important Distinction

- Role of government
- Role of the regulatory authority

Role of Government in Clinical Studies

- Establish a legal framework for GCP
  - Protect rights and safety of subjects (including requirements for informed consent and IEC review)
  - Ensure quality of studies/data, quality of regulatory decisions, and implementation of quality systems
  - Sanctions/penalties for violators
- Licensure of medical professionals
  - Qualifications of clinical investigators/staff
- Provide mandates to the regulatory authority

Role of Regulatory Authority in Clinical Studies –1-

- Must act according to laws to implement and enforce the laws

Role of Regulatory Authority in Clinical Studies –2-

- In general, the regulatory authority bears responsibility for:
  - Allowing a protocol to proceed
  - Ensuring the quality of the investigational product
  - Ensuring subject rights and safety during a study
  - Assuring and using quality study data for regulatory decision-making

Role of Regulatory Authority in Clinical Studies –3-

- Inspecting the parties who conduct or oversee the study
- Receiving and acting on complaints about a clinical study
- Educating the parties who conduct or oversee the study

Allowing a Protocol to Proceed

- Should ensure that both scientific and ethical review have been performed
  - Regulatory Authority's Review
    - May include inspection of non-clinical (animal toxicology) studies/facilities supporting the protocol
  - Independent Review(s)
    - Expert review(s); Ethics Committee review
- Should include authority for the regulator to NOT allow the protocol to proceed or to require modification of the protocol before proceeding

Ensuring the Quality of the Investigational Product

- In accordance with national/local laws and regulations, regulators may
  - Establish Good Manufacturing Practice (GMP) requirements for investigational products
  - Review manufacturing data submitted in support of research permits
  - Inspect manufacturing facilities
  - Establish requirements for the import of investigational products

Ensuring Subject Rights and Safety during the Study

- Should include the regulator's receipt and review of safety information (especially serious and unanticipated adverse experiences) during the study
- Should include knowledge by the regulator of safety concerns with the investigational product in other studies of the product
- May include the regulator's requesting or requiring independent data and safety monitoring boards (DSMBs) for the study

Ensuring Subject Rights and Safety during the Study

- Should include assurance to the regulator that informed consent and ethical (IEC) review is conducted prior to initiating the study and continued during the study
- Regulatory authorities also need to be alert to the issue of subject confidentiality and any applicable national/local laws and regulations for handling private medical information
- Regulators should have the authority to stop a study if they find that subjects are or will be exposed to an unreasonable risk

Establishing a System of Ethical Review

- States should promote the establishment of Ethics Committees (WHO)
  - Promote development of independent ethical review within a country
  - Ensure clear and efficient communication between committees
  - Ensure ongoing education of IEC members
  - Establish procedures for the review of protocols carried out at more than one site in a country or in more than one country

IEC: Regional Organizations

- Regional organizations or forums can encourage the exchange of information among IECs and assist in the development of high quality ethics committees
  - FERCAP (Forum of Ethics Review Committees of Asia-Pacific): Asia-Pacific forum initiated by WHO-TDR

Study Data -1-

- Regulators must be able to rely on the study data in making regulatory decisions
  - Allowing other studies of that investigational product to proceed
  - Approving the product for marketing
  - Labeling of the product

Study Data -2-

- Regulators, regardless of their specific job (reviewer, inspector, educator, administrator), should understand and be able to assess and apply the basic elements of data quality and integrity

Inspecting -1-

- Regulators should have authority to inspect on-site each of the parties under GCP
  - Investigators and site staff
  - Sponsors/monitors/contractors
  - IECs
- Inspections should be conducted in accordance with written procedures
- Inspections may be carried out routinely, randomly, and/or for specific reasons

Inspecting -2-

- The regulator's authority should include direct access to the subject's original medical records for verification of clinical study procedures and/or data
  - Subjects should be made aware of this provision (required element of informed consent)
  - Regulatory authorities should handle private information with respect for subject confidentiality

Receiving and Acting On Complaints

- Subjects and others involved in clinical studies should be able to report complaints (concerning subject safety, subject rights, data quality/integrity, or other aspects of study conduct) to the regulatory authority
- The regulatory authority should implement procedures to receive, review, evaluate, and as appropriate, follow-up (e.g., by inspection) on any such complaints

Ensuring GCP Compliance

- Regulators should be promptly notified when a sponsor identifies serious and/or persistent GCP noncompliance on the part of an investigator or institution
- Regulators should have enforcement options and authority when serious and/or persistent GCP noncompliance is observed and confirmed through due process

Written Procedures

- The regulatory authority should develop SOPs and quality systems for internal regulatory activities, including
  - Reviewing product applications and safety reports
  - Conducting GCP inspections
  - Communicating findings to inspected/ regulated parties
  - Establishing an infrastructure for due process and imposing sanctions on parties who violate laws/regulations

Regulatory Authority: Educational Role

- Regulators have a role in educating those parties that conduct or oversee regulated clinical studies
  - What is expected/required under national and local laws/regulations
  - Internationally recognized standards (GCP)
- Regulatory review and inspection should serve an educational as well as a compliance/enforcement function

Capacity-Building: Where is Capacity Still Needed ?

- For the inspector:
  - Recognizing which of the regulatory responsibilities for GCP are strongest and which still need strengthening
- For the regulatory authority/inspectorate
  - Commitment
  - Prioritization
  - Planning/Coordination
  - Implementation/Assessment

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