Good Clinical Practice

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• Mission
  - “To create, develop and nurture world class clinical product development capacity in India”

• Formed on 23 Sep 2009 by Dept. of Biotechnology, MoS & T, Government of India as an extramural unit of Translational Health Science and Technology Institute

• Registered as ‘Not-for-Profit’ under Societies Registration Act on 28 Sep 2010

• Based at Faridabad, NCR Biotech Science Cluster
Focus

1. Training in Clinical Research for Young Researchers
2. Clinical Study Support Services
   - Regulatory Advice
   - Monitoring Support
   - Medical Affairs
   - Data Management
   - Statistics
   - Audit
3. Collaboration with CoEs
Overview of Good Clinical Practice
What is Good Clinical Practice?

• An international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials.
Applicability of GCP

• Principles of GCP apply to:
  1. All clinical research involving human subjects, and not just research involving pharmaceutical or other medical products
  2. Studies of a physiological, biochemical, or pathological process, or of the response to a specific intervention – whether physical, chemical, or psychological – in healthy subjects or in patients
  3. Controlled studies of diagnostic, preventive or therapeutic measures, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation
Applicability of GCP

4. Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures
   • Diseases that have could be prevented by just changing behaviors and exposures (affected by environmental factors, genetic predisposition, disease agents, and lifestyle choices)
     – Adults can *delay or prevent type 2 diabetes through modest lifestyle changes* — losing a small amount of weight, eating a healthy diet, and being physically active a total of two and a half hours per week
     – increasing condom use, limiting sex partners and delaying sex, *increasing acceptance of male circumcision in certain cultures*, and increasing access to substance abuse treatment programs reduces the spread of HIV/AIDS
5. Studies concerning human health-related behavior in a variety of circumstances and environments
   - The Back to Sleep health awareness campaign that promotes infant backsleeping cut the incidence of sudden infant death syndrome, by $>50\%$ in a 12-year period
Applicability of GCP

6. Studies that employ either observation or physical, chemical, or psychological intervention. Such studies may generate records or make use of existing records containing biomedical or other information about individuals who may or may not be identifiable from the records or information.
Why is GCP important?

• Compliance with GCP provides public an assurance that:
  - **Data and reported results are credible and accurate**
  - **Rights, safety, well-being of study subjects involved in the research are protected and respected**, consistent with the principles enunciated in the Declaration of Helsinki and other internationally recognized ethical guidelines, and
  - **Ensures the integrity of clinical research data**
GCP – Stakeholders

• Conduct of Clinical Research is complex
• Complexity compounded by the need to involve a number of different individuals with a variety of expertise
• Stakeholders to share a common goal in adhering to ethics and quality data
Guidelines
Declaration of Helsinki 1964 - 2000

- World Medical Association
- Forms the basis for the ethical principles that underlie the ICH-GCP guidelines
- Recommendations guiding medical doctors in biomedical research involving human subjects.
  1. Duty of physician to protect the life, health, privacy and dignity of the human subject
  2. Review of proposed research by independent ethics committee
  3. Medical research involving human subjects conducted by scientifically qualified persons and under the supervision of a clinically competent medical person
  4. Physician to obtain the subject’s freely-given consent, preferably in writing
  5. Stress on publication of results - negative or positive
ICH

• International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in April 1990
• Unified standard for the European Union (EU), Japan, and the United States to comply with the regulatory authorities in these countries.
• Topics:
  – Quality
  – Safety
  – Efficacy
    • E6: GCP: Apr 1995
    • E6(R1): Finalised Guideline in May 1996; Adopted in EU in July 1996 and by US FDA in May 1997
  – Multidisciplinary
ICH-E6 (GCP)

- Based on a set of regulatory and ethics requirements, standards, recommendations that apply to numerous tasks, processes and roles in the conduct of clinical research
  - Design
  - Performance
  - Audit
  - Termination
  - Reporting of clinical trial
  - Conduct
  - Monitoring
  - Recording
  - Analysis
ICH-E6 (GCP)

• Cardinal Principles
  – *Protection of Subject’s rights:* To ensure that the rights, integrity and confidentiality of trial participants are protected
  – *Data Integrity:* To provide assurance that the data and reported results are credible and accurate
CDSCO – GCP

- Central Drugs Standard Control Organization
- GCP Guidelines for Clinical Trials on Pharmaceutical Products (2001)
- Guidelines that have been evolved with consideration of WHO, ICH, and ICMR - Ethical Guidelines for Biomedical research on Human Subjects
- To be followed for carrying out all biomedical research in India at all stages of drug development, whether prior or subsequent to product registration in India
  - Drugs
  - Ayurveda, Siddha and Unani Medicine (Mar 2013)
  - ISO 14155 for conducting clinical investigations of medical devices
13 Principles of CDSCO-GCP

**Ethics:**
1. Ethical conduct of clinical trials
2. Benefits justify risks
3. Rights, safety, and well-being of subjects prevail

**Protocol and Science:**
4. Nonclinical and clinical information supports the trial
5. Compliance with a scientifically sound, detailed protocol
13 principles of CDSCO-GCP

Responsibilities:
6. IRB/IEC approval prior to initiation
7. Medical care/decisions by qualified physician
8. Each individual is qualified (education, training, experience) to perform his/her tasks

Informed Consent:
9. Freely given from every subject prior to participation
13 principles of CDSCO-GCP

Data Quality and Integrity:
10. Accurate reporting, interpretation, and verification
11. Protects confidentiality of records

Investigational Product:
12. Conform to GMP and used per protocol

Quality Control/Quality Assurance:
13. Systems with procedures to ensure quality of every aspect of the trial
CDSCO – GCP

- http://cdsco.nic.in/forms/list.aspx?lid=1585&Id=1
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  i. Declaration of Helsinki  
  ii. Schedule Y  
  iii. Format for submission of Pre-clinical and Clinical data for r-DNA based vaccines, diagnostics and other biologicals  
  iv. Investigator’s Brochure  
  v. Essential Documents |
GCP – Organisation of Document

• Each section contains:
  – Specific definitions
  – Elements that must be contained in IB and Protocol
  – Outlines the responsibilities of each stakeholder in conducting the clinical trial
2.3. Protocol

• 2.3.1.1. General Information
  a. Protocol title, PIN, date, amendment number and date
  b. Name, address and contact numbers of Sponsor, Monitor/ CRO

• 2.3.1.2. Objectives and Justification
  a. Aims and objectives of the study
  b. Name and description of the investigational product
2.3. Protocol

• 2.3.1.4. Study Design
  a. Specific statement of primary and secondary endpoints

• 2.3.1.5. Inclusion, Exclusion and Withdrawal of Subjects
  a. Criteria for inclusion and exclusion

• 2.3.1.10 Data Handling and Management

• 2.3.1.14 Publication Policy
2.4. Ethical & Safety Considerations

- 2.4.2. Ethics Committee
  - 2.4.2.1. Basic Responsibilities
  - 2.4.2.2. Composition
  - 2.4.2.8. Record Keeping

- 2.4.3. Informed Consent Process
  - 2.4.3.2. Essential information for prospective research on subjects

- 2.4.5. Compensation for Participation
3.1. Sponsor Responsibilities

- 3.1.1. Investigator and Institution Selection
- 3.1.2 Contract
- 3.1.13 Monitoring
- 3.1.17 Role of Foreign Sponsor
3.2. The Monitor

• 3.2.1 Qualifications
• 3.2.2 Responsibility
  a. The Monitor should verify that the investigator(s) have the adequate qualifications, expertise and the resources to carry out the study. Monitor should also confirm that the investigator(s) shall be available throughout the study period.
3.3. Investigator Responsibilities

- 3.3.1 Qualifications
- 3.3.4 Communications with Ethics Committee
- 3.3.5. Compliance with the protocol
- 3.3.7. Selection and recruitment of study subjects
4. Record Keeping and Data Handling

• 4.2 Corrections
• 4.3. Electronic Data Processing
• 4.4. Validation of Electronic Data Processing Systems
• 4.6. Responsibilities of the Investigator
  - Investigator should ensure that the observations and findings are recorded correctly and completely in the CRFs and signed by the responsible person(s) designated in the Protocol
5. Quality Assurance

• The Sponsor is responsible for the implementation of a system of Quality Assurance in order to ensure that the study is performed and the data is generated, recorded and reported in compliance with the Protocol, SOP, GCP and other applicable requirements.
6. Statistics

• 6.1. Role of Biostatistician
• 6.2. Study Design
• 6.3. Statistical Analysis
  – The type(s) of Statistical Analyses to be used must be clearly identified and should form basis of the statistical model for the Study. Any subsequent deviation(s) should be described and justified in the Final Report
7. Special Concerns

• 7.1. Clinical Trials of Vaccines
• 7.2. Clinical Trials of Contraceptives
• 7.3 Clinical trials with surgical procedures/ medical devices
• 7.4. Clinical trials for Diagnostic Agents - Use of Radio-active Materials and X- Rays
• 7.5. Clinical trials of Herbal Remedies and Medicinal Plants
8. Appendices

- Appendix I: *WMA Declaration of Helsinki*
- Appendix II: *Schedule Y*
- Appendix III: *Format For Submission Of Preclinical and Clinical Data* for r-DNA based Vaccines, Diagnostics and other Biologicals
- Appendix IV: *Investigator’s Brochure*
- Appendix V: *Essential Documents for the Conduct of a Clinical Trial*
GCP – Conclusion

1. **Non-malfeasance**: Do no harm to subject
2. **Beneficence**: Study to benefit subject and society
3. **Justice**: Fair distribution of risk vs. benefit
4. **Autonomy**: Protect rights and dignity (Privacy, anonymity and confidentiality)
5. **Essentiality**: Need for study or sub-studies?
6. **Non-exploitation**
7. **Accountability and Transparency**
8. **Public Domain**
9. **Totality of Responsibility**
GCP – Conclusion

- Conduct of clinical research in accordance with the principles of GCP (irrespective of drug trial or observational study) helps to ensure that clinical research participants are not exposed to undue risk, and that data generated from the research are valid and accurate
Thank You