Good clinical practice in pharmacovigilance

By Prof. Satish Sharma, Dean, School of Pharmacy
• GCP is defined as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies
Why is GCP important

- GCP compliance provides public assurance that the rights, safety and well-being of human subjects involved in research are protected
- Improved trial methods
- Clinical trial concept better understood
- Public/Political Concern over Safety Aspects
Goals of GCP

• To protect the rights, safety and welfare of humans participating in research
• To assure the quality, reliability and integrity of data collected
• To provide standards and guidelines for the conduct of clinical research
• Good Clinical Practice = Ethics + Quality Data
ICH-GCP

• GCP is an international quality standard that is provided by the International Conference on Harmonization (ICH)
• Goals: Harmonize technical procedures and standards; improve quality; speed time to market
• In 1997, the FDA endorsed the GCP Guidelines developed by ICH
• ICH guidelines have been adopted into law in several countries, but used as guidance for the FDA in the form of GCP
## Historical background

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tr>
<td>4600 BC</td>
<td>Hippocratic oath</td>
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<td>1930</td>
<td>US Food Drug and Cosmetic Act</td>
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<tr>
<td>1947</td>
<td>Nuremberg code</td>
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<td>1948</td>
<td>Declaration of human rights</td>
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<tr>
<td>1962</td>
<td>Kefauver-Harris Amendment</td>
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<td>1964</td>
<td>Declaration of Helsinki</td>
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<td>1979</td>
<td>The Belmont Report</td>
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<td>1982</td>
<td>International Guidelines for Biomedical Research Involving Human Subjects</td>
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<td>1996</td>
<td>ICH-GCP guidelines issued</td>
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<td>1997</td>
<td>ICH-GCP guidelines becomes law in some countries</td>
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• Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the:
  29th WMA General Assembly, Tokyo, Japan, October 1975
  35th WMA General Assembly, Venice, Italy, October 1983
  41st WMA General Assembly, Hong Kong, September 1989
  48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
  52nd WMA General Assembly, Edinburgh, Scotland, October 2000
  53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
  55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
  59th WMA General Assembly, Seoul, Republic of Korea, October 2008
  64th WMA General Assembly, Fortaleza, Brazil, October 2013
Preamble

“promote and safeguard the health of the people. The physician’s knowledge and conscience are dedicated to the fulfilment of this duty”
Belmont Report

- Respect for persons
- Beneficence
- Justice
Principles of ICH-GCP

- Ethical conduct of clinical trials
- Benefits justify risks
- Rights, safety, and well-being of subjects prevail
- Nonclinical and clinical information supports the trial
- Compliance with a scientifically sound, detailed protocol
Principles of ICH-GCP

- Responsibilities: IRB/IEC approval prior to initiation
- Medical care/decisions by qualified physician
- Each individual is qualified (education, training, experience) to perform his/her tasks
- Informed Consent freely given from every subject prior to participation
Principles of ICH-GCP

- Data quality and integrity
- Accurate reporting, interpretation and verification
- Protects confidentiality of records and investigational products
- Conform to GMP/GLP: quality control/quality assurance
- Systems with procedures to ensure quality of every aspect of the trial
### Who is responsible for compliance of ICH-GCP

- Sponsors
- Clinical Investigators (CIs)
- Independent Ethics Committees (IECs)
- Institutional Review Boards (IRBs)
- Contract Research Organizations (CROs)
- Research Nurses
- Clinical Research Coordinators (CRCs)
- Clinical Research Associates (CRAs)
- Data Entry Personnel
Responsibilities of Institutional Review Board

- Should safeguard the rights, safety, and well-being of all trial subjects
- Should review a proposed clinical trial within a reasonable time and document its views in writing
- Should review both the amount and method of payment to subjects
- Should obtain trial protocol(s)/amendment(s), written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g., advertisements), written information to be provided to subjects, Investigator’s Brochure (IB), available safety information
• The investigator should be thoroughly familiar with the appropriate use of the investigational product(s)
• The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies)
• should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
• should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
Investigator’s Responsibilities

• should have sufficient time to properly conduct and complete the trial within the agreed trial period.

• should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.

• should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions

• is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site
Investigator’s Responsibilities

• Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IRB/IEC for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects should

• the investigator/institution should provide the IRB/IEC with a current copy of the Investigator’s Brochure

• During the trial the investigator/institution should provide to the IRB/IEC all documents subject to review
Investigator’s Responsibilities

• The investigator should not implement any deviation from, or changes of, the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IRB/IEC of an amendment

• Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator/institution

• The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product’s delivery to the trial site, the inventory at the site, the use by each subject
Informed consent of the subjects

• In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB/IEC’s written approval/favorable opinion of the written informed consent form and any other written information to be provided to subjects.

• None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject’s legally acceptable representative to waive or to appear to waive any legal rights.
Informed consent of the subjects

- The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject’s legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval/ favorable opinion by the IRB/IEC.

- The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject.
Informed consent of the subjects

- All questions about the trial should be answered to the satisfaction of the subject or the subject’s legally acceptable representative.
- Prior to a subject’s participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject’s legally acceptable representative, and by the person who conducted the informed consent discussion.