Good Clinical Practice (GCP)
Key Topics

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Office of the Commissioner

FDA Clinical Investigator Training Course
November 13, 2018

Objectives

- Definition and Goals of GCP
- Investigator Responsibilities
- Clinical Investigator Financial Disclosure
- HSP/GCP Resources

What is Good Clinical Practice (GCP)?

- Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.

What is Good Clinical Practice (GCP)?

- While FDA regulations do not have a stand alone definition of GCP, it is defined in 21 CFR 312.120 (*Foreign clinical studies not conducted under an IND*):
  - For the purposes of this section, GCP is defined as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials in a way that provides assurance that the data and reported results are credible and accurate and that the rights, safety, and well-being of trial subjects are protected.

What is Good Clinical Practice (GCP)?

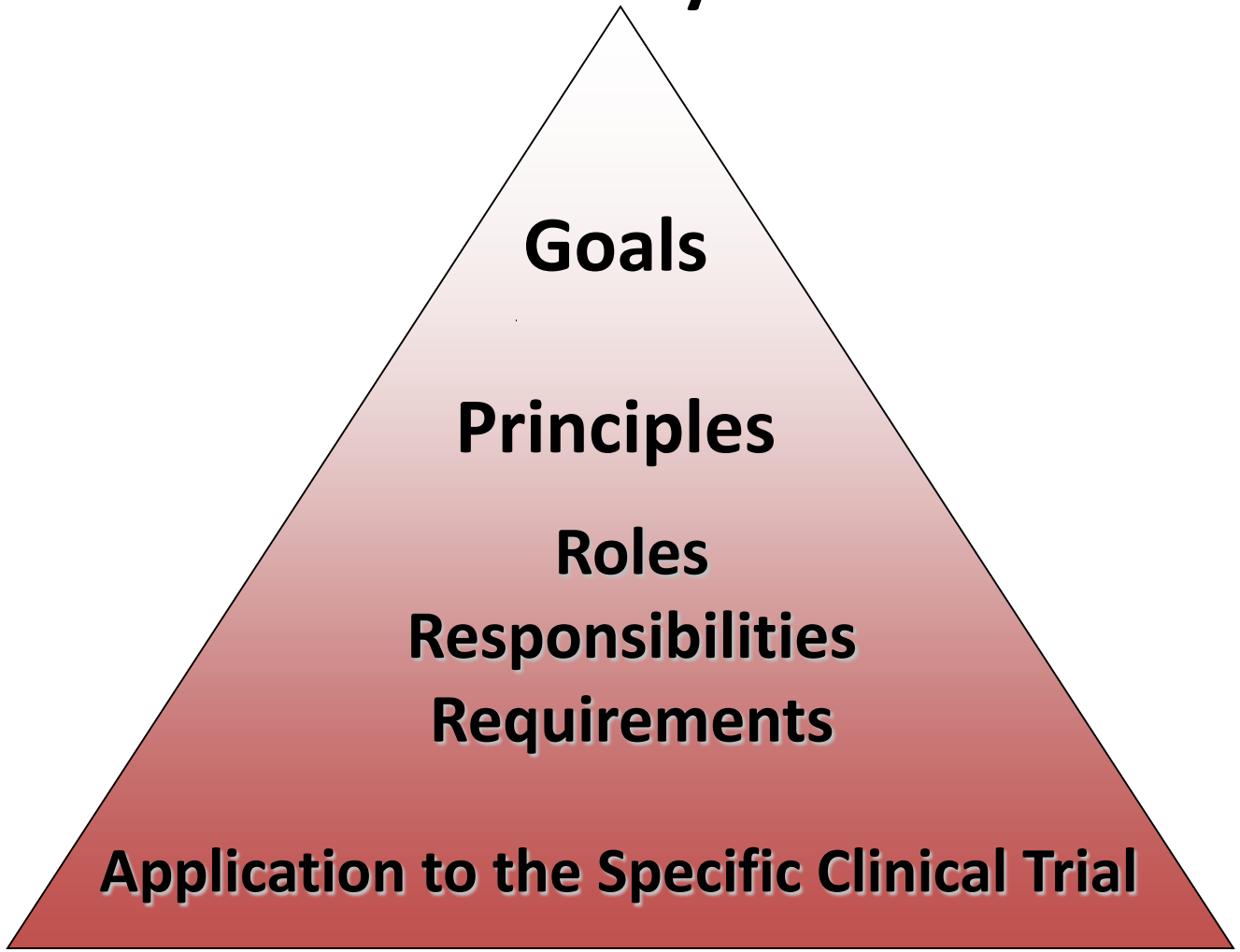
GCP stand alone definition in the 1996 ICH GCP E6 consolidated guidance:

- A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that *the rights, integrity and confidentiality* of trial subjects is protected.

GCP: Overarching Themes

- Responsibility(-ies)
- Attention to Detail
- Documentation
- Quality
  - Data/Scientific Quality; Ethical Quality; Process Quality
- Risk and Risk Management
- Validation/Verification/Inspection

The Hierarchy of GCP



The Goals of GCP

To provide standards and guidelines for the conduct of clinical research that include provisions for:

- Protecting Research Subjects
  - Subject safety
  - Rights as subjects (research ethics)
    - Right to be informed
    - Right NOT to participate
    - Right to withdraw at any time
    - Right to protection of privacy
    - … and other Rights

The Goals of GCP

- Ensuring the quality and integrity of research data for regulatory decision-making
  - Based on a scientifically sound protocol that is designed to meet its stated objectives
  - Based on the quality conduct and oversight of the clinical study

The Goals of GCP

- Assuring the existence and operation of “quality systems”
  - Including but not just for the current study
  - By each party (investigator, sponsor, IRB, and regulatory authority)
  - Based on written procedures
  - Assured through self- and cross-evaluation
  - Leveraged: Regulatory authority can’t do it all

Good Clinical Practice = Ethics + Quality Data

Why is GCP important?

- Adherence to the principles of GCPs, including adequate human subject protection (HSP) is universally recognized as a critical requirement to the conduct of research involving human subjects.

Why is GCP important?

- GCP compliance provides public assurance that the rights, safety and wellbeing of human subjects involved in research are protected.

- Promotes data integrity and reliability.

GCP/Laws and Regulations

- Many countries have adopted GCP principles as laws and/or regulations.

- The FDA's regulations for the conduct of clinical trials, which have been in effect since the 1970s, address both GCP and HSP.

What Constitutes GCP in Clinical Trials?

- IRB-approved protocol
- Valid Informed Consent
- Monitoring Plan
- Adverse Event (AE) Reporting
- Proper documentation
- Valid data collection/reporting procedures

How does FDA implement GCP?

- 21 CFR 11 – Electronic Records & Signatures
- 21 CFR 50 – Informed Consent
- 21 CFR 54 – Financial Disclosure
- 21 CFR 56 – Institutional Review Boards
- 21 CFR 312 – Investigational New Drug Applications

How does FDA implement GCP?

- 21 CFR 314 – New Drug Applications
- 21 CFR 320 – Bioavailability & Bioequivalence Requirements
- 21 CFR 601 – Biologic License Applications
- 21 CFR 812 – Investigational Device Exemptions
- 21 CFR 814 – Premarket Approval of Medical Devices

Shared Responsibilities

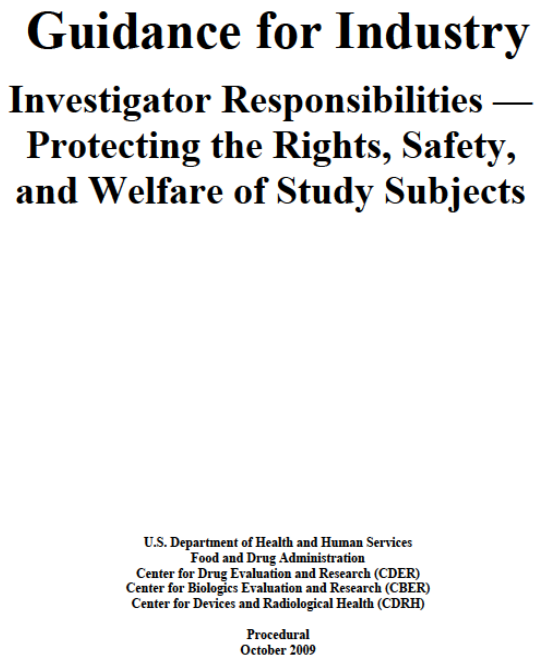
- Responsibility for GCP is shared by all parties involved in a clinical trial including:
  - Sponsors
  - Contract Research Organizations (CROs)
  - Investigators
  - Study site staff
  - IRBs
  - Research Subjects
  - FDA/other regulators

Investigator responsibilities

21 CFR Parts 312 and 812

- Personally conduct and/or supervise the study
  - Cannot contract out any responsibilities; is entirely responsible for study conduct at site
  - Needs to ensure qualifications and training of anyone delegated study duties and meet with study staff on a regular basis
  - SOPs for site's conduct of studies and handling of problems
- Lack of appropriate study oversight by the CI is a commonly cited noncompliance in bioresearch monitoring (BIMO) inspections

Investigator Responsibilities



- Final Guidance issued October 2009
- Intended to clarify certain investigator responsibilities:
  - Appropriate Delegation
  - Adequate Training
  - Supervision of staff, including contracted personnel
  - Subject protections, including necessary medical care

Investigator Responsibilities

October 2009 Guidance

- Appropriate delegation of study tasks
  - Individuals to whom a task is delegated:
    - Should be qualified by education, training, and experience (and state licensure where relevant)
    - Must meet protocol specific requirements
  - A qualified Physician (or dentist) should be responsible for trial-related medical decisions and care
  - Recommend maintaining a list of qualified individuals and their delegated tasks

Investigator Responsibilities

October 2009 Guidance

- Adequate training of study staff
  - Familiarity with protocol and study purpose
  - Adequate understanding of study in order to perform delegated task(s)
  - Knowledge of applicable regulations and HSP and GCP principles
  - Individuals competent or trained to perform delegated task(s)
  - Updates and additional training provided, as needed

Investigator Responsibilities

October 2009 Guidance

- Supervision of staff, including contracted personnel
  - Level of supervision should be appropriate to the staff, nature of the trial, and the subject population
  - A supervisory plan should include routine meetings with study staff and procedures for determining appropriate completion of delegated tasks

Investigator Responsibilities

October 2009 Guidance

- Supervision of staff, including contracted personnel
  - Oversight extends to study staff not directly supervised by the investigator:
    - Site management organization (SMO) staff
    - Contracted providers (e.g., radiologists, laboratories)
    - Medical device engineers

Investigator Responsibilities

October 2009 Guidance

- Subject protections, including necessary medical care
  - Reasonable medical care for study-related medical problems
  - Provisions for access to medical care when specialized care is required
    - Study subjects should be informed on how to obtain medical care
  - Minimize risks to subject by adhering to study protocol

Clinical Investigator Financial Disclosure

21 CFR Part 54

Proposed rule	September 2, 1994
Final rule	February 2, 1998
Revised final rule	December 31, 1998
⇨ Effective date	**February 2, 1999**

Clinical Investigators Financial Disclosure

21 CFR Part 54

Ensures that financial interests and arrangements of clinical investigators ***(that could affect reliability of data submitted to FDA in support of product marketing applications)*** are identified and disclosed to the agency

Clinical Investigators Financial Disclosure

21 CFR 54.2(d)

Definition of Clinical Investigator includes:

- Investigators
- Subinvestigators (those who play a significant role in the conduct of a study)
- Spouses and dependent children

The definition does not include:

- Full- or part-time employees
- Hospital or office staff who do not make a significant contribution to the data

Clinical Investigators Financial Disclosure

21 CFR 54.4(b)

Clinical Investigator Responsibilities:

- Must provide “sufficient accurate financial information to allow the sponsor to submit complete and accurate certification of disclosure statements...”
- Must update the information if any relevant changes occur during the study or 1 year after study completion

Clinical Investigators Financial Disclosure

21 CFR Part 54

Requires Applicant of a marketing application to either:

1. Certify that there are no financial arrangements with investigator

OR

2. Disclose specific financial arrangements and what is being done to minimize bias

Clinical Investigators Financial Disclosure

21 CFR Part 54

Disclosable Arrangements:

1. Compensation where the value could be affected by study outcome (e.g., royalties)
2. Significant Payments of Other Sorts (SPOOS) to the investigator or institution with a monetary value of $25,000 or more (e.g., grants, equipment, retainers for ongoing consultation, honoraria) ***not including the cost of conducting the trial***

Clinical Investigators Financial Disclosure

21 CFR Part 54

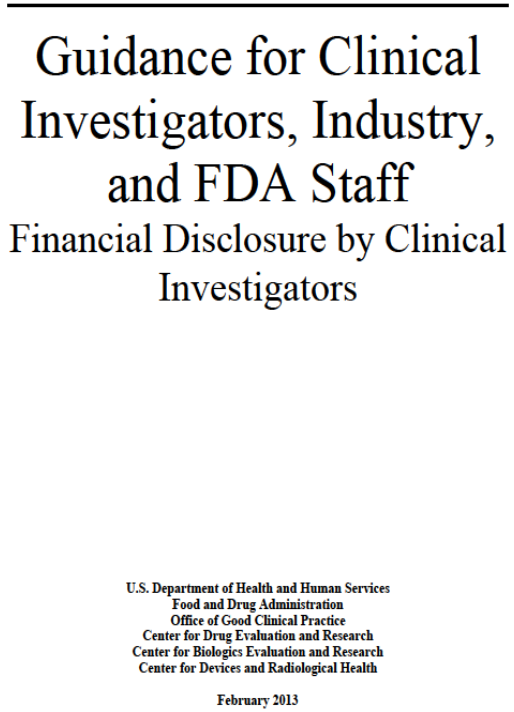
Disclosable Arrangements:

3. Proprietary interest in product, such as a patent, trademark, copyright or licensing agreement

4. Equity interest in a publicly traded company whose value > $50,000 ***OR***

   Equity interest such as ownership interest or stock options whose value cannot be readily determined through reference to public prices

Financial Disclosure by Clinical Investigators


Guidance for Clinical Investigators, Industry, and FDA Staff

Financial Disclosure by Clinical Investigators

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Good Clinical Practice
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research
Center for Devices and Radiological Health

February 2013

- Final Guidance issued February 2013
- Specifically, the guidance describes:
  - Financial disclosure requirements
  - Responsibilities of various parties
  - Further explanation of the terminology used in the regulations
  - How FDA reviews financial disclosure information
- Describes FDA's policy to publicly post FDA's reviews summarizing financial disclosure information related to an approved marketing application

HSP/GCP Resources

Office of Good Clinical Practice (OGCP) website –
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm
alias – www.fda.gov/gcp

Access to HSP/GCP-related Regulations, Guidance, Information Sheets, Educational Materials, Compliance and BIMO-related information

Clinical Trials and Human Subject Protection
Bioresearch Monitoring Program (BIMO)
BIMO Inspection Metrics
HSP/BIMO Initiative
Regulations
Report Problems to FDA
Complaints relating to Clinical trials
Guidance Documents (Including Information Sheets) and Notices
Proposed Regulations and Draft Guidances
Compliance & Enforcement
Educational Materials
Replies to Inquiries to FDA on Good Clinical Practice
FDA's Role: ClinicalTrials.gov Information

Resources for You

- ClinicalTrials.gov (NIH)
- FDA Basics
- FDA Basics for Industry
- Laws Enforced by FDA
- Freedom of Information
- Dockets Management
- Approvals of FDA-Regulated Products
- Websites with Information About Clinical Trials

Clinical Trials and Human Subject Protection

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

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Bioresearch Monitoring

FDA's bioresearch monitoring (BIMO) program conducts on-site inspections of both clinical and nonclinical studies performed to support research and marketing applications/submissions to the agency. Links to the compliance programs for each inspection type and contact information for each Center's BIMO program are also accessible from this site.

Office of Good Clinical Practice

See the Office of Good Clinical Practice's (OGCP's) mission statement on the OGCP's Web page.

Sign up for Good Clinical Practice/Human Subject Protection e-mail updates

In June 2009, FDA redesigned its web site. As a result, some links (URLs) embedded within Guidance documents, Rules, and other documents are no longer valid. If you find a link that does not work, please try searching for the document using the document's title. For additional assistance, go to Contact FDA. We apologize for any inconvenience this redesign might have caused.

Workshops and Meetings

In The News

- FDA and OHRP Announcement to extend the comment period on the draft guidance document entitled, "Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs."
- Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs (November 2015)
- Acceptance of Medical Device Clinical Data from Studies Conducted Outside the United States - Draft Guidance for Industry and Food and Drug Administration Staff (PDF - 649KB)
- Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers (PDF - 110KB)
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- Informed Consent Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors (July 15, 2014)
- FDA's HSP/BIMO Initiative Accomplishments: Update June 2014
- Good Clinical Practice: Previous "In the News" Items

Contact FDA

301-796-8340
gcp.questions@fda.hhs.gov

Office of Good Clinical Practice
Food and Drug Administration
Office of Good Clinical Practice
Office of Special Medical Programs
10903 New Hampshire Ave.,
WO32-5103

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Redacted Email Inquiries

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Workshops and Meetings

- Conferences on FDA clinical trial requirements

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OGCP's Query Mailbox

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OGCP's Listserv for notifications of new guidance documents, regulations, etc. as well as FDA webinars

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Resources

- Guideline for Good Clinical Practice: E6(R2) – Integrated Addendum, March 2018
  - http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf
- Guidance for Industry, Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf
- Financial Disclosure by Clinical Investigators, Guidance for Industry
  - http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM341008.pdf


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