



Making Life Better
through Research, Education & Healthcare. *

**STANDARD OPERATING PROCEDURES
FOR THE
CONDUCT OF CLINICAL RESEARCH AT USF HEALTH
MORSANI CLINICAL RESEARCH CENTER (CRC)**

Compiled by

**USF Health
Office of Clinical Research
12901 Bruce B. Downs Blvd., MDC 28
Tampa, FL 33612
Tel: (813) 974-3336
Fax: (813) 905-9997**

Office email: OCR@health.usf.edu

Website: [USF Office of Clinical Research](#)

TABLE OF CONTENTS

INTRODUCTION and BACKGROUND

I GENERAL ADMINISTRATION (GA)

- 101 Writing and maintaining SOPs
- 102 Training Clinical Research Staff
- 103 Responsibilities of the Research Team
- 104 Clinical Study Conduct
- 104 Role of the Office of Clinical Research
- 106 Document Control

II. REGULATORY AFFAIRS (RA)

- 201 Regulatory Documentation
- 202 Privacy and Confidentiality
- 203 IRB Submissions
- 204 Adverse Event Reporting
- 205 Institutional Conflicts of Interest

III. PROJECT MANAGEMENT (PM)

- 301 Study Feasibility
- 302 Site Qualification Visit
- 303 Site Initiation Visit
- 304 Communication Practices
- 305 Investigational Product Accountability
- 306 Blinding
- 307 Venipuncture
- 308 Specimen Collection and Management
- 308 Preparing Injectable Medications
- 310 Site Monitoring Visits
- 311 Study Close-Out Visit
- 312 Protocol Compliance

IV. SUBJECT MANAGEMENT (SM)

- 401 Subject Recruitment
- 402 Informed Consent Process
- 403 Eligibility and Enrollment
- 404 Protecting Confidential Information
- 405 Study Visits

V DATA MANAGEMENT (DM)

- 501 Case Report Form Completion
- 502 Source Documentation
- 503 Electronic Records Management
- 504 Archiving Study Records
- 505 Printing and Certifying Medical Records

VI. QUALITY ASSURANCE (QA)

- 601 Quality Control
- 602 Audits
- 603 Corrective Action Plan to Audit Findings
- 604 Equipment Maintenance and Calibration
- 605 Temperature Monitoring

VII APPENDICES

ie: flowcharts, checklists, logs, guidance docs

DRAFT

INTRODUCTION

Clinical research has grown exponentially over the last several decades into a multi-billion dollar global business with intense regulation and control imposed on the industry by the federal government. To ensure that the safety and welfare of human research participants are protected, biomedical research requires clinical investigators and research personnel to be adequately trained in Good Clinical Practice (GCP) and credentialed with a working knowledge of regulatory requirements and medical ethics. Failure to understand the complexities of conducting clinical trials may result in a flawed clinical trial. A flawed clinical trial may lead to errors during study implementation, compromised data integrity, and ultimately deemed unacceptable to regulatory authorities.

BACKGROUND

Historical events have provided a framework leading up to the formation of the International Conference on Harmonisation (ICH) - GCP guidelines. For example, the Nuremberg Code of 1947 was created as a result of the unethical, biomedical experiments carried out by German physicians during World War II on Nazi war camps prisoners. This code serves as the basis for the protection of human subjects, and all clinical research should have its origin in it.

In 1964, the World Medical Association developed the Declaration of Helsinki which formed the foundation for the ethical principles outlined in the ICH-GCP guidelines. Protecting the rights of human subjects was the focus of this declaration as evident in its introduction that states, "The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty."

Another important milestone that led to the development of the ICH-GCP is the Belmont Report established in 1979 by the National Commission for protection of Human Subjects of Biomedical and Behavioral Research. This report identifies the following three, basic ethical principles that provide a moral framework for the conduct of biomedical and behavioral research involving human subjects:

1. **Respect for Persons:** This principle acknowledges the autonomy of every individual and requires that persons with diminished autonomy are protected.
2. **Beneficence:** This principle requires that researchers maximize benefits and minimize harm associated with research. Research-related risks must be reasonable in light of the expected benefits.
3. **Justice:** This principle requires equitable selection, recruitment and fair treatment of research subjects.

In recent years, international GCP standards have been developed in an effort to unify standards for clinical research, to reduce waste and redundancy, and to expedite approval by the appropriate regulatory authorities. In 1996, the International Conference on Harmonisation (ICH) guidance entitled, "Good Clinical Practice: Consolidated Guideline" (ICH-E6) was established to provide a unified standard for the United States, European Union (EU) and Japan. The main aim of the ICH GCP guidelines is to protect and preserve human rights.

INTRODUCTION

The ICH-GCP guidance document is based on the following 13 core principles:

1. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favorable opinion.
7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
12. Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

The ICH GCP guidance has been adopted by industry and academia worldwide. Sponsors, researchers and institutions who comply with this guideline establish an institutional culture where clinical research is conducted in ethically and scientifically sound manner. This guidance document, along with numerous other guidelines and codes, such as the Nuremberg Code which serves as a basis for the protection of human subjects, provide a measure of quality in the conduct of clinical research. Collectively, these documents serve as the gold standard for the conduct of clinical research.

The guidance document can be accessed on the FDA website URL:

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm122044.htm>

INTRODUCTION

OVERVIEW OF GCP

The rights and welfare of the individual clinical research subject must always be the paramount consideration for ethical research. Therefore, clinical research must be conducted in a manner that protects the rights, welfare and confidentiality of the human subject and also assures data credibility by protecting the integrity of data that has been collected according to the approved protocol.

Good Clinical Practice (GCP) is defined as “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 are protected.” When researchers comply with this standard, it provides public assurance that the rights, safety and welfare of the research subjects are protected. Moreover, compliance with this guideline promotes transparency which enhances accountability, raises performance, and boosts credibility of the clinical trial data.

GCP is a shared responsibility by all parties involved in the conduct of clinical research to include sponsors, the Principal Investigator (PI) and his/ her research team, clinical research organizations (CROs), ethics committees and regulatory authorities.

OVERVIEW OF STANDARD OPERATING PROCEDURES (SOPs)

The ICH defines Standard Operating Procedures (SOPs) as a set of standardized, written procedures with detailed instructions that document routine operations, processes and procedures followed within an organization. The development and use of SOPs are an integral part of a successful quality system as it provides individuals with the information to perform a job properly. They help to ensure consistency, compliance, accountability and efficiency of the investigator and the investigator's team when they are conducting clinical trials. The advantage of having well-written, comprehensive and practical clinical research specific SOPs is that writing SOPs impels an investigator to take the critical steps of reading and interpreting GCP regulations and guidelines and then applying them to his or her particular clinical research operations. Without clinical research specific SOPs, investigators run a high risk of GCP noncompliance and poor productivity.

The aim of this SOP manual with attached appendices that include checklists, logs and flowcharts is to provide researchers a way to standardize processes and documentation relating to clinical trials while fostering conformance to Good Clinical Practice (GCP) requirements in clinical research. When implemented, these SOPs will be the first step in establishing an institutional culture of excellence by providing uniform quality, safety, and integrity performance during the conduct of clinical studies.

REFERENCES:

1. Belmont Report- http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf
2. USF Institutional Review Board (IRB) HRPP Policy & Procedures
<https://arc.research.usf.edu/Prod/Doc/0/PVVIQBCNKI84V80KBQ6PU5BHDE/USF%20HRPP%20Policy%20and%20Procedures%20Manual.pdf>
3. USF Institutional Review Board (IRB) HRPP Investigator Guide located in HRPP Guidance Documents
4. Compliance Program Guidance Manual for FDA Staff – Compliance Program 7348.811
5. Bioresearch Monitoring: Clinical Investigators;
<http://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/ucm133562.htm>
6. Device Advice, FDA Center for Devices and Radiological Health (CDRH):
<http://www.fda.gov/cdrh/devadvice/> .
7. Good Clinical Practice in FDA-Regulated Clinical Trials:
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/>
8. Office for Human Research Protections: <http://www.hhs.gov/ohrp/>
9. Office of Human Subjects Research – Nuremberg Code-
<http://ohsr.od.nih.gov/guidelines/nuremberg.html>
10. Office of Human subjects Research- Declaration of Helsinki
11. Form FDA 1572 Statement of Investigator:
<http://www.fda.gov/opacom/morechoices/fdaforms/FDA-1572.pdf>
12. Code of Federal Regulations:
 - 21 CFR 50 ----- Protection of Human Subjects
 - 21 CFR 54 ----- Financial Disclosure by Clinical Investigators
 - 21 CFR 56 ---- Institutional Review Boards
 - 21 CFR 312 --- Investigational New Drug Application
 - 21 CFR 314 --- Applications for FDA Approval to Market a New Drug
 - 21 CFR 812 --- Investigational Device Exemptions
 - 21 CFR 814--- Premarket Approval of Medical Devices
 - 45 CFR 46 ----- Protection of Human Subjects
 - 45 CFR 160 --- General Administrative Requirements
 - 45 CFR 164----Security and Privacy

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm>

13. ICH E2A – FDA Guideline for Industry – Clinical Safety Data Management: Definitions and Standards for Expedited Reporting; March 1995
14. ICH E2C – FDA Guideline for Industry – Clinical Safety Data Management: Periodic
15. Safety Update Reports for Marketed Drugs; November 1996
16. ICH E6 – FDA Guidance for Industry – Good Clinical Practice: Consolidated Guidance;

DRAFT