



## **Academic Affairs:**

A centralized resource to facilitate financial management of research efforts of the Cleveland Clinic. This includes Research Operations, Office of Sponsored Research and Projects (OSRP) and Research Finance Operations (RFO). Research Operations is further divided into the areas of CTMS, CROP, and ROC which will be further explained in the glossary.

## **Academic Research Organization (ARO):**

An academic organization engaged by a research sponsor to coordinate the management and performance of a sponsored research project and which may assume responsibility for certain regulatory obligations of the research sponsor under applicable federal regulations. Also see the definition of Contract Research Organization (CRO). The primary distinction between an ARO and a CRO is that an ARO is dedicated to the furtherance of its academic and educational objectives and will often serve in the role of primary investigator and lead author for the study results.

## **Adverse Event (AE):**

Any undesirable event that occurs to a research subject whether or not it is considered related to the trial product. This includes events not seen at baseline, or that worsen from baseline. See [IRB policy IRB-60](#).

## **Association for Accreditation of Human Research Subject Protection Program (AAHRPP):**

[AAHRPP](#) is a voluntary accreditation program for clinical research formed by AAMC and recognized by the FDA and OHRP. Accreditation requires completion of a detailed self-assessment of current programs for protection of human subjects as part of the application process. Written policies and procedures must be provided as evidence of satisfaction of the accreditation standards, as well as examples of program implementation, including: training, education tools, Q & A and audit results.

The accreditation standards are organized in five (5) Domains –

- Domain I - Organization
- Domain II – IRB
- Domain III - Investigators
- Domain IV- Sponsored Research
- Domain V – Participant Outreach

Within each Domain are multiple elements and standards that must be individually identified and satisfied by written policies and procedures or documentation of CCHS' process and practices.

[http://www.aahrpp.org/AAHRPP\\_Evaluation\\_Instrument\\_With\\_Regulations.htm](http://www.aahrpp.org/AAHRPP_Evaluation_Instrument_With_Regulations.htm)

# Cleveland Clinic Research Glossary of Terms

## **Belmont Report:**

[Document](#) issued in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which established an ethical framework for clinical research activities in the United States.

## **Basic Ethical Principles:**

**Respect for Persons:** the principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy (the ethical principle that refers to an individual's right to self-determination) and the requirement to protect those with diminished autonomy.

### **Beneficence:**

Ethical principle that attempts to provide benefits and to limit risk.

### **Justice:**

Ethical principle that applies fairness in the selection of subjects.

## **Biological Resources Unit (BRU):**

The [Biological Resources Unit](#) provides support in matters related to animal experimentation to all Cleveland Clinic scientists who use animals in their research projects.

## **Budget:**

The financial plan for a specific research activity or project includes all estimated costs to complete the project and anticipated revenues from all payment sources, including but not limited to corporate sponsors, governmental awards and third party payers as well as personnel, salaries, fringe benefits, subcontractor services, lease or purchase of equipment, space rental, space renovation costs, patient care costs, and consumable supplies.

## **Case Report Form (CRF):**

A printed, optical, or electronic document designed to record protocol-required information to be reported to sponsor on each trial subject.

## **Clinical Investigation:**

Any experiment that involves a test article and one or more human participants.

## **Code of Federal Regulations:**

Annually revised codification of general and permanent rules published in the *Federal Register*. Title 21, Parts 11, 50, 54, 56, 312, 314 and 812 pertain to human subject research.

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## **Conflict of Interest (COI):**

A **Conflict Of Interest** may exist when a CCF Staff member or employee, or a member of his or her immediate family or an entity directed or controlled by any of them, has an interest in (including relationships with) a non-CCF party—whether investment, compensation, or otherwise—that could be reasonably perceived as influencing his or her activities in patient care, research, administrative decisions, or business transactions for CCF. Cleveland Clinic maintains a comprehensive [conflict of interest program](#) for staff physicians, other employees, and trustees to assure a professional and commercial integrity in all matters. It is designed to ensure that all potential conflicts, including institutional conflicts, are transparent and properly addressed.

## **Contract:**

A contract is formed when two or more parties have a mutual intent to be entered into a binding and legally enforceable agreement with respect to an activity or project. A contract identifies the rights and responsibilities of each party.

## **Contract Research Organization (CRO):**

A contract organization engaged by a research sponsor to coordinate the management and performance of a sponsored research project and which may assume responsibility for certain regulatory obligations of the research sponsor under applicable federal regulations. Also see the definition of Academic Research Organization (ARO).

## **Declaration of Helsinki:**

Set of professional [guidelines](#) established by physicians of the World Medical Association to apply the principles of the Nuremberg Code to human experimentation. First released in 1964, with revisions in 1975, 1983, 1989, 1996, 2000, 2002 and 2004.

## **Department of Health and Human Services (DHHS):**

Is the United States government's principal [agency](#) for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves. The Department includes the NIH, CDC, FDA, HIS, HRSA, SAMHSA, AHRG, CMS (MEDICARE AND MEDICAID), ACF AND AOA.

## **Environmental Health and Safety (EHS):**

The mission of [Environmental Health and Safety](#) (EHS) is to create, promote, and maintain a safe and healthful environment for all individuals at the Clinic. Sections include: [Hazardous Chemicals](#), [Radiation Safety](#), [Fire Safety](#), [Ergonomics](#), [Biosafety](#), [Industrial Hygiene](#).

## **First Coast Service Options, Inc:**

The [organization](#) (AKA: Carrier and Fiscal Intermediary) responsible for processing Florida's Part A and Part B Medicare Claims.

# Cleveland Clinic Research Glossary of Terms

## **Food and Drug Administration (FDA):**

Promotes and protects the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use. FDA's regulatory approaches are as varied as the products it regulates. Some products -- such as new drugs and complex medical devices -- must be proven safe and effective before companies can put them on the market. The [FDA](#) requires clinical research trials to be conducted on new drugs and devices for which safety and effectiveness have not been proven.

## **Good Clinical Practice (GCP):**

Is the term coined by the pharmaceutical and medical device industries to encompass the federal regulations and industry accepted standards that govern clinical trials on humans conducted to support applications and subsequent amendments for approval by the U.S. Food and Drug Administration (FDA) of new drugs, biologics and medical devices. These regulations and standards apply to the conduct of the studies, record keeping, informed consent of subjects, collection of scientific data, and submissions of information needed in order for the FDA to make an evaluation to approve or disapprove the product. The FDA has a site specific to the [Good Clinical Practice in FDA Regulated Clinical Trials](#).

## **Health Information Portability and Accountability Act (HIPAA):**

The [Health Insurance Portability and Accountability Act](#) (HIPAA) of 1996 mandates significant changes in the legal and regulatory environments governing the provision of health benefits, the delivery and payment of healthcare services, and the security and confidentiality of individually identifiable, protected health information.

## **Human subject:**

*Human subject* means a living individual about whom an Investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. [45CFR46.102 (f)] Human Subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. [21CFR56.102 (23)(e)]. See [IRB policy-05](#).

## **Informed Consent:**

A form of written agreement between the investigator and subject to a research study based upon a full discussion with the investigator regarding the purpose, participation requirements, procedures involved, risks, benefits and alternatives.

## **Institutional Review Board (IRB):**

Established under federal regulations to protect the rights safety and welfare of research participants and to uphold the ethical principles for human research (Also known as the Research Ethics Committee at some institutions). CC employee may not conduct human based research if the CC IRB has not approved it. The [Cleveland Clinic IRB](#) has the authority to approve, require modifications to

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secure approval and disapprove all research activities overseen and conducted by the organization.

## **International Conference on Harmonisation (ICH) on GCP:**

[Guidance](#) developed with consideration of the current good clinical practices of the European Union, Japan and the United States, as well as those of Australia, Canada, the Nordic countries, and the World Health Organization (WHO). These principles have their origin in the Declaration of Helsinki, and are often adhered to in global clinical research trials. The [ICH Guideline for GCP](#) was published in the Federal Register 9 May 1997, making it an FDA guideline.

## **Investigational Drug Service from Pharmacy:**

The [Investigational Drug Service](#) provides assistance to investigators who conduct research involving investigational and approved medications at the Cleveland Clinic Foundation.

## **Investigational New Drug (IND):**

The investigational new drug (IND) application permits a sponsor to use an investigational drug in a clinical trial (human trial). During the clinical trial, an investigational drug is administered to humans and is evaluated for its safety and efficacy in treating, preventing, or diagnosing a specific disease or condition. An IND may be required when the principal intent of the investigational use of a drug is to develop information about the product's safety or efficacy. Contact the Center for Clinical Research [IND/IDE Office](#) prior to submitting an IND application.

## **Investigational Device Exemption (IDE):**

If a medical device has not received FDA approval (or has not yet been approved for a particular use), the manufacturer must generally obtain an "investigational device exemption" ("IDE") from the FDA to use the device in a clinical trial. IDE numbers are preceded with a "G" and have six positions, i.e., G123456. When the FDA grants a manufacturer an IDE for a device, the agency will assign a special identifier number and categorize the device as either a Category A or Category B device. Contact the Center for Clinical Research [IND/IDE Office](#) prior to submitting an IDE application. Refers to the regulations under 21 CFR 812.

**FDA Category A Device:** An experimental, new and innovative device for which "absolute risk" has not yet been established (i.e. the initial questions of safety and effectiveness have not yet been resolved). FDA has approved the device trial in order to establish the safety and effectiveness data. CMS may cover routine (or standard of care) costs associated with device trial, if the device is to be used for patients who have an immediately life threatening disease or condition, where there is a reasonable likelihood that death will occur within a matter of months, or in which premature death is likely without early treatment. The cost of the Category A device itself will not be covered.

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**FDA Category B Device:** An investigational, non-experimental device, often a modified version of a previously approved device. The device may be categorized by the FDA as Class I, II or III, depending upon the levels of risk associated with the device. Safety and effectiveness of earlier or *predicate* devices has been established

**Legally Authorized Representative (LAR):**

*Legally authorized representative* means an individual, judicial, or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. [21 CFR §50.3(l)] [45 CFR §46.102(c)]. Individuals chosen as the surrogate or proxy should be the highest in the following priority order: attorney-in-fact (under a Durable Power of Attorney for Health Care), legal guardian, spouse, majority of adult children, parents, majority of siblings. In the case of a legally authorized representative, the surrogate should be a person that is likely to understand the subject's situation and act in the subject's best interest. Additionally, the LAR should be given the opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research if such action appears in the subject's best interest. See [IRB policy -75](#).

**Minimal risk:**

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**National Institute of Health (NIH):**

The [National Institutes of Health](#) (NIH) is one of the world's foremost medical research centers. An agency of the Department of Health and Human Services, the NIH is the Federal focal point for health research. NIH is the steward of medical and behavioral research for the Nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.

**Nuremberg Code:**

Ten principles that address human experimentation, established by the judges at Nuremberg following the Nazi Doctors Trial. This document can be found on the Office of Human Subject Research [website](#).

**Office of Corporate Compliance (OCC):**

The Cleveland Clinic is committed to programs, policies and procedures to ensure that Cleveland Clinic and its affiliates (collectively "CCHS"), and their members, trustees, directors, officers, independent contractors and employees (collectively "employee" or "employees" as applicable) conduct activities in full compliance with applicable federal, state and local laws and ethical standards. In furtherance of this obligation, the Board of Trustees of CCHS (the "Board of Trustees") adopted "The Cleveland Clinic Corporate Compliance Program" (the "Program") in May of 1996. The Program restated many existing policies and procedures, and is intended to prevent and detect any violations of

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federal, state or local laws by CCHS. Each affiliate of CC is required either to apply the Program to its operations, or to adopt its own program to ensure compliance with applicable laws. <http://intranet.ccf.org/compliance/>

## **Office of General Counsel (OGC):**

Of the Cleveland Clinic is the Health System's Legal Department. It employs the attorneys and other legal support staff who are charged with the responsibility of advising the CCHS on legal matters on a day-to-day basis. Generally speaking the [Office of General Counsel](#) reviews all sponsored research agreements involving clinical research.

## **Office for Human Research Protections (OHRP):**

The [Office for Human Research Protections](#) (OHRP) provides leadership and oversight on all matters related to the protection of human subjects participating in research conducted or supported by the U.S. Department of Health and Human Services (HHS). OHRP helps ensure that such research is carried out in accordance with the highest ethical standards and in an environment where all who are involved in the conduct or oversight of human subjects research understand their primary responsibility for protecting the rights, welfare, and well being of subjects.

OHRP:

- Establishes criteria for and approves assurances of compliance for the protection of human subjects with institutions engaged in HHS-conducted or –supported human research,
- Provides clarification and guidance on involving humans in research,
- Develops and implements educational programs and resource materials, and
- Promotes the development of approaches to enhance human subject protections.

## **Office of Research Integrity (ORI):**

Oversees and directs Public Health Service (PHS) research integrity activities on behalf of the Secretary of Health and Human Services. Organizationally the [ORI](#) is located within the [Office of Public Health and Science](#) (OPHS) within the Secretary of Health and Human Services (OS).

## **Office of Sponsored Research and Projects (OSRP):**

The administrative arm of the Division of Clinical Research and the Lerner Research Institute. [OSRP](#) provides oversight of processes and procedures used to administer all sponsored research grants and contracts funded by corporations, federal, state, or local governments, private foundations, or CC internal sources. OSRP interfaces with sponsoring agencies or corporations and directs project development, contracting, pre and post award project management, project tracking, and project closeout and analysis.

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## **Phases of a Research Study:**

### **Phase 1 Study:**

Earliest phase of a drug development in which a limited number of human subjects are exposed to the test article. The objective of this phase of clinical trial is to establish a drug's safety and toxicity profile.

### **Phase 2 Study:**

Expands the numbers of patients exposed to the drug; initial collection of data to evaluate efficacy.

### **Phase 3 Study –**

Phase of study designed to demonstrate drug efficacy in research subject populations with specific disease indications, and to collect additional safety data in a larger cohort of subjects. These multicentered studies usually involve hundreds to thousands of subjects.

### **Phase 4 Studies:**

Post-marketing studies may be requested by the FDA to provide additional data, or are intended to expand labeling to other populations or other indications, or simply to market the drug in a variety of clinical settings.

## **Placebo:**

An inert substance that is intended to act as a comparator for the active drug in controlled clinical trials.

## **Principal Investigator (PI)**

### **(Responsible for overall conduct of study)**

Personnel, typically staff or scientist, employed by the Cleveland Clinic, who is responsible for carrying out the design, conduct, review and reporting of the project. The PI is also accountable for meeting the terms and conditions of a grant or contract. In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team.

## **Point of Care Testing (POCT):**

Any type of analytical patient testing performed on blood, urine or other specimen that takes place outside of the central clinical laboratory at or near the point of patient care (intensive care units, emergency departments, outpatient facilities or similar). The mission of the [POCT Compliance Council](#) (Office of Accreditation) is to provide healthcare professionals with the tools and latest information relevant to point of care (POC) through a specialized POCT program.

## **Protocol:**

Document that describes and directs how a clinical trial will be implemented.

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## **Research** *(as defined by funding source):*

Includes all research projects at CC that are separately budgeted and accounted for. It includes:

- Sponsored research-research and development projects that are sponsored by federal and non-federal agencies and organizations, including industry sources;
- Internal research- all research and development projects where internal sources fund the project (e.g., departmental funds).

## **Research Compliance:**

[Research Compliance](#) exists within the Office of Corporate Compliance and is responsible for providing information, training and support to those needed to meet the laws, regulations and policies governing research in the most efficient and effective manner training and support.

## **Responsible Conduct of Research (RCR):**

Includes many elements: the proper treatment of human or animal subjects, managing conflicts of commitment or interest, responsible peer review, the education of new scientists through mentoring, the management of data so as to preserve privacy and integrity, etc.

## **Risk/benefit ratio:**

The potential toxicity or harm compared to the potential for beneficial effects, usually used in reference to receiving an investigational drug, device or biologic.

## **Serious Adverse Event (SAE):**

A **SAE** is defined as any adverse experience occurring that results in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. See [IRB policy IRB-60](#).

## **Sponsored Research Contracts:**

Written agreements with external parties for support or performance of a research project or program. Contracts are distinguished from Grants for this purpose as agreements that may require a certain degree of review and negotiation between the parties to outline their respective rights and obligations for the performance of the research, while Grants are generally non-negotiable and are governed by Terms and Conditions that are imposed by virtue of acceptance of the award funding. Contracts are routed either to the Office of General Counsel (OGC), CCF Innovations (CCFI) or to both if the contract is a hybrid requiring review by both offices.

## **Standard Operating Procedure (SOP):**

SOPs briefly describe a topic's purpose, give staff contact information, and provide procedures to follow, usually including staff and investigator roles. Focusing on steps to accomplish a task, they give links to more detailed background information on policy and regulations. SOP's require annual review and sign off by those who follow them.

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## **Sub-investigator or Co-Investigator:**

The term Sub-Investigator (Sub-I) may include any other individual member of the research team. [21CFR 312.3] and is generally understood to mean those individuals engaged in the informed consent process or who will have a significant role in the design or conduct of the research.

## **Tissue Procurement:**

[Tissue Procurement](#) provides services to obtain specimens and biopsies as required by research study guidelines.

## **Tuskegee Study:**

An unethically conducted [study](#) from 1932 – 1972 examining the natural history and progression of untreated syphilis in black men in rural Alabama.

## **Voluntary:**

Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research study.