

<b>DEPARTMENT:</b> Clinical Operations Group – Research	<b>POLICY DESCRIPTION:</b> Research - Guiding Documents and Definitions
<b>PAGE:</b> 1 of 5	<b>REPLACES POLICY DATED:</b> 3/1/12, 9/1/13
<b>EFFECTIVE DATE:</b> February 22, 2019	<b>REFERENCE NUMBER:</b> COG.RSH.001 (formerly CSG.RSH.001)
<b>APPROVED BY:</b> Ethics and Compliance Policy Committee	

**SCOPE:** This policy applies to all Company-affiliated facilities (i.e., hospitals, surgery centers, physician practices, administrative offices, etc.).

**PURPOSE:** To provide the facility with a quick reference to the appropriate federal and local laws pertaining to clinical research as well as appropriate guidance. To provide consistent definitions of key terms (either specifically defined by, or consistent with, regulations) used across all research compliance policies in a single location for easy reference.

**POLICY:**

**A. Endorsed Guidance Documents**

1. The Belmont Report;
2. All current guidance of the DHHS Office of Human Research Protections;
3. All current guidance of the Food and Drug Administration;
4. All current guidance of the Office for Civil Rights pertaining to privacy and research;
5. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidance # E6(R1) Guideline For Good Clinical Practice (GCP) (May 1996);
6. World Medical Association’s Declaration of Helsinki (1989 Version only).

**B. Resolving Conflicts Between Laws, Guidance and These COG.RSH Compliance Policies**

1. Laws and regulations take precedence over guidance and policies.
2. When laws and regulations differ, the more conservative approach must be taken whenever possible to be compliant with all differing laws.
3. Any resolution inconsistent with compliance policies must involve the Corporate Responsible Executive for Clinical Research.
4. Any conflicts between laws (federal, State and local), guidance documents and these COG.RSH compliance policies must be brought to the attention of the Corporate Responsible Executive for Clinical Research.
5. The ultimate authority on resolving interpretation issues regarding these policies and guidance documents is the Corporate Responsible Executive for Clinical Research. The ultimate authority on resolving interpretation issues in matters of law is the legal department in consultation with the Corporate Responsible Executive for Clinical Research.

**C. Sponsoring Research Operations Outside The United States**

1. When a U.S. based Facility is a sponsor of research and such research is conducted outside of the United States, the Facility shall ensure the research performed in other countries meets equivalent levels of protection that would be required in its principal location, taking into account local laws and cultural context. Essentially, all policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate. Additionally, the Facility must adopt local policies specifically pertaining to how the Facility will:
  - a. Ensure appropriate expertise and knowledge of the country either through IRB membership or consultants;

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- b. Confirm the qualifications of the researchers and research staff for conducting research in that country;
- c. Ensure initial review, continuing review, and review of modifications/amendments occur as per local policy;
- d. Provide knowledge and guidance regarding local laws;
- e. Describe post-approval monitoring;
- f. Outline a process to handle complaints, non-compliance, and unanticipated problems involving risk to participants or others;
- g. Ensure a consent process is in place and addresses other language barrier issues;
- h. Ensure communication and coordination with local IRBs or other regional Ethics Committees when appropriate; and
- i. Provide for training and tracking of the Foreign Corrupt Practices Act.

#### D. Common Acronyms Used in the Policies

The following abbreviations and definitions are for use in the Clinical Operations Group– Research policies, COG.RSH.001 through COG.RSH.010.

CFR	Code of Federal Regulation
DHHS	The United States Department of Health and Human Services
FDA	The United States' Food and Drug Administration
FWA	Federal-Wide Assurance
GCP	The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)'s Guidance Entitled "E6: Good Clinical Practices)
HDE	Humanitarian Device Exemption
HIPAA	The Health Insurance Portability and Accountability Act of 1996.
HUD	Humanitarian Use Device
IBC	Institution Biosafety Committee
IDE	Investigational Device Exemption
IND	Investigational New Drug
NIH	DHHS's National Institutes of Health
OHRP	The Office of Human Research Protections under DHHS
PHI	Protected Health Information as defined by HIPAA
RDRC	Radioactive Drug Research Committee

#### E. Definitions of Common Terms Used in the Policies

**Clinical Investigation:** Defined at 21 CFR 56.102(c) as "*Clinical investigation* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application

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for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies.

**Engaged In Research:** The facility adopts the criteria put forth by the OHRP guidance document entitled “Guidance on Engagement of Institutions in Human Subjects Research” published October 16, 2008 and its successors. Please read the guidance document for examples and criteria.

**Exempt Research:** Research determined to be research with human subjects that has been statutorily exempt from the regulations based on meeting certain criteria set forth in 45 CFR 46.104. Clinical Investigations cannot be Exempt.

**External IRB:** An Institutional Review Board that is not under the operational control of the Facility. An External IRB may or may not be in the same local community as the Facility.

**Human Protections Administrator:** The contact person for any research-related issues pertaining to human subject protection. If the Facility operates an IRB, this individual is usually the IRB manager/administrator. If the Facility does not operate an IRB, this person is usually the primary person who interfaces with the External IRB(s). This person can also be the Institutional Official. This person is to be listed as the Human Protections Administrator on any Federal-Wide Assurance with DHHS.

**Human Subject:** For purposes of FDA governed studies, a “human subject” is defined at 21 CFR 56.102(e) as meaning “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.” For all other purposes, a human subject is defined by the OHRP definition at 45 CFR 46.102(e) as meaning “a living individual about whom an investigator (whether professional or student) conducting research (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens or (2) obtains, uses, studies, analyzes, or generates identifiable private information identifiable private information or identifiable biospecimens.”

**Humanitarian Device Exemption (HDE):** An HDE is submitted for FDA review and approval by a manufacturing company/company/sponsor. The purpose of the HDE is, to the extent consistent with the protection of the public health and safety and with ethical standards, to encourage the discovery and use of devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect fewer than 8,000 individuals in the United States. Although a device may have HDE approval, it still falls under the category of an HUD.

**Humanitarian Use Device (HUD):** An HUD is a device that is (1) intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year; (2) the device would not be available to a person with such a disease or condition unless the exemption is granted; (3) no comparable device (other than a device that has been granted such an exemption) is available to treat or diagnose the disease or condition; and (4) the device will not expose patients to an unreasonable or significant risk of illness

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or injury, and the probable benefit to health from using the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

**Institutional Official:** The individual designated to authorize the necessary administrative or legal actions pertaining to the protection of human subjects at the Facility. This person would be listed as the Signatory Official on any Federal-Wide Assurance with DHHS.

**Internal IRB:** An Institutional Review Board that is under the operational control of the Facility.

**Investigational Device Exemption (IDE):** Devices under investigation and required to adhere to the FDA regulations.

**Principal Investigator:** An individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

**Research:** Defined at 45CFR46 as meaning “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Clinical Investigations are one type of research. 45 CFR 46.101(l) has certain research activities excluded from this definition for regulatory purposes.

**Routine Costs (in Clinical Trials):** CMS defines routine costs in clinical trials to include: 1) Items or services that are typically provided absent a clinical trial (e.g., conventional care); 2) Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and 3) Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for the diagnosis or treatment of complications.

**Second Institution:** This is an FDA-defined term describing a facility which is not engaged in the research but administers a test product (i.e., an investigational drug, device or biologic) subsequent to the routine care they provide. Specifically, the subject’s (now patient’s) treatment or hospitalization is not related to the research, the admission is medically necessary, and the admitting physician determines that the subject (now patient) should continue on the test product. In this case, the facility is providing incidental medical care and is not participating as a research site.

**Signatory Official:** See Institutional Official

**Sponsor:** A person or other entity that initiates a clinical investigation but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that

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it has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered investigators.

**Standard of Care:** See Usual Care

**Unrelated Study:** A study in which a Facility patient is participating in but is unrelated to their care at the facility and such participation does not alter their care at the Facility.

**Usual Care:** Non-investigational care given to a patient because their medical condition warrants it. This includes items and services typically provided to a patient absent a research protocol (noting that non-investigational treatment for a research-related injury because their medical condition warrants it is considered usual care). Usual care does not include protocol-driven procedures that are in addition to, instead of, or at a frequency different from the care given (or that would be given) absent a protocol.

**REFERENCES:**

1. IRB Related Definition and Common Acronyms Policy, [COG.IRB.001](#)
2. Clinical Operations Group Research Policies in the COG.RSH series (COG.RSH.001 through COG.RSH.010)