DEPARTMENT: Clinical Operations Group - Research	**POLICY DESCRIPTION:** IRB Related Definitions and Common Acronyms
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EFFECTIVE DATE: February 22, 2019	**REFERENCE NUMBER:** COG.IRB.001(formerly CSG.IRB.001)
APPROVED BY: Ethics and Compliance Policy Committee	

SCOPE: This policy applies to all Company-affiliated facility-run Institutional Review Boards (IRBs).

PURPOSE: To provide consistent definitions of key terms (either specifically defined by, or consistent with, regulations) used across all IRB compliance policies in a single location for easy reference.

POLICY: The following abbreviations and definitions are for use in the Institutional Review Board policies, COG.IRB.001 through COG. IRB.011.

CFR	Code of Federal Regulations
DHHS	Unites States Department of Health and Human Services
FDA	United States' Food and Drug Administration
HIPAA	The Health Insurance Portability and Accountability Act of 1996
IRB	Institutional Review Board
NIH	United States' National Institutes of Health
OHRP	DHHS's Office for Human Research Protections
PHI	Protected Health Information
UPIRSO	Unanticipated Problems Involving Risk To Subjects Or Others

DEFINITIONS:
The following definitions apply to the compliance policies in the COG.IRB series. Additional definitions may be found in the Guiding Documents and Definitions Policy, COG.RSH.001.

Assent: A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Adverse Event (AE): Any untoward occurrence in a patient or clinical investigation subject which does not necessarily have to have a causal relationship with their participation in the study. Adverse Drug Experiences and Adverse Drug Reactions may be Adverse Events (AEs) as may abnormal lab findings, symptoms or disease concurring with the research. Adverse events may also be non-medical in nature such as economic or social harms.

Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

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 Food Drug and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Food Drug and Cosmetic 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 for a research or marketing permit. The term does not include experiments that must meet the provisions of 21 CFR 58, regarding nonclinical laboratory studies."

Clinical Investigator: Any listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects.

Conflict of Interest: A conflict of interest exists when the designated official(s) or IRB reasonably determines that a non-research interest (*i.e.*, a significant financial interest or personal relationship) could directly and significantly affect the design, conduct, or reporting of research activity, consequently, such conflicts may bear directly on issues of human subject protection. Conflicts of interest can be actual, potential or perceived.

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 subsequent successors.

Expedited Review: Both the FDA and OHRP have established and published in the *Federal Register* a list of categories of research that may be reviewed by the IRB through an expedited review procedure. No other non-exempt research with human subjects can be reviewed through this procedure.

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.

Federal Wide Assurance (FWA): A formal written, binding commitment that is submitted to OHRP in which an institution promises to comply with DHHS regulations governing the protection of human subjects in research. An FWA is only required for an institution that is engaged in the review and approval process for DHHS conducted or supported (*i.e.*, federally- funded) human research. Terms of Assurance can be accessed at: https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/fwa-protection-of-human-subjecct/index.html.

Fetus: The product of conception from implantation until delivery.

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

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(f) 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 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 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.

Informed Consent: The knowing consent of a human subject, or his/her legally authorized representative, who is able to exercise free power of choice without undue inducement or any form of force, fraud, deceit, duress or other form of constraint or coercion.

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

Investigational New Drug (IND): New drugs/biologics or new uses for approved drugs/biologics under investigation that require adherence to the FDA regulations.

Institutional Review Board (IRB): An appropriately constituted group that the facility's governing body has formally designated to review and monitor research involving human subjects to protect the rights and welfare of the subjects. The IRB also provides for oversight and monitoring of such protections. In accordance with the Common Rule, HIPAA Privacy Standards, the FDA regulations and applicable State regulations, the IRB has the responsibility for approving, requiring modification (to secure approval) or disapproving research.

IRB Approval: The determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

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.

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Minimal Risk in Prisoner Research: The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Minor Changes: Changes in research not affecting the relationship of likely subject risk to benefit relied upon to approve the protocol; or the rights, safety, or welfare of the human subjects involved in the investigation.

Office for Human Research Protections (OHRP): A division of the DHHS which is responsible for overseeing human subject research subjects protection functions and related functions where research involves the use of human subjects. It includes four sections: Office of the Director, Division of Policy and Assurance, Division of Compliance Oversight and Division of Education and Development. The OHRP website is located at: http://www.hhs.gov/ohrp/.

Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research.

Parent: A child's biological or adoptive parent.

Pregnancy: The period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

Principal Investigator (PI): 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.

Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and detained pending arraignment, trial, or sentencing.

Protocol: The formal design or plan of an experiment or research activity. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

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

Serious Adverse Events (SAEs): An adverse event that results in any one of the following: 1) Death; 2) Life Threatening condition; 3) Hospitalization (or prolongation of an existing hospitalization); 4) Congenital anomaly; 5) Persistent or significant disability/incapacity; or 6) the need for intervention to prevent any one of the above criteria. SAEs have very prompt reporting requirements to the Sponsor of research as well as possibly to the IRB.

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

Sponsor-investigator: An individual who both initiates and actually conducts, alone or with others, a clinical investigation, *i.e.*, under whose immediate direction the test article is administered or dispensed to, or used involving a subject. The term does not include any person other than an individual, *e.g.*, it does not include a corporation or agency. The obligations of the sponsor-investigator under federal regulations include both those of the sponsor and those of an investigator.

Test Article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to relevant regulations.

Unanticipated Problem Involving Risks To Subjects or Others (UPIRSO): A problem that is all three 1) unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; 2) related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and 3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Waiver of Authorization to Release Protected Health Information (PHI): Elimination of the requirement to obtain a HIPAA compliant research authorization from each research subject to disclose PHI. This is not the same thing as Waiver of Informed Consent or Waiver of Documentation of Informed Consent and must be evaluated separately.

Waiver of Documentation of Informed Consent: A waiver of the requirement to obtain written documentation of informed consent. This is not synonymous, and not to be confused, with a Waiver of Informed Consent, which has different criteria.

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Waiver of Informed Consent: A waiver of all or some of the requirements of informed consent. This may only be authorized by an IRB. This is not synonymous, and not to be confused with, a Waiver of Documentation of Informed Consent, which has different criteria.

REFERENCES:

1. Guiding Documents and Definitions Policy, COG.RSH.001
2. Clinical Operations Group Research policies in the COG.IRB series: COG.IRB.001 – COG.IRB.011