1.0 Purpose:

1.1 This policy defines the applicability of the United States Code of Federal Regulations, 21 CFR Part 812 - Investigational Device Exemptions (IDE) and the procedures the Human Research Protections Program (HRPP) requires an investigator to follow when applying for and conducting a device investigation.

1.2 All non-exempt human subjects research and clinical investigations reviewed and approved by the IRB must comply with FDA regulations for devices intended for human use.

1.3 The investigator working with devices must be knowledgeable and compliant with these regulations.

2.0 Definitions:

2.1 **Research** (45 CFR 46.102(l) - A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

2.2 **Human Subject** (45 CFR 46.102(e) - 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

- *Intervention* includes both physical procedures by which data or biospecimens are gathered (i.e., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- *Interaction* includes communication or interpersonal contact between investigator and subject.
- *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (i.e., medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

2.3 **Subject -** A human who participates in an investigation, either as an individual on whom or on whose specimen and investigational device is used or as a control. A subject may be in normal health or have a medical condition or disease. [21 CFR 812.3(p)]

2.4 **Investigation -** Research involving one or more subjects to determine the safety and efficacy of a device. [21 CFR 812.3(h)]

2.5 **Sponsor -** A person who initiates, but does not actually conduct, the investigation. The investigational device is administered, dispensed, or used under the direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. [21 CFR 812.3(n)]

2.6 **Sponsor-investigator -** An individual who both initiates and conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed or used. The term does not include any person other than an individual. The obligations of a sponsor-investigator include those applicable to an investigator and a sponsor. [21 CFR 812.3(o)].

2.7 **Medical Device -** An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component part or accessory, which is:

- recognized in the official National Formulary or the United States Pharmacopoeia, or any supplement to them;
- intended for use in the diagnosis of disease, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes [21 U.S.C. 321(h)].

2.8 **Custom Device –** A device that:

- Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order or an individual physician or dentist;
- Is not generally available to, or generally used by, other physicians or dentists;
- Is not generally available in finished form for purchase or for dispensing upon prescription;
- Is not offered for commercial distribution through labeling or advertising; and
- Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

2.9 **Investigational Device -** A device, including a transitional device that is the object of an investigation.

2.10 **Transitional Device –** A device that was regulated by the FDA as a new drug before May 28, 1976.

3.0 Procedure:

3.1 Investigators submit all required protocol-related documents via the Research Application process to the IRB for review at a convened meeting.

3.2 When the research involves a device, the investigator is required to provide the IRB with sufficient information about the device, including FDA status, to assess the risks and potential benefits to subjects. Procedures for receipt and disposition of the devices are to be included in the protocol.

3.2.1 If the IRB determines that an IDE is needed, the investigator must provide the IRB with a copy of the letter from the FDA with the IDE assignment for the clinical investigation under review or a letter from the FDA stating that an IDE is not needed.

3.2.2 To prevent situations where researchers begin studies that require regulatory authority approval, such as an IDE, before the FDA has issued a number, the IRB will evaluate whether the IDE number is valid. Validation will be done by determining that an approval number (IDE) granted by the FDA matches the sponsor protocol, or communication from the sponsor, or communication from the FDA.

3.2.3 In the case of an investigator-held IND, the number should match information provided by the government regulatory agency.

3.2.4 IRB approval for any clinical investigation of an investigational device will not be given unless the IDE is in effect.

3.3 Investigations of FDA-approved devices off-label or non-FDA approved devices intended for human use are considered “investigational” and subject to the requirements of the IDE regulations 21 CFR part 812 when being evaluated for safety and effectiveness, unless exempt. **Exempt studies include**:

3.3.1 Consumer preference testing, testing of a device modification, or testing of two or more devices in commercial distribution if the testing does not collect safety or effectiveness data or put subjects at risk [21 CFR 812.2(c)(4)]

3.3.2 Studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling. [21 CFR 812.2(c)(1)(2)]

3.3.3 Diagnostic device studies (e.g., in vitro diagnostic studies) under certain circumstances. [21 CFR 812.2(c)(3)]

3.4 IDE exempt studies that are being conducted to collect data to support either a clinical investigation or a marketing application must comply with the requirements for IRB review and informed consent.

3.5 As part of the IRB review, the IRB categorizes the investigation as either “significant risk” (SR) or “non-significant risk” (NSR).

3.5.1 Significant Risk Device:

3.5.1.1 Is intended as an implant and presents a potential for serious risk to the health, safety or welfare of a subject;

3.5.1.2 Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or

3.5.1.3 Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

3.5.1.4 Otherwise presents potential for serous risk to the health, safety, or welfare of a subject.

3.5.2 The sponsor generally makes the determination of risk; however the IRB is responsible for making the determination when the sponsor has not submitted an IDE application to the FDA. The IRB bases the risk on the proposed use of the device in the investigation, and not on the device alone. If the proposed use of the device involves a procedure, i.e., a surgical procedure, the IRB considers the potential harm that could be caused by the procedure as well as the device.

3.5.3 The IRB reviews information such as reports of prior investigations conducted with the device, the proposed investigational plan, the sponsor's risk assessment and the rationale used in making its determinations, the description of the subject selection criteria, and monitoring procedures that will be used.

3.5.4 A non-significant risk device is one that does not meet the definition for a significant risk study and the risk to the subjects is determined to be minimal in accordance with 21 CFR 56.102(i). IRB approval is still required.

3.5.5 If a protocol is originally submitted as a NSR device and the IRB determines the device is SR, the study may not be approved until the FDA has reviewed and either granted the IDE or determines that the device is, in fact, NSR. The investigator and sponsor are notified of the IRB decision.

3.5.6 Once an IDE is obtained by the sponsor, the IRB review will continue.

3.6 Non-significant Risk Device Investigations:

3.6.1 If approved by the IRB as a NSR device, the sponsor and investigator must comply with "abbreviated" IDE requirements as defined in 21 CFR 812.2(b), and informed consent regulations. The abbreviated requirements include the following:

3.6.1.1 The device must be labeled appropriately. The label must include information on the manufacturer, packer or distributor, the quantity of contents, if appropriate and the following statement: "CAUTION – Investigational Device. Limited by Federal (or U.S.) law to investigational use." The label shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings and precautions. The labeling may not contain false or misleading statements that imply the device is safe or effective for the purpose investigated.

3.6.1.2 The investigator must obtain and maintain IRB approval after presenting a brief explanation of why the device is not SR.

3.6.1.3 Ensure that each investigator participating in the investigation obtains and documents informed consent from each subject, unless documentation is waived by the IRB.

3.6.1.4 Comply with all monitoring requirements and reporting of unanticipated adverse events.

3.6.1.5 Maintain accurate, complete and current records relating to participation in the investigation which include:

3.6.1.5.1 All correspondence with other investigators, the IRB, the sponsor, monitors, or FDA, including reports;

3.6.1.5.2 Records of receipt, use or disposition of a device;

3.6.1.5.3 Records of each subject's case history and exposure to the device (dates, times), informed consent documents, written concurrence of a licensed physician, all relevant observations including adverse events (whether anticipated or unanticipated), results of diagnostic tests, etc.;

3.6.1.5.4 The protocol, amendments, documentation of dates and reasons for deviations from the protocol, if any;

3.6.1.5.5 Any other records that the FDA requires to be maintained by regulation or specific requirement;

3.6.1.6 Prepare and submit complete, accurate and timely reports to include:

3.6.1.6.1 Unanticipated adverse events;

3.6.1.6.2 Withdrawal of IRB approval;

3.6.1.6.3 Progress reports to the sponsor, monitor and reviewing IRB;

3.6.1.6.4 Deviations from the investigational plan;

3.6.1.6.5 Use of a device without obtaining informed consent (within 5 working days after the use occurs);

3.6.1.6.6 Final report within 3 months following termination or completion of the investigation;

3.6.1.6.7 Additional reports requested by the IRB or FDA about any aspect of the investigation.

3.7 Significant Risk Device Investigations:

3.7.1 If approved as a significant risk device investigation, the investigator must comply with the human subject protection (informed consent and additional safeguards for children in research), IRB and IDE regulations. (See the attached checklist)

3.7.2 Investigator Requirements:

3.7.2.1 Assure IRB review and approval by maintaining all IRB documentation at the study site, including initial review, continuing review, amendments, adverse event reports, protocol deviations, and any other IRB correspondence.

3.7.2.2 Ensure that co-investigators and research staff are qualified by training and experience.

3.7.2.3 Conduct the study according to the signed investigator statement, protocol and all applicable regulations. Report violations/deviations to the IRB, protect the rights, safety and welfare of subjects, obtain informed consent in accordance with provisions in 21 CFR 50, promptly report any adverse events in accordance with IRB requirements and maintain all applicable documentation.

3.7.2.4 Maintain adequate and accurate case histories on each participant in the study including documentation of all source data, progress notes, concomitant medications recorded, subject eligibility documented, case report files, appropriately documented consent forms, documentation the informed consent was obtained prior to study procedures, and the subject was given a copy of the signed and dated consent form, and signature and date of staff obtaining data.

3.7.2.5 Ensure control of the investigational device:

3.7.2.5.1 The device is only administered to those subjects enrolled in the study and under the investigator or designee's supervision.

3.7.2.5.2 Maintain adequate record of receipt and shipment of investigational device.

3.7.2.5.3 Assure return of all unused investigational devices.

3.7.2.5.4 Maintain written records of any disposition of the device.

3.7.2.6 Permit FDA officers to access, copy and verify any records or reports.

3.7.2.7 Maintain all pertinent correspondence between the sponsor, monitor or FDA (if applicable).

3.7.2.8 If performed under Good Clinical Practice (GCP) guidelines

3.7.2.8.1 Maintain copies of pertinent laboratory certifications, and normal laboratory values.

3.7.2.8.2 Maintain a signature log of staff signatures/initials.

3.7.3 Sponsor Requirements:

3.7.3.1 All correspondence with the FDA is maintained including the original IDE application, the FDA letter of no objection, amendments, IDE safety reports, correspondence with investigators, annual reports ensuring all the protocol, protocol amendments, additions of new investigators, etc.

3.7.3.2 Select principal investigators (PI) qualified by training and experience.

3.7.3.3 Ship investigational products only to investigators participating in the study.

3.7.3.4 Maintain complete and accurate records involving investigator's financial disclosure.

3.7.3.5 Maintain a file with signed Investigator agreements (IA), CVs, financial disclosures for PI and anyone else on the IA, and clinical protocols.

3.7.3.6 Ensure ongoing monitoring of investigations.

3.7.3.6.1 Select monitors by training and experience.

3.7.3.6.2 Ensure proper monitoring.

3.7.3.6.3 Ensure PI compliance or discontinue shipments of the investigational device.

3.7.3.6.4 Review and evaluate device safety and effectiveness.

3.7.3.6.5 Discontinue investigation within 5 working days when unreasonable and significant risk to subject are identified.

3.7.3.7 Keep each investigator informed of new observations discovered by or reported to the sponsor on the investigational product.

3.7.3.8 Permit FDA officer to access, copy and verify any records or reports made by the investigator.

3.7.3.9 Maintain all pertinent correspondence with investigators (enrollment numbers, adverse events, financial information and any changes in financial information).

3.7.3.10 Maintain all correspondence with monitors and FDA (if applicable).

3.8 Humanitarian Use Devices (HUD):

3.8.1 HUDs with approved Humanitarian Device Exemptions (HDEs) may be used for the FDA-approved indication only with approval of the IRB. The IRB may vote to allow continuing review to be conducted following the

expedited review procedure, as long as the HUD is used within the scope of its approved labeling. The FDA does not consider the use of an HUD within its approved labeling to be research.

3.8.2 When HUDs are being evaluated for safety and effectiveness beyond the scope of the FDA-approved HDE indication, they are subject to the requirements of device investigations as noted above.

3.9 Custom Devices:

3.9.1 Custom devices made in a specific form for a given patient on the order of a physician or dentist as part of their professional practice are not subject to the requirements for device investigations **unless** the devices are being evaluated for safety and effectiveness. In such cases, custom devices are subject to the requirements of device investigations as noted above.

3.10 Non-FDA Approved Devices Used as a Tool to Study Human Physiology:

3.10.1 Non-FDA approved devices used in research to study human physiology are not subject to the 812 IDE regulations, but must meet the criteria for NSR devices to be used in human subjects. When the device is electrically powered, the device must also be evaluated for electrical safety by the Biomedical Engineering department.

3.11 Non-Hospital Inventory FDA-Approved Medical Devices Used for monitoring or Data Collection:

3.11.1 Commercially available FDA-approved medical devices used in research according to the FDA-approved labeling are not subject to the 812 IDE regulations, but must meet the same hospital safety standards as medical devices being used for patient care..

4.0 Documentation:

4.1 The HHC HRPP office will maintain all records related to the implementation of this policy, electronic communications and notifications to investigators, funding or regulatory agencies, etc.

4.2 Records will be archived for a period of at least six (6) years following the termination or completion of the research activities.

5.0 References:

5.1 21 CFR 50 – *Protection of Human Subjects*

5.2 21 CFR 56 – *Institutional Review Boards*

5.3 21 CFR Part 812 – *Investigational Device Exemptions*

5.4 FDA Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors - Frequently Asked Questions About Medical Devices (January 2006) http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf

5.5 FDA Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors - Significant Risk and Nonsignificant Risk Medical Device Studies (January 2006) http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

5.6 Institutional Review Board Management and Function, Bankert, E. A., Amdur, R. J., 2nd Edition, 2006

6.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
01	EHP	7/1/11	Conversion to new policy template; significant expansion of policy New Issue
02	CLB	3/15/20	General review. Expanded Section 3.2; updated definitions and regulatory citations.

Element I.7.A., I.7.B.