Obtaining and Maintaining an Investigational Device Exemption (IDE)

1. BACKGROUND:

The Food and Drug Administration (FDA) medical device regulations establish specific responsibilities of sponsors for ensuring (1) the proper conduct of research for submission to the FDA, and (2) the protection of the rights and welfare of subjects involved in this research.

A DF/HCC Investigator who sponsors device research may be required to hold and maintain an Investigational Device Exemption (IDE). Additional information on IDE Application requirements can be found on the FDA website.

2. ASSOCIATED DF/HCC POLICIES:

2.1. RCO-100

3. DEFINITIONS:

3.1.1. **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 (1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) 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. Investigational device means any device, including a transitional device, which is the object of an investigation.

3.1.2. **Investigation:** A clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

3.1.3. **Investigational Device Exemption (IDE):** Sponsors and investigators of certain device studies are allowed to use an investigational device in a clinical study in order to collect safety and effectiveness data. The exemption only applies to investigations in which 510(k) products are being used in accordance with the labeling cleared by the FDA.

3.1.4. **IDE Number:** This is generally a 6-digit number (ex. 060025) beginning with a letter (for example: G) that the FDA assigns the investigational device being used in a specific clinical trial. It references the product(s) used under a specific IDE application. This number must be referenced on all correspondence to the FDA.

3.1.5. **Significant risk (SR):** Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- 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
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

3.1.6. **Non-significant risk (NSR):** A NSR device study does not meet the definition for a SR device study. The sponsor must comply with the abbreviated IDE requirements.

4. PROCEDURE:

4.1. Determination of Risk

4.1.1. The sponsor of an investigational device study is responsible for the initial risk determination and presenting it to the Institutional Review Board (IRB). The risk determination should be based on the proposed use of a device in an investigation and not on the device alone.

4.1.2. The IRB must review the sponsor's determination for every investigational medical device study and modify the determination if the IRB disagrees with the sponsor.

4.1.2.1. If the FDA has already made the risk determination for the study, the agency's determination is final.

4.1.3. For assistance with risk determination, the FDA Office of Device Evaluation (ODE) should be contacted. Correspondence with the ODE should be made in writing and include:

- A request for a written response from the ODE
- A description of the device
- The clinical protocol or detailed summary of the clinical protocol including the potential risks to subjects
- Rationale for initial risk determination by the sponsor / Principal Investigator

4.1.4. The sponsor's risk determination submission must include an investigational plan comprised of:

- Purpose: The name and intended use of the device and the objectives and duration of the investigation.

- Protocol: A written protocol describing the methodology to be used and an analysis of the protocol demonstrating that the investigation is scientifically sound.
- Risk analysis: A description and analysis of all increased risks to which subjects will be exposed by the investigation; the manner in which these risks will be minimized; a justification for the investigation; and a description of the patient population, including the number, age, sex, and condition.
- Description of device: A description of each important component, ingredient, property, and principle of operation of the device and of each anticipated change in the device during the course of the investigation.
- Monitoring procedures: The sponsor's written procedures for monitoring the investigation and the name and address of any monitor.
- Labeling: Copies of all labeling for the device.
- Consent materials: Copies of all forms and informational materials to be provided to subjects to obtain informed consent.
- IRB information: A list of the names and locations of all IRBs that have been or will be asked to review the investigation and a certification of any action taken by any of those IRBs with respect to the investigation.
- Other institutions: The name and address of each institution at which a part of the investigation may be conducted.

4.2. **Responsibilities and Reporting - Significant Risk Device Studies (SR)**

4.2.1. SR device studies must be conducted in accordance with the full IDE requirements within and may not commence until 30 days following sponsor's submission of an IDE application to the FDA.

4.2.2. The sponsor must submit an IDE application to the FDA and obtain the agency's approval of the study.

4.2.3. The sponsor must advise its investigators about the SR status and obtain their agreement to comply with the applicable regulations governing such studies. Sponsors should provide the IDE number and/or a copy of the IDE approval letter to the IRB when requested. All communications with investigators are maintained in the Sponsor Regulatory File.

4.2.4. Sponsors may send their SR device study to an IRB for review before the IDE application is approved by the FDA. However, the FDA cautions that an SR device study may not begin until the FDA approves the IDE.

4.2.5. Once an IDE application is approved, the following requirements must be met in order to conduct the investigation in compliance with the IDE regulation:

- Labeling: The device must be labeled in accordance with the labeling provisions of the IDE regulation and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use." A copy of the approved label and all updates are maintained in the Sponsor Regulatory File.

- Distribution: Investigational devices can only be distributed to qualified investigators. Records for distribution are maintained in the Sponsor Regulatory File.

- Informed Consent: The sponsor will provide a template of the informed consent document to each investigator. The investigator will obtain approval from their local IRB. Any changes to the informed consent document will be reviewed and consideration given to updating the overall consent for the trial. This assessment must be maintained as an official record. All communications and informed consent documents are maintained by the sponsor in the Sponsor Regulatory File. Each subject must be provided with and sign an informed consent document before being enrolled in the research.

- Monitoring: All investigations must be properly monitored, as outlined in the sponsor developed monitoring plan that was submitted to and approved by the FDA, to protect the human subjects and assure compliance with approved protocols.

- Prohibitions: Commercialization, promotion, and misrepresentation of an investigational device and prolongation of the study are prohibited.

- Records and Reports: Sponsors and investigators are required to maintain specified records and make reports to investigators, IRBs, and the FDA.

4.2.6. Once an IDE is in effect, the sponsor must adhere to the following periodic IDE submission requirements set by the FDA. The local IRB must receive and review all information submitted to the FDA.

Type	Description	Requirements
IDE Supplement	Changes in investigational plan that are likely to have significant effect on the scientific soundness of the research design and/or validity of the data resulting from the research, such as: changes in indication; changes in type or nature of study control; changes in primary endpoint;	Must be submitted prior to implementation

	changes in method of statistical evaluation; early termination; expanding the research by increasing the number of investigational sites or number of subjects.	
	Developmental changes / changes to the basic principles of operation of a device.	Must be submitted within 5 working days of the change.
	Changes in clinical protocol that do not affect the validity of the data or the risk to benefit relationship in the approved protocol, scientific soundness of the investigational plan or the safety and welfare of the subjects. Examples of these types of changes include modifications of inclusion/exclusion criteria; increasing frequency of data collection; inclusion of additional observations or measurements; and modifying secondary endpoints.	Must be submitted within 5 working days of the change.
	New facilities	May be submitted at one time or at 6 month intervals.
Deviations	Informed consent not obtained	Must be submitted within 5 working days of learning of the occurrence.
	All other prospective deviations	Must be submitted prior to the protocol change or deviation if it affects study integrity or subject safety.
Safety	Unanticipated Adverse Effect Reports	Must be submitted within 10 working days of receiving notification. Refer to www.fda.gov/medwatch
Routine Reporting	Current investigator list	Must be submitted at 6 month intervals.
	Progress report	Must be submitted annually.
	Financial disclosure information	Must be submitted at the time of change and for one (1) year following study completion.
	Final report	Must be submitted within six (6) months of study completion
Termination	Withdrawal of IRB approval	Must be submitted within 5 working days of receiving the withdrawal notice from the IRB.
	Recall of device	Must be submitted within 30 days of occurrence.
	Study termination due to unreasonable risk	Must be submitted within five (5) working days of study termination and no later than fifteen (15) working days after receiving notice of effect.
	Study completion notification	Must be submitted within 30 days of study completion.

4.3. **Responsibilities - Nonsignificant Risk Device (NSR)**

4.3.1. If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination and should provide any other information that may help the IRB in evaluating the risk of the study (e.g. a description of the device, reports of prior investigations with the device, the proposed investigational plan, subject selection criteria, and other information the IRB may need).

4.3.2. NSR device studies do not require an IDE application to be approved by the FDA.

4.3.2.1.1. An NSR device study may be initiated at the institution without prior FDA approval as long as the IRB has reviewed and approved the study.

4.3.2.1.2. Sponsors and IRBs do not have to report IRB approval of an NSR device study to the FDA.

4.3.2.1.3. If an IRB determines that a device is a significant risk device (SR), and the sponsor had proposed that the IRB consider the device not to be significant risk device, the sponsor shall submit to the FDA a report of the IRB's determination within five (5) working days after the sponsor learns of the IRB's determination.

4.3.3. The sponsor also must comply with the following requirements for NSR device studies:

- Labeling: The device must be labeled in accordance with the labeling provisions of the IDE regulation and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use" A copy of the approved label and all updates are maintained in the Sponsor Regulatory File.

- IRB Approval: The sponsor must obtain and maintain Investigational Review Board (IRB) approval throughout the investigation as a nonsignificant risk device study.

- Informed Consent: The sponsor will provide a template of the informed consent to each investigator. The investigator will obtain approval from their local IRB. Any changes to the informed consent should be reviewed and consideration given to updating the overall consent for the trial. This assessment must be maintained as an official record. All communications and consents are maintained by the sponsor in the Sponsor Regulatory File. The sponsor must assure that investigators obtain and document informed consent from each subject.

- Monitoring: All investigations must be properly monitored, as outlined in the Sponsor developed monitoring plan that was submitted to and approved by the FDA, to protect the human subjects and assure compliance with approved protocols.

- Records and Reports: Sponsors are required to maintain specific records and make certain reports as required by the IDE regulation.

- Investigator Records and Reports: The sponsor must assure that participating investigators maintain records and make reports as required.

- Prohibitions: Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited.

4.4. **Ensuring Safety for both SR and NSR research**

4.4.1. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects must terminate all investigations or parts of the investigations presenting that risk as soon as possible for SR and NSR trials.

4.4.1.1. Termination must occur no later than five (5) working days after the sponsor makes this determination and no later than fifteen (15) working days after the sponsor first received notice of the effect.

4.4.2. A sponsor may not resume a terminated investigation without IRB approval. If a non significant risk (NSR) study was terminated for unanticipated adverse device effects, the sponsor must also obtain FDA approval to continue.

4.5. **Responsibilities - IDE Exempt Device Studies:**

4.5.1. IRB submission of Sponsor risk determination is required.

4.5.2. Studies exempt from the IDE regulation include:
- The device must be used in accordance with its labeling;
- If it is a diagnostic device, it must comply with the labeling requirements in §809.10(c)

4.5.3. Consumer preference testing, testing of a modification, or testing of a combination of devices if the device(s) are legally marketed device(s), that is, the devices have an approved PMA, cleared Premarket Notification 510(k), or are exempt from 510(k)] AND if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

4.6. **Emergency Use Devices**

4.6.1. An investigator may treat a patient with an unapproved medical device in an emergency situation if he/she concludes the following:

- The patient has a life-threatening condition that needs immediate treatment
- No generally acceptable alternative treatment for the condition exists.
- Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.
- All emergency uses of an unapproved medical device must be reported to the IRB within five (5) working days.
- All essential regulatory documents are maintained in the protocol specific regulatory file.