Guidance on Requirements of the Sponsor and the Investigator as a Sponsor

University of Colorado Denver (UCD) secures assurances from the sponsor or the Sponsor Investigator* that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations.

** Sponsor-Investigator refers to a situation in which the individual investigator is a UCD investigator and is the holder of the IND or IDE and therefore assumes the duties of the sponsor of the clinical investigation under the applicable FDA regulations as well as being an investigator conducting the study under whose immediate direction the investigational device is administered, dispensed, or used.*

Responsibilities of an Investigator acting as an Investigator

Under FDA regulations and guidance, investigators (and sponsor-investigators) are responsible for the conduct of the study and for leading the team of individuals conducting the study. Their responsibilities include the following:

- Ensuring informed consent of each subject is obtained
- Ensuring the investigation is conducted according to the investigational plan
- Personally conducting or supervising the investigation
- Protecting the rights, safety, and welfare of participants
- Preparing and maintaining adequate, current, and complete case histories or records
- Retaining records for two years following the date the marketing application is approved or withdrawn
- • Providing timely reports to the COMIRB, including reports of changes in the research activity needed to avoid immediate hazards to participants, unanticipated problems involving risks to participants or others, including adverse events to the extent required by the COMIRB
- Complying with the requirements of the Controlled Substances Act, when applicable
- Complying with all FDA test article requirements
- Adequately maintaining control of test articles, including appropriate tracking documentation for test articles to the extent that such control and documentation are not centrally administered • Supervising the use and disposition of the test article
- Ensuring that all associates, colleagues, and employees assisting in the conduct of the investigation(s) are informed about their obligations in meeting the above commitments.

Responsibilities of the Sponsor-Investigator when acting as the Sponsor
These studies are typically called investigator initiated studies that use an investigational drug or device or use an approved drug or device for investigational purposes.

The **sponsors**' responsibilities include the following:

- Selecting qualified investigators
- Providing investigators with the information they need to conduct the investigation properly
- Ensuring proper monitoring of the investigation
- Ensuring that the FDA and (for devices) any reviewing IRB or (for drugs) all participating investigators are promptly informed of significant new information about an investigation.

Collecting financial information about the individual investigators in accordance with the regulations

Assuring that the investigational product is properly managed and its use it properly documented

Investigator-Sponsors
In reviewing research involving FDA regulated articles, the COMIRB determines if the study involves a sponsor-investigator. If so, the COMIRB informs the investigator that there are sponsor responsibilities, including reporting requirements to the FDA, (as well as the investigator responsibilities) and all these requirements are his/her responsibility.

Sponsor-investigators who submit protocols to the COMIRB involving FDA test articles must include all supporting FDA documentation for their IND or IDE and any UCD required approvals for applying for an IND or IDE. Additionally, if the IND or IDE product will be manufactured at UCD, the Principal Investigator must submit documentation that:

1. The product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in issuing the IND or IDE.

2. The GMP plan has been approved by the applicable UCD official.

3. If a UCD investigator-sponsor, the GMP plan has been reviewed and accepted by the Affiliate Hospital Risk Management and the Office of Regulatory Compliance.

The IND or IDE product must be stored, secured, dispensed, and documented in accordance with the policies of UCD. If it will be managed external to the affiliate hospital's pharmacy then the investigational product management plan will need prospective review and approval by the UCD Investigational Product Review Committee prior to study initiation.

An investigator-sponsor for an IDE protocol must follow the FDA regulations in 21 CFR 812 applicable to sponsor responsibilities, particularly Subpart C. This includes:

- the record keeping requirements of 21 CFR 812.140(b), and
- the required notification under 21 CFR 812.150(b)(1) to the FDA and all participating investigators of any evaluation of an unanticipated device effect within ten (10) working days of first receiving notice of the effect.

An investigation of a device other than a significant risk device is considered to have an approved application for IDE, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required, if the device is not a banned device and the sponsor:

(i) Labels the device in accordance with 812.5;
(ii) Obtains COMIRB approval of the investigation after presenting the COMIRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
(iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by the COMIRB under 56.109(c).
(iv) Complies with the requirements of 812.46 with respect to monitoring investigations;
(v) Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);
(vi) Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1),
(2), (5), and (7); and
(vii) Complies with the prohibitions in 812.7 against promotion and other practices.

An investigator-sponsor for an IND protocol must follow the FDA regulations in 21 CFR 312 applicable to sponsor responsibilities, particularly Subpart D. This includes:

- the record keeping requirements of 21 CFR 312.57, and
- promptly reporting as required in 21 CFR 312.55(b) to the FDA and all participating investigators of significant new adverse effects or risks with respect to the drug or biologic.

When the organization or an individual assumes the sponsor function by holding an IND or IDE, the following additional FDA regulations may apply:

Drugs or devices:

* 21 CFR §11 (Electronic records and electronic signature) * 21 CFR §54 (Financial Disclosure by Clinical Investigators) **Drugs and Biologics:**
* 21 CFR §210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General)
* 21 CFR §211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
* 21 CFR §312 (Investigational New Drug Application)
* 21 CFR §314 (Drugs for Human Use)
* 21 CFR §320 (Bioavailability and Bioequivalence Requirements)
* 21 CFR §330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded)
* 21 CFR §601 (Biologics Licensing) **Devices:**
* 21 CFR §812 (Establishment Registration and Device Listing for Manufacturers and Initial Importers Of Devices)
* 21 CFR §812 (Investigational Device Exemptions)
* 21 CFR §814 (Premarket Approval of Medical Devices)
* 21 CFR §820 (Quality System Regulation)
* 21 CFR §860 (Medical Device Classification Procedures)

Monitoring

In order to ensure proper administration and monitoring of compliance with regulatory requirements, the sponsor-investigator will select one of the following:

- Assume responsibility for compliance with all FDA regulatory requirements of sponsors and arrange to undergo an audit by a Contract Research Organization to ensure that procedures are in place so that all regulatory requirements will be met.
- Assign responsibility for compliance with all FDA regulatory requirements to a Contract Research Organization.
- Assign responsibility for compliance with some FDA regulatory requirements to a Contract Research Organization and have the investigator obtain an audit from a Contract Research Organization to ensure that procedures are in place so that all other FDA regulatory requirements of sponsors will be met.

- Assign responsibility for compliance with some FDA regulatory requirements to an internal research entity and have the investigator obtain an audit from the internal research entity to ensure that procedures are in place so that all other FDA regulatory requirements of sponsors will be met. The credentials detailing the expertise and resources of the internal research entity must be reviewed and approved by the Office of Regulatory Compliance before the study can be approved by COMIRB.

Quality Assurance Requirements

The Office of Regulatory Compliance will assess the site audit findings and will evaluate whether the investigator is knowledgeable about the regulatory requirements of sponsor-investigators and will follow them. The sponsorinvestigator's proposal, site and resources will be evaluated before initiation of the research to determine compliance with these FDA regulatory requirements. If compliance has been demonstrated, the sponsor-investigator may begin the research. An audit will also be required at the time of and prior to the renewal, of the protocol by the COMIRB.