OFFICE OF THE INSTITUTIONAL REVIEW BOARD

Guidance on FDA Regulated Drugs and Devices

FDA Regulated Drugs

The UNM IRB does not review projects involving the administration of investigational drugs. Instead, these projects are deferred to a qualified, accredited external IRB.

An investigational drug is a substance that has been tested in the laboratory and has been approved by the U.S. Food and Drug Administration (FDA) for testing in people. Clinical trials test how well investigational drugs work and whether they are safe to use. An investigational drug may be approved by the FDA for use in one disease or condition but still be considered investigational in other diseases or conditions. Also called experimental drug, IND, investigational agent, and investigational new drug. Supplements may or may not be considered a drug in some instances; if you intend to conduct human research with supplements, contact the OIRB.

When proposing research that involves administration of non-investigational FDA approved drugs, the researcher must complete the **Drug Information Form** and provide certification to the IRB of the following (based on IND regulations at 21 CFR 312):

1. The project is neither intended to be reported to the FDA as a well-controlled project in support of a new indication for use nor intended to be used in support of any other significant change in labeling for the drug;
2. The project is not intended to support a significant change in the advertising for the product;
3. The project does not involve a route of administration or dosage level or use in a clinical population or other factor that significantly increases the risk associated with the use of the drug; and
4. The drug is not represented in a promotional context as safe or effective for the purposes under investigation.

FDA Regulated Devices

The Investigational Device Exemptions (IDE) regulation (21 CFR 812) describes three types of device projects: significant risk (SR), nonsignificant risk (NSR), and exempt projects. The UNM IRB does not review projects involving significant risk devices. Sponsors (or sponsor/investigators) are responsible for making the initial risk determination and presenting it to the IRB. If the sponsor/investigator identifies a device as NSR, they must complete the **Device Information Form** providing the IRB an explanation of its determination and any other information that may help the IRB in evaluating the risk of the research. For example, a description of the device, reports of prior investigations with the device, the proposed investigational plan, participant selection criteria, and other information the IRB may need in the protocol.

In order to conduct research using FDA regulated devices, the device must either be FDA approved for the proposed indication, have an Investigation Device Exemption (IDE) issued by

the FDA or meet abbreviated requirements at 21 CFR 812.2(b) as follows (regulatory references are detailed below):

1. It is an investigation of a nonsignificant risk (NSR) device;
2. The device is not a banned device in the United States; and
3. The sponsor (investigator):
   i. Labels the device in accordance with 21 CFR 812.5;
   ii. Obtains and maintains IRB approval of the investigation;
   iii. Obtains and documents the informed consent of each participant, unless documentation is waived by the IRB;
   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.

Important Regulatory References:

Sec. 812.5 Labeling of investigational devices.

(a) *Contents.* An investigational device or its immediate package shall bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor (in accordance with 801.1), the quantity of contents, if appropriate, and the following statement: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use." The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

(b) *Prohibitions.* The labeling of an investigational device shall not bear any statement that is false or misleading in any particular and shall not represent that the device is safe or effective for the purposes for which it is being investigated.

Sec. 812.46 Monitoring investigations.

(a) *Securing compliance.* A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a participant.

(b) *Unanticipated adverse device effects.*

(1) A sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect.

(2) A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to participants shall terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first received notice of the effect.

(c) *Resumption of terminated studies.* If the device is a significant risk device, a sponsor may not resume a terminated investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor may not resume a terminated investigation without IRB approval and, if the investigation was terminated under paragraph (b)(2) of this section, FDA approval.

Sec. 812.140 Records.

(a) *Investigator records.* A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

(3) Records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and any medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

(i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the research.

(b) *Sponsor records.* A sponsor shall maintain the following accurate, complete, and current records relating to an investigation:

(4) For each investigation subject to 812.2(b)(1) of a device other than a significant risk device, the records described in paragraph (b)(5) of this section and the following records, consolidated in one location and available for FDA inspection and copying:

(i) The name and intended use of the device and the objectives of the investigation;

(ii) A brief explanation of why the device is not a significant risk device:

(iii) The name and address of each investigator:

(iv) The name and address of each IRB that has reviewed the investigation:

(v) A statement of the extent to which the good manufacturing practice regulation in part 820 will be followed in manufacturing the device; and

(vi) Any other information required by FDA.

(5) Records concerning adverse device effects (whether anticipated or unanticipated) and complaints.

Sec. 812.150 Reports

(a) *Investigator reports.* An investigator shall prepare and submit the following complete, accurate, and timely reports:

(1) Unanticipated adverse device effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(2) Withdrawal of IRB approval. An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

(5) Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

(7) Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

(b) *Sponsor reports.* A sponsor shall prepare and submit the following complete, accurate, and timely reports:

(1) Unanticipated adverse device effects. A sponsor who conducts an evaluation of an unanticipated adverse device effect under 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

(2) Withdrawal of IRB approval. A sponsor shall notify FDA and all reviewing IRB's and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

(3) *Withdrawal of FDA approval.* A sponsor shall notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.

(5) *Progress reports.* At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRB's.

(6) *Recall and device disposition*. A sponsor shall notify FDA and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.

(7) *Final report.* In the case of a device that is not a significant risk device, the sponsor shall submit a final report to all reviewing IRB's within 6 months after termination or completion of the project.

(8) *Informed consent.* A sponsor shall submit to FDA a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.

(9) *Significant risk device determinations.* If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.
(10) *Other.* A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Sec. 812.7 Prohibition of promotion and other practices.
A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not:
(a) Promote or test market an investigational device, until after FDA has approved the device for commercial distribution.

(b) Commercialize an investigational device by charging the participants or researchers for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

(c) Unduly prolong an investigation. If data developed by the investigation indicate in the case of a class III device that premarket approval cannot be justified or in the case of a class II device that it will not comply with an applicable performance standard or an amendment to that standard, the sponsor shall promptly terminate the investigation.

(d) Represent that an investigational device is safe or effective for the purposes for which it is being investigated.

ICH 4.6.3
The investigator/institution or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial participants. Investigators should maintain records that document adequately that the participants were provided the doses specified by the protocol and reconcile all investigational product(s) received from the sponsor.