UNLV | Office of RESEARCH INTEGRITY HUMAN SUBJECTS

Guidance - Food and Drug Administration (FDA) Requirements

General Description

Research that is regulated by federal agencies often times have agency-specific requirements. This guidance is the assist researchers and the IRB in identifying additional regulatory considerations.

21 CFR 50.1 Scope

> (a) This part applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.
>
> Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or monitor clinical investigations involving particular test articles may also be found in other parts (e.g., parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of subjects involved in investigations filed with the Food and Drug Administration pursuant to sections 403, 406, 409, 412, 413, 502, 503, 505, 510, 513-516, 518-520, 721, and 801 of the Federal Food, Drug, and Cosmetic Act and sections 351 and 354-360F of the Public Health Service Act.

When it applies/context

This guidance may be used by members of the UNLV Human Research Protection Program, Researchers and the IRB. Researchers should review this guidance when conducting research covered by the Food and Drug Administration (FDA). The IRB should use this guidance to review for agency-specific requirements in research covered by the FDA.

Considerations & Best Practices

Considerations

The definition of activities covered by the UNLV Human Research Protection Program involve clinical investigations and human subject(s) as defined by FDA regulations. Specifically:

- Clinical Investigations-any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later 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 are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies.

- Human Subject-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 human or a patient.

Additionally, FDA definitions per 21 CFR 50.3 apply to all clinical investigations with human subject(s). The PI should consider these definitions during the development of the protocol (if applicable) and during the conduct of the clinical investigation, and educate all research staff about these definitions. These definitions will be considered by UNLV official and the IRB when overseeing and/or reviewing clinical investigation.

Requirements/Best Practices

Policies and procedures describe the reporting of serious or continuing non-compliance to FDA. (SOP 11.02 Researcher Noncompliance Investigation Reporting and Corrective Action)

Consent

The IRB has the option to observe, or have a third party observe, the consent process and the conduct of the research. (SOP 6.02 Informed Consent; 6.02 Informed Consent Children; Rules & Procedures)

Consent will be obtained in accordance with FDA regulations, or the circumstances meet the exception to the requirement for consent in FDA regulations.

21 CFR 50.20 General Requirements for informed consent

IND/IDE

When research involves the use of a drug other than a marketed drug in the course of medical practice, policies and procedures describe the process to confirm that:

- The drug has an IND or the research meets one of the FDA exemptions from the requirement to have an IND. (SOP 8.01 FDA Regulated Drugs and Biologics)

When research is conducted to determine the safety or effectiveness of a device, policies and procedures describe the process to confirm:

- The device has an IDE issued by the FDA, the device fulfills the requirements for an abbreviated IDE, or the research meets one of the FDA exemptions from the requirement to have an IDE.
- The IRB or EC makes a determination whether the device is a significant or non-significant risk device. The IRB minutes document the rationale for significant risk/non- significant risk device determinations.

When research involves a drug with an IND or a device with an IDE, policies and procedures describe the process to confirm that the IND or IDE number is valid.

For FDA-regulated research involving an investigational drug conducted outside of the U.S., an IND is not required provided the study is conducted in accordance with the Good Clinical Practice guidelines and FDA is able to validate the data from the study through an onsite inspection if FDA deems it necessary.

For FDA-regulated research involving an investigational drug where FDA requires an IND, the research does not commence until a valid IND is in place.

Emergency Use

Under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

In order to use a test article in a life threatening situation without prior IRB or EC review, the following criteria must be met:

- The participant is in a life-threatening or severely debilitating situation.
- No standard acceptable treatment is available
- There is not sufficient time to obtain IRB or EC approval.
- The use is reported to the IRB or EC within five working days.
- Any subsequent use of the test article is subject to IRB or EC review.

Institutional Review Board

Responsibilities:

- The criteria for exemptions are consistent with FDA regulations.
- The designation by the IRB chair of IRB member(s) who may conduct review using the expedited procedure.
- The evaluation by the reviewer of whether research undergoing initial review and continuing review using the expedited procedure:
    - Meets all applicability criteria.
    - Represents one or more approvable categories of research.

- The report of unanticipated problems involving risks to participants or others be sent to the FDA, when the research is FDA-regulated is required.
- The prompt reporting of suspensions and terminations of IRB approval to FDA.

- The IRB reviews advertising to ensure that advertisements do not:
    - Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
    - Use terms, such as "new treatment," "new medication," or "new drug," without explaining that the test article is investigational.
    - Allow compensation for participation in a trial offered by a Sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

- The IRB determines
    - The required and appropriate additional elements of disclosure are included in the consent process.
    - The consent document embodies the basic and required additional elements of disclosure.
    - There is a statement noting the possibility that the FDA may inspect the records that will be provided to each participant.
    - There is a statement a description of the clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. law. The website will not include information that can identify the participant. At most the website will include a summary of the results. The participant can reach the website at any time.
    - The participant or the participant's legally authorized representative will sign and date the consent document.

- The Researcher will give either the participant or the legally authorized representative adequate opportunity to read the consent document before it is signed.
- For the use of the short form of consent documentation,
  - The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant's legally authorized representative.
  - A written summary embodies the basic and required additional elements of disclosure.
  - There will be a witness to the oral presentation.
  - For participants who do not speak English, the witness is conversant in both English and the language of the participant.
  - The participant or the participant's legally authorized representative will sign the consent document.
  - The witness will sign both the short form and a copy of the summary.
  - The person actually obtaining consent will sign a copy of the summary.
  - A copy of the signed short form will be given to the participant or the legally authorized representative.
  - A copy of the signed summary will be given to the participant or the legally authorized representative.

- With regard to data retention when participants withdraw from a clinical trial,
  - When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
  - A Researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non- invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.
  - The Researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB or EC must approve the consent document.
  - If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the Researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a Researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

- The IRB is prohibited from waiving or altering the consent process.
- The IRB or EC is allowed to waive the requirement to document the consent process by determining that the regulatory criteria for waivers are met.
  - When the IRB considers waiving the requirement to obtain written documentation of the consent process, the IRB will review a written description of the information that will be provided to participants.

- When granting waivers of the requirement to obtain written documentation of the consent process, the IRB will consider requiring the Researcher to provide participants with a written statement regarding the research.

Research Involving Children

- The IRB or EC follow the requirements specified in Subpart D for research involving children.
- When research involves children, the IRB follows the requirements in Subpart D pertaining to obtaining assent of children and permission of the parents or guardian.
- For research that involves no more than minimal risk or more than minimal risk with the prospect of direct benefit to the individual children, the IRB determines whether:
  - The permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child, or the permission of one parent is sufficient.
- For research that involves more than minimal risk without the prospect of direct benefit to the individual children, the IRB determines that the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- IRB will determine and document that assent is a requirement of:
  - All children.
  - Some children.
  - None of the children.
- When the IRB determines that assent is not a requirement for some or all children, the IRB determines and documents one or more of the following:
  - The children are not capable of providing assent based on the age, maturity, or psychological state.
  - The capability of the children is so limited that they cannot reasonably be consulted.
  - The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
  - Assent can be waived using the criteria for waiver of the consent process
- When the IRB determines that assent is a requirement, the IRB determine:
  - Whether assent will be documented.
  - If so, the process to document assent.

Planned Emergency Research

- Policies and procedures describe the criteria to approve planned emergency research. The research plan must be approved in advance by the FDA and the IRB or EC, and publicly disclosed to the community in which the research will be conducted.

Researchers and Research Staff

- When the long form of consent documentation is used, Researchers or Research Staff follow regulatory and IRB requirements.
- When the short form of consent documentation is used, Researchers or Research Staff follow regulatory and IRB requirements.

Resources

- 21 CFR 11, 21 CFR 54, 21 CFR 50, 21 CFR 56, 21 CFR 210, 21CFR 211, 21 CFR 312, 21 CFR 314, 21 CFR 320, 21 CFR 330, 21 CFR 601, 21 CFR 807, 21 CFR 812, 21 CFR 814, 21 CFR 820, 21 CFR 860
- Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND
- Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
- Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Frequently Asked Questions About Medical Devices
- Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Continuing Review After Clinical Investigation Approval
- Frequently Asked Questions: IRB Organization, A Guide to Informed Consent, Recruiting Study Subjects, Payment to Research Subjects
- FDA Information Sheets: A Guide to Informed Consent
- Frequently Asked Questions: Informed Consent Document Content, Recruiting Study Subjects, IRB Procedures
- FDA Information Sheets: Frequently Asked Questions: Informed Consent Process, Data Retention When Subjects Withdraw from FDA- Regulated Clinical Trials
- Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception From Informed Consent Requirements for Emergency Research
- FDA Information Sheets: Frequently Asked Questions: IRB Records
- Guidance for Clinical Investigators, Industry, and FDA Staff: Financial Disclosure by Clinical Investigators
- FDA-Good Clinical Practice
- Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs – Improving Human Subject Protection