Policy
Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XI.B
Section: Investigational Drugs, Biologics, and Devices
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Subject: Investigational Drugs, Agents, and Biologics

Definitions:
1. Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
2. Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.
3. Investigational Drugs/Investigational Biologics (Test Articles): A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used in vitro for diagnostic purposes. Investigational drugs or biologics may include:
   a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
   b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).
4. Investigational New Drug (IND): FDA granting of permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data that has determined that a particular product is safe and effective for a specific use. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.
5. Expanded Access to Investigational Drugs for Treatment Use: Mechanism established by the FDA to make available to patients with serious diseases or conditions investigational new drugs (and approved drugs with conditional limited availability) when there is no comparable or satisfactory alternative therapy to treat their disease or condition.
6. Immediately life-threatening disease of condition: A stage of a disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
7. Serious disease or condition: A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity does not have to be irreversible if it is persistent or recurrent.

Policy:
It is the policy of the Human Research Protections Program that the use of investigational drugs, agents, and/or biologics be reviewed and approved for use in accordance with the federal regulations.

I. IRB Requirements for the Use of an Investigational Drug, Agent, or Biologic.
   A. The IRB will conduct initial approval and ongoing approvals of all investigational drugs, agents, and biologics used in human subjects research under its jurisdiction. Included in this process is a review by the IRB review is required even if a waiver from IRB
regulations has been granted by the FDA for use of the investigational drug, agent, or biologic.

B. FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

1. **Compassionate Use:** The term “compassionate use” is used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available.

2. **Individual Patient IND (for treatment use):** The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting an individual patient IND to the FDA requesting authorization to use the investigational drug for treatment use. Prospective IRB review and approval is required.

3. **Emergency IND:** Please see the “Emergency Use of FDA Regulated Products” policy and procedure (See HRPP Policy XI.E for details).

4. **Treatment IND or Treatment Protocol or Biologics:** A mechanism for providing widespread treatment use of investigational drugs (as early in the drug development process as possible) to eligible subjects for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

   The FDA identifies two special considerations when a patient is to be treated under expanded access or a Treatment IND or Treatment Protocol:

   a. **Informed Consent.** Informed consent is especially important in expanded access for treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential subjects are fully aware of the risks involved in participation.

   b. **Charging for Investigational Drugs for Treatment Use under Expanded Access:** The FDA permits charging for the drug, agent, or biologic under expanded access if certain conditions are met. Therefore, the IRB Committee should pay particular attention to expanded access submissions in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB should balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

5. **Group C Treatment Investigational New Drug (IND):** A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the VU IRB requires prospective IRB review and approval.

6. **Open-Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The
he IDS Pharmacy representative on the IRB committee. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.

7. **Parallel Track**: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the IRB.

B. Where a protocol is subject to review under more than one department or agency’s regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with Treatment Investigational New Drugs where both the FDA and HHS have jurisdiction over the research. The use of an unapproved investigational drug, agent, and/or biologic requires an FDA investigational new drug application (IND).

II. Use of an Investigational Drug, Agent, or Biologic by an Investigator.
   A. In order for an investigational drug, agent, or biologic to be used in clinical research, an Investigational New Drug (IND) must be on file with the FDA and an IND number granted.
   B. Clinical investigations of a drug, agent, or biologic that is lawfully marketed in the United States are exempt from the requirements of an IND, if all of the following conditions are met:
      1. Use of the investigational drug, agent, or biologic is not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product;
      2. The use of the investigational drug, agent, or biologic is not intended to support a significant change in the advertising of the product;
      3. The use of the product does not involve a route of administration, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the use of the drug, agent, or biologic;
      4. The use will be conducted in compliance with the IRB approval and informed consent procedures;
      5. The use will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR Sec. 312.7; and
      6. The use does not intend to invoke exception from informed consent requirements for emergency use.
   C. A clinical investigation involving an in vitro diagnostic biological product (as listed below) is exempt if the diagnostic test was intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established diagnostic product or procedure and the diagnostic test was shipped in compliance with 21 CFR 312.60.
   D. Clinical investigations of an in vitro diagnostic biologic product that involves one or more of the following are exempt from the requirements of an IND:
      1. blood grouping serum;
      2. reagent red blood cells; and/or
      3. anti-human globulin.
   E. A clinical investigation involving the use of placebo is exempt if it does not otherwise require IND submission.
   F. Research involving combinations of FDA approved drugs, agents, or biologics that are currently approved as single use, do not require an IND. However, use of these drugs, agents, or biologics in research must still be prospectively reviewed and approved by the IRB.
G. The Investigator administering an investigational drug, agent or biologic must meet the following requirements in order to use an investigational drug, agent, or biologic in research conducted under the jurisdiction of the IRB.

1. The drug, agent, or biologic must be used only in accordance with the plan of investigation as described in the FDA-approved IND application and the IRB-approved protocol;
2. The drug, agent, or biologic may only be used in participants under the Principal Investigator’s personal supervision or under the supervision of physicians who are directly responsible to the Investigator; and
3. Informed consent from the participant or the participant’s legally authorized representative is prospectively obtained, unless a waiver of consent has been approved by the IRB.

H. Research with the use of an investigational drug, agent, or biologic must be conducted in accordance with all HRPP policies and procedures.

III. Advertising or Recruitment for Studies Involving Investigational Drugs, Agents, or Biologics (See HRPP Policy X.G on Recruitment and Advertising).

A. Advertisements or recruiting tools must not include the term “new treatment”, without explaining that the drug, agent, or biologic is “investigational, meaning non-FDA approved”. A phrase such as “receive new treatment” implies that all study subjects will be receiving newly marketed products of proven worth. It is not a treatment since its effectiveness has not been proven or established. The term “new” is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive; and

B. Advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g. drug, agent, biologic). The use of the word “free” could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

IV. Informed Consent in Research that Involves an Investigational Drug, Agent, or Biologic.

A. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (See HRPP Policy IV.A);

B. No claims are to made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;

C. The informed consent document must contain a statement that the drug, agent, or biologic is “investigational, meaning non-FDA approved”;

D. The informed consent document must contain a statement that the FDA may have access to the participant's medical records as they pertain to the study; and

E. The Investigator must assure that throughout the consenting process and study participation the participant understands that the investigational drug, agent, or biologic is under investigation, and that its benefits for the condition under study are unproven.

F. For Phase I studies, the informed consent document must disclose that the purpose of the research includes examining the drug's safety. For Phase II and Phase III studies, the informed consent document must disclose that the purpose of the research includes examining the drug’s safety and efficacy (effectiveness).

References:
21 CFR 50, 56, and 312