HRPP POLICY APPROVAL & IMPLEMENTATION
OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

Policy Number: 500
SOP Title: Research Involving Drugs, Biological, and Nutritional Products

Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB Chairs, IRB Administrators, Protocol Navigators

Revision Approval:
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A. PURPOSE

1. Describe the responsibilities of NIH investigators, non-NIH investigators, NIH sponsors, and the NIH Institutional Review Board (IRB) when conducting or reviewing human subjects research (HSR) that involves the use of drugs, biological products, or nutritional products (e.g., dietary supplements or foods) that are under the oversight of the Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS).

B. SCOPE

1. This policy applies to NIH investigators when conducting FDA-regulated research involving drugs, biological products, or nutritional products (referred to in this policy as “test articles”), whether or not the research is conducted under an Investigational New Drug application (IND)\(^1\).

2. This policy applies to non-NIH investigators when conducting FDA-regulated research involving the use of drugs, biological products, or nutritional products, when the NIH IRB is the Reviewing IRB.

3. This policy applies to the NIH IRB as the Reviewing IRB.

C. POLICY

1. NIH investigators and non-NIH investigators conducting human subjects research involving drugs, biological products, or nutritional products, must comply with all applicable FDA regulations including, but not limited to, 21 CFR parts 50, 56, 312 and 600 as well as those set forth in HHS regulations at 45 CFR 46.

2. When reviewing and approving research that involves drugs, biological products, or nutritional products, the NIH IRB must apply the applicable FDA regulations including, but not limited to, 21 CFR parts 50, 56, 312 and 600 as well as those set forth in HHS regulations at 45 CFR 46.

\(^1\) Information regarding treatment use and expanded access to investigational drugs, biological products or nutritional products is addressed in NIH Policy 502 Expanded Access, Including Emergency Use of Investigational Drugs, Biologics, and Medical Devices.
3. By NIH policy, NIH investigators may not be Sponsors, effective January 15, 2018. However, investigators may have sponsor responsibilities when required by regulation.

D. DEFINITIONS

1. **Adverse event (AE)** – Any untoward medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in research, whether or not considered related to the subject’s participation in the research. (Policy 801 Reporting Research Events)
   a. **Adverse Event (In the context of FDA-required reporting)** - Any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. (21 CFR 312.32 (a))

2. **Biological product** – (1) a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings. (2) The term “biosimilar” or “biosimilarity”, in reference to a biological product that is the subject of an application under subsection (k) [of 42 USC 262], means (A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and (B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. (3) The term “interchangeable” or “interchangeability”, in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. (4) The term “reference product” means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k). (42 USC 262(i)(1))

3. **Clinical Investigation** – 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. (21 CFR 50.3(c))

a. **Clinical Investigation (involving drugs)** – Any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. (21 CFR 312.3(b))

4. **Color Additive** – A material which – (A) is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and (B) when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto; except that such term does not include any material which the Secretary, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring. (2) The term “color” includes black, white, and intermediate grays. (3) Nothing in subparagraph (1) of this paragraph shall be construed to apply to any pesticide chemical, soil or plant nutrient, or other agricultural chemical solely because of its effect in aiding, retarding, or otherwise affecting, directly or indirectly, the growth or other natural physiological processes of produce of the soil and thereby affecting its color, whether before or after harvest. (Federal Food Drug and Cosmetic Act at 21 USC 301(t))

5. **Dietary Supplement** – (1) Means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);

(2) means a product that – (A)(i) is intended for ingestion in a form described in section 350(c)(1)(B)(i) of this title; or (ii) complies with section 350(c)(1)(B)(ii) of this title; (B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and (C) is labeled as a dietary supplement; and

(3) does – (A) include an article that is approved as a new drug under section 355 of this title or licensed as a biologic under section 262 of title 42 and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and
dosages set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title; and (B) not include – (i) an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of title 42, or (ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter. Except for purposes of paragraph (g) and section 350f of this title, a dietary supplement shall be deemed to be a food within the meaning of this chapter. (21 USC 321(ff))

6. Drug – (A) articles recognized in the official United States Pharmacopœia, official Homeopathic Pharmacopœia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement. (2) The term “counterfeit drug” means a drug which, or the container or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor. (21 USC 321(g)(1))

Note: Biological products are generally included within this definition and are covered by some of the same laws and regulations, but differences exist regarding their
manufacturing processes (chemical process versus biological process; see definition for “biological product”).

7. **Human Subject (2018 Common Rule definition)** – (1) A living individual about whom an investigator (whether professional or student) conducting research:

   (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

   (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

(2) **Intervention** – includes both physical procedures by which information or biospecimens are gathered (e.g. venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

(3) **Interaction** – includes communication or interpersonal contact between investigator and subject.

(4) **Private information** – includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g. a medical record).

(5) **Identifiable private information** – is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

(6) **Identifiable biospecimen** – is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. ([45 CFR 46.102(e) 2018 Common Rule])

8. **Human Subject (Pre-2018 Common Rule definition)** – A living individual about whom an investigator (whether professional or student) conducting research obtains: 1) Data through intervention or interaction with the individual, or 2) Identifiable private information. ([45 CFR 46.102(f) pre-2018 Common Rule])

9. **Investigational New Drug** – A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms “investigational drug” and “investigational new drug” are deemed to be synonymous for purposes of this part. ([21 CFR 312.3(b)])
10. **IND [Application]** – An investigational new drug application. For purposes of this part, “IND” is synonymous with “Notice of Claimed Investigational Exemption for a New Drug.” ([21 CFR 312.3(b)](https://www.gpo.gov/fdsys/pkg/CFR-2010-title21-vol1/content-detail.html#sec312.3c))

11. **Investigator (for research involving investigational drugs)** – An individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. “Subinvestigator” includes any other individual member of that team. ([21 CFR.312.3(b)](https://www.gpo.gov/fdsys/pkg/CFR-2010-title21-vol1/content-detail.html#sec312.3c))

12. **NIH Investigator** – An NIH federal employee (intramural or extramural), Special Volunteer, Intramural Research Training Awardee (IRTA) and Cancer Research Training Awardee (CRTA) who is conducting human subjects research on behalf of the NIH. This may include a contractor in accordance with policy.

13. **Non-Compliance** – Failure of an investigator to follow the applicable laws, regulations, or institutional policies governing the protection of human subjects in research, or the requirements or determinations of the IRB, whether intentional or not.
   a. **Serious non-compliance** – Non-compliance, whether intentional or not, that results in harm or otherwise materially compromises the rights, welfare and/or safety of the subject. Non-compliance that materially effects the scientific integrity or validity of the research may be considered serious non-compliance, even if it does not result in direct harm to research subjects.
   b. **Continuing non-compliance** – A pattern of recurring non-compliance that either has resulted, or, if continued, may result in harm to subjects or otherwise materially compromise the rights, welfare and/or safety of subjects, affect the scientific integrity of the study or validity of the results. The pattern may comprise repetition of the same non-compliant action(s), or different non-compliant events. Such non-compliance may be unintentional (e.g. due to lack of understanding, knowledge, or commitment), or intentional (e.g. due to deliberate choice to ignore or compromise the requirements of any applicable regulation, organizational policy, or determination of the IRB) ([Policy 802 Non-compliance in Human Subjects Research](https://p3cycles.com/))

14. **Protocol Deviation (PD)** – Any change, divergence, or departure from the IRB-approved research protocol.
   a. **Major Deviations** – Deviations from the IRB approved protocol that have, or may have the potential to, negatively impact, the rights, welfare or safety of the subject, or to substantially negatively impact the scientific integrity or validity of the study.
b. **Minor Deviations** – Deviations that do not have the potential to negatively impact the rights, safety, or welfare of subjects or others, or the scientific integrity or validity of the study. *(Policy 801 Reporting Research Events)*

15. **Serious adverse event (SAE) or Serious Suspected Adverse Reaction (SUSAR)** – An adverse event or suspected adverse reaction is considered “serious” if, in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse. *(21 CFR 312.32(a))*

16. **Sponsor (for drugs and biologics)** – Means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. *(21 CFR 312.3(b))*

17. **Sponsor-Investigator (for drugs and biologics)** – Means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor. *(21 CFR 312.3(b))*

18. **Subject (FDA- for study of investigational drugs)** – A human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease. *(21 CFR 312.3(b))*

19. **Test Article (for FDA regulated research)** – Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n). *(21 CFR 50.3(j))*
20. **Unanticipated Problem Involving Risks to Subjects or Others (UP)** – Any incident, experience, or outcome that meets all the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; and
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects, or others (which may include research staff, family members or other individuals not directly participating in the research) at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or expected. (Policy 801 Reporting Research Events)

### E. RESPONSIBILITIES AND REQUIREMENTS

1. **Principal Investigator Responsibilities:**

   NIH Principal Investigators (PIs) are responsible for:

   a. When the research involves the clinical investigation of a test article, the PI will provide documentation in the protocol whether the test article(s) for use is under an IND or provide written justification for why the test article(s) is exempt from the requirement for an IND. (21 CFR 312.2) (See FDA guidance, Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND, September 2013.)

   I. If the Office of IRB Operations (IRBO) does not concur with the investigator that the test article is exempt, the IRBO may require the investigator to submit to the FDA for a formal determination prior to further review of the study. The FDA determination as to whether the test article is exempt or requires an IND is final.

   II. If the FDA has indicated the test article is exempt from the IND regulations, documentation from FDA confirming this determination should be kept in the regulatory binder and provided to the IRB upon submission for initial review or upon request.
III. If the use of the test article is not exempt from the requirement for an IND, the IRBO will not further review the study and research may not begin until a valid IND is in effect. The PI is responsible for providing documentation to the IRB confirming that an IND is in effect. A valid IND will be considered to be in effect:

   i. Thirty days after the FDA receives the IND application, unless the FDA notifies the sponsor that the investigations described in the IND are subject to a clinical hold; (21 CFR parts 312.40 and 312.42); OR

   ii. An earlier notification by FDA that the clinical investigations in the IND may begin.

IV. Investigators should provide documentation from the FDA verifying the IND number and indicating the study is safe to proceed (e.g., the FDA letter assigning the IND number and safe to proceed letter). If the safe to proceed letter has not been received, the IRB will accept documentation from the Sponsor indicating the FDA’s confirmation that the study may proceed.

V. The PI must include either the Package insert (in the case of an approved drug) or Investigator Brochure (IB) if one exists, with protocol submission to the NIH IRB.

   i. If no IB exists for an investigational drug, the investigator must include in the protocol all relevant preclinical and clinical safety and efficacy data to support the proposed use of the test article in the research.

   ii. During the course of the research, updated IBs must be provided to the IRB within 7 days of receipt if the changes to the IB reflect, in the investigators judgment, an increase in risks to subjects or decrease in the acceptability of risks, or within 30 days of receipt if the changes do not adversely impact risk-benefit.

   b. Conducting the investigation according to the signed investigator statement provided by the Sponsor (for studies being conducted under an IND), the investigational plan, IRB approved protocol, and applicable regulations.

   c. Obtaining informed consent from each human subject to whom the drug is administered consistent with 21 CFR part 50 Subpart B, except as provided in 21 CFR 50.23 or 21 CFR 50.24.
d. Ensuring control of drugs under investigation, including documentation, maintenance, and tracking of the test article. (21 CFR 312.61)

e. Ensuring that the protocol has a maintenance and tracking plan for the test article that includes, but is not limited to, the receipt, storage, handling, and dispensing of the test article. (21 CFR 312.62(a))

   I. Some or all of the duties associated with this responsibility may be delegated to other appropriate individuals. For example, at the NIH CC, the CC Pharmacy Department is responsible for the receipt, storage, dispensing and disposition of all investigational drugs

f. Ensuring safety reporting requirements are met. (21 CFR 312.64(b))

   I. Principal Investigators are required to promptly report serious adverse events (SAEs) to sponsors. (21 CFR 312.64(b))

   II. The PI must report Adverse Events (AEs), Serious Adverse Events (SAEs), Deaths, Unanticipated Problems (UPs), protocol deviations, and noncompliance consistent with the sponsor reporting requirements in the protocol, NIH Institute/Center (IC) policy, and per Policy 801 Reporting Research Events.

  g. In addition to safety reporting (see E.1.f. above), submitting required reports to the Sponsor (e.g., annual reports, final reports, and financial disclosure reports). (21 CFR 312.64)

h. Ensuring recordkeeping and record retention requirements are met. (21 CFR 312.57 and NIH Manual Chapter 1743-3000 Records Retention)

   I. The PI must prepare adequate and accurate case histories, records of subjects’ conditions before, during and after the clinical investigation, progress notes that record observations and other data about each subject and assure that research data is verifiable in the source documents. (21 CFR 312.62)

   II. The PI must follow record retention requirements such that at the closure of the trial, the Investigators and Sponsors must retain the records and reports required for the longest of the following intervals: 1) at least 3 years as required by the NIH Manual Chapter 1743-3000 Records Retention; 2) two years after a marketing application is approved for the drug or, 3) if an application is not approved for the drug, records must be maintained for 2 years after shipment and delivery of the drug for investigational use is
III. When a subject withdraws from a study conducted under an IND, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The investigator may not continue to access the subject’s medical record or other confidential records for additional research purposes unless the subject has provided consent to do so.

i. If the PI terminates or suspends a trial without prior agreement of the sponsor, the PI must inform the IRB and the sponsor promptly. Communication from the PI to the IRB and the sponsor will include a detailed written explanation of the reasons for termination or suspension.

j. If the sponsor terminates or suspends a trial, the PI must promptly inform the IRB and provide the Board with a detailed written explanation of the termination or suspension.

k. If the Reviewing IRB terminates or suspends its approval of a trial, the PI will promptly inform the sponsor.

I. When a trial is terminated, the PI will work with the IRB to create a plan to promptly inform the study subjects about suspension/termination and should ensure appropriate therapy and follow-up for subjects. If the reason for termination/suspension could be relevant for former study subjects, the PI and the IRB will consider whether former subjects should also be notified.

2. Sponsor Responsibilities (when the sponsor is the NIH or an NIH employee):

a. The Sponsor is responsible for:

I. Submitting an IND to the FDA for each clinical investigation, unless exempt from IND requirements as defined in 21 CFR 312.2(a). (21 CFR 312.20)

II. Selecting qualified investigators. (21 CFR 312.53)

III. Providing investigators with the information they need to conduct an investigation properly. (21 CFR 312.50)

IV. Maintaining adequate records showing the receipt, shipment, or other disposition of the investigational drug including disposition of unused supply of investigational drug. (21 CFR 312.62)

V. Ensuring proper monitoring of the investigation(s). (21 CFR 312.50)
VI. Ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND. *(21 CFR 312.50)*

VII. Notifying FDA and all participating investigators (i.e., all investigators to whom the sponsor is providing drug under its INDs or under any investigator's IND) in an IND safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting. *(21 CFR 312.32)*

VIII. Maintaining an effective IND with respect to the investigations, including maintaining the Sponsor’s Regulatory binder.

IX. Submitting an annual report to the FDA within 60 days of the anniversary date that the IND went into effect. *(21 CFR 312.33)*

X. Prompt reporting to the FDA and to investigators when an IND is withdrawn. *(21 CFR 312.38)*

3. Sponsor-Investigator

   a. By NIH policy, INDs shall be held by the IC, rather than by the NIH PI on the clinical protocol.

   b. Investigators may serve as the sponsor for expanded access protocols. (See Policy 502 Expanded Access, Including Emergency Use of Investigational Drugs, Biologics, and Medical Devices (Test Articles).)

      I. When a PI holds the IND (Sponsor-Investigator), s/he assumes all responsibilities of both the Investigator (see E.1, above) as well as the Sponsor (see E.2, above). (See 21 CFR 312 Subpart E and 21 CFR 312 Subpart I.)

4. IRB Responsibilities

   a. When the NIH IRB is the Reviewing IRB, it is responsible for the following:

      I. In its review and approval of FDA-regulated research the NIH IRB must apply the applicable FDA regulations including, but not limited to, 21 CFR parts 50, 56, 312 and 600 as well as those set forth in HHS regulations at 45 CFR 46. (See Policy 204 Levels of IRB Review and Criteria for IRB Approval of Research and Policy 301 Informed Consent.)
b. If the IRB does not have the necessary expertise in its membership to review the specific research activity, additional consultation will be sought consistent with requirements specified in Policy 201 IRB Membership and Composition.

c. When a PI indicates that the use of the test article is exempt from IND requirements, the IRB Analyst, IRBO Director, Executive IRB Chair or designee, will confirm that the Investigator’s justification meets the criteria for exemption. If it is determined that the proposed use of the study drug does not meet the criteria for exemption from the IND requirements, the PI will be required to submit an IND application to the FDA or ask the FDA for a formal determination as to whether an IND is needed. The FDA determination is final.

d. The IRBO will not further process the submitted IRB application until a determination has been reached by the FDA, or 30 days has elapsed since submission of the IND application to the FDA and no clinical hold has been placed on the clinical investigation.

e. The IRB will confirm that the test article has an IND issued by the FDA, or the use of the test article in the study meets all of the requirements for exemption from the requirement for an IND as defined in 21 CFR 312.2(a).

f. For expedited review, the NIH IRB must continue to comply with both the most current FDA regulation at 21 CFR 56, and as appropriate, the HHS regulations at 45 CFR 46. (See Policy 204 Levels of IRB Review and Criteria for IRB Approval of Research.)

g. For continuing review, the NIH IRB must continue to comply with both the most current FDA regulations at 21 CFR 56, and as appropriate, the HHS regulations at 45 CFR 46. (See Policy 204 Levels of IRB Review and Criteria for IRB Review of Research.)

h. The IRB will review proposed advertising to ensure that advertisements do none of the following:

I. Make claims, either explicitly or implicitly, that the drug, biologic or nutritional products is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biologic or nutritional products;

II. Use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational;
III. 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.

i. When the Reviewing IRB suspends or terminates a study, the IRB will report its actions to the investigator, NIH Institutional officials, and OHSRP. OHSRP will report termination or suspension of a trial to the FDA and OHRP consistent with Policy 801 Reporting Research Events.

5. Responsibilities related to FDA Inspections include the following;

a. Investigators, Sponsors, IRBs, and other FDA regulated entities (e.g. the NIH Radioactive Drug Research Committee, Pharmacy, etc.) must make records available for FDA inspection. (21 CFR parts 56.115(b) and 312.68).

   I. NIH researchers who are informed of an FDA inspection must immediately notify their Clinical Director, Clinical Center (CC) CEO, ORSC, and OHSRP.

b. Researchers must cooperate with guidance provided by the Clinical Director, CC CEO, OHSRP and ORSC staff with respect to such inspections, including allowing appropriate NIH personnel to participate in the inspection.

c. Any written responses to the FDA submitted by NIH researchers must first be approved by the Clinical Director, CC CEO, ORSC, and OHSRP. The appropriate party must provide a draft response to the Clinical Director, CC CEO, ORSC, and OHSRP at least four business days before it must be submitted to the FDA.

d. If there is disagreement between a researcher and a Clinical Director, CC CEO, ORSC representative, or OHSRP about a response to the FDA, the Deputy Director for Intramural Research (DDIR) will make the decision about the appropriate response.

e. Any written responses to the FDA submitted by an NIH IRB in response to an FDA inspection must first be approved by the Director, OHSRP with input from ORSC, as needed. The IRB must provide a draft response to the ORSC and OHSRP Director at least four business days before it must be submitted to the FDA.

F. REFERENCES

1. Federal Regulations:

   HHS: 45 CFR 46; 45 CFR 46.109(f)(1); 45 CFR 46.110(b)
   FDA: 21 CFR 50, 56, and 312
2. NIH Policies

Policy 201 IRB Membership and Composition
Policy 204 Levels of IRB Review and Criteria for IRB Approval of Research
Policy 206 Reporting Research Events
Policy 301 Informed Consent
Policy 502 Expanded Access, Including Emergency Use of Investigational Drugs, Biologics, and Medical Devices (Test Articles)
Policy 801 Reporting Research Events
Policy 802 Non-compliance in Human Subjects Research
NIH Manual Chapter 1743-3000 Records Retention

3. Guidance and Tools

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 (August 2013)

Guidance Document - Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects (October 2009)

Guidance for Sponsors, Clinical Investigators, and IRBs - Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials (October 2008)

Information for Sponsor-Investigators Submitting Investigational New Drug Applications (INDs) (Content current as of: 6/27/2017)


G. APPENDICES: NA

H. REVISION HISTORY: NA

I. SUPERSEDES DATE: 10/22/2020
SOP 15 – Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications

SOP 15A – Research Regulated by the Food and Drug Administration (FDA): Information and Policies Specific to Research Involving Investigational New Drugs (Including Biological Products)