



**DUKE UNIVERSITY HEALTH SYSTEM**  
**Human Research Protection Program**

**RESEARCH INVOLVING DRUGS OR  
BIOLOGICS**

**3/26/2021**

Research investigating or evaluating drugs or biologics must be conducted under an IRB approved protocol, under the direction of the approved investigator(s) and must comply with FDA regulations.

When research involves the use of drugs or biologics other than the use of a FDA approved, marketed drug/biologic in the course of medical practice, the IRB will confirm and document that either:

1. The drug/biologic has a valid IND number. The IND for each drug/biologic must be supported by one of the following:
  - The sponsor protocol imprinted with the IND number
  - A written communication from the sponsor documenting the IND number
  - A written communication from the FDA documenting the IND number  
*(required if an investigator listed on this protocol holds the IND)*

**OR**

2. The protocol meets all of the requirements in one of the following FDA exemptions to an IND [Categories in 21 CFR 312.2(b) and 21 CFR 320.31].

**Exemption 1**

- The clinical investigation is of a drug/biologic product that is lawfully marketed in the United States
- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug/biologic
- The investigation proposed is not intended to support a significant change in the advertising for the drug/biologic
- The investigation does not involve a route of administration, dose, patient population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug/biologic
- The investigation will be conducted in compliance with FDA regulations for the Protection of Human Subjects and Institutional Review Boards (21 CFR 50 and 56)
- The investigation will be conducted in compliance with the FDA requirements for Promotion and Charging for Investigational Drugs (21 CFR 312.7)

- The investigation is not intended to invoke an exception from informed consent requirements for planned emergency research under 21 CFR 50.24

#### Exemption 2

- The clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following:
  - Blood grouping serum
  - Reagent red blood cells
  - Anti-human globulin
- The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure
- The diagnostic product will be shipped in compliance with FDA Regulations for Drugs for investigational use in laboratory research animals or in vitro tests (21 CFR 312.160)

#### Exemption 3

- The drug/biologic is intended solely for tests in vitro or in laboratory research animals and is shipped in accordance with FDA Regulations for Drugs for investigational use in laboratory research animals or in vitro tests (21 CFR 312.160)

#### Exemption 4

- The clinical investigation involves the use of a placebo and the investigation does not otherwise require submission of an IND

#### Exemption 5

- The clinical investigation involves an *in vivo* bioavailability or bioequivalence study **unless**:
  - The test product contains a new chemical entity\*\* as defined in 21 CFR 314.108(a) [\*\*a drug that contains no active moiety that has been approved by FDA in any other application]
  - The study involves a radioactively labeled drug product
  - The study involves a cytotoxic drug product
  - The investigator will conduct a bioavailability or bioequivalence study in humans using a drug product that contains an already approved, non-new chemical entity and the study will involve a single dose in normal subjects or patients where either the maximum single or total daily dose exceeds that specified in the labeling of the drug product that is the subject of an approved new drug application or abbreviated new drug application
  - The investigator will conduct a bioavailability or bioequivalence study in humans using a drug product that contains an already approved, non- new chemical entity and the study will involve a multiple-dose study in normal subjects or patients where either the single or total daily dose exceeds that specified in the labeling of the drug product that is the subject of an approved

- new drug application or abbreviated new drug application, or
- The investigator will conduct a bioavailability or bioequivalence study in humans using a drug product that contains an already approved, non- new chemical entity and the study will involve a multiple-dose study on an extended release product on which no single-dose study has been completed

### **Combination Drug Products and Multi-Drug Studies**

The DUHS IRB has adopted the definitions of “Combination Product” set forth in 21 CFR Part 3. For those research studies using Combination Products, the IRB considers the Primary Mode of Action (“PMOA”), as defined in 21 CFR Part 3, or, in cases where it is impossible to determine PMOA, the primary therapeutic benefit, and uses this consideration in its review of the need for an IND and/or IDE for this Combination Product. The IRB is ultimately guided by the FDA’s determination of any IND/IDE requirements for the Combination Product.

For a research study that involves multiple drugs that are administered separately, review is conducted at two levels: (i) each drug is independently assessed at a convened IRB meeting for the necessity of obtaining an IND number, and (ii) the novel combination of drugs is assessed for the necessity of obtaining an IND number.

### **Investigator-Held IND**

An investigator in a proposed research project who is also the IND holder is a sponsor-investigator and is responsible for complying with both FDA sponsor and investigator regulations, and the DUHS Policy on Responsibilities of an Investigator Who is also a Sponsor.

### **Control, Handling and Documentation of Drugs or Biologics Used in Investigations**

As part of their submission, investigators must provide a description of their process for control, handling and documentation of drugs or biologics investigated or evaluated in the proposed research study. A member of the IRB will evaluate whether the proposed plan is adequate. A pharmacy member of the IRB may evaluate whether proposed plans related to drugs or biologics are adequate. The pharmacy member is not required to be a primary reviewer and the review may occur at the time of the IRB meeting. If a pharmacy member will not be present at the IRB meeting, a pharmacy member may be consulted regarding the proposed plan.

Duke investigators must use the Investigational Drug Service (IDS) for control, handling and documentation of investigational drugs and biologics administered in the inpatient setting, and must use the IDS or an IRB-approved plan for control, handling and documentation of investigational drugs and biologics administered in the outpatient setting.

### **When Questions Arise During the IRB Approval Process or During the Course of an Investigation**

If the IRB determines that an IND is required for a Duke investigator-initiated clinical research study, then approval of the protocol will not be granted unless the FDA-provided IND number has been registered with Duke's Office of Regulatory Affairs and Quality (ORAQ), the sponsor-investigator has completed training with ORAQ staff, and documentation of the IND either being in effect or FDA acknowledgement that it is safe to proceed has been received by the IRB.

If, after a study begins, it is found that an IND is required (e.g., based on a regulatory assessment or adjudication by an external IRB, etc.), further accrual to the study will be put on hold until an IND is obtained and registered with the Regulatory Affairs and Quality office (ORAQ), any required investigator training is completed, and the IRB has approved resumption of accrual to the study.

If the IRB is in doubt about the requirement for an IND, the investigator must inquire about the issue with the FDA. All correspondence with the FDA about the necessity of an IND must be shared with the IRB via the IRB electronic system. The study will not be approved by the IRB until either an IND has been issued by FDA and registered with ORAQ and any required investigator training is completed, or FDA has confirmed that an IND is not required.

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