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

**Drugs or Biologics**

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 one of the following FDA exemptions from the requirements to have an IND [Categories in 21 CFR 312.2(b) and 21 CFR 320.31]

   **Exemption 1**
   - The drug/biologic 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 in this protocol is not intended to support a significant change in the advertising for the drug/biologic
   - The investigation does not involve a route of administration or dosage level or use in a 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:
  o Blood grouping serum
  o Reagent red blood cells
  o 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 test 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 will be 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:
  o 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]
  o The study involves a radioactively labeled drug product
  o The study involves a cytotoxic drug product
  o 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
  o 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
  o 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

Exemption 6

- The clinical investigation involves a combination of drug products and each
drug in the combination has been approved by the FDA for marketing in the
United States

If the IRB determines that an IND is required for a drug or biologic for a specific
research study, that determination may be satisfied by a letter from the FDA stating
that an IND for that drug or biologic is not required.

Devices

When the research is conducted to determine the safety or effectiveness of a device
the IRB will confirm and document for each device that either:

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

2. The device fulfills the requirements for an abbreviated IDE [Criteria in 21 CFR
812.2(b)(1)]
   - The device is not a banned device
   - The device is labeled by the sponsor in accordance with the FDA
Investigational Device Exemptions at 21 CFR 812.5
   - The sponsor will obtain IRB approval of the investigation after presenting the
reviewing IRB with a brief explanation of why the device is not a significant risk
device, and maintains such approval
   - The sponsor will ensure that each investigator participating in the investigation
of the device obtains from each subject under the investigator’s care, consent
as required by FDA Regulations on the Protection of Human Subjects (21 CFR
50) and documents it, unless documentation is waived by the IRB
   - The sponsor will comply with the requirements of the FDA Investigational
Device Exemptions at 21 CFR 812.46 with respect to monitoring
investigations;
   - The sponsor will maintain the records required under the FDA Investigational
Device Exemptions at 21 CFR 812.140(b) (4) and (5) and makes the reports
required under the FDA Investigational Device Exemptions at 21 CFR
812.150(b) (1) through (3) and (5) through (10);
• The sponsor will ensure that participating investigators maintain the records required by the FDA Investigational Device Exemptions at 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
• The sponsor complies with the prohibitions in the FDA Investigational Device Exemptions at 21 CFR 812.7 against promotion and other practices.

OR

3. The device fulfills one of the IDE exemption categories [Criteria in 21 CFR 812.2(c)]:

A. The device, other than a transitional device, was introduced into commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time
B. The device, other than a transitional device, was introduced into commercial distribution on or after May 28, 1976, that FDA had determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that was used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence
C. The device is a diagnostic device and the sponsor will comply with applicable requirements in 21 CFR 809.10(c) and the testing:
   • Is noninvasive
   • Does not require an invasive sampling procedure that presents significant risk
   • Does not by design or intention introduce energy into a participant
   • Was not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
D. The device is undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing was not for the purpose of determining safety or effectiveness and does not put participants at risk
E. The device is intended solely for veterinary use
F. The device is shipped solely for research on or with laboratory animals and labeled in accordance with the FDA Investigational Device Exemptions at 21 CFR 812.5(c)
G. The device is a custom device as defined in the FDA Investigational Device Exemptions at 21 CFR 812.3(b) and is not being used to determine safety or effectiveness for commercial distribution

If the IRB determines that an IDE for the device is required for a specific research study, that determination may be satisfied by a letter from the FDA stating that an IDE for that device is not required.

**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 or IDE**

An investigator in a proposed research project who is also the IND/IDE 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, Biologics and Devices Used in Investigations**

As part of their submission, investigators must provide a description of their process for control, handling and documentation of drugs, biologics and devices 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 will 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.

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. For control, handling and documentation of investigational devices, investigators use an IRB-approved plan.

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

If the IRB determines that an IND or IDE is required for a Duke investigator-initiated clinical research study, then approval of the protocol will not be granted unless the FDA-provided IND/IDE number has been registered with the Duke Translational Medicine Institute (DTMI) Regulatory Affairs office, and the sponsor-investigator has completed training with DTMI Regulatory Affairs office staff.

If, after a study begins, it is found that an IND/IDE 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/IDE is obtained and registered with the DTMI Regulatory Affairs office, 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/IDE, the investigator must inquire about the issue with the FDA. All correspondence with the FDA about the necessity of an IND/IDE must be shared with the IRB via the eIRB. The study will not be approved by the IRB until either an IND/IDE has been issued by FDA and registered with the DTMI Regulatory Affairs office and any required investigator training is completed, or FDA has confirmed that an IND/IDE is not required.

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