Dartmouth-Hitchcock

WORKSHEET: Drugs and Biologics

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The purpose of this worksheet is to provide support for IRB staff pre-reviewing research involving drugs. This worksheet is to be used. It does not need to be completed or retained.

1 Drug Applicability

☐ Does the activity involve any the following? **(Check all that apply) If "No" to both, FDA regulations do not apply.**

- ☐ In the United States: The use of a drug[i] or a biological product (biologic)[ii] in one or more persons other than use of an approved drug in the course of medical practice[iii].
- ☐ Data regarding subjects or control subjects submitted to or held for inspection by FDA[iv].

2 IND Requirements[v] (Check if **"Yes"**. One must be **"Yes"** If all are **"No"** IND information is not complete.)

- ☐ The drug has a valid IND. (Complete Sections 3 and 4)
- ☐ The drug is exempt from the IND requirements (Complete Section 5)
- ☐ The research is conducted outside of the United States and is conducted under ICH-GCP.

3 IND Validation (Check if **"Yes"**. At least one must be **"Yes"** If all are **"No"** IND cannot be validated.)

- ☐ Sponsor protocol imprinted with the IND number.
- ☐ Written communication from the sponsor documenting the IND number.
- ☐ Written communication from the FDA documenting the IND number. *(Required if the investigator holds the* IND.*)*

4 Drug or Biologic Control (Check if **"Yes"**. Must be **"Yes"** If **"No"** information regarding drug control is incomplete.)

- ☐ The plan for storage, control, and dispensing of the drug or biologic is adequate to ensure that only authorized investigators will use the drug and that they will use the drug only in subjects who have provided consent.[vi]

5 IND Exemptions (Check if **"Yes"**. All criteria for one category must be **"Yes"** to be met. If none are met, the drug is not exempt from an IND.)

☐ **Category #1 - Lawfully Marketed Drugs (21 CFR 312.2(b)(1)) or Biologics**

- The drug or biologic is lawfully marketed in the United States.
- ☐ The research is not intended to be reported to the 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.
- ☐ The research is not intended to support a significant change in the advertising for the product.
- ☐ The research 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 product.
- ☐ The research is conducted in compliance with the marketing limitations described in 21 CFR §312.7.

☐ **Category #2 - Serological Tests (21 CFR 312.2(b)(2))**

- ☐ A clinical investigation for an in vitro diagnostic[vii] biological product that involves one or more of the following: (1) Blood grouping serum; (2) Reagent red blood cells; or (3) 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 is shipped in compliance with 21 CFR §312.160.

☐ **Category #3 - Placebos (21 CFR 312.2(b)(5))**

- ☐ A clinical investigation involving use of a placebo when the investigation does not otherwise require submission of an IND.

☐ **Category #4: Bioavailability/Bioequivalence Studies (21 CFR 320.31(b) and (d))**

- ☐ The active moiety in the drug product is identical to that in an FDA approved drug.
- ☐ The drug product is not radioactively labeled.
- ☐ The drug product is not cytotoxic.
- ☐ The dose (single or total daily) does not exceed the dose in the labeling of the approved version of the drug product.
- ☐ The sponsor meets the requirements for retention of test article samples in 21 CFR 320.31(d)(1).

☐ **Category #5: Radioactive Drugs for Research Use (21 CFR 361.1)**

- ☐ The drug has been approved by Radioactive Drug Research Committee as a radioactive drug for certain research use under the criteria in 21 CFR 361.1(b)

☐ **Category #6: Cold Isotopes for Research Use (FDA enforcement discretion[viii])**

- ☐ The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry.
- ☐ The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject.
- ☐ The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies.
- ☐ The quality of the cold isotope meets relevant quality standard.

6 IND Oversight for investigators who hold the IND (Check if **"Yes"**. One of the following must be **"Yes"** if the investigator

	holds the IND)
☐	The FDA requirements of a sponsor (including GMP when applicable) have been assumed by a contract research organization.
☐	An audit has documented that the investigator is compliant with FDA sponsor requirements (including GMP when applicable).

[i] The term ''drug'' means:
(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia 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 and dietary supplements) 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).

[ii] The term "biological product" means 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.

[iii] "Other than the use of an approved drug in the course of medical practice" refers to a practitioner providing an approved drug to a patient because the practitioner believes the drug to be in the best interests of the patient. If the protocol specifies the use of the drug, it is not in the course of medical practice unless use of the drug is completely up to the discretion of the practitioner.

[iv] This is specific to submissions that are part of an application for a research or marketing permit. However, unless otherwise indicated, assume all submissions to FDA meet this requirement.

[v] If there are questions about which category is appropriate, have the investigator apply for an IND following 21 CFR §312.23.

[vi] The investigator or other designated individual must maintain records of the product's delivery to the clinical trial site, the inventory at the site, the use by each subject, and the return to the Sponsor or alternative disposition of unused products. These records include dates, quantities, batch or serial numbers, and Expiration Dates (if applicable), and the unique code numbers assigned to the investigational products and trial subjects. The investigator must maintain records that document adequately that the subjects are provided the doses specified by the protocol and reconcile all investigational products received from the Sponsor.

[vii] An in vitro diagnostic (IVD) products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. IVD products are devices as defined in section 201(h) of the Act and may also be biological products subject to section 351 of the Public Health Service Act.

[viii] (FDA Guidance for Clinical Investigators, Sponsors, and IRBs Investigational New Drug Applications (INDs)) Determining Whether Human Research Studies Can Be Conducted Without an IND, September 2013: https://www.fda.gov/downloads/drugs/guidances/ucm229175.pdf.