## 8.2 INVESTIGATIONAL USE OF DRUGS OR BIOLOGICS

### A. Investigational New Drug (IND)

Federal law prohibits the distribution of a new drug or biological product until the FDA has reviewed clinical data and determined that the agent is safe and effective for a specific indication in humans. Investigational New Drug (IND) means a new drug or biological product that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. A biological product is a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, 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. An IND application must be submitted by the sponsor of a new drug or biological product to the FDA before tests on human subjects can begin. All information related to the IND must be provided at the time a sponsor applies for IRB approval to conduct the research.

In accordance with 21 CFR 312.40, 30 days after the FDA receives the IND application the sponsor may begin clinical investigations, unless the FDA notifies the sponsor that the clinical investigation described in the IND application are subject to a clinical hold.

### B. Exemptions from IND Requirement

Investigations involving drugs/biologic that are considered exempt from IND regulations must still be reviewed by the IRB. The Sponsor must provide the IRB with documentation that the investigation with the drug/biologic meets one of the FDA exemptions from the requirement to have an IND.

i. Exemption 1

- The drug product 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;
- If the drug/biologic that is undergoing investigation is lawfully marketed as a prescription product, the investigation is not intended to support a significant change in the advertising for the product;
- 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 product;
- The investigation is conducted in compliance with the requirements for IRB review and obtaining informed consent; and
- The investigation is conducted in compliance with the requirements of 21 CFR 312.7 (waiver of informed consent requirements for emergency research).

ii. Exemption 2

- A clinical investigation involving one of the following in vitro diagnostic biological product: (a) blood grouping serum; (b) reagent red blood cells; and (c)

anti-human globulin is exempt if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure, and (b) it is shipped in compliance with 21 CFR 312.160.

iii. Exemption 3

- A drug intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160.

iv. Exemption 4

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

The IRB can request that the investigator contact the FDA for review of the proposed clinical investigation to determine whether the use qualifies for an exemption from the IND requirements.

## 8.3 EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC

The emergency use provision in the FDA regulations (21 CFR 56.104(c)) is an exemption from prior review and approval by the IRB if time does not allow. The exemption, allows for one emergency use of a drug/biologic for the treatment of a single patient only. Any subsequent use of the test article at the institution is subject to IRB review.

FDA regulations are not intended to "limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law" (21 CFR 50.25(d)).

Emergency use of an investigational drug/biologic for a patient may be appropriate if the FDA determines that the following criteria are met:

1. The patient, or patients, to be treated have a serious **or** immediately life-threatening disease or condition, **and** there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition (21 CFR 312.305(a));

    - *Serious disease or condition* means 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 need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

    - *Immediately life-threatening* disease or condition means a stage of 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.

2. The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; *and*