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*

3. Providing the investigational drug/biologic for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use (21 CFR 312.310(a)).
4. The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; *and*
5. FDA must determine that the patient cannot obtain the drug under another IND or protocol.

The emergency use of an unapproved investigational drug/biologic requires an IND. The FDA may authorize expanded access for an individual patient without a written submission and by telephone if there is "an emergency that requires the patient to be treated before a written submission can be made." The licensed physician or sponsor, however, must agree to submit an expanded access IND or protocol within 15 working days of FDA's authorization of the use (312.310(d)(2)).

The contact information for the FDA review division and required forms can be found at: http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

If there is sufficient time, the following is to be submitted via Cayuse IRB for acknowledgment of the use:

a. Initial Application in Cayuse IRB, which includes: A description of the patient's disease including recent medical history and previous treatments; a summary outlining the rationale for the use, including an explanation of why there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; and the rationale for why this investigational drug/biologic is preferable. The submission is also to include the method of administration and duration of therapy, and a description of the clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the drug/biologic and minimize its risks. This summary information must support the criteria for emergency use as described above.
b. A copy of the informed consent that will be used. The consent form must explain the purpose of the use of drug/biologic, and must not include references to a research investigation. It must include an explanation of what data will be collected and the reporting requirements to the FDA and/or sponsor. If the physician is unable to obtain consent, the submission must meet the criteria for exception to obtaining informed consent as described below.
c. The emergency expanded access IND letter from the FDA, or, documentation that verbal authorization was obtained from the FDA due to time constraints.
d. The statement from the supplier of the drug/biologic that they will ship the product and authorize its use under the emergency IND or verbal FDA authorization.
e. A letter of support from the Research Pharmacy if it will dispense the drug/biologic.

The IRB Chair will confirm that the necessary requirements for an emergency use are met. Once the review is completed, an Acknowledgement letter will be forwarded to the treating physician, along with a stamped version of the consent document (as applicable).

Within five-working days after administration, whether the drug/biologic was administered with prior IRB acknowledgement or not, the treating physician must submit to the IRB the following:

a. A summary of the administration of the test article and outcome.

b. A summary of any unexpected fatal or life-threatening suspected adverse reactions because of the administration of the drug/biologic.

c. If IRB acknowledgement was not obtained prior to administration, the treating physician is required to submit all the elements listed above for prior IRB notification.

If the treating physician determines that there is a likelihood of treating additional patients with the drug/biologic, the treating physician should consider submitting an expanded access IND or protocol to the FDA and submit an Initial Application via Cayuse IRB to obtain IRB review approval for the prospective use.

A. Exception from the Informed Consent Requirement for Emergency Use

An exception from the requirement to obtain informed consent for the emergency use of a drug/biologic is permissible if both the physician and a physician who is not otherwise participating in the patient's treatment certify in writing that the emergency meets each of the following (21 CFR 50.23(a)):

1. The subject is confronted by a life-threatening situation necessitating the use of the drug/biologic;
2. Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the patient;
3. Time is not sufficient to obtain consent from the patient's legally authorized representative; and
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

If the investigator cannot obtain the independent assessment of a physician to certify the above, then within five days after the use of the drug/biologic a physician who is not otherwise participating in the clinical investigation must document in writing that the above criteria were satisfied. This determination is to be included in the five working day report to the IRB.

B. Reporting Responsibilities

The treating physician is responsible for reporting the use of the drug/biologic to the FDA:

a. If an expanded access IND for emergency use was obtained by the treating physician prior to the administration of the drug/biologic, the treating physician is responsible to submit the following (using Form 3926):

- Submit written progress reports required at intervals not exceeding one year and are due within 60 days of the application anniversary date (i.e., the date granted the IND).
- Report any unexpected fatal or life-threatening suspected adverse reactions to no later than 7 calendar days after initial receipt of the information.

- Report any (1) serious, unexpected suspected adverse reactions, (2) findings from other clinical, animal, or in-vitro studies that suggest significant human risk, and (3) a clinically important increase in the rate of a serious suspected adverse reaction to the FDA and to all investigators (as applicable) no later than 15 calendar days after determining that the information qualifies for reporting .
- When the treating physician has completed treatment of the patient with the drug/biologic or if it has been decided not to treat the patient, the FDA must be notified so that the IND may be withdrawn. The final report to the FDA should include a summary of the results of treatment, including adverse effects, and information concerning the disposition of any unused supplies of the test article.

b. If no prior expanded access IND was obtained (only verbal FDA approval), the following reporting actions are required:

- Submit an expanded access IND application **within 15 working days** of FDA's initial authorization of the expanded access use (21 CFR 312.310(d)(2)).

8.4 EXPANDED ACCESS USE OF INVESTIGATIONAL DRUGS/BIOLOGICS

Expanded access refers to the use of an investigational drug/biologic when the primary purpose is to diagnose, monitor, or treat a patient rather than to obtain the kind of information about the drug/biologic (i.e., safety and efficacy data) that is generally derived from clinical trials. Expanded access to an investigational drug/biologic can only be provided under an expanded access IND or protocol if the sponsor is actively pursuing marketing approval of the drug/biologic for the expanded access use.

Expanded access, access, and treatment use may also refer to (1) use in situations when a drug/biologic has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks; (2) use of a similar, but unapproved drug/biologic (e.g., foreign-approved product) to provide treatment during a shortage of the approved drug/biologic; (3) use of an approved drug/biologic where availability is limited by a risk evaluation and mitigation strategy (REMS) for diagnostic, monitoring, or treatment purposes, by patients who cannot obtain the drug/biologic under the REMS; or (4) use for other reasons.

There are three categories of expanded access to an investigational drug/biologic:

- Expanded access for individual patients, including for emergency use.
- Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol — a treatment protocol is submitted as a protocol to an existing IND by the sponsor)
- Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations)

For each category of expanded access, there are two types of regulatory submissions that can be made:

1. Expanded access ***protocol*** submitted as a protocol amendment to an existing IND (i.e., an expanded access protocol). An expanded access protocol submission for expanded access should be used only if the sponsor has an existing IND — typically under which