Department: **UAMS Human Research Advisory Committee**
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Section: **Drugs and Devices**
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SUBJECT: Emergency Use of an Investigational Drug (IND) or Biologic

Treatment use of an investigational new drug. A drug that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease condition in patients for whom no comparable or satisfactory alternative drug or other therapy is available. During the clinical investigation of the drug, it may be appropriate to use the drug in the treatment of patients not in the clinical trials, in accordance with a treatment protocol or treatment IND. The purpose of this section is to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible, before general marketing begins, and to obtain additional data on the drug's safety and effectiveness. In the case of a serious disease, a drug ordinarily may be made available for treatment use under this section during Phase 3 investigations or after all clinical trials have been completed; however, in appropriate circumstances, a drug may be made available for treatment use during Phase 2. In the case of an immediately life-threatening disease, a drug may be made available for treatment use under this section earlier than Phase 3, but ordinarily not earlier than Phase 2. For purposes of this section, the ``treatment use'' of a drug includes the use of a drug for diagnostic purposes. If a protocol for an investigational drug meets the criteria of this section, the protocol is to be submitted as a treatment protocol under the provisions of this section (21 CFR312.34; 45 CFR).

FDA shall permit an investigational drug to be used for a treatment use under a treatment protocol or treatment IND if:

1. The drug is intended to treat a serious or immediately life-threatening disease;

2. There is no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;

3. The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and

4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence.

Serious disease. For a drug intended to treat a serious disease, the Commissioner may deny a request for treatment use under a treatment protocol or treatment IND if there is insufficient evidence of safety and effectiveness to support such use.

Immediately life-threatening disease. For a drug intended to treat an immediately life-threatening disease, the Commissioner may deny a request for treatment use of an investigational drug under a treatment protocol or treatment IND if the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the
drug:

1. May be effective for its intended use in its intended patient population; or

2. Would not expose the patients to whom the drug is to be administered to an unreasonable and significant additional risk of illness or injury.

3. For the purpose of this section, an ``immediately life-threatening'' disease means a stage of a disease in which there is a reasonable likelihood that

death will occur within a matter of months or in which premature death is likely without early treatment.

Safeguards. Treatment use of an investigational drug is conditioned on the sponsor and investigators complying with the safeguards of the IND process, including the regulations governing informed consent (21 CFR part 50) and institutional review boards (21 CFR part 56) and the applicable provisions of part 312, including distribution of the drug through qualified experts, maintenance of adequate manufacturing facilities, and submission of IND safety reports.

Clinical hold. FDA may place on clinical hold a proposed or ongoing treatment protocol or treatment IND in accordance with Sec. 312.42.

Obtaining an Emergency IND. The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means (21 CFR312.36; 45 CFR).

Consent. Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the requirements of exception for consent in emergency research detailed in section 15.2 of this manual).

If, in the investigator's opinion, immediate use of the test article (investigational drug or biologic) is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. **The investigator must notify the HRAC within 5 working days after the use of the test article** (21 CFRIf, in the investigator's opinion, immediate use of the test article (investigational drug or biologic) is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. **The investigator must notify the HRAC within 5 working days after the use of the test article** (21 CFR50.23c).