

Clarification of FDA Regulations and Guidance on "Compassionate" and "Humanitarian" Use

The following FDA regulations and guidance make provision for the so-called "compassionate use" of investigational drugs and devices. Investigators should note that the term "compassionate use" does not appear in FDA regulations, and its use is actively discouraged by the FDA Center for Drug Evaluation and Research (CDER). The term does appear in guidance issued by the FDA Center for Devices and Radiological Health (CDRH). That guidance is summarized in Section B (Devices) of this document.

The Compassionate Use situations described in Section A (Drugs) and Section B (Devices) of this guidance should be distinguished from the Humanitarian Use Device (HUD) and the Humanitarian Device Exemption (HDE) described in Section C.

I. DRUGS

- (B) TREATMENT IND. During the clinical investigation of a drug, it may be appropriate to use the drug in treatment of patients not in the clinical trials. Such use requires FDA approval under a treatment protocol (21 CFR 312.35) or a treatment IND (21 CFR 312.34), as well as IRB review and approval and informed consent.
- (C) SINGLE-PATIENT TREATMENT IND. The Single-Patient Treatment IND is not described in regulations yet, but was added to the law under the FDA Modernization Act (FDAMA) in 1997. From an operational standpoint, the Single-Patient IND must meet the same requirements as a standard IND, and requires IRB review and approval and informed consent.
- (D) GROUP C TREATMENT IND. Group C drugs are Phase 3 study drugs that have shown evidence of efficacy in a specific tumor type. Group C drugs are distributed by the National Cancer Institute (NCI) with a Guideline Protocol and an informed consent document. Informed consent is required, and although FDA and NCI permit the use of Group C drugs without local IRB review, this Institution's policy normally requires review and approval by the IRB. Investigators who are considering use of Group C drugs should contact the IRB Chairperson for guidance.
- (E) ORPHAN DRUGS. The term "orphan drug" refers to a product that treats a rare disease affecting fewer than 200,000 Americans. The treatment use of orphan drugs requires prospective IRB review and approval and informed consent (21 CFR 316.40 and 312.34).

- (F) PARALLEL TRACK STUDIES. FDA also permits wider access to promising new drugs for HIV/AIDS related diseases under a “separate access” protocol that “parallels” the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. These so-called “parallel track” studies require prospective IRB review and informed consent.

II. DEVICES

- (B) TREATMENT IDE. Treatment use of an investigational device facilitates the availability of promising new devices to desperately ill patients as early as possible before general marketing begins. Such use may occur when: (i) the patient has a serious or immediately life-threatening condition; (ii) there is no comparable or satisfactory alternative available; (iii) the device is under investigation in a controlled trial for the same use (or such trials have been complete); (iv) the Sponsor is pursuing marketing approval/clearance; (v) the Sponsor has submitted and the FDA has approved an IDE under 21 CFR 812.36. Such use permits wide access to the device dependent upon patient need. IRB review and approval and informed consent are required.
- (C) COMPASSIONATE USE. Compassionate use of an unapproved device may occur when a device that is being tested in a clinical trial is the only option available for a patient faced with a serious condition. Such uses require prior FDA approval of a protocol deviation under 21 CFR 812.35(a). Prior FDA approval for compassionate use should be obtained before the device is used.

On occasion, compassionate use may occur even if there is no IDE for the device. Under this situation, the physician would submit the compassionate use request directly to FDA.

Compassionate use of an unapproved device also requires as many of the following patient protections as possible: (i) informed consent; (ii) clearance from the institution; (iii) concurrence of the IRB chairperson (this concurrence does not constitute IRB approval); (iv) an independent assessment of an uninvolved physician; and (v) authorization from the IDE sponsor. Follow-up reports should be provided to the Sponsor. Such use may involve an individual patient or a small group of patients.

The compassionate use of an investigational device may take place only where the FDA has specifically approved the use. IRB approval and the informed consent of the patient-subject must be obtained prior to the use, unless the criteria for emergency use of devices described above have been satisfied.

III. HUMANITARIAN USE DEVICES and HUMANITARIAN DEVICE EXEMPTIONS

A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. FDA developed this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

The HUD regulation provides for Humanitarian Device Exemption (HDE) applications. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

An approved HDE authorizes marketing of the HUD. However, a HUD may only be used after the institution's convened (full) IRB has approved the use of the device at the institution. The IRB's responsibility in this case is to conduct a special limited review simply to verify that the proposed (non-research) use of the device is consistent with the HDE's FDA-approved indication. (21 CFR 814.124(a)). After granting initial approval, the IRB may use expedited procedures for conducting subsequent continuing reviews, which must be performed at least annually. Informed consent of patients is not required because the use of the HUD in a manner consistent with its marketing approval under the HDE does not constitute research.