



Humanitarian Use Devices

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Section 520(m) of the Food, Drug and Cosmetic Act

“... to encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States.” [yearly]

Intent of HDE Provisions

Provide incentive for development of devices intended for treatment or diagnosis, **in small patient populations where otherwise a device manufacturer's R&D costs could exceed market returns**

Regulatory History

- Safe Medical Devices Act 1990
 - created HDE pathway
- FDA Modernization Act 1997
 - 75 days, IRB approval
- FDA Amendments Act 2007
 - pediatric provisions added

HDE vs. PMA

- Both are marketing approvals
- Both subject to post-market Medical Device Reporting (MDR) requirements
- Approval thresholds differ:
 - PMA: safety and **effectiveness**
 - HDE: safety and **probable benefit**
 - No regulatory definition of probable benefit

Statutory Conditions

- Approval (HDE) authorizes **marketing** of a humanitarian use device (HUD)
- IRB approval required before the device is used (except in emergency situations)
- Labeling must clearly identify device as a HUD, and that effectiveness for that indication has not been demonstrated

Statutory Conditions (cont.)

- Device not otherwise available (through a 510(k) or PMA)
- No comparable **device** currently available (through a 510(k) or PMA)
- Device under consideration:
 - Does not pose unreasonable risk of illness or injury (i.e., **safety** is demonstrated), **AND**
 - **Probable benefit** outweighs the risk (i.e., exempt from effectiveness requirements of a PMA)

FDA Approval Threshold

Device does not expose patients to unreasonable risk of illness or injury, AND probable benefit outweighs the risks of using the device, taking into account the probable risks and benefits of alternative therapies

HUD Designation (21 CFR 814 Subpart H)

Part One of the two-part review/approval process:
Request submitted to FDA's Office of Orphan
Products (Office of the Commissioner)

- Designates the intended population for the device
 - Must be <4000/year in the U.S.
 - If subset of a larger population, must be “medically plausible” subset
- 45 day review
- HDE can be submitted for a narrower, but not a broader, subset

Medically Plausible Subset

If the disease or conditions occurs in > 4,000 patients/year, the device **could** be used in a subset of the disease or condition AS LONG AS sponsor shows the subset is medically plausible (NOT just “readily identifiable”). A medically plausible subset is one in which use of the device is limited to that subset because of some inherent property of the device and/or the disease. That is, the sponsor must explain why the device couldn't also be used in all patients with the disease or condition.

HDE Review

Part Two of the two part review/approval process:

- Follows HUD designation granted by Office of Orphan Products
- 75 day review
- Explanation why device would not otherwise be available
- Statement that no comparable device exists

HDE Review (continued)

- Device description
- Bench and animal testing
- Clinical experience: data, literature, investigation(s), marketing experience (OUS, or same device for a different indication)
 - Clinical trials are usually not randomized or controlled due to small sample size and lack of a comparable marketed device

HDE Review (continued)

- Manufacturing information:
Quality Systems Regulation (QSR) applies (unless elements waived)
- Labeling (physician and patient), including HUD statement (that no effectiveness demonstrated)
- Cost cannot exceed R&D, fabrication and distribution (unless pediatric)

Key Points

- HDE is marketing approval
- Exempt from requirement to establish effectiveness – must show probable benefit
- IRB approval required
- No requirement to submit PMA/510(k)
- Can have multiple HDEs for same indication from different sponsors

Points of Confusion

- HDE devices are **marketed, NOT investigational**, devices
- Informed consent is not an FDA requirement, but can be (and often is) a state, local, institutional or IRB requirement
- A clinical trial for a new indication requires an IDE for significant risk (SR) devices (so far, all HDEs are SR)

2010 Guidance

Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff:

<http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm110194.htm>

- **52 approved HDEs since 1996**
- **List of approved HDEs and their Summaries of Safety and Probable Benefit (SSPB) available at:**

<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm>

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