Orphan Drug Development Guidebook

Building Block U202

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	Humanitarian Device Exemption (HDE) Humanitarian Use Device (HUD) Program
References	FDA HDE: https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/humanitariandeviceexemption/default.htm FDA Designating HUD: https://www.fda.gov/forindustry/developingproductsforrarediseasesconditions/designatinghumanitarianusedeviceshuds/default.htm FDA Guidance: https://www.fda.gov/industry/designating-humanitarian-use-device-hud/education-and-media-resources-hud-program
Description	In 1990, a new provision was created in the US under the Safe Medical Devices Act to create a new regulatory pathway for device products intended for diseases or condition that affect small (rare) populations that defined HDEs and HUDs. A HUD is “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the US per year.” [21CFR 814.3(n)]. An HDE is a marketing application for a HUD. An HDE is exempt from the effectiveness requirements of the Food, Drug and Cosmetic Act, and is subject to certain profit and use restrictions. An HDE is similar to a premarket approval application (PMA) in that the applicant must demonstrate a reasonable assurance of safety; however, it differs from a PMA in that the applicant is exempt from the requirement of demonstrating a reasonable

assurance of effectiveness. For safety, a HUD designated device is eligible for HDE approval if, among other criteria, "the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment." [21CFR 814.104(b)(2)].

HUD designation is the first step in seeking marketing approval of an HDE and is a prerequisite for submitting an HDE marketing application to FDA CDRH or CBER. In order to obtain HUD designation, an applicant must provide documentation to demonstrate that the device meets the population use definition and a description of the rare disease or condition that the device treats or diagnoses. The required contents of the HUD are set forth in 21CFR 814.102 and described in detail in the FDA HUD Designation Guidance: https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM336515.pdf

HDEs may be subject to some conditions of approval, including:

- Labeling
- Post-approval record-keeping requirements
- Names and addresses to which the HUD was shipped, IRB records
- Mandatory reporting
- Periodic, post-approval study reports, supplements, annual Medical Device Reports (MDRs), annual incidence reassessment to ensure use continues to fall below 8,000 patients per year
- Post-approval studies may be required
- IRB approval at the site, before the HDE-approved device is used at that site (but not for each patient at that site). A HUD-designated device may only be used in facilities with functioning IRBs.
- May not be sold for profit except in certain circumstances.
- For Pediatric devices, Pediatric Advisory Committee annual review is performed, which is coordinated through FDA's Office of Orphan Products

The humanitarian use device program was established to "encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect not more than 8,000 individuals in the US per year." [21CFR814.100(a).

HUD designation request applications are reviewed with a 45-day goal timeline.

	The HDE review goal date timeline is 180 days, which is the same as for a PMA. (There are no fast track or priority review designations for devices).
Category	Regulatory Building Block
Geographical scope	United States of America
Availability	Applicants developing medical devices intended for the treatment or diagnosis of a rare disease.
Scope of use	The goal of this building block, along with other tools of the FDA Office of Orphan Products Development (OOPD) is to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. Device manufacturers may wish to consider HUD designation for their qualifying products.
Stakeholders	• Medical device manufacturer • FDA Office of Orphan Products Development (OOPD) • FDA review center, CDRH or CBER
Enablers / Requirements	HUD designation is the first step in seeking marketing approval of an HDE and is a prerequisite for submitting an HDE marketing application to FDA CDRH or CBER. For HUD designation, an applicant must provide justification that the medical device is intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the US per year. Devices are eligible for HDE if they are HUD-designated and there is no legally marketed device for the same disease or condition granted under premarket notification (501(k) or PMA.
Output	The final product is an HDE marketing authorization under the Humanitarian Use Device pathway.
Best time to apply and time window	HUD designation must be obtained prior to submitting an HDE in the premarket period. Early consultation with OOPD is recommended.

Expert tips	Extensive information, guidance and advice on the Humanitarian Use Device pathway is available on FDA OOPD's website: https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/DesignatingHumanitarianUseDevicesHUDS/default.htm Interested parties may also request assistance from OOPD staff at (301) 796-8660 or by email at: orphan@fda.hhs.gov PROs: – The main incentive of the HDE is that it is exempt from the effectiveness requirements for a PMA. Manufacturers of HUD devices are exempt from the usual PMA requirement to provide reasonable assurance of effectiveness in the premarket period for an HDE approval. – User fees for marketing applications are waived for HUD-designated devices. CONs: – There are considerable regulatory burdens and restrictions on profits for HDE devices. For example, prior IRB approval and oversight at the site at which the device is used is required, as well as significant reporting requirements. HDE authorization may also be withdrawn by FDA should population use restrictions be exceeded (<8,000 patients per year in the US), or another device receives marketing authorization for the same indication.