HDE Preparation Guide

Digital Health
Regulatory Pathways

The Humanitarian Device Exemption (HDE) is a FDA regulatory pathway for certain digital health products that are intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year - the FDA's definition of a "rare" disease.

As the research investment and development cost of such a product could exceed the market returns, this pathway provides an incentive for innovators to develop these products for use in the treatment or diagnosis of diseases affecting these smaller populations.

<8000

Individuals per year in the US

Two key terms to keep in mind:

HUD	HDE
Humanitarian Use Device	*Humanitarian Device Exemption*
A Humanitarian Use Device is a 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 United States per year.	A Humanitarian Device Exemption is a marketing application that is submitted to the FDA to obtain an approval for an HUD (Humanitarian Use Device).

DOWNLOAD **At-a-Glance Overview on HDE**

What should I know?

12 step process as a general guide for preparing a HDE submission:

1. Determine if the device is eligible for an HDE by reviewing FDA guidance and regulations.
2. Classify the device according to FDA regulations.
3. Conduct a thorough risk analysis and develop a comprehensive quality system.
4. Prepare a pre-submission package and submit it to the FDA for feedback.
5. Revise the device or submission package based on FDA feedback.
6. Prepare and submit the HDE application to the FDA.
7. Address any issues or concerns raised by the FDA during the review process.
8. Conduct any necessary clinical studies to demonstrate the safety and effectiveness of the device.

9. Submit any additional information requested by the FDA.
10. Receive clearance or approval for the HDE from the FDA and comply with post-approval reporting and record-keeping requirements.
11. Continuously monitor the safety and effectiveness of the device and make any necessary changes to the device or quality system.
12. Be prepared to address any issues or concerns that may arise during the life-cycle of the device.

How is the HDE process different from Premarket Approval (PMA)?

Differences between the PMA and HDE processes:

Category	**PMA** (Premarket Approval)	**HDE** (Humanitarian Device Exemption)
FDA Oversight Language	Approved	Approved
Indication for Use	Proposed by Applicant	Based on HUD designation
Target population	General public	Patient with rare disease (<8000 patients in US/year)
Safety	Reasonable Assurance of Safety	Will not expose patients to an unreasonable or significant risk of illness or injury
Effectiveness	Reasonable Assurance of Effectiveness	Demonstration of Probable Benefit, exempt from demonstrating effectiveness
Timeline	180 days – if no panel 320 days – if panel	75 days
Cost	Standard Fee: $441,547 Small Business Fee: $110,387	No fee
Institutional Review Board (IRB) Oversight After Approval	No	May only be used at facilities that have IRB oversight
Restrictions on Profit	No	Yes

DOWNLOAD **Comparison Chart of Regulatory Pathways for Digital Health**

What should I include?

Items to consider to prepare for an FDA HDE request:

- Complete HUD description
- Copy of the HUD designation letter
- Explanation of why the product would not be available unless an HDE were granted
- Statement declaring no comparable legally marketed product exists for the intended use (other than another approved HUD)
- Explanation of why the probable benefit to health from the use of the product outweighs the risk of injury or illness from its use
- All required information under 21 CFR 814.20(b)
- Sufficient technical information:
    - Non-clinical studies
    - Clinical investigations
- Quality System information
- Amount charged for the product:
    - If the product is profitable, request an exception to the profit prohibition
- Physician and patient labeling (if applicable)

It is important to carefully review the FDA's guidance on Humanitarian Device Exemption requests to ensure that all necessary information is included in the submission.

DOWNLOAD HDE Checklist

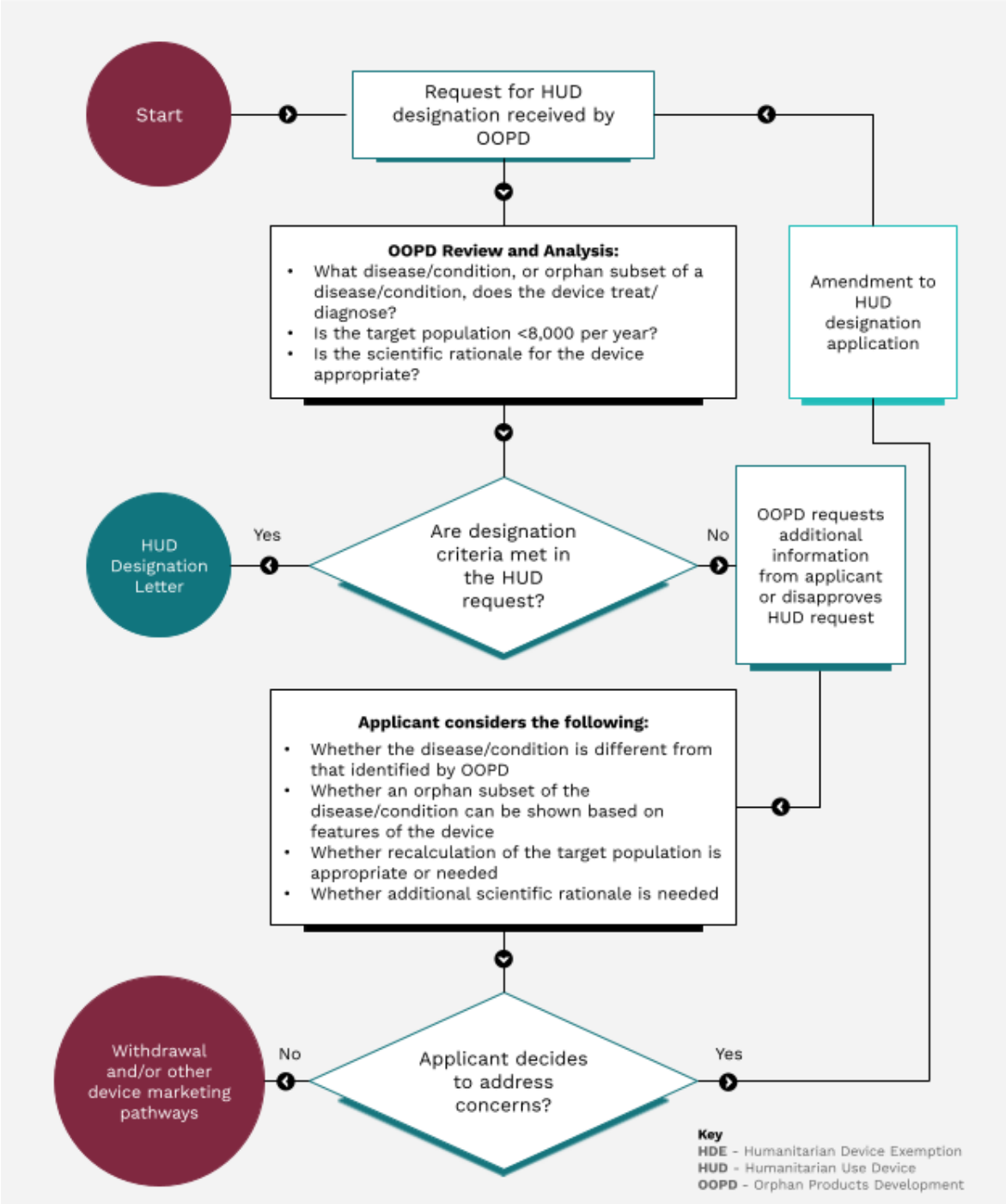
What is the FDA HDE process?

Two-step process

Before an innovator submits an HDE application, complete step 1:

- The company must first prepare and submit a marketing approval request for Humanitarian Use Device (HUD) designation to the FDA's Office of Orphan Products Development (OOPD).
- Over a period of 45 days, OOPD may determine that the product does or does not meet the statutory standards of an HUD.
- If an HUD designation letter is granted, go to Step 2.

What is the review process for a HUD request and granting of a HUD Designation?



DOWNLOAD HDE Decision Making Flowchart

Step 2:

- Once the digital health product is designated as an HUD, the company then submits an HDE application, which is similar to a Premarket Approval Application (PMA) in both form and content, but is exempt from the effectiveness requirements of a PMA (i.e., it must demonstrate safety and probable benefit).
- To be eligible to submit an HDE application, an applicant must have obtained HUD designation, and there cannot be another comparable product that is legally marketed for the same intended use (other than another approved HUD). In determining whether a comparable product exists, the FDA will consider:
    - The product's indications for use and technological characteristics.
    - The patient population to be treated or diagnosed with the product.
    - Whether the product meets the needs of the identified patient population.
- HDE applications should be submitted in an electronic format (eCopy) to the proper FDA Premarket Review Center: either the Center for Devices and Radiological Health (CDRH), or the Center for Biologics Evaluation and Research (CBER), depending on which Center has jurisdiction of your product.

What should I expect?

Outcomes to expect for an FDA HDE request decision

Based on the information provided by the company for their digital health product, the FDA will complete a substantive review of an HDE application and make a decision notifying the applicant by issuing one of the following:

#	FDA Decision	Description
1	**Approval Order**	**Allows** the product to be **legally marketed** in the US. FDA lists the **approved indication for use** and any conditions of approval. Provides the **Annual Distribution Number (ADN)**, if the FDA determines that the HDE holder is eligible to sell the device for profit.
2	**Approvable Letter**	**Identifies minor deficiencies** (e.g. labeling related items, postapproval study, etc.) that must be resolved in order for the application to be approved.
3	**Major Deficiency Letter**	**Identifies major outstanding deficiencies** that must be resolved in order for the application to be approved. Generally issued if deficiencies cannot be resolved interactively but do not require new clinical and/or substantive nonclinical evidence.

4	**Not Approvable Letter**	**Identifies significant deficiencies** that must be resolved in order for the application to be approved, usually involving new clinical and/or substantive nonclinical evidence.

Humanitarian Device Exemption (HDE)

Search FDA HDE Database	*DiMe Resources*			
	 At-a-Glance	 Preparation Guide	 Checklist	 FAQs

Access DiMe's Digital Health Regulatory Pathway Resources

 **Identify** your regulatory pathway

 **Build** your regulatory strategy

 **Interact** with regulators