# **HDE** Submission Checklist

Digital Health **Regulatory Pathways**

As you plan for the submission of the Humanitarian Device Exemption (HDE), check out the table below for the FDA's Checklist for HDEs.

*Note: Throughout the document, the term "product" refers to a digital health product that entails either a medical device and/or a combination product unless indicated otherwise for specific reasons.*

| # | Title | Information | Yes | No | N/A |
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| **Preliminary questions** | | | | | |
| 1 | Is the product a device or a combination product with a device constituent part?<br><br>NOTE: If the product is a combination product with a device constituent part, it may not be appropriate for HDE review. | | ☐ | ☐ | ☐ |
| 2 | Is there a copy of, or reference to the determination made by the Office of Orphan Product Development that the product qualifies as a Humanitarian Use Device (HUD)? | | ☐ | ☐ | ☐ |
| 3 | Has a Request for Designation (RFD) been submitted?<br><br>*If no, mark N/A.* | • Does the product have the same design/formulation as that presented in the RFD submission? | ☐ | ☐ | ☐ |
| | | • Are the products and indications for use the same in the HDE and RFD submission? | ☐ | ☐ | ☐ |
| 4 | Is the product eligible for HDE? | | ☐ | ☐ | ☐ |
| 5 | Is the manufacturer currently on the FDA's Application Integrity Policy (AIP) list? | | ☐ | ☐ | ☐ |
| **Organizational and Administrative Elements** | | | | | |
| 1 | For the HDE content: | Are all required sections in English or accompanied with an English translation? (Includes written or translated reports, literature, articles, etc.) | ☐ | ☐ | ☐ |
| | | Is there a table of contents? | ☐ | ☐ | ☐ |
| 2 | For the HDE/HUD information: | Is there an explanation of why the product would not be available unless an HDE was granted? | ☐ | ☐ | ☐ |

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| | | Is there a statement that no other comparable product, other than another approved HUD under an HDE or a product under an approved investigational device exemption (IDE), is available to treat or diagnose the disease or condition? | ☐ | ☐ | ☐ |
| | | Is there a discussion of the risks and benefits of currently available products/alternative forms of treatment? | ☐ | ☐ | ☐ |
| | | Is there an explanation of why the probable benefit to health from the use of the product outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available products/ alternative forms of treatment? | ☐ | ☐ | ☐ |
| | | Has the amount to be charged for the product been provided, and, if >$250, is a report or attestation provided verifying that the amount charged does not exceed the costs of the product's research, development, fabrication, and distribution? | ☐ | ☐ | ☐ |
| 3 | Is a bibliography provided? | | ☐ | ☐ | ☐ |
| 4 | If a product sample has been requested by the FDA, has it been provided, or, if impractical to submit, has the applicant offered alternatives to allow FDA staff to view or access the product? | | ☐ | ☐ | ☐ |
| 5 | Is there a summary of the contents of the HDE? | | ☐ | ☐ | ☐ |
| 6 | Is the description of the product included?<br><br>*If no, mark N/A.* | Does it include pictorial representations and material specifications of the product? | ☐ | ☐ | ☐ |
| | | Is a description of the principles of operation of the device (including components) and properties relevant to clinical function present? | ☐ | ☐ | ☐ |
| 7 | Is the Device Manufacturing Section included and has a description of the methods, facilities, and controls used in the manufacture, processing, packing, storage, and installation of the device been provided? Learn more. | | ☐ | ☐ | ☐ |

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| 8 | Are summaries of the nonclinical laboratory studies and full test reports provided for the following?:<br><br>*If no, mark N/A.* | a. Sterilization | ☐ | ☐ | ☐ |
| | | b. Biological/Microbiological | ☐ | ☐ | ☐ |
| | | c. Immunological | ☐ | ☐ | ☐ |
| | | d. Toxicological/Biocompatibility | ☐ | ☐ | ☐ |
| | | e. Engineering (stress, wear, etc.) | ☐ | ☐ | ☐ |
| | | f. Chemistry/Analytical (typically for In-Vitro Diagnostics) | ☐ | ☐ | ☐ |
| | | g. Shelf Life | ☐ | ☐ | ☐ |
| | | h. Animal Studies | ☐ | ☐ | ☐ |
| | | i. Other Essential Laboratory Testing | ☐ | ☐ | ☐ |
| 9 | Is a summary of the clinical investigation(s) and results provided?<br><br>*If no, mark N/A.* | Are the final versions of the clinical protocols included? | ☐ | ☐ | ☐ |
| | | Is a description of study population demographics provided? | ☐ | ☐ | ☐ |
| | | Is a description of adverse events (e.g., adverse reactions, complaints, discontinuations, failures, replacements) given? | ☐ | ☐ | ☐ |
| | | Have report forms for patients who died or who did not complete the investigation been provided (i.e. to resolve potential bias)? | ☐ | ☐ | ☐ |
| 10 | Are statistical analyses of the clinical investigations, as well as their results, provided? | | ☐ | ☐ | ☐ |
| 11 | Has appropriate draft physician and patient labeling been submitted?<br><br>*If no, mark N/A.* | **Physician Labeling**<br>1. Are indications for use included? | ☐ | ☐ | ☐ |
| | | 2. Are contraindications, warnings, and precautions included? | ☐ | ☐ | ☐ |
| | | 3. Are instructions for use included? | ☐ | ☐ | ☐ |
| | | 4. Does it include the statement “Humanitarian Device. Authorized by Federal law for use in the [treatment | ☐ | ☐ | ☐ |

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| | | or diagnosis] of [specific disease or condition]. The effectiveness of this device for this use has not been demonstrated." | | | |
| | | **Patient Labeling**<br>Check "N/A" if the FDA's Center for Devices and Radiological Health (CDRH) has indicated that patient labeling is not necessary. | ☐ | ☐ | ☐ |
| | | **Technical/operators manual** | ☐ | ☐ | ☐ |
| **Statements/Certifications/Declarations of Conformity** | | | | | |
| 1 | Does the application utilize voluntary consensus standard(s)?:<br><br>*If not, mark N/A.* | If yes, does the application include: a Declaration of Conformity (DOC) as outlined in FDA's guidance document, "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," **or,** if citing general use of a standard, an explanation of any deviation from the standard? | ☐ | ☐ | ☐ |
| | | If the application cites non-FDA-recognized voluntary consensus standard(s), does the application explain any deviation from the standard? | ☐ | ☐ | ☐ |
| 2 | Investigator Financial Disclosure | Has the applicant provided documentation to establish that they have followed the recommendations in applicable FDA guidance/ guidelines or otherwise met applicable statutory or regulatory criteria? | ☐ | ☐ | ☐ |
| | | Has the applicant submitted either a signed and dated Certification Form (3454) or a signed and dated Disclosure Form (3455)? | ☐ | ☐ | ☐ |
| | | For a Certification Form (3454): Is the required list of all investigators and subinvestigators attached to the Form? Or does the Form include the reason(s) why financial disclosure information could not be obtained? | ☐ | ☐ | ☐ |

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| | | For a Disclosure Form (3455): Does the application provide details of the financial arrangements and interests of the investigator(s) or subinvestigator(s), along with a description of any steps taken to minimize potential bias? | ☐ | ☐ | ☐ |
| 3 | Is an environmental assessment included (ONLY required for devices that present new environmental concerns)? Or, if claiming a categorical exclusion to the environmental assessment requirement, does the application include information to justify the exclusion? | | ☐ | ☐ | ☐ |
| 4 | FDA Form 3674 | Does the application include a completed FDA form 3674: Certification with Requirements of ClinicalTrials.gov Data Bank? | ☐ | ☐ | ☐ |
| | | Does the form indicate if:<br>1. There are no clinical trials referenced in submission, OR | ☐ | ☐ | ☐ |
| | | 2. The requirements are not applicable to referenced clinical trials, OR | ☐ | ☐ | ☐ |
| | | 3. The requirements are applicable and have been met? | ☐ | ☐ | ☐ |
| 5 | For all clinical investigations conducted in the US, does the application include one of the following for each investigation: | A statement of compliance with 21 CFR parts 50, 56, and 812, **or** a brief statement of the reason for noncompliance with 21 CFR parts 50, 56, and 812? | ☐ | ☐ | ☐ |
| 6 | For all clinical investigations conducted outside of the US, does the application include one of the | A statement that the clinical investigations were conducted in accordance with good clinical practice (GCP) as described in 21 CFR 812.28(a)(1);<br>**or**<br>A brief statement of the reason for not conducting the investigation in accordance with GCP and a description of steps taken | ☐ | ☐ | ☐ |

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| | following for each investigation: | to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected;<br>**or**<br>A waiver request in accordance with 21 CFR 812.28(c)? | | | |
| **Pediatric Use Provisions** | | | | | |
| 1 | Does the application include a description of any pediatric subpopulations (and the number of pediatric patients) that suffer from the disease or condition that the device is intended to treat, diagnose, or cure, or a statement that no pediatric subpopulation exists for the disease or condition for which the device is intended? This statement does not mean the device is indicated for treating pediatric patients. | | ☐ | ☐ | ☐ |
| **History of the Application** | | | | | |
| 1 | Does the applicant list prior submissions or state that there were no prior submissions? If so, which of these are included?<br>*If not, mark N/A.* | 1. **510(k)**<br>If this device has been the subject of a Not Substantially Equivalent (NSE) decision, does the HDE address any issues relating to safety or effectiveness? | ☐ | ☐ | ☐ |
| | | 2. **IDE**<br>Have the data presented in the HDE taken into account any safety or effectiveness concerns (e.g., "future considerations") previously communicated through IDE correspondence? | ☐ | ☐ | ☐ |
| | | 3. **Prior PMA**<br>If a previously submitted PMA for this device has been withdrawn or denied, does the current HDE application address any issues related to safety or effectiveness raised during review of the prior PMA? | ☐ | ☐ | ☐ |
| | | 4. **HDE**<br>If a previously submitted HDE application for this device has been withdrawn or denied, does the current HDE application take into account any issues related to safety or probable benefit raised during review of the prior HDE application? | ☐ | ☐ | ☐ |

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| 2 | If a modular HDE was submitted, has the number of modules in the following categories?<br>1. If yes, number of modules submitted #_____<br>2. How many modules were closed? #_____ | | ☐ | ☐ | ☐ |
| 3 | Does the applicant list Q-Submission (s) regarding the device or this application in which FDA feedback regarding data or information related to safety and/or effectiveness in the HDE was provided by email or during a meeting (in person or by phone), or state that there were no prior Q-Submission interactions with the FDA regarding this application?<br><br>*If not, mark N/A.* | If applicant lists Q-submissions, does the application include, as applicable:<br>• Q-Submission #_____ | ☐ | ☐ | ☐ |
| | | • Meeting date(s)#_____ | ☐ | ☐ | ☐ |
| | | • Copy of minutes from each meeting or other written feedback? | ☐ | ☐ | ☐ |
| | | Were all staff concerns or action items previously presented to the applicant in the Q-Submission minutes,<br><br>**or**<br><br>feedback was addressed in the HDE,<br><br>**or**<br><br>has the applicant provided a detailed scientific or clinical justification for an alternative approach? | ☐ | ☐ | ☐ |

## 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