

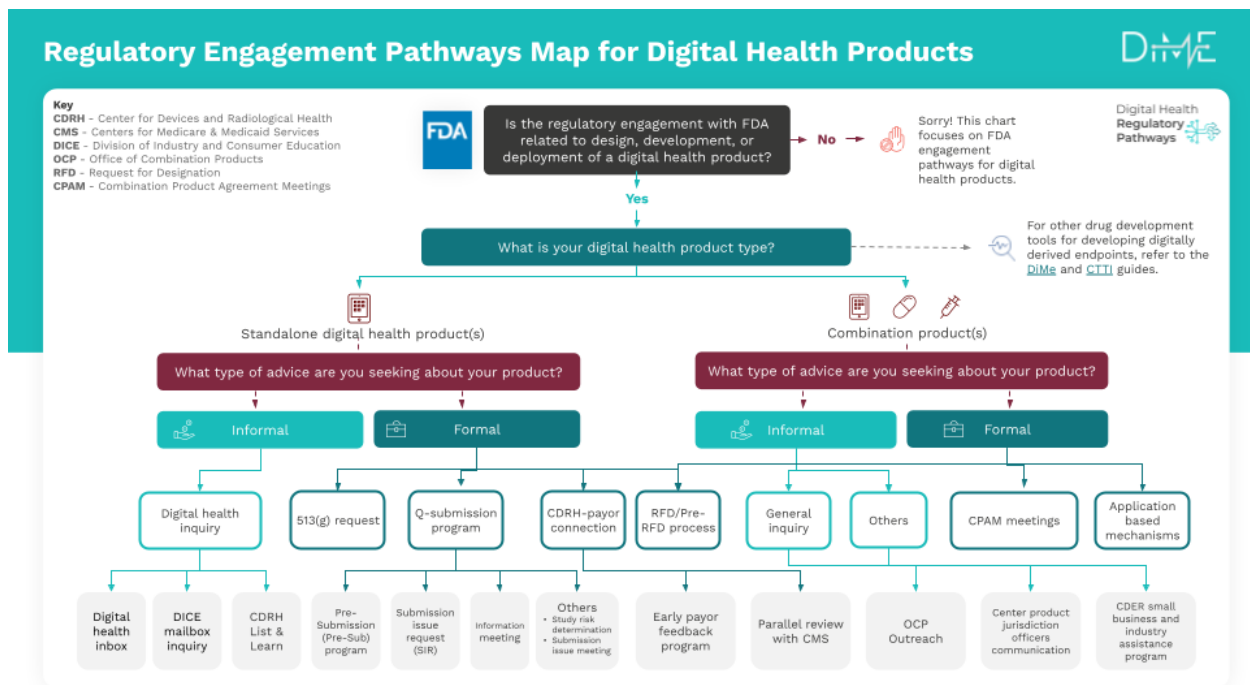
Engagement Pathways to Communicate with

U.S. Regulators (FDA - Food and Drug Administration)

A QUICK GUIDE FOR DIGITAL HEALTH & COMBINATION PRODUCTS PURSUING MARKET ACCESS IN THE U.S.

Interacting with the U.S. regulatory body can be a complex and intimidating process, especially for businesses that are new to the process or are unfamiliar with the specific regulations and guidelines that apply to their industry. By interacting with regulators early in the development process, companies can gain a better understanding of the needs and requirements and can work to ensure that their product meets these requirements. This interaction can make the process more efficient by streamlining regulatory review, thereby reducing risk of delays or misunderstanding when bringing new digital health products to market.

Use this quick guide to gain an understanding about various formal and informal engagement pathways and resources to further communicate with FDA.



DOWNLOAD Regulatory Engagement Pathways for Digital Health Product 

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Formal Engagement Pathways

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Combination products only:

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Basic Terms First

Digital Health Product	Combination Product(s)
<p>A digital health product includes technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes; capture, store, or transmit health data; and/or support life science and clinical operations.</p> <p>Source: Digital health industry categorization</p>	<p>A combination product is a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product.</p> <p>Source: FDA</p>

Note: For the purpose of this guide, we will focus on digital health and combination products. For engagement pathways for drug development tools when developing digitally derived endpoints, refer to the [DiMe](#) and [CTTI](#) guides.



Informal Engagement Pathways

For digital health products and combination products

DIGITAL HEALTH INQUIRY

Digital Health Inbox Outreach

Overview

Individuals and/or organizations can informally communicate questions about their digital health product to the FDA by utilizing the [digital health inbox](#) at the Digital Health Center of Excellence (DHCoE). DHCoE serves to empower digital health stakeholders to advance healthcare by fostering responsible and high-quality digital health innovation. Some of their functional areas of focus include:

- Digital Health Policy and Technology Support and Training
- Medical Device Cybersecurity
- Artificial Intelligence/Machine Learning
- Regulatory Science Advancement
- Regulatory Review Support and Coordination
- Advanced Manufacturing
- Real World Evidence and Advanced Clinical Studies
- Regulatory Innovation
- Strategic Partnerships



Reason for communication

To navigate the FDA's current policies on digital health products and receive informal feedback on the possible regulatory status of products in development.

Contacting the DHCoE is an informal, non-binding form of feedback regarding digital health products in development (or already developed) that includes but is not limited to questions about medical device regulations, interpreting digital health guidance, upcoming premarket submission, determining product risk classification, and more.

Contact details

Please send these questions to the Division of Digital Health:

Email: DigitalHealth@fda.hhs.gov

Learn more

Check out additional resources:

[Digital Health Center of Excellence Services](#)

DICE Mailbox Inquiry

Overview

Individuals and/or organizations can informally communicate questions related to appropriate product classification or understanding FDA regulations or policies to the FDA via an inquiry sent to the Division of Industry and Consumer Education (DICE) mailbox. This communication method can be helpful when navigating the FDA's medical device regulations, such as when bringing a digital health product to market, finding FDA databases, and/or making general inquiries to the office of communication and education. Some example questions to ask via this channel include:

- *“Can you help me determine whether the FDA would consider my digital health product to be an actively regulated product?”*
- *“Can you help me understand the FDA definition of a low-risk product, as referenced in the General Wellness guidance document?”*

How to prepare

You should include the following information within your Device Determination email request:

- Intended Use (for example, what is the product supposed to treat or diagnose?)
- Physical description and mechanism of action
- Any claims you intend to publicly make about the product
- Your contact information

Contact details



Department: Division of Industry and Consumer Education (DICE)

- Email: DeviceDetermination@fda.hhs.gov or DICE@cdrh.fda.gov
- Phone: 800-638-2041 or 301-796-7100

CDRH List & Learn

Overview

The FDA Center for Devices and Radiological Health's (CDRH) **Learn program** provides various tools and resources to provide the digital health industry with information that is comprehensive, interactive, and easily accessible.

The FDA Center for Devices and Radiological Health's (CDRH) **Email List** provides updates and information via email about various digital health related news, product approvals/recalls, new guidelines, and more.

Learn more 🔍

- Check out the resources: [CDRH Learn](#)
- Sign up for the FDA updates: [Subscribe to CDRH Email Lists](#)

PRE-RFD PROCESS

Overview

The Pre-RFD (Request For Designation) process is a way to receive informal, non-binding written feedback regarding the regulatory identity or classification of a human medical product such as a drug, device, biological product, or combination product. This process inform the submitter about a non-combination or combination product's assignment to the appropriate Agency Center [Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), or Center for Biologics Evaluation and Research (CBER)] for regulatory oversight for the digital health product.

Reason for communication

- To determine whether the medical product will be regulated as a drug, a device, a biologic, or a combination product.
- If the medical product will be regulated as a combination product, to identify which FDA medical product center will have the primary jurisdiction over the product.



Category	Pre-RFD	RFD
Submission Type	Informal	Formal
Information	Recommended	Required
Description of Product	Yes	Yes
Proposed Use or Indications for Use	Yes	Yes
Description of Manufacturing Process	Optional (if available)	Yes
Supportive Data/Studies	Optional (if available)	Yes
Description of How a Product Achieves its Intended Therapeutic Effect	Yes	Yes
Description of Related Products	Optional (if available)	Yes
Manufacturer Recommendation	Optional (if available)	Yes
Page Limit	No	Yes



Informal Engagement Pathways

For combination products only

OFFICE OF COMBINATION PRODUCT OUTREACH

Overview

Individuals and/or organizations seeking information on guidance, regulations, and standard operating procedures that apply to the regulation of combination products should reach out to the Office of Combination Products (OCP). OCP provides non-binding information on the classification of products and information on potentially relevant FDA centers for premarket review and postmarket safety oversight.



Reason for communication

- To clarify uncertainties about the classification or assignment of products, as well as to ask questions regarding pre-market or post-market considerations for combination products.

Contact details

Office of Combination Products (OCP)

Email: combination@fda.gov

Phone: (301) 796-8930

Fax: (301) 847-8619

Address:

Office of Combination Products
Office of Clinical Policy and Programs
Food and Drug Administration
10903 New Hampshire Ave.
WO-32, Room 5129
Silver Spring, MD 20993

Learn more

About policies and procedures involved in the FDA collaborative review process:

- [Intercenter Consultative/ Collaborative Review Process](#)

Check out OCP's resources for product classification, jurisdiction, and combination products:

[Combination Products Guidance Documents](#)

CDER PRODUCT JURISDICTION OFFICE COMMUNICATION

Overview

The Center for Drug Evaluation and Research's (CDER) enhanced communication team provides general information about which review division to contact for a product, as well as help in navigating challenges in communicating with the review team regarding an application.

Reason for communication

- To ask general questions about the drug development process or for clarification on which review division to contact with questions.
- For assistance in evaluating the issues to determine appropriate next steps and then working with the review team and the manufacturer to facilitate resolution.
- To identify best practices for enhanced communication.



Contact details

Department: Division of Industry and Consumer Education (DICE)

- Email: ONDCommunications@fda.hhs.gov

Include the following details in your outreach:

- Dates of the communications with the Review Division or Office
- The subject of the communication with the Review Division or Office
- Name of the Review Division or Office
- Application number
- Method of submission: email, phone, formal submission dated DD/MM/YYYY (include the names of those contacted by email or phone)

SMALL BUSINESS AND INDUSTRY ASSISTANCE (SBIA)

Overview

The FDA Center of Drug Evaluation and Research's (CDER) SBIA helps to navigate the wealth of information that the FDA offers as well as assistance in understanding human drug product regulation. SBIA outreach is the first step for a small pharmaceutical business trying to contact the Agency. Though the FDA's focus with this program is on small businesses, CDER SBIA serves as a channel for engagement of the regulated pharmaceutical industry, both domestically and internationally.

Reason for communication

- To access resources, education, and training for a more clearly informed and efficient developmental process.

Contact details

Send direct inquiries to the SBIA

- Email: CDERSBIA@fda.hhs.gov
- Phone: (301) 796-6707 or (866) 405-5367

Learn more

Check out for important regulatory information and training resources.

- [CDER Small Business & Industry Assistance](#)





Formal Engagement Pathways

For digital health products and combination products

513(G) PROGRAM

Overview

A [513\(g\) Request](#) is a solicitation for formal written feedback regarding a digital health product's classification (i.e., as a medical device, as a combination product, etc.), the FDA device category it falls into (e.g. risk class, generic panel, etc.), and whether additional FDA requirements may apply. The 513(g) request is also known as a "Request for Information" from the FDA.

Reason for communication

- To obtain information regarding classification and regulatory requirements applicable to the digital health product that will potentially aid in informing appropriate regulatory pathways for the product.
- Sometimes, 513(g) requests are also submitted to determine if an innovator needs a 510(k) submission based on modifications to their product, or to identify an optimized pathway for regulatory oversight.

DOWNLOAD

513(g) Checklist



Output from the communication



What to expect in a response from the FDA

- The response will inform the innovator if the product does not meet the requirements for classification as a device.
- If the product meets the requirements, the FDA will share information regarding their assessment of the type and class of the device and any requirements that apply to the class to which the device belongs.
- The response will provide information on which application is necessary: a premarketing approval application (PMA), a 510(k) application, or neither.
- The response will provide information on whether guidance on this particular class of device have been issued and whether any other requirements may apply (e.g., those regarding radiation-emitting products).



What NOT to expect in a response from the FDA

- The response will not provide information on whether the device is substantially equivalent.
- The response will not provide information on the safety and efficacy of the device.
- The response will not make final determinations on the class of the device or authorizations to market the device.
- The response will not provide information on the type of studies necessary for approval and marketing of a product.



Note: Innovator should keep in mind that any information released in response to a 513(g) request does not constitute any final decision or action on the part of the FDA.

Q-SUBMISSION PROGRAM

There are several components of the Q-Submission Program, such as:

- **Pre-Submissions (Pre-Sub)** - To obtain formal feedback about a potential and planned digital health product in-development, including any specific questions regarding product development, submission preparation, or clinical/nonclinical evaluation.
- **Submission Issue Request (SIR)** - To request FDA feedback on a proposed approach to address issues; intended to quickly resolve or clarify issues or outstanding questions in the formal responses.
- **Study Risk Determination (SRD)** - To request FDA determination regarding whether a planned medical device clinical study is of significant risk (SR), non-significant risk (NSR), or exempt from Investigational Device Exemption (IDE) regulations.
- **Informational Meeting** - To share information with the FDA without the expectation of receiving feedback, to provide an overview of ongoing product development, and to familiarize the FDA review team with new product(s) with significant technology differences compared to currently available products.
- **Others** include:
 - PMA Day 100 Meeting
 - Formal Early Collaboration Meetings
 - Agreement and Determination Meeting
 - Breakthrough Devices Program
 - Accessory Classification Request

Learn more 🔍

Check out additional information about the Q-submission programs:

- [Q-Submission](#)



Pre-Submission Program (Pre-Sub)

Overview

The FDA Pre-Submission (aka Pre-Sub) program is an opportunity to obtain FDA feedback “prior” to an intended formal FDA application for your digital health product. The Pre-Sub is applicable to:

- **Investigational applications:** Investigational New Drug (IND) Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE), Master Files, Special Protocol Assessments.
- **Marketing applications:** New Drug Application (NDA), Premarket Approval (PMA), Biologics License Application (BLA), Premarket Notification [510(k)], Evaluation of Automatic Class III Designation (De Novo Request).
- **Other:** Accessory Classification Requests, Clinical Laboratory Improvement Amendments (CLIA), CLIA Waiver by Applications (CW), Dual: 510(k) and CLIA Waiver by Application.

Note: Pre-Sub is not applicable for general FDA inquiries, discussion when an application is already under FDA review, or an appeal meeting.

Reason for communication

To obtain information regarding the classification and the regulatory requirements applicable to the digital health product that will potentially aid in informing appropriate regulatory pathways for the product. Examples of situations where the Pre-Sub process may be helpful include:

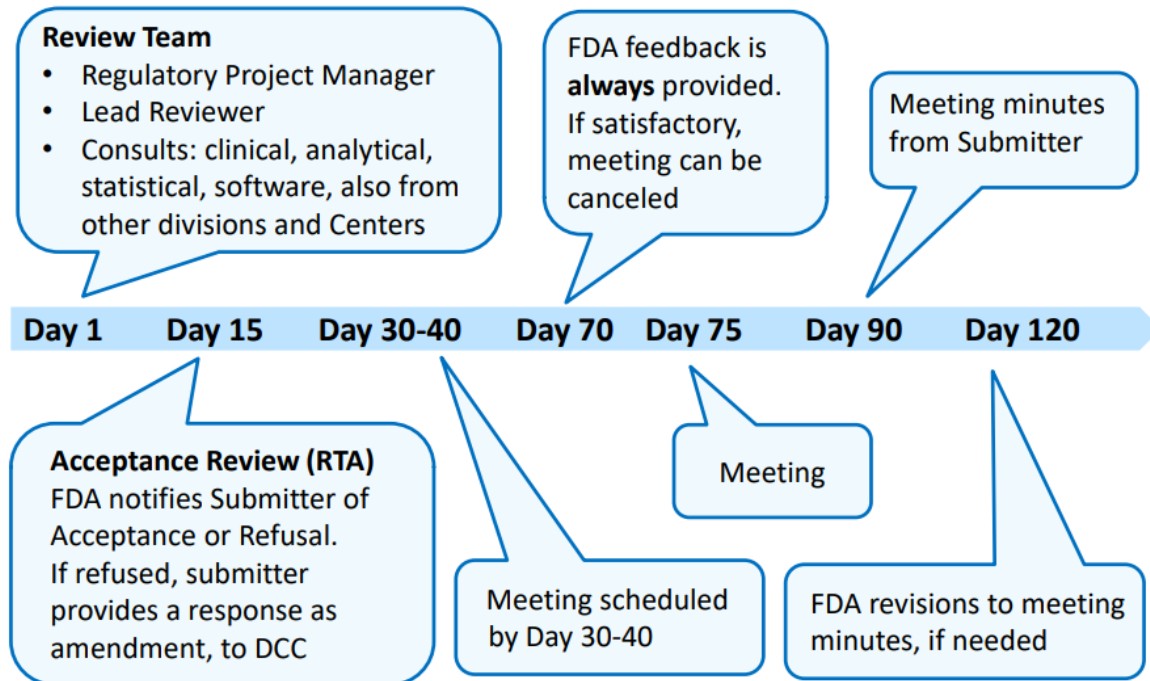
- A new product does not clearly fall within an established regulatory pathway
- Innovators are planning a study that will support a future application
- An investigational or marketing application has been submitted to:
 - Share product specifications with the Agency
 - Collect early feedback into potential hurdles for approval or clearance

DOWNLOAD

Pre-Sub Checklist



Timeline



Source: FDA

CDRH-PAYOR CONNECTION

Early Payor Feedback Program

Overview

The [early payor feedback program](#) is intended to facilitate communication between manufacturers and payors to potentially shorten the time to FDA approval or clearance and coverage decisions.

Reason for communication

- To obtain payor input on clinical trial design or other plans for gathering clinical evidence needed to support positive coverage decisions, thereby expediting patient access to digital health products.
- To receive formal feedback about clinical evidentiary requirements of the digital health product's needs to support positive coverage decisions.
- To gather information about coverage, procurement, and reimbursement decisions from public payors such as the Center for Medicare & Medicaid Services (CMS), private health plans, health technology assessment groups, and others.



Contact details

For questions, additional information, or inquiries, reach out to the department at:

- Email: CDRHPayorCommunications@fda.hhs.gov

Note: Voluntary opportunity for digital health manufacturers and coverage organizations. The decision of a digital health manufacturer to participate or not to participate in this Early Payor Feedback opportunity will not alter the regulatory and evidentiary standards the FDA uses for decision making.

Payor participants in the program:

- Aetna
- BlueCross BlueShield Association
- CareFirst BlueCross BlueShield (HealthWorx)
- Center for Medicare & Medicaid Services (CMS)
- Cigna
- Clover Health
- Duke Evidence Synthesis Group, Duke Clinical Research Institute, Duke University
- ECRI Institute Headquarters
- EXCITE International Health Innovations
- Highmark, INC
- Humana
- Kaiser Permanente
- National Institute for Health and Care Excellence (NICE)
- Premier Inc.
- UnitedHealth Group

Parallel Review with CMS

Overview

The [Parallel Review with the Centers for Medicare and Medicaid Services \(CMS\)](#) is a program designed to help decrease the time between the FDA's approval of a premarket application and the subsequent CMS national coverage determination (NCD). Both the FDA and CMS independently review the data to determine if the applicant meets their standards. The review happens in two stages:

1. The FDA and CMS meet with the manufacturer to provide feedback on the proposed pivotal clinical trial within the Early Payor Feedback Program or other mechanism.
2. The FDA and CMS concurrently review (“in parallel”) the clinical trial results submitted in the Premarket Approval (PMA) or De Novo request.

Reason for communication

- To strategize submission of clinical data to the FDA and CMS for a simultaneous review with timely outreach to both agencies



- To receive formal feedback after independent review of the data by both the FDA and CMS to determine whether it meets their respective Agency's standards.

Prerequisite criterias

- Product addresses the public health needs of the Medicare population.
- Product needs a De Novo or PMA application.
- Product is far enough along in its development (e.g., indications for use are nearly finalized) to determine if it is not excluded by statute from Part A and/or Part B Medicare coverage.
- Manufacturer intends to meet jointly with both the FDA and CMS using the FDA's Q-Submission program.

Note: Participation in Parallel Review is voluntary and does not change the existing separate and distinct review standards for FDA device approval or clearance and CMS national coverage determination.

Contact details ✉

Parties interested in Parallel Review can reach out via email:
Parallel-Review@fda.hhs.gov.

Include the following details in your outreach:

- Manufacturer name and contact information
- Product name (include proposed indications for use/intended use)
- Product description (include stage of development of the technology)
- Regulatory history (include previous FDA interactions, submission, feedback, resolution, and/or relevant submission numbers)
- Brief statement explaining why the product is an appropriate candidate for Parallel Review





Formal Engagement Pathways

For combination products only

COMBINATION PRODUCT AGREEMENT MEETINGS (CPAMs)

Overview

Combination product agreement meetings (CPAMs) are designed for manufacturers to gain clarity and certainty regarding combination products. The purpose of a CPAM is to address the standards and requirements for marketing authorization of the combination product, as well as other issues related to post-market modification of the product.

Manufacturers may choose to submit a request for a face-to-face meeting, a teleconference, or written feedback. The FDA's final written feedback should include the agreed-upon proposals and an indication of the FDA's agreement with the proposal; whether the FDA does not agree with the proposal and why the FDA does not consider the manufacturer's proposal acceptable; or whether the FDA cannot agree to the proposal at the time of the response due to inadequate or insufficient information.

Reason for communication

- To seek agreement from the FDA on an approval approach if previous feedback under an application-based mechanism has not been provided
- To obtain clarity and certainty on combination products for which the lead center assignment is not clear [i.e., the Center for Devices and Radiological Health (CDRH) vs. the Center for Drug Evaluation and Research (CDER)]
- To address the standards and requirements for marketing authorization of a combination product
- To address other issues relevant to a combination product, such as requirements related to postmarket modification of the product or Current Good Manufacturing Practice (CGMP) Regulations

Learn more

Check out additional information about the CPAMs – the request process, checklist, outcomes, and more:

- [Requesting FDA Feedback on Combination Products](#)



APPLICATION-BASED MECHANISMS

Overview

Application-based mechanisms for interacting with the FDA are most efficient and effective for combination products, specifically to address product issues. These processes provide general information and feedback on product development, application preparation, or postmarket issues, including proposed approaches to address specific deficiencies identified during a review of certain types of device applications or responses to questions related to a clinical study design, as well as responses to requests for device-led combination products to be designated as Breakthrough Devices, etc.

All interactions are coordinated through the lead center as identified by the FDA and using the application-based mechanisms of that center, regardless of the feedback being requested. For example, if a manufacturer has general questions on the drug constituent part of a device-led combination product, that interaction would occur through the Center for Devices and Radiological Health (CDRH), and the appropriate application-based mechanism would be the pre-submission meetings process.

Reason for communication

- To obtain feedback on scientific issues, study design, testing approaches, or application preparation considerations for combination products
- To obtain clarification on topics for which the FDA has already published technical guidance
 - Manufacturers should also review associated guidance relevant to the specific application based mechanism

Learn more

Check out additional information about application-based mechanisms:

- [Requesting FDA Feedback on Combination Products](#)

Access DiMe's Digital Health Regulatory Pathway Resources



Identify your regulatory pathway



Build your regulatory strategy



Interact with regulators

