

# PMA Preparation Guide

Premarket approval (PMA) is the process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices used by the US Food and Drug Administration (FDA) for products that support or sustain human life, are of substantial importance in preventing impairment of human health, or that present a potential, unreasonable risk of illness or injury. PMA is the most stringent type of marketing application required by the FDA, and fewer than 10% of marketed digital health products have been approved using the PMA pathway.

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**At-a-Glance Overview on  
PMA Applications**



## What should I know about the FDA PMA Application Process?

### General guide for preparing a FDA PMA application filing:

1. Identify the intended use of the digital health product and determine if it meets the criteria for a PMA classification using [the FDA's product classification database](#).
2. Determine if other substantially similar product exist on the market:
  - a. If substantially similar products exist, determine the risk level of those products using the product classification database. If existing similar products are classified as Class III, your digital health product will likely require a PMA submission.
  - b. If no substantially similar products exist, determine the risk level of your own product to understand if the PMA or De Novo pathway is the best fit (novel digital health products for which there is not a substantially similar marketed equivalent product typically qualify for PMA status; however, novel digital health products with a lower risk profile may qualify for [De Novo](#) status)
3. If it is unclear whether your digital health product requires a PMA, use the three letter product code generated by the product classification database to search the [Premarket Approval \(PMA\) database](#) and the [510\(k\) Premarket Notification database](#).
4. Assemble a team of experts, including a regulatory affairs consultant, to assist with the submission.
5. Review FDA guidance documents relevant to the product and its intended use.
6. Determine which [PMA application method](#) is most suitable for your product:
  - a. For products that have completed clinical evaluation, the **Traditional PMA** application method will likely be the best fit.

- b. For earlier-phase products, the **Modular PMA** application may be the best fit as this method allows applicants to compile and complete a PMA application over time and to submit data and analysis in modules according to a pre-defined PMA shell created by the applicant and the FDA.
  - c. For products that rely on well-established technology, the **Product Development Protocol** might be the best fit. This method allows the applicant and the FDA to pre-define a plan for establishing the product's safety and effectiveness and for the applicant to execute that plan at their own pace.
  - d. For products designed for conditions that impact fewer than 8,000 patients per year, applicants may apply for a **Humanitarian Device Exemption**.
7. Determine the need for pre-submission feedback from the FDA and follow the pathways available in the agency's [Q-Submission Program](#) based on the desired feedback ([Q-Sub](#) is for feedback on specific questions necessary to guide product development and/or submission preparation, examples are provided below).
8. Attend a pre-submission meeting with the FDA, if requested.
9. Develop a summary section for the PMA application that includes:
  - a. A detailed description of the product, including the indication for which it will be used, a description of each of its functional components (with pictorial representations, as appropriate), and marketing history.
  - b. A summary of nonclinical and clinical studies for the product and conclusions drawn from those studies.
10. Develop a detailed technical report that includes significant detail regarding nonclinical investigations, including those involving animal subjects, as well as clinical investigations.
11. Prepare a detailed submission cover letter that summarizes the product, its intended use, and the information provided in the submission.
12. Prepare and submit a PMA filing request and all supporting documentation, including basic administrative and scientific elements listed in [21 CFR 814.20](#), to allow the FDA to decide if a substantive review should proceed after a limited scientific and administrative review.
13. If accepted, the application will undergo a substantive and panel review process before a final FDA decision is returned. For more detail on this process, see page 7.

Please note that the FDA may refuse to accept a PMA Application filing request if:

1. The application is incomplete, i.e. it does not contain all information required under sections 515(c)(1) of the FD&C Act.
2. The PMA request does not contain every item required under Section 814.20, or justification for those items omitted (or included justification is inadequate).



3. There is a pending 510(k) request for the same product and a determination has not been made that a PMA is required.
4. The application contains a false statement of material fact.
5. The financial certification or financial disclosure statement was not included.

It's important to carefully review the [FDA's guidance on PMA Applications](#) to ensure that all necessary information is included in the submission.

Please also note that this guide provides general information and the submission process may vary depending on the specific product and circumstances. It is important to carefully and thoroughly complete all required sections of the PMA submission guidance in order to increase the chances of obtaining FDA approval to market your digital health product. Prior to submitting a PMA application to the FDA, here are a few recommendations:

1. Consider submitting a **Pre-Submission** (Pre-Sub) to obtain feedback from the appropriate premarket review division (the Pre-Sub can include feedback on cybersecurity considerations for the product, non-clinical testing protocols, design and performance of clinical studies and acceptance criteria, etc.).
2. Consult an **FDA regulatory expert** (e.g. onboard an advisor, reach out to a consultant, hire a regulatory affairs lead, etc.) to help with the plan and execute a request on your behalf.



## How is a PMA submission different from 510(k) and De Novo submissions?

Differences between PMA, 510(k), and De Novo pathways

Category	PMA	510(k)	De Novo
<b>FDA Oversight Language</b>	Approved	Cleared	Granted
<b>Risk</b>	Highest	Low to Moderate	Low to Moderate
<b>Medical Device Product Class</b>	Class II, III	Class I, II	Class I, II
<b>Control</b>	General Controls PMA Controls (Manufacturing & Design Controls, Quality Inspection)	General Controls Special Controls	General Controls Special Controls
<b>Safety</b>	Established Safety	No Substantial Equivalence	Reasonable Assurance of Safety
<b>Effectiveness</b>	Established Effectiveness		Reasonable Assurance of Effectiveness
<b>Clinical Data</b>	Yes, clinical and often laboratory data	10-15% require clinical data	Yes
<b>Timeline</b>	180 days (up to)	90 days (traditional)	150 days
<b>Cost</b>	Standard Fee: \$441,547 Small Business Fee: \$110,387	Standard Fee: \$12,745 Small Business Fee: \$3,186	Standard Fee: \$132,464 Small Business Fee: \$33,116
<b>Annual reporting requirement</b>	Yes (more info <a href="#">here</a> )	No	No
<b>Good Manufacturing Practice (GMP) requirement</b>	Yes	No	Yes
<b>Medical Device Reporting (MDR) requirement</b>	Yes	No	Yes



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



## What is the FDA PMA review process?

- Step 1.** Filing review.
- Step 2.** Statistical review for filing.
- Step 3.** Review of manufacturing information for compliance with the Quality System regulation (21 CFR 820).
- Step 4.** PMA filing decision.
- Step 5.** Day-100 Meeting to discuss the status of the pending PMA submission, innovators must request this meeting within 70 days of original submission.
- Step 6.** Quality System Inspection(s) by the FDA field personnel. An FDA manufacturing inspection may be conducted for all original PMAs and may be conducted for PMA supplements requesting approval of alternate or additional manufacturing and sterilization facilities.
- Step 7.** Bioresearch Monitoring (BIMO) Audit (audit of clinical study data).
- Step 8.** Substantive review coordination and completion in areas such as:
  - Preparation of FDA Summary of Safety and Effectiveness Data (SSED)
  - Nonclinical Studies [Microbiological, Toxicological, Immunological, Biocompatibility, Shelf Life, Analytical (for IVDs), Animal, Engineering (Stress, Wear, Fatigue, etc.)]
  - Clinical Studies
  - Panel Meeting Decision and Mailing (if panel meeting is appropriate)
  - Panel Date (if appropriate)
  - Transcripts Received, Reviewed, and Placed in Administrative Record
  - QS/GMP Clearance
  - Final Response for GMP/BIMO
  - Final Decision Memo
  - Approval Package
  - Approval Order, SSED, Final Draft Labeling

Check out the required elements for PMA Application [here](#).

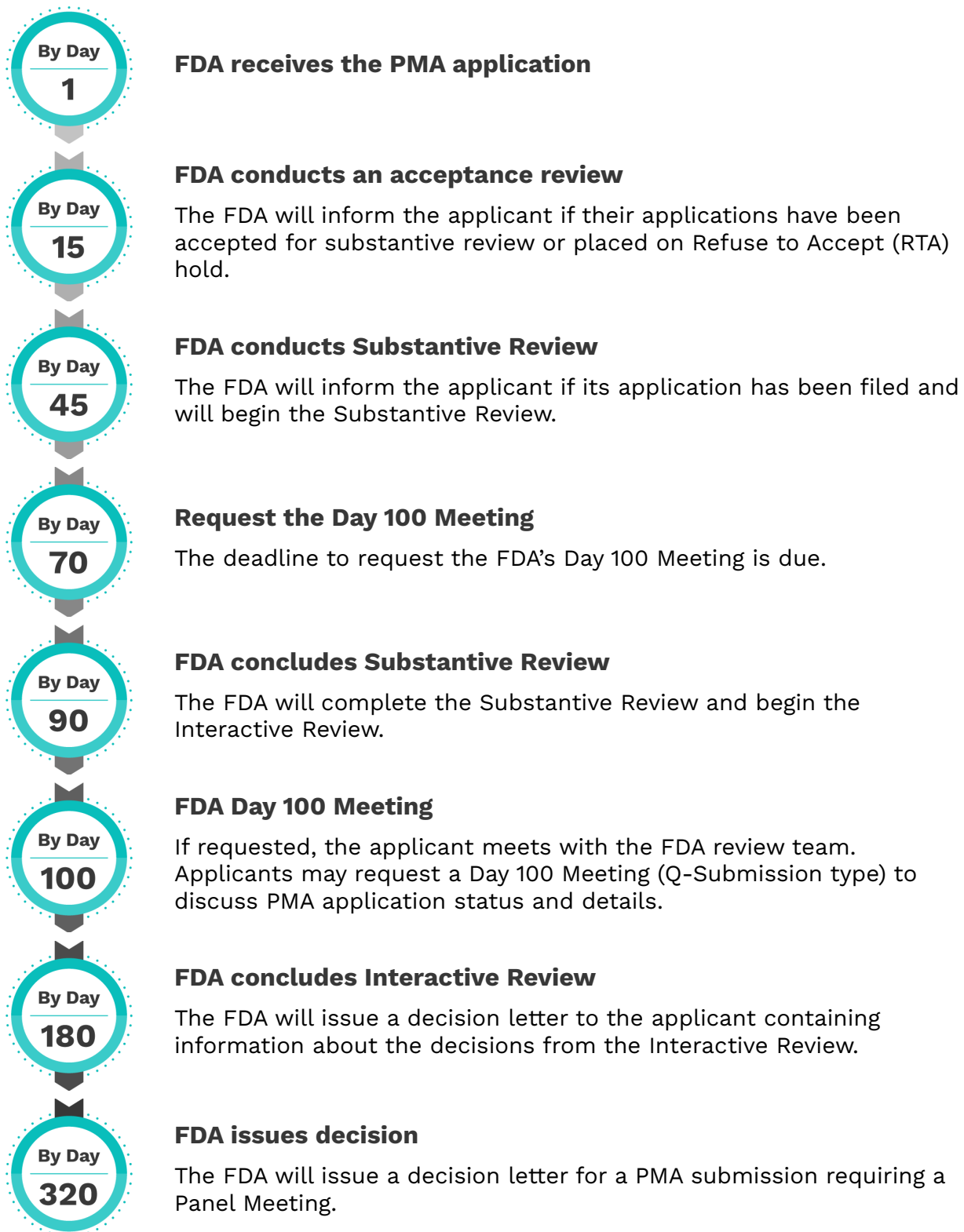
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**PMA Acceptance Checklist**

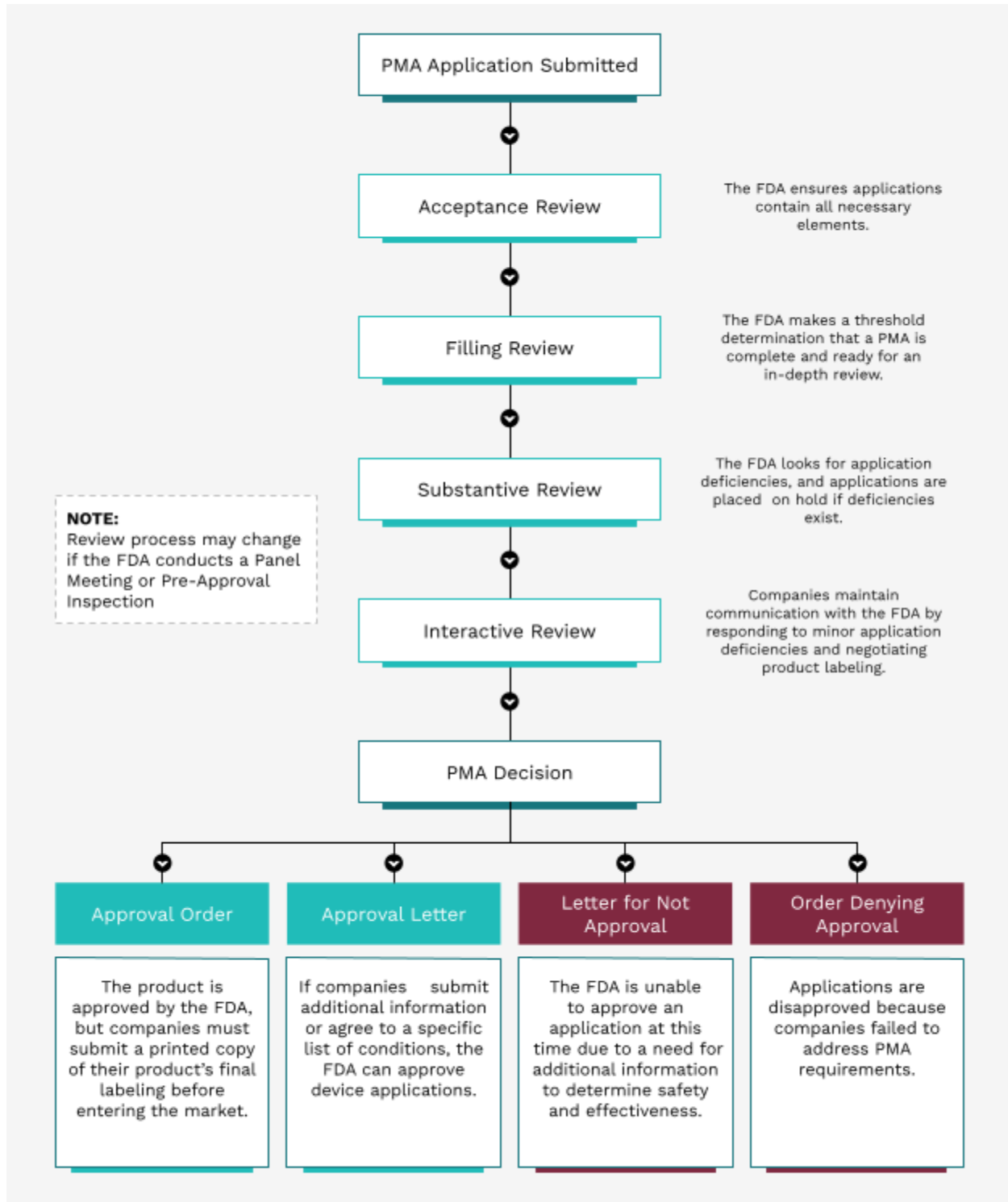


## What is the FDA PMA process timeline?

### The submission process timeline for Pre-market approval submission



## What is the FDA PMA review process?



Source: AdvaMed

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**PMA Request  
Review Process**



## What should I expect?

### Potential outcomes of a final FDA PMA decision based on substantive review:

Based on the information provided by the company for their digital health product, the FDA will assess product safety and effectiveness and determine whether the probable benefits of the product outweigh the probable risks. Results could include:

- The FDA **approves** the PMA application – if the probable benefits of the product outweigh the probable risks and the controls are adequate to demonstrate it.
- The FDA **denies** the PMA application – if the application does not contain sufficient valid scientific evidence that provides a reasonable assurance of safety and effectiveness, or the benefit of the product does not outweigh the probable risk.



### Approved



### Denied

If the FDA approves a PMA application:

- The new product is authorized to be marketed. It must now comply with applicable regulatory controls.
- A new classification regulation is established for the product.
- The new product can be used as a predicate for future 510(k) submissions, when applicable.
- The FDA publishes a notice in the Federal Register announcing the new classification regulation and, for Class II devices, the new special controls.
- The FDA generates and publicly discloses a decision summary and posts a copy of the granting order notifying the requester about marketing authorization.
- Continued approval of the PMA is contingent upon the submission of required postapproval annual reports.






If the FDA denies a PMA application:

- The denial is likely because the submission does not contain sufficient valid scientific evidence that provides a reasonable assurance of safety and effectiveness or that the benefit of the product does not outweigh the probable risk.
- The product shall not be legally marketed.
- The FDA issues a non approval letter describing why the application cannot be approved or if there is insufficient information to make a determination
- The applicant may resubmit the PMA with additional information necessary to comply with the requirements of section §515(c)(1)(A)-(G) of the FD&C Act and 21 CFR 814.20. A resubmitted PMA must include the PMA reference number of the original submission.





## Pre-Market Approval (PMA)

 Search <a href="#">FDA PMA Database</a>	<i>DiMe Resources</i>			
	 <a href="#">At-a-Glance</a>	 <a href="#">Preparation Guide</a>	 <a href="#">Checklist</a>	 <a href="#">FAQs</a>

Access DiMe's Digital Health Regulatory Pathway Resources



**Identify** your regulatory pathway



**Build** your regulatory strategy



**Interact** with regulators

