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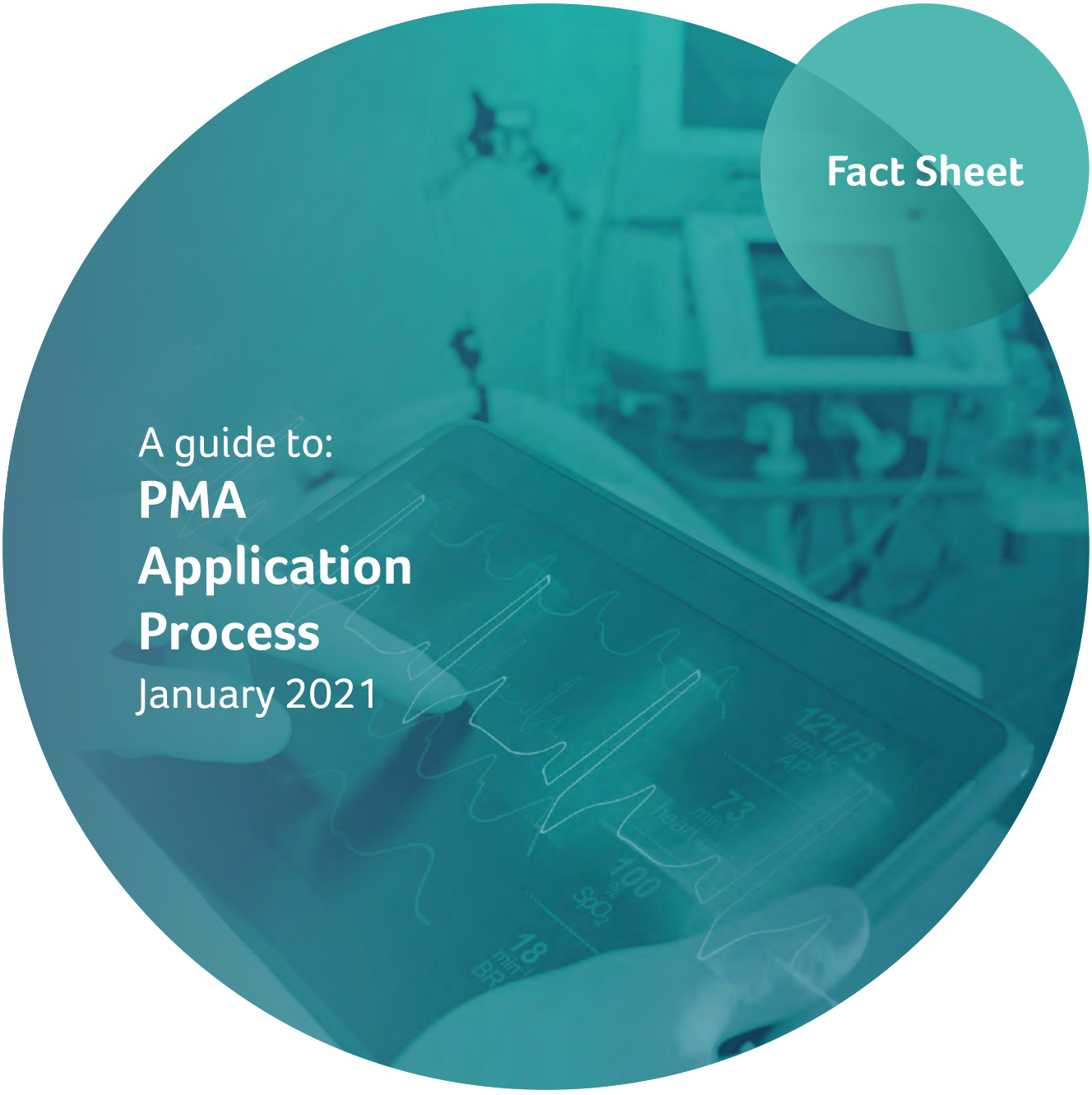

Fact Sheet

A guide to:

PMA Application Process

January 2021

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A guide to the PMA Application Process

Introduction

Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that:

- **Support or sustain human life**
- **Are of substantial importance in preventing impairment of human health**
- **Present a potential, unreasonable risk of illness or injury**

Due to the level of risk associated with Class III devices, the FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of Class III devices.

As such, these devices require a Premarket Approval (PMA) application in order to obtain marketing approval. Some Class III pre-amendment devices may require a Class III 510(k) (see our 510(k) fact sheet for more on this).

3 quick facts about the PMA application process:

1. **PMA is the most stringent type of device marketing application required by the FDA** (because Class III devices fall within the most stringent regulatory category for medical devices)
2. **Approval of your PMA application** must be received prior to marketing your device
3. **PMA approval is based on** a determination by the FDA that your application contains **sufficient valid scientific evidence** to assure that the device is safe and effective for its intended use(s)

This fact sheet covers answers to the following questions:

- **When is a PMA is required?**
- **What is involved in the submission?**
- **How long does a PMA application take?**

When is a PMA required?

To help ascertain whether your device requires a PMA, the first step is to classify your device:

Device product classification can be found in the Product Classification Database. The database search provides:

- The name of the device
- The device classification
- A link to the Code of Federal Regulations (CFR), if any are applicable

No classification regulation in the CFR?

- If your PMA device involves a new concept and is not of a type that has been marketed prior to the Medical Device Amendments, your device will not have a classification regulation in the CFR.
- In this case, the product classification database will only cite the device type name and product code.
- If it is unclear whether your unclassified device requires a PMA, use the three letter product code to search the Premarket Approval (PMA) database and the 510(k) Premarket Notification database.
- If there are 510(k)'s cleared by the FDA and your new device is substantially equivalent to any of these cleared devices, then you should submit a 510(k).

Device not found in the Product Classification Database?

- If your device is a new type of high-risk device that cannot be found in the product classification database, and has been found to be not substantially equivalent (NSE) to a Class I, II, or III [Class III requiring 510(k)] device, then your device must have an approved PMA.
- Some devices that are found to be not substantially equivalent to a cleared Class I, II, or III (not requiring PMA) device, may be eligible for the De Novo process as a Class I or Class II device.

The fees for your PMA application:

The Fees for Fiscal Year 2021 (October 1, 2020 - September 30, 2021) are as follows:

Standard Fee	Small business fee
$365,657	$91,414
Note: the 510(k) fee by comparison is $12,432	Note: the 510(k) fee by comparison is $3,108

What is involved in the submission?

There are administrative elements of a PMA application, but good science and scientific writing is key to gaining approval. The checklist below identifies some key considerations to bear in mind as you prepare your submission:

- ✓ Ensure all the elements listed in the administrative checklist are included
- ✓ Take care to include valid clinical information and scientific analysis based on sound scientific reasoning
- ✓ Make sure your application is complete, accurate, consistent, and has all critical information incorporated
- ✓ Perform a quality control audit of your PMA application before sending it to the FDA to ensure that it is scientifically sound and presented in a well-organised format
- ✓ Your Technical sections containing data and information are particularly important, as these sections should allow the FDA to determine whether or not to approve your application. Divide these sections into non-clinical laboratory studies and clinical investigations
- ✓ Your Non-clinical Laboratory Studies section should include information on microbiology, toxicology, immunology, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests. Non-clinical studies for safety evaluation must be conducted in compliance with 21 CFR Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies)
- ✓ Your Clinical Investigations section should include study protocols, safety and effectiveness data, adverse reactions and complications, device failures and replacements, patient information, patient complaints, tabulations of data from all individual subjects, results of statistical analyses, and any other information from the clinical investigations
- ✓ Any investigation conducted under an Investigational Device Exemption (IDE) must be identified as such. You should also include Form FDA-3674, which is the Certification of Compliance with the Requirements of ClinicalTrials.gov Data Bank

Some advice for your submission:

FDA may refuse to file a PMA if they determine that any of the following applies:

- The application is incomplete because it does not contain all the information required under section 515(c)(1)(A)-(G) of the FD&C Act
- The PMA does not contain each of the items required under Sec. 814.20 and justification for omission of any item is inadequate
- The applicant has a pending Premarket Notification 510(k) with respect to the same device, and FDA has not determined whether the device falls within the scope of Sec. 814.1(c).The PMA contains a false statement of material fact
- The PMA is not accompanied by a statement of either certification or disclosure as required by 21 CFR 54 Financial Disclosure by Clinical Investigators

Top tip:

The FDA suggests early collaboration to obtain further guidance prior to the submission of your PMA, either via a Presubmission Request or via a Determination Meeting.

How long does a PMA application take?

Step 1: Acceptance & Filing Review | Administrative & limited scientific review to determine completeness

Within **45 days** after your PMA is received by the FDA, you will be notified whether your application has been filed. Expedited review status, if appropriate, may be communicated at this time.

The date of filing is the date that a PMA accepted for filing was received by the FDA.

ACCEPTANCE

Application filed, proceed to Substantive review. The **180-day period** for review starts on the date of filing.

REFUSAL

FDA will refuse to file your application for substantive review if it does not meet a minimum threshold of acceptability. In this case, you will receive a refusal to file notice.

If the FDA refuses to file your PMA, you may submit a written request to review the decision via informal conference with the Office of Health Technology Director.

You need to submit this request within **10 working days** of the date of receipt of the notice refusing to file the PMA.

You may receive clarification on the deficiencies stated in the Not Filing Letter by communicating with the Review Team (rather than by requesting an informal conference with OHT Director)
If you decide to request a meeting to discuss the Not Filing Letter, you need to choose either:

1. An informal conference or
2. A meeting to review the decision not to file the application, including the specific deficiencies and measures necessary to correct them

The FDA will not grant requests for both.

The informal conference is held by the OHT Director within **10 working days** after receiving the request

The OHT Director makes their decision on filing within **5 working days** after the informal conference

ACCEPTANCE

If the OHT Director accepts the PMA for filing, the date of filing will be the date of the decision to accept the PMA for filing.

REFUSAL

If the OHT Director upholds the not filing decision and does not reverse the decision, you may submit a request for reconsideration from the Office of Product and Evaluation Quality (OPEQ) Director **within 30 days** of receipt of the FDA's notice of upholding the not filing decision.

The OPEQ Director will provide a written decision **within 60 days** of receipt of the request.

ACCEPTANCE

If the OPEQ Director accepts the PMA for filing, the date of filing will be the date of the decision to accept the PMA for filing.

REFUSAL

If the OPEQ Director does not reverse the not filing decision, then the PMA remains not filed. The OPEQ Director's decision will constitute the final administrative action for the purpose of judicial review.

How long does a PMA application take? (continued)

Step 2: Substantive Review | In-depth scientific, regulatory, and Quality System review

FDA will begin substantive review of the PMA after it is accepted for filing.

During the review process, FDA will notify you via major/ minor deficiency letters of any information needed by them to complete the review of your application.

You may request to meet with the FDA within **100 days** of the filing of the PMA to discuss the review status of the application.

The procedure for "**Day-100 Meetings**" can be found in the guidance document here.

If you need to submit a PMA amendment which contains significant new data from a previously unreported study, significant updated data from a previously reported study, detailed new analyses of previously submitted data, or significant required information previously omitted, the review period may be extended up to **180 days.**

Step 3: Panel Review | Review & recommendation by the appropriate advisory committee

The FDA may refer your PMA to an outside advisory committee. In general, all PMA's for the first-of-a-kind device are referred. However, as soon as FDA believes that:

1.The pertinent issues in determining the safety and effectiveness for the type of medical device are understood and

2.The FDA has developed the ability to address those issues,

future PMA's for devices of that type are not be taken before an advisory panel unless a particular application presents an issue that can best be addressed through panel review.

- During the review process, FDA may communicate with you or the committee to respond to questions that may be raised by committee members, or to provide additional information to the panel.
- The advisory committee will hold a public meeting to review the PMA in accordance with 21 CFR 14
- They will then submit a final report to the FDA including their recommendation (which can be in the form of a meeting transcript signed by the committee chairperson)

- FDA then takes into consideration the transcript of the meeting, the panel`s recommendations, and other information to reach a final decision on your PMA
- You will then be informed whether the FDA agrees or disagrees with the panel`s recommendation, and what additional information you need to provide.
- If the application is deemed approvable, you must agree to the "Conditions of Approval."

How long does a PMA application take? (continued)

Step 4: Final deliberations, documentation, and notification of the FDA's decision

ACCEPTANCE

Approval letter

- You will receive an approvable letter if your application substantially meets the requirements of the FD&C Act, and the FDA believes that it can approve the application if you agree to specific conditions / submit additional information
- The approvable letter will describe the additional information required to obtain approval

Approval order

- The FDA will issue an order to you that your PMA is approved
- They will approve your application on the basis of draft final labelling
- Approval will be based on the condition that you submit a copy of the final printed labelling to the FDA before marketing.

REFUSAL

Not approvable letter

- You will receive a not approvable letter if the FDA believes that the application may not be approved for specific reasons, or if they are unable to reach an approvable decision due to a lack of significant information in your application
- The not approvable letter will describe the deficiencies in your application, including each applicable ground for denial
- When practical, FDA will identify what is necessary to make the PMA approvable

If you receive a not approvable letter you can:

- Amend your PMA as requested
- Consider the not approvable letter to be a denial of approval of the PMA and request an administrative review by filing a petition for reconsideration
- Withdraw your PMA

Order denying approval

Your PMA application will be denied if:

- You fail to follow the requirements of the PMA regulations
- The FDA determines any grounds for denying approval as specified in the FD&C Act
- Your PMA contains a false statement of material fact
- Your device`s proposed labelling is non-compliant
- You do not permit an authorised FDA employee to inspect your manufacture facilities and controls
- An essential nonclinical laboratory study described in your PMA was not conducted in compliance with the good laboratory practice (GLP) regulations in 21 CFR 58, with no valid reason for noncompliance provided
- A clinical investigation involving human subjects described in your PMA was not conducted in compliance with the applicable regulations, such that the rights or safety of human subjects were not adequately protected.

The order denying approval will outline the deficiencies in your PMA, and where practical, will identify measures required to place your PMA in approvable form. It will also include notice of an opportunity to request a review.

Further reading:

- www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma
- www.fda.gov/medical-devices/premarket-approval-pma/pma-review-process
- www.fda.gov/medical-devices/premarket-approval-pma/pma-guidance-documents
- www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/guidance-pma-interactive-procedures-day-100-meetings-and-subsequent-deficiencies-use-cdrh-and
- www.fda.gov/media/91429/download
- www.fda.gov/medical-devices/premarket-approval-pma/pma-conditions-approval
- www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/early-collaboration-meetings-under-fda-modernization-act-fdama-final-guidance-industry-and-cdrh