Draft Guidance for Industry and Food and Drug Administration Staff

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Acceptance and Filing Review for Premarket Approval Applications (PMAs)

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
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For questions regarding this document, contact the Premarket Approval Staff at 301-796-5640. For questions regarding submissions to the Center for Biologics Evaluation and Research, contact CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

When final, this document will supersede the following guidance documents:
Premarket Approval Application Filing Review, dated May 1, 2003.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

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Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER) by written request, Office of Communication, Outreach and Development (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, by telephone, 1-800-835-4709 or 301-827-1800, by email, ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm.

Draft Guidance for Industry and Food and Drug Administration Staff

Acceptance and Filing Review for Premarket Approval Applications (PMAs)

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

Purpose

As discussed in more detail below, the PMA regulation (21 CFR 814.42(e)) identifies the criteria that, if not met, may serve as a basis for refusing to file a PMA. These criteria are discussed in the guidance document "Guidance for Industry and FDA Staff: Premarket Approval Application Filing Review," dated May 1, 2003 (2003 PMA Filing Guidance). These documents have been used by FDA staff and the device industry to help elucidate the broad preclinical and clinical issues that need to be addressed in a PMA and the key decisions to be made during the filing process.

Focusing the Agency's review resources on complete applications will provide a more efficient approach to ensuring that safe and effective medical devices reach patients as quickly as possible. Moreover, with the enactment of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA), the Medical Device User Fee Amendments of 2007 (MDUFA II) and the Medical Device User Fee Amendments of 2012 (MDUFA III),[1] FDA agreed to performance goals based on the timeliness of reviews. Acceptance review therefore takes on additional importance in both encouraging quality applications from PMA applicants and allowing the Agency to appropriately concentrate resources on complete applications.

Therefore, we have modified the PMA filing guidance and checklist. We have separated the criteria for PMA filing into 1) acceptance criteria and 2) filing criteria. Acceptance review

[1] *See* Title II of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-114), amending sections 737, 738, and 738A of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

involves assessment of the completeness of the application, and informing the applicant in a written response within the first 15 calendar days of receipt of the application whether any elements are missing, and if so, identifying the missing element(s). In order to enhance the consistency of our acceptance and filing decisions and to help applicants better understand the types of information FDA needs to conduct a substantive review of a PMA, this guidance and associated checklist clarify the necessary elements and contents of a complete PMA application. The process we outline is applicable to all devices reviewed in a PMA application and has been compiled into a checklist for use by FDA review staff.

FDA staff and industry should note that this guidance is not significantly different from the previous PMA filing checklist and guidance document, as the PMA filing criteria defined in the regulation have not changed. The "preliminary questions" remain the same and the "filing review questions" have been separated into "acceptance decision questions" (i.e., whether the file is administratively complete) and "filing decision questions" (i.e., whether the data are consistent with the protocol, final device design, and proposed indications). In the 2003 PMA Filing Guidance, we stated that delayed submission of the manufacturing section would not preclude filing a PMA, and, if this section is not included in the original PMA application, recommended submitting this section within 90 days. However, delayed submission of the manufacturing section has rarely occurred in recent years, and in many cases this section is submitted prior to other sections of the PMA, as part of a modular PMA submission. Therefore, we are now including the manufacturing section in the checklist for a complete PMA application.

FDA encourages all submitters to provide an electronic copy (eCopy)[2] in place of one of the six hard copies of the PMA application. For more information regarding recommended formatting of eCopies for submissions sent to the Center for Devices and Radiological Health (CDRH), please refer to our website for guidelines for submitting both general information (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm) as well as clinical data (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm). For more information regarding recommended formatting of eCopies and inclusion of hard copies for submissions sent to CBER, please refer to "Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format-General Considerations" (http://www.fda.gov/RegulatoryInformation/Guidances/ucm124737.htm) as well as "CBER SOPP8110: Submission of Paper Regulatory Applications to CBER" (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079467.htm).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance documents means that something is suggested or recommended, but not required.

[2] Section 745A(b) of the FD&C Act, added by section 1136 of FDASIA provides statutory authority to require eCopy (*See* Public Law 112-114). FDA intends to issue guidance on the eCopy program to implement this statutory requirement.

Introduction

The purpose of the PMA acceptance and filing reviews is to make a threshold determination about whether an application is administratively complete for the Agency to undertake a substantive review. The PMA regulation (21 CFR 814.42(e)) states that FDA may refuse to file a PMA if **any** of the following applies:

(1) The PMA is incomplete because it does not on its face contain all the information required under section 515(c)(1)(A)-(G) of the FD&C Act.

(2) The PMA does not contain each of the items required under section 814.20 and justification for omission of any item is inadequate.

(3) The applicant has a pending premarket notification under section 510(k) of the FD&C Act with respect to the same device, and FDA has not determined whether the device falls within the scope of section 814.1(c).

(4) The PMA contains a false statement of material fact.

(5) The PMA is not accompanied by a statement of either certification or disclosure as required by 21 CFR Part 54.

Section 814.20 of the regulation further specifies that PMAs must include, among other things, "*technical sections which shall contain data and information in sufficient detail to permit FDA to determine whether to approve or deny approval of the application*" (21 CFR 814.20(b)(6)). FDA staff has frequently expressed the need for more specific guidance in applying this regulatory standard to the PMA application filing decision-making process.

The goal of this document is to clarify the criteria for accepting and filing a PMA, thereby enhancing the consistency of our acceptance and filing decisions. The decision-making process presented in this document is captured in "Checklists for Acceptance and Filing of PMAs," (see Appendix A). FDA staff will use these checklists during the acceptance and filing review process.

Scope

The information presented in this document is intended to provide FDA staff with a clear, consistent approach to making acceptance and filing decisions on original PMA applications and panel-track PMA supplements. FDA's decision to accept and/or file a PMA does not imply that the data provided in the PMA demonstrate reasonable assurance of the safety and effectiveness of your device or assure approval of the PMA. Modular PMAs are not addressed in this document; please refer to the guidance document entitled "Premarket Approval Modular Review" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089764.htm) for additional information regarding Modular PMAs.

In addition, it should be noted that this document is focused on the regulatory and scientific criteria for making an "Accept" or "Refuse to Accept" decision as well as "File" or "Not File" decision for a PMA. It specifically does not alter the following administrative aspects of the PMA filing process: the time frame for the filing review phase (i.e., 45 days); the processes for document tracking, distribution, and handling; and the procedures for assembling the review team and setting up the filing meeting.

This document does not discuss the statutory criteria for expedited (or priority) designation. Information pertaining to expedited designation can be found in the "Guidance for Industry and FDA Staff: Expedited Review of Premarket Submissions for Devices," published on February 29, 2008. (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089643.htm).

This document does not address the monetary aspects or the MDUFA goals associated with PMAs. For information pertaining to the fees and payment procedures for submission of a PMA, please refer to "Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products." (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089726.htm)

Pre-Submission Interaction

Prior to interacting with review staff, applicants should consult CDRH's Division of Small Manufacturers, International and Consumer Assistance (DSMICA) or CBER's Manufacturers Assistance and Technical Training Branch for general information regarding the PMA regulations. Before submitting a PMA, we encourage applicants to interact with FDA review staff. Such pre-submission interaction is an important way of improving the quality and completeness of a PMA. Also, we encourage applicants to meet face to face with FDA staff before preparing the PMA to discuss issues related to their specific device and PMA. For additional information regarding the Pre-Submission process, please refer to the Draft Guidance "Medical Devices: The Pre-Submission Program and Meetings with FDA Staff."[3] (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm)

In addition, CDRH's Device Advice, (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm) as well as other applicable CDRH device-specific and cross-cutting guidance documents, (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm) provide valuable information for preparing PMAs.

[3] Once finalized, this guidance will represent the Agency's current thinking on this topic.

Basic Review Policies and Procedures

Review policies for acceptance

To facilitate a more efficient review process, FDA staff will conduct an acceptance review of all original PMAs and Panel-Track PMA Supplements based on objective criteria using the Checklist for Acceptance Review (see Appendix A) to ensure that the PMA is administratively complete. In order for the submission to be accepted, all organizational and administrative elements should be present or a rationale should be provided for those elements determined by the sponsor to be not applicable. The acceptance review should be conducted and completed within 15 calendar days of the Agency receiving the PMA application. If the application contains all of the information outlined in the checklist, FDA staff should notify the applicant in writing that it has been "Accepted" and proceed to the filing review. Should FDA fail to complete the acceptance review within 15 calendar days, the submission should be considered accepted, the applicant should be notified in writing, and FDA should commence with the filing review.[4]

If one or more of the items on the acceptance checklist are not present, the staff conducting the acceptance review should obtain management concurrence that the application should be designated "Refuse to Accept," and notify the designated PMA contact person that the application has not been accepted. FDA staff should also provide the applicant with a copy of the completed acceptance checklist indicating which item(s) are the basis for the "Refuse to Accept" designation.

The PMA applicant may respond to the "Refuse to Accept" notification by providing the missing information identified in the checklist. The applicant should submit this information to be included in the file (i.e., as an amendment) under the originally assigned PMA number. A new application and new user fee are not necessary. Nor should the submitter re-send the entire PMA application, unless FDA determines otherwise (e.g., because the majority of the submission was not in English, or the submission pages were not numbered). It is sufficient to submit and address only the information requested per the acceptance checklist.

Upon receipt of the newly submitted information, FDA staff should conduct the acceptance screening again following the same procedure within 15 calendar days of receipt. If the submission is still found to be incomplete, FDA staff should notify the contact person and provide the new checklist indicating the missing item(s).

Review policies for filing

Once the application is found to be administratively complete, FDA staff should notify the applicant that the PMA has been accepted and begin the filing review according to the Checklist for Filing Review. The objective of the filing review is to determine the basic adequacy of the technical elements of the PMA. In order for the submission to be filed, the application should be

[4] In the case of extenuating circumstances such as a government closure during the 15-day review period, the review period may be extended by a comparable number of business days that the FDA buildings are closed. If the submitter receives an automated notice that the acceptance review was not completed because the screening period has exceeded 15 days, FDA may send a correction notice to the submitter.

sufficiently complete to permit a substantive review. Once the filing review is complete, staff will notify the applicant in writing within 45 calendar days of receipt whether the PMA has been "Filed" or "Not Filed." See 21 CFR 814.42(a). If the PMA has been "Filed," the agency will identify the date of receipt of the PMA or of the amendment to the PMA that enabled FDA to file the PMA.

The PMA applicant may respond to the "RTF" notification by providing the missing information identified in the letter. The applicant should submit this information to be included in the file (i.e., as an amendment) under the originally assigned PMA number. Upon receipt of the newly submitted information, FDA staff should conduct the filing review again following the same procedure within 45 calendar days of receipt.

During the filing review, review staff may ask for any information that should have resulted in an "RTA" designation during the acceptance review. Likewise, once the submission has been filed, FDA may ask for any information during the substantive review that may have been unintentionally overlooked during the acceptance or filing reviews.

FDA Review Clock

As explained in section VIII.C. of the commitment letter for MDUFA III referenced in Title II of FDASIA, Public Law 112-114, "FDA days begin on the date of receipt of the submission or of the amendment to the submission that enables the submission to be accepted (510(k)) or filed (PMA)."[5] Since the PMA acceptance criteria are a subset of the PMA filing criteria under 21 CFR 814.42, an application that is "Not Accepted" is not one that enables the submission to be filed. Thus, the FDA review clock does not start when an application is designated "Not Accepted" or "Not Filed." The FDA review clock also would not start if we receive an unsolicited amendment during the acceptance review period. Once FDA has both "Accepted" and "Filed" an application, the FDA review clock begins as of the date of receipt of the most recent submission or amendment that made the PMA complete and on which the FDA based its "Accepted" and "Filed" decisions. This date will not change even if FDA later requests information it should have requested during acceptance or filing review.

Acceptance and Filing Review Principles

In order to use this guidance appropriately, FDA staff should review the following basic principles in bold followed by a description of FDA's review policies and procedures. These principles, and the objective criteria outlined in the Acceptance and Filing Checklists, inform FDA's PMA acceptance and filing decisions.

The contents of the PMA should allow the substantive review to proceed

The PMA must contain the basic administrative and scientific elements listed in 21 CFR 814.20.

[5] MDUFA III Commitment Letter, available at http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf (this document is dated April 18, 2012; it has not changed since then).

The specific questions in the acceptance and filing checklists are intended to help FDA ensure that the PMA contents are not so disorganized or incomplete so as to prevent the review team from proceeding with a substantive review of the application.

The acceptance decision and filing decision should not be based on a substantive review of the studies in the PMA

The acceptance review and filing review are conducted to ensure that the PMA is administratively complete and to determine the basic adequacy of the technical elements of the PMA, respectively. Notably, in determining whether a PMA should be accepted and filed, the submitted information should not be evaluated to determine whether there is a reasonable assurance of safety and effectiveness. The checklist is a tool to ensure that the submission contains the necessary information in order to conduct a substantive review (i.e., FDA should not designate an application "Refuse to Accept" or refuse to file a PMA because we have reviewed the data and believe that the application is ultimately not approvable). Subsequently, the substantive review of the PMA will evaluate the quality of the content and lead to a decision regarding the safety and effectiveness of the PMA product.

Concerns identified by the Agency during the acceptance or filing review regarding **results and outcomes** of nonclinical and clinical studies **would not preclude acceptance or filing**. Examples of information that would typically fall into this category include:

- demographic information for the study population
- conclusions regarding statistical analyses
- report or assessment of protocol deviations
- reports of device failures or malfunctions.

Staff should consider the applicant's justifications for any alternative approaches

If the applicant believes any criteria in the checklist are not applicable, it should explain its rationale. Likewise, the applicant should provide a rationale for any deviation from a device-specific or cross-cutting guidance document or FDA-recognized standard. It is FDA's expectation that any item in the checklist that is missing will be addressed with a rationale explaining why it is not applicable and that any deviations will be explained.[6] A given criterion in the checklist will be considered not "Present" if the submission fails to include either the information requested or a rationale for omission. See Acceptance Review section below for further explanation.

[6] The presence of a justification is particularly relevant in the acceptance review stage, while the adequacy of such justification falls within the scope of the substantive review phase.

PMA acceptance and filing review

The decision to "Accept" an application or designate it "Refuse to Accept" should be made by the lead reviewer with concurrence from the immediate supervisor or designee. The decision to "File" or "Not File" a PMA should be made at the division level in collaboration with the PMA review team (in particular the medical officer and statistician) and the appropriate managers in the reviewing division(s).

The Checklist – Preliminary Questions

Within 15 calendar days of receipt of the PMA and prior to the formal filing review, the PMA lead reviewer should answer the preliminary questions below, and complete the Administrative Checklist to make an Acceptance Decision.

The preliminary questions are included on the first page of the "Checklists for Accepting and Filing PMAs." Depending upon the answers to these preliminary questions, the remainder of the acceptance and filing reviews may or may not be necessary. If the responses to the preliminary questions and subsequent consultation with the Center personnel identified below indicate that the PMA acceptance and filing reviews should not continue,[7] the PMA team leader should promptly:

- inform the PMA review team (including consulting reviewers); and
- notify the applicant using proper administrative procedures.

The preliminary questions are:

1. **Is the product a device (per section 201(h) of the FD&C Act) or a combination product (per 21 CFR 3.2(e)) with a device constituent part subject to review under PMA?**

   If the product does not appear to meet the definition of a device under section 201(h) of the FD&C Act, or does not appear to be a combination product with a device constituent part subject to review under PMA, then the PMA team leader should consult with the CDRH Jurisdictional Officer or the CBER Office Jurisdiction Liaison to determine the appropriate action, and inform division management. If they agree that the product does not appear to be a device or a combination product with a device constituent part subject to review under PMA, the PMA review team should stop the review and notify the applicant.

[7] There are three (3) additional criteria for not processing a PMA that has been received: i) the application is not submitted with the required user fee per the Medical Device User Fee Amendments of 2012, ii) the application is not signed or countersigned by a U.S. representative per 21 CFR 814.20(a), and iii) the firm did not submit the correct number of copies per 814.20(b)(2). Since any PMA not meeting these three criteria will not be processed by the CDRH Document Mail Center or CBER Regulatory Project Manager, they are not included in the checklist.

2. Is the application with the appropriate Center?

If the application is for a single-entity device and appears to be subject to review in a Center different from the one to which it was submitted, or if it is for a combination product with a device constituent part and it appears that a Center different from the one to which it was submitted has the lead, the PMA team leader should consult with the CDRH Jurisdictional Officer or the CBER Office Jurisdiction Liaison to determine the appropriate action and inform division management. If the PMA is submitted to CDRH and CDRH staff determines that the application is not subject to CDRH review, or the PMA is submitted to CBER and CBER staff determines that the application is not subject to CBER review, the PMA review team should stop the review and notify the applicant.

3. Is class III/PMA review required for the device?

Our goal is to apply the appropriate level of regulation to provide a reasonable assurance of safety and effectiveness. Therefore, early in the filing review process, FDA should consider the regulatory burden and the available mechanisms to apply the proper degree of regulation. In making this determination, staff should consider how similar devices are being regulated.

Class III devices are those that cannot be classified as Class I or Class II devices and either (1) are purported to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health; or (2) present a potential unreasonable risk of illness or injury. See section 513(a)(1)(C) of the FD&C Act. Devices may also automatically be classified in class III under section 513(f)(1) of the FD&C Act.

Generally, PMA review is required if the device is:

- a transitional device that has not been reclassified (see section 520(l) of the FD&C Act),
- the subject of a final "call for PMA" under section 515(b) of the FD&C Act, or
- automatically classified into Class III under section 513(f) of the FD&C Act, including devices found to be Not Substantially Equivalent (NSE) in response to a 510(k) premarket notification.

If regulation under PMA does not appear to be required, the PMA lead reviewer should consult division management and other Center resources to determine the appropriate action. If the review division agrees that review in a different type of marketing submission may be an option, the PMA review team should notify the applicant to discuss the most appropriate path forward.

4. Is there a pending 510(k) for the same device with the same indications for use?

FDA may decide not to file a PMA if the applicant has a 510(k) for the same device pending (21 CFR 814.42(e)(3)). If there is a pending 510(k), the review team should stop the review.

Under these circumstances, the applicant should be asked to withdraw either the 510(k) or the PMA. The PMA team leader should consult division management and other Center resources to determine which premarket review pathway applies to the device. Staff should also consult division management and other Center resources if a 510(k) and PMA have been submitted for the same device type by different applicants.

5. Is the submitter the subject of the Application Integrity Policy (AIP)[8]?

The lead reviewer should refer to the AIP list. (http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134453.htm) If the applicant is on the list, the reviewer should consult the CDRH Office of Compliance/Division of Bioresearch Monitoring (OC/DBM - BIMO) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action.

The Checklist – Acceptance Review

If the answers to the above preliminary questions indicate that PMA review should continue, the acceptance review should proceed by answering questions in the "Acceptance Review" section of the checklist. This section of the checklist collects information regarding the completeness of the PMA (i.e., "Inventory of Organizational and Administrative Elements") and guides FDA staff through the process necessary to arrive at a decision to "Accept" a PMA or designate it "Refuse to Accept."

The specific issues that are critical to the PMA acceptance decision-making process (i.e., the "Acceptance Decision Questions") are individually discussed below. The numbering scheme used for these decision questions corresponds to the checklist. Each Acceptance Decision Question should be answered. Only if questions are answered "YES" can the PMA application be accepted for filing review.

Acceptance Decision 1: Is the PMA administratively <u>complete</u>?

The questions in Section A of the checklist are intended to outline each of the administrative elements required by 21 CFR 814.20 that are necessary for substantive review of the PMA. If, on its face, the PMA is missing one or more required element or sections as described by the questions in Section A (including manufacturing information as discussed above), the answer to the above question is "NO" and the PMA team leader should note the specific omission(s) on the checklist. A section will be considered missing if it is not in English and not accompanied by an English translation. If such omissions exist, the review division should not accept the PMA.

[8] When data in a pending application has been called into question by certain wrongful acts (fraud, untrue statements of material facts, bribery, or illegal gratuities), FDA intends to defer substantive scientific review of such data until completion of a validity assessment and questions regarding reliability of the data are resolved. (*See* FDA Guide 7150.09 Compliance Policy Guide, Chapter 50 – General Policy – Subject: Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities, 56 FR 46191).

Acceptance Decision 2: From only an administrative review, does the PMA include data that appears to constitute valid scientific evidence?

The answer to this question is "NO" if it is **clear** that the only information provided in the PMA is information that is not regarded as valid scientific evidence under 21 CFR 860.7 (i.e., "isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions"). If none of the data, on their face, constitute valid scientific evidence, the division should not accept the PMA.

Acceptance Decision 3: Does the PMA address the key nonclinical and clinical issues identified by FDA prior to submission of the PMA application, OR has the applicant provided a scientific or clinical justification for an alternative approach?

Section B of the checklist outlines questions intended to identify when the FDA has previously provided specific guidance to the applicant about the content of the PMA through one or more mechanisms, such as a prior PMA application, a prior "Not Substantially Equivalent" decision on a 510(k), Investigational Device Exemption (IDE) letters, Pre-Submission feedback, a Determination or Agreement meeting(s), or other substantive communication with FDA, or through a published guidance document. If such information has been communicated to the applicant through one or more of these mechanisms, and the PMA application addresses each of the key nonclinical and clinical issues identified by FDA, the answer to the above question is "YES." Furthermore, if some of these key issues previously identified by FDA are not addressed, but the PMA application contains a scientific or clinical justification for the omission or deviation, the answer to the above question is "YES." These cases do not preclude the review division from accepting the PMA.

In this context, the term "key issues" is meant to refer to issues that are central to our review of device safety and effectiveness under section 515(c) and (d) of the FD&C Act. Examples of key issues include: need for long-term nonclinical studies (e.g., biocompatibility, carcinogenicity, or other animal studies), and certain clinical trial parameters (e.g., sample size, patient population, statistical hypothesis, study design, and endpoints). These key issues typically are device-specific. As a result, the decision of the review division to "Refuse to Accept" a PMA application based on this criterion can only be made after carefully considering these questions:

Are the types of necessary nonclinical and clinical studies well-known in the scientific and medical communities for the particular device?

For an "established" device type, the types of nonclinical and clinical studies that we would expect in a PMA are likely to be well-known both within FDA and in the scientific and medical communities and, as such, are often included as part of an FDA guidance document and/or consensus standard.

Were the issues conveyed to the applicant as part of a documented regulatory process?

Examples of a documented regulatory process include:

- pre-submission interaction,
- prior PMA application,
- prior "Not Substantially Equivalent" decision on a 510(k),
- IDE letters, or
- letter(s) issued as a result of Determination or Agreement meetings.

Staff should only designate a PMA "Refuse to Accept" based on a "NO" response to "Acceptance Decision 3" in instances where the key issues were identified by staff as part of a documented regulatory process.

The Checklist – Filing Review

If the answers to the above preliminary questions and acceptance decision questions indicate that PMA review should continue, the formal filing review should proceed by answering questions in the "Filing Review" section of the checklist. This section of the checklist assesses the basic adequacy of the technical elements (i.e., "Filing Assessment of Technical Elements") and guides FDA staff through the process necessary to arrive at a decision to "File" or "Not File" a PMA.

The specific issues that are critical to the PMA filing decision-making process (i.e., the "Filing Decision Questions") are individually discussed below. The numbering scheme used for these decision questions corresponds to that of the checklist. Each Filing Decision Question should be answered. Only if all questions are answered "YES" can the PMA application be filed.

We do not anticipate that a single member of the PMA review team will be able to answer all of these questions. Rather, we expect that the PMA team leader will complete this checklist in consultation with the team members, in particular the medical officer and statistician.

Filing Decision 1: Were the clinical study data collected and analyzed per the protocol?

If the clinical data submitted in support of PMA approval were collected and analyzed consistent with the major elements of the clinical protocol (i.e., objectives, study population, endpoints, study design, hypothesis, sample size, and follow-up duration), **or** the applicant provides a scientific or clinical justification for the use of an alternative approach, the answer to the above question is "YES" and the PMA team leader will note any specific deviations or justifications on the checklist. In addition, if the sample size is smaller or the follow-up duration is shorter than specified in the clinical protocol, but such changes are supported by either: (i) the recommendation of a Data Monitoring Committee

(DMC) or (ii) statistical plans that incorporate interim stopping rules, substantive review of the PMA may proceed. That is, these cases do not preclude the division from filing the PMA.

If the study deviated from the clinical protocol with respect to the major elements identified in the paragraph above **and** the applicant provided no justification for doing so, the answer to the above question is "NO" and the PMA team leader will note the specific deviation(s) on the checklist. In these cases, the division should not file the PMA.

As discussed above, occasionally, applicants have submitted PMAs with incomplete clinical data (i.e., the sample size is smaller or follow-up duration for the primary analysis is shorter than specified in the clinical protocol). If no justification is provided and/or the applicant indicates they intend to update the PMA with necessary additional clinical data, we will consider such PMAs to be submitted prematurely and therefore incomplete. If the PMA is viewed as a premature submission, the answer to the above question is "NO." In these cases, the review division should not file the PMA.

Filing Decision 2: Were the nonclinical and clinical data collected on the final design of the device (i.e., the device design intended to be marketed)?

If the nonclinical and pivotal clinical data submitted in support of PMA approval were collected on the final device design, or the differences between the study device and final device clearly do not affect safety or effectiveness of the device and/or clinical outcome, the answer to the above question is "YES" and any device changes will be noted on the checklist. Furthermore, if the clinical data were collected on an earlier design of the device **and** the applicant provides a scientific or clinical justification describing why the study results on the earlier device design apply to the proposed design, the answer to the above question is "YES" and the justification will be noted on the checklist. These cases do not preclude the review division from filing the PMA.

If changes that could potentially impact safety and/or effectiveness were made to the device design either during or after the pivotal nonclinical and clinical studies, **and** no justification is provided as to why these data are applicable to the new design, the answer to the above question is "NO." In this case, the PMA team leader will note the specific device change(s) on the checklist, and the review division should not file the PMA.

Filing Decision 3: Were the patient/study[9] population and endpoints consistent with the proposed indications?

If, upon an administrative review, the patient population (as defined by the inclusion and exclusion criteria) in the pivotal study matches the device's proposed indications for use and the endpoints that were selected were agreed to by FDA and/or appear to be clinically relevant, the answer to the above question is "YES." Additionally, if the patient population and/or endpoints are inconsistent with the proposed indications **but** the applicant provides a

[9] Note that in the case of PMAs submitted to CBER, the study population may be blood donors rather than patients.

611 detailed scientific or clinical justification for this approach, the answer to the above
612 question is "YES." These cases do not preclude the review division from filing the PMA.
613
614 If either the patient population or endpoints of the pivotal study, **on their face**, do not
615 match the proposed indications for use **and** no justification is provided for this alternative
616 approach, the answer to the above question is "NO." In addition, if the pivotal study was
617 conducted outside the U.S. and the applicant has not addressed how such data are adequate
618 to support approval (including addressing how the local medical practice and/or patient
619 population match those of the U.S. or why any differences would not impact the
620 applicability of the study results to the U.S. patient population), answer "NO" to the above
621 question. In these cases, the PMA should not be filed.
622

623

Appendix A. Checklists for Acceptance and Filing of PMAs

Checklist for Acceptance Decision for PMAs

(should be completed within 15 days of DCC receipt)

PMA Number: _____ **Date Received:** _____
Device: _____ **Procode:** _____
Company Name/ Address: _____
Contact Name/Phone Numbers: _____
Lead Reviewer Name: _____

Preliminary Questions		
Answers in the shaded blocks indicate consultation with Center advisor is needed.	**Yes**	**No**
1. Is the product a device (per 201(h) of the FD&C Act) or a combination product with a device constituent part subject to review under PMA? If it appears not to be a device or such a combination product, or you are unsure, consult with the CDRH Jurisdictional Officer or appropriate CBER Jurisdiction Liaison to determine the appropriate action and inform your division management. *Provide summary of Jurisdictional Officer's/Liaison's determination.* If the product does not appear to be a device or such a combination product, mark "No."		
2. If the product is a device or a combination product with a device constituent part, is it subject to review by the Center in which the submission was received? If you believe the application is not with the appropriate Center or you are unsure, consult with the CDRH Jurisdictional Officer or CBER Office Jurisdiction Officer to determine the appropriate action and inform your division management. *Provide a summary of the Jurisdictional officer's determination.* If application should not be reviewed by your Center mark "No."		
3. Is class III/PMA review required for the device? **NOTE: If you believe an application is for a new type of device for which we have never received a marketing application and is thus class III/PMA, you should (1) complete the 510(k) decision tree to document why the device would be found NSE (*attach copy*) and (2) obtain concurrence from the CDRH 510(k) Program Director and ODE Deputy Office Director for Science and Regulatory Policy or appropriate CBER staff prior to the accepting the Original PMA. *Attach a copy of the 510(k) Staff's concurrence.***		
4. Is there a pending 510(k) for the same device with the same indications for use? The regulations allow FDA to refuse to file a PMA if a 510(k) for the same device is pending (21 CFR 814.42(e)(3)).		
5. Is the applicant the subject of an Application Integrity Policy (AIP)? If yes, consult with the CDRH Office of Compliance/Division of Bioresearch Monitoring (OC/DBM - BIMO) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action. Check on web at http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134453.htm		

If the answer to 1 or 2 appears to be "No," then stop review of the PMA and issue the "Original Jurisdictional Product" letter.

If the answer to 3 is no, the PMA lead reviewer should consult division management and other Center resources to determine the appropriate action.
If the answer to 4 is "Yes," then stop review of the PMA, contact the CDRH 510(k) Staff and PMA Staff, or appropriate CBER staff.
If the answer to 5 is "Yes," then contact CDRH/OC/DBM – BIMO or CBER/OCBQ/DIS/BMB, provide a summary of the discussion with the BIMO Staff, and indicate BIMO's recommendation/action.

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)								
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.								
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.						**Present** (with section or page number)	**Not Present**
							Yes / **N/A**	
A.	PMA Content							
	1.	Are all required sections in English or accompanied with an English translation?					☐	☐
	2.	Is there a table of contents?					☐	☐
	3.	Is a bibliography provided?					☐ ☐	☐
		a.	Have copies of key articles been provided and are English translations included, if appropriate? Check N/A if applicant includes a statement that upon searching they found no literature related to their device				☐ ☐	☐
	4.	If a device sample has been requested by FDA, has it been provided or if impractical to submit, has the applicant provided other means to provide access to the device?					☐ ☐	☐
	5.	Is there a summary of the contents of the PMA?					☐	☐
	6.	Device Characteristics						
		a.	Is a description of device included?				☐	☐
			i.	Pictorial representations?			☐	☐
			ii.	Materials specifications?			☐	☐
				•	If there is a color additive present: • has the color additive been identified by common name and chemical name, and		☐ ☐	☐

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)								
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.								
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.					**Present** (with section or page number)		**Not Present**
						Yes	**N/A**	
					• has the amount of each color additive in the formulation by weight percent of the colored component and total amount (e.g., µg, ppm) in the device been provided?			
		b.	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? (see Guidance for the Preparation of PMA Manufacturing Information) For Original PMA or a Panel Track Supplement with a new manufacturing site or substantially different manufacturing procedures:				☐	☐	☐
		a.	Has a description of the methods, facilities, and controls used in the manufacture, processing, packing, storage, and installation of the device been provided?			☐		☐
	8.	Are a summary of the nonclinical laboratory studies and full test reports* provided? Note: the applicant can reference data located in other submissions. Check "Yes" if nonclinical data is not provided in the current submission, but found in another submission. State where the data were provided (e.g., modular submission, licensing PMA). *Full test report includes objective of the test, description of test methods and procedures, study endpoint(s), pre-defined pass/fail criteria, results summary, discussion of conclusions)				☐	☐	☐
		a.	Sterilization			☐	☐	☐
		b.	Biological/Microbiological			☐	☐	☐
		c.	Immunological			☐	☐	☐
		d.	Toxicological/Biocompatibility			☐	☐	☐

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)							
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.							
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.				**Present** (with section or page number)		**Not Present**
					Yes	**N/A**	
		e.	Engineering (stress, wear, etc.)		☐	☐	☐
		f.	Chemistry/Analytical (typically for IVDs)		☐	☐	☐
		g.	Shelf Life		☐	☐	☐
		h.	Animal Studies		☐	☐	☐
		i.	Other Essential Laboratory Testing		☐	☐	☐
	9.	Is a summary of the clinical investigation(s) and results provided?			☐		☐
		a.	Are the final versions of the clinical protocols included? (If performed under IDE, these should be the final FDA-approved versions of the clinical protocols.)		☐		☐
		b.	Is a description of study population demographics provided?		☐		☐
		c.	Is a description of adverse events (e.g., adverse reactions, complaints, discontinuations, failures, replacements) given?		☐		☐
		d.	Have report forms for patients who died or who did not complete the investigation been provided (i.e., to resolve potential bias)? Check "N/A" only if no patients died or were discontinued.		☐	☐	☐
	10.	Are statistical analyses of the clinical investigations provided?			☐		☐
		a.	Are the results of all analyses identified in the protocol provided?		☐		☐
	11.	Has appropriate draft labeling been submitted?					
		a.	Physician Labeling		☐		☐
			i.	Are indications for use included?	☐		☐
			ii.	Are contraindications, warnings, and precautions included?	☐		☐
			iii.	Are instructions for use included?	☐		☐

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)						
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.						
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.			**Present** (with section or page number)		**Not Present**
				Yes	**N/A**	
		b.	Patient Labeling (OHIP/ODE Memorandum of Understanding) Check "N/A" only if OCER (formerly OHIP) has indicated that patient labeling is not necessary. Put a copy of the OCER reviewer's decision memo in the admin binder.	☐	☐	☐
		c.	Technical/Operators Manual	☐	☐	☐
	12.	Statements/Certifications/Declarations of Conformity				
		a.	Has the applicant provided documentation to establish conformance with applicable performance standards and/or voluntary standards? Check "N/A" only if no standards are used.	☐	☐	☐
		b.	Has the applicant provided documentation to establish that it has followed the recommendations in applicable FDA guidance/ guidelines or otherwise met applicable statutory or regulatory criteria? Check "N/A" only if no guidance/guidelines are used.	☐	☐	☐
		c.	Investigator Financial Disclosure For additional information refer to the guidance document "Guidance for Industry – Financial Disclosure by Clinical Investigators" (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126832.htm) *Document in your filing review memo or checklist any discussions and actions taken.* As required by 21 CFR Part 54, has the applicant submitted either: 1. A signed and dated Certification Form (3454) or 2. A signed and dated Disclosure Form (3455) Note: the signature should be from a responsible corporate official or representative of the applicant.	 ☐ ☐	 ☐ ☐	 ☐ ☐

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)							
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.							
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.				**Present** (with section or page number)		**Not Present**
					Yes	**N/A**	
			i.	For a Certification Form (3454): Is the required list of all investigators and subinvestigators attached to the Form?	☐	☐	☐
			ii.	If box 3 is checked, does the Form include an attachment with the reason(s) why financial disclosure information could not be obtained?	☐	☐	☐
			iii.	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?	☐	☐	☐
		d.	Environmental Assessment under 21 CFR 25.20(n) ((d)(i) or (ii) must be marked YES)		☐		☐
			i.	If claiming a categorical exclusion, information to justify the exclusion, OR	☐	☐	
			ii.	An environmental assessment (ONLY required for devices that present new environmental concerns)	☐	☐	
		e.	Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (42 U.S.C. 282(j)(5)(B)) Note: Enter the NCT number(s) in CTS or other regulatory tracking database		☐		☐
			Data from FORM FDA 3674 (mark YES for the applicable one):				
			i.	No clinical trials referenced in submission.	☐	☐	
			ii.	Requirements are not applicable to referenced clinical trials.	☐	☐	
			iii.	Requirements are applicable and have been met.	☐	☐	
	13.	Pediatric Use - Per 515A(a)(2) of the FD&C Act, did the submission					

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)								
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.								
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.						**Present** (with section or page number) **Yes**	**N/A**	**Not Present**
		include:							
		a.	A description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure. This does not mean the device is indicated for treating pediatric patients.				☐	☐	☐
		b.	The number of affected pediatric patients.				☐	☐	☐
B.	Issues Identified by FDA Prior to PMA Submission - history of the applicant with this device								
	1.	Does the applicant list prior submissions or state that there were no prior submissions? (may be located in CDRH Coversheet Form 3514, Section F) If the applicant lists prior submissions, address the applicable questions below:					☐		☐
		a.	510(k) #_____				☐	☐	
			i.	If this device has been the subject of an NSE decision, does the PMA address any issues relating to safety or effectiveness?			☐	☐	☐
		b.	IDE #_____				☐	☐	
			i.	Have the data presented in the PMA taken into account any safety or effectiveness concerns (e.g., "future considerations") previously communicated through IDE correspondence?			☐	☐	☐
		c.	PMA #_____				☐	☐	

Inventory of Organizational and Administrative Elements (21 CFR 814.20 unless otherwise indicated)							
Check "Yes" if item is present, "N/A" if it is not needed and "Not Present" if it is not included but needed.							
	• Any "Not Present" answer will result in a "Refuse to Accept" decision. • Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.				**Present** (with section or page number) **Yes**	**Present** (with section or page number) **N/A**	**Not Present**
			i.	If a previously submitted PMA for this device been withdrawn, does the current PMA address any issues related to safety or effectiveness raised during review of the prior PMA?	☐	☐	☐
		d.	Modular PMA #_____		☐	☐	
			i.	If yes, how many modules submitted? _____ How many modules were closed? _____			
			ii.	If there are modules that are on hold, does the PMA address outstanding deficiencies?	☐	☐	☐
	2.	Does the applicant list Pre-Submission(s) regarding the device or this submission in which FDA feedback regarding data or information related to safety and/or effectiveness in the PMA was provided by email or during a meeting (in person or by phone), or state that there were no prior Pre-Submission interactions with the FDA regarding this submission? If the applicant lists Pre-Submissions, address the applicable questions below:				☐		☐
		a.	Pre-Submission #_____ Meeting date(s), if applicable_____				
		b.	Copy of minutes from each meeting or other written feedback?		☐	☐	☐
		c.	Were all staff concerns or action items previously presented to the applicant in the Pre-Submission minutes or feedback addressed in the PMA or has the applicant provided a detailed scientific or clinical justification for an alternative approach?		☐	☐	☐

Acceptance Decision Questions			
		Yes	**No**
Decision 1	**Is the PMA complete?** **If, on its face, the PMA is missing one or more required elements (identified above), answer "No."**	☐	☐
Decision 2	**From only an administrative review, does the PMA include data that appears to constitute valid scientific evidence?** **Only answer "No" if it is clear that the PMA is supported solely by information that 21 CFR 860.7 identifies as not constituting valid scientific evidence:** • **isolated case reports** • **random experience** • **reports lacking sufficient details to permit scientific evaluation** • **unsubstantiated opinions** **Comments:**	☐	☐
Decision 3	**Does the PMA address the key nonclinical and clinical issues identified by FDA prior to submission of the PMA application?** **OR** **Has the applicant provided a detailed scientific or clinical justification for the alternate approach?** ***See the guidance document (*Premarket Approval Application Acceptance and Filing Review*) for interpretation of this criterion.***	☐ ☐	☐ ☐

Decision: Accept ___ Refuse to Accept ___

If Accept, notify applicant; if Refuse to Accept, notify applicant in writing and include a copy of this checklist.

PMA Team Leader Signature: _____ Date: _____

Supervisory Signature: _____ Date: _____

Only proceed to the "Filing Review" section if the file is Accepted, indicating that review can continue.

Checklist for Filing Decision for PMAs

Filing Assessment of Technical Elements – Clinical Studies						
Check "Yes" if the information submitted is considered adequate to permit substantive review, "N/A" if it is not needed and "No" if it is not included.						
If data were collected in a study outside the U.S., then the applicant is expected to provide valid scientific justification for all components of the clinical protocol.						
				Present		**Not Present**
				Yes	**N/A**	
A.	Consistency of study data 1) with the protocol in the approved IDE, 2) with recommendations from a Pre-Submission interaction, and/or 3) in accordance with a device-specific guidance document					
	1.	Sample size/number of patients enrolled and completing the study(i.e., the number of evaluable patients at the primary endpoint timeframe)		☐		☐
	2.	Follow-up duration for the primary analysis		☐		☐
	3.	Follow-up evaluations for the primary analysis		☐		☐
	4.	Study Objectives		☐		☐
	5.	Study Population/Enrollment Criteria		☐		☐
	6.	Study Endpoints		☐		☐
	7.	Study Design		☐		☐
	8.	Hypothesis		☐		☐
	9.	Statistical Analysis		☐		☐
		a.	Effectiveness	☐		☐
		b.	Safety Analyses	☐		☐
B.	Appropriateness of key aspects of the protocol					
	1.	Does the patient/study population match the intended use?		☐		☐
	2.	Have clinically significant endpoints been selected?		☐		☐
	3.	If the primary study is based on foreign clinical data, does the sponsor provide a justification with respect to how the data are adequate to support approval (e.g., do the population and medical practices match those in the U.S., or if not, has a justification been provided for why any differences would not impact the applicability of the study results to the		☐		☐

Filing Assessment of Technical Elements – Clinical Studies					
Check "Yes" if the information submitted is considered adequate to permit substantive review, "N/A" if it is not needed and "No" if it is not included.					
If data were collected in a study outside the U.S., then the applicant is expected to provide valid scientific justification for all components of the clinical protocol.					
			Present		**Not Present**
			Yes	**N/A**	
		U.S. patient population [21 CFR 814.15(b) and 814.15(d))			

Filing Decision Questions			
The Filing Decision Questions are shaded and bolded. Some Filing Decision Questions are preceded by introductory questions (denoted by suffixes "a" and "b") to ensure that those Filing Decision Questions are answered appropriately.			
		Yes	**No**
Decision 1a	Was each study completed and analyzed per the protocol (answers to A1-9 under "Filing Assessment of Technical Elements")? • If "yes," answer "yes" to Decision 1 below. • If "no," describe and continue on to Decision 1b. Comments:	☐	☐
Decision 1b	If any study was not completed per the protocol, did the applicant provide a detailed scientific or clinical justification for this alternate approach, without the intention of updating the PMA with additional data? • If "yes," describe and answer "yes" to Decision 1 below. • If "no" (i.e., no justification is provided, or a clinical update is intended), describe and answer "no" to Decision 1 below. Comments:	☐	☐
Decision 1	**Were the clinical study data collected and analyzed per the protocol?**	☐	☐
Decision 2a	Were the studies performed using the final device design (i.e., the device design intended to be marketed)? • If "yes," answer "yes" to Decision 2 below. • If "no," describe and continue on to Decision 2b. Comments:	☐	☐

Filing Decision Questions			
The Filing Decision Questions are shaded and bolded. Some Filing Decision Questions are preceded by introductory questions (denoted by suffixes "a" and "b") to ensure that those Filing Decision Questions are answered appropriately.			
		Yes	**No**
Decision 2b	If the studies were performed using an earlier device design, did the applicant provide a detailed scientific or clinical justification for why the changes made do not impact safety AND effectiveness? • If "yes," describe and answer "yes" to Decision 2 below. • If "no" (i.e., device changes were made that could impact safety OR effectiveness and no justification is provided), describe and answer "no" to Decision 2 below. Comments:	☐	☐
Decision 2	**Were the nonclinical and clinical data collected on the final design of the device (i.e., the device design intended to be marketed)?**	☐	☐

Decision 3a	Does the patient/study population match the device's indication for use, are the endpoints clinically relevant, and, if the pivotal study was conducted outside the U.S., does the sponsor discuss why the data are adequate to support approval in that the foreign data/patient population and medical practice are applicable to those of the U.S. (answers to B1-3 under "Filing Assessment of Technical Elements")? • If "yes," answer "yes" to Decision 3 below. • If "no," describe and continue on to Decision 3b. Comments:	☐	☐
Decision 3b	If "no" to question 3a, did the applicant provide a detailed scientific or clinical justification? • If "yes," describe and answer "yes" to Decision 3 below. • If "no," describe and answer "no" to Decision 3 below. Comments:	☐	☐
Decision 3	**Were the patient/study population and endpoints selected appropriately?**	☐	☐

Decision: Review Team Recommendation: File ___ Not File ___

Priority Review:

*Complete attached **Priority Review Form** whether or not requested by sponsor.*

Priority review requested: Yes___ No___
Priority review granted: Yes___ No___

Lead Reviewer Signature: _____ Date: _____

Supervisory Signature: _____ Date: _____

Division Director Signature: _____ Date: _____

Priority[10] Review Form

Applicant: _____

Device: _____

Use/Indications: _____

Document #: _____

Justification for Priority Review		**Check if YES (✓)**
1.	Does the device affect a condition that is life-threatening or irreversibly debilitating?	☐
2.	Does the device address an unmet medical need, as demonstrated by any one of the following:[11] a. breakthrough technology b. no approved alternative c. significant clinically meaningful advantage d. in the best interest of patients.	☐ ☐ ☐ ☐
3.	Are the answers to 1 & any one part of 2 a YES response?	☐
		If yes, go to 4.
		If no, skip to 5.
Priority Review Assessment (check only one)		
4.	The application qualifies for priority review status	☐
5.	The application does not qualify for priority review status	☐

Identify review lead reviewer & consultants:

Attach tentative review timeline.

Signature: _____
Lead reviewer & Date

Signature: _____
Supervisor & Date

Signature: _____
Division Director & Date

[10] Formerly called Expedited

[11] See **"Expedited Review of Premarket Submissions for Devices"** at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/ucm089643.htm for a more detailed description of the statutory criteria for priority review. FDA will verify the applicability of any justification proposed.