The 21st Century Cures Act (Cures), signed into law on December 13, 2016, amended several sections of the Federal Food, Drug, and Cosmetic Act. This guidance was developed and issued prior to the enactment of Cures, and certain sections of this guidance may no longer be current as a result. FDA is assessing how to revise this guidance to represent our current thinking on this topic. For more information please contact CDRH-Cures@fda.hhs.gov.

Guidance for Industry and Food and Drug Administration Staff

Priority Review of Premarket Submissions for Devices

Document issued on: May 17, 2013

This document supersedes the following guidance document: Expedited Review of Premarket Submissions for Devices" dated February 29, 2008.

For questions regarding the use or interpretation of this guidance in the review of PMAs, please contact the PMA Staff at (301) 796-5640.

For questions regarding the use or interpretation of this guidance in the review of 510(k)s, including the Evaluation of Automatic Class III Designation classification actions (de novo review), please contact the Premarket Notification (510(k)) Staff at 301-796-5640.

For questions regarding the use or interpretation of this guidance in the review of devices regulated by CBER, please contact CBER's Office of Communication, Outreach and Development (OCOD) at 1-800-835-4709 or 301-827-1800.

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

Public Comment

You may submit written comments and suggestions at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Submit electronic comments to www.regulations.gov.

Identify all comments with Docket No. 1998D-0173. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 301-827-8149 to receive a hard copy. Please use the document number (108) to identify the guidance you are requesting.

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 (OCOD) (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.

Table of Contents

Guidance for Industry and Food and Drug Administration Staff

Priority Review of Premarket Submissions for Devices

This guidance represents 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.

I. Introduction

The Medical Device User Fee Amendments of 2012[1] (MDUFA III), amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to authorize FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2012. The additional funds obtained from user fees will enable FDA, with the cooperation of industry, to improve the device review process to meet certain performance goals and implement improvements for the medical device review process.

This guidance document incorporates changes set forth in MDUFA III related to priority (formerly expedited) submissions. Specifically, the terminology "Expedited" is updated to "Priority" to be consistent with Section 515(d)(5) of the FD&C Act. In addition, for the purposes of evaluating performance goals,[2] Premarket Approval Application (PMA) cohorts will not be defined by whether or not a PMA has been designated priority; rather PMA cohorts will be defined by whether or not a PMA is taken to an advisory committee

[1] *See* Title II of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-114)

[2] Performance goals are outlined in the letter from the Secretary of Health and Human Services (the Secretary) to Congress (MDUFA III Commitment Letter). See "MDUFA Performance Goals and Procedures" (April 18, 2012), available at http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf) (attachment to letter dated July 16, 2012 from Secretary of Health and Human Services Kathleen Sebelius to The Honorable Fred Upton, Chairman, U.S. House of Representatives Committee on Energy & Commerce

panel meeting for review. The PMAs that receive priority review designation will, however, still be reported in the MDUFA annual performance reports.

FDA's guidance documents, including this guidance document, do not establish legally enforceable responsibilities. Instead, guidance documents 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.

II. Scope

This document has the following purposes: (1) develop a common understanding of the statutory criteria for granting priority review to premarket submissions for medical devices, and (2) outline standard procedures that should be followed to achieve an efficient priority review process.

While Section 515(d)(5) of the FD&C Act only applies to PMAs, because of the potential public health importance of devices warranting priority review status, FDA also has applied the priority review criteria to all premarket submissions, including devices evaluated under a protocol development product (PDP), the Evaluation of Automatic Class III Designation process (also known as the "de novo" or "risk based" classification process), premarket notification submissions (510(k)s), and Biologics License Applications and Supplements (BLAs/BLSs) for medical devices regulated under section 351 of the PHS Act.

III. Devices Appropriate for Priority Review

Using the criteria in section 515(d)(5) of the FD&C Act, FDA considers a device or a combination product containing a device,[3] appropriate for priority review if the device or combination product:

1. **is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition, and**

2. **meets at least one of the following:**

    a. **The device represents a breakthrough technology that provides a clinically meaningful advantage over existing technology.** Breakthrough technologies should be demonstrated to lead to a clinical improvement in the treatment or diagnosis of the life-threatening or irreversibly debilitating condition.

[3] Combination products are eligible for priority review under the MDUFA goals when CDRH or CBER has been designated as the lead Center.

b. **No approved alternative treatment or means of diagnosis exists.**

c. **The device offers significant, clinically meaningful advantages over existing approved alternatives.** The device should provide for a clinically important earlier or more accurate diagnosis or offer important therapeutic advantages in safety and/or effectiveness over existing alternatives. Such advantages may include demonstrated superiority over current treatments for effects on serious outcomes (e.g., morbidity), ability to provide clinical benefit for those patients unable to tolerate current treatments, or ability to provide a clinical benefit without the serious side effects associated with current treatments.]

d. **The availability of the device is in the best interest of patients.** That is, the device provides a specific public health benefit, or meets the need of a well-defined patient population. This may also apply to a device that was designed or modified to address an unanticipated serious failure occurring in a critical component of an approved device for which there are no alternatives, or for which alternative treatment would entail substantial risk of morbidity for the patient.

IV. Special Considerations

Manufacturers who are working with a federal agency in the development of medical devices to address a national security issue should include a letter in the premarket submission from the federal agency (e.g., Department of Defense, Department of Homeland Security) identifying the specific device or device type and indicating that commercial availability is of particular importance to our national security to support the request for priority review. The letter should be printed on official agency letterhead and signed by an individual with appropriate authority for making the request.

V. Priority Review: Its Meaning and Impact

A. Priority Review Queue

Granting priority review status means that a marketing application that is determined to be appropriate for priority review is placed at the beginning of the appropriate review queue and receives additional review resources, as needed.[4] If multiple applications for the same type of device offering comparable advantage over existing approved alternatives have been granted priority review, they are reviewed with priority assigned on a first-in-first-reviewed (FIFR) basis for each review cycle.

[4] Note that in the case of BLAs or Efficacy supplements granted priority review status, the place in the review queue is not changed. Rather, the priority is reflected in a reduced review time. Under the MDUFA III Commitment Letter, Standard BLAs and Efficacy supplements are reviewed within 10 months whereas Priority BLAs and Efficacy supplements are reviewed within 6 months.

Furthermore, if one of these applications is approved, the remaining priority applications will retain their priority status until a final decision is rendered. Any new application filed after the approval or clearance of a device of the same type will not be given a priority status unless covered under Section IV (Special Considerations).

B. Impact of Priority Review

While all device submissions granted priority review status are prioritized by FDA, there is no assurance that a device will receive FDA marketing authorization in a more timely manner when compared with submissions not granted priority status. The reasons for this outcome are varied, such as that the devices involve new technology or present complex scientific and regulatory issues often warranting more in-depth review; a failure by the manufacturing facility to be prepared for inspection; or a failure of the applicant to provide adequate scientific data in its submission.

In order to benefit from the priority review process, the commitment on behalf of the applicant to resolve all scientific and regulatory issues should match that of FDA. It will only be through effective communication (i.e., interactive review) and a total commitment to fulfilling all regulatory and scientific requirements that FDA and the applicant can speed market authorization for safe and effective products.[5]

In addition, FDA strongly recommends that industry sponsors developing a device that might qualify for priority review to submit a Pre-Submission.[6]

VI. Requesting Priority Review

The responsibility for identifying devices that are appropriate for priority review is a responsibility jointly shared by industry and FDA. A primary objective of this guidance document is to promote a common understanding of which device submissions may be granted priority review status to facilitate an early recognition of devices that merit such review.

A. Industry Responsibilities

[5] FDA has issued a draft guidance document entitled "Types of Communication During the Review of Medical Device Submissions," available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm341918.htm. When final, this document will represent the Agency's current thinking on this topic.

[6] FDA has issued a draft guidance document on Pre-submissions entitled "Medical Devices: The Pre-Submission Program and Meetings with FDA Staff" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm). Once final, this document will represent the Agency's current thinking on this topic.. For CBER IND and BLA/BLS submissions for devices, please refer to CBER's meeting procedures webpage at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPs/ucm079448.htm.

Opportunities to identify a device as a candidate for priority review occur throughout the device development process. Some of the factors described earlier in this guidance document that indicate that a device should be granted priority review status may be apparent during the early stage of development, while other factors that indicate a device should be granted priority review status may not be apparent until there has been an actual assessment of patient outcomes. As an example, a device in the early design stage may qualify for priority review if, for a certain life-threatening disease or condition, there exists no approved alternative treatment (i.e., see conditions 1 and 2b in Section III (Devices Appropriate for Priority Review) of this guidance document). Alternatively, a device further along in the development process that has undergone clinical testing may be eligible for priority review based on significant advances in safety and effectiveness by satisfying conditions 1 and 2c in Section III (Devices Appropriate for Priority Review).

FDA recommends that industry requests for priority review of a premarket submission be made in writing and accompany any materials submitted in preparation for a meeting or with the application that is to be priority. The request for priority review should cite the relevant priority review criteria described in this guidance document that have been met and include information sufficient to justify the request. In cases where FDA has granted priority review status in advance of the submission of a marketing application, the applicant should include a copy of the FDA correspondence conveying that decision in the marketing application. Note that while FDA can make a priority review determination prior to receipt of a marketing application, the decision will only apply to a future PMA, PDP, 510(k) or DeNovo submission of this type and the decision will be reassessed when the marketing application is received in case other devices of the same type have already gained marketing clearance or approval.

Once FDA grants priority review status for a marketing application, industry responsibilities do not end. If the priority review program is to function effectively and efficiently, industry should give priority to resolving all scientific and regulatory issues that surface during the review process. This may involve redistributing resources from other activities to resolving pending issues, or by providing complete responses to FDA requests for additional information in as timely a manner as possible. It will only be through a complete commitment by all parties involved that priority review will result in safe and effective devices getting to market in as short a time as possible.

B. FDA Responsibilities

FDA staff are also responsible for considering whether new devices are appropriate for priority review, regardless of whether an applicant has identified its device as a potential candidate for this program. Pre-Submission interactions are a prime opportunity for FDA to identify devices eligible for priority review. The review divisions should monitor incoming submissions for devices of the same type that may also be appropriate for priority review status. If more than one pending submission is appropriate for priority review, both submissions should be granted priority review status.

C. FDA Timeframes for Determinations

The Division Director responsible for evaluation of a device is authorized to grant priority review status for a premarket submission, whether requested by the applicant or initiated by FDA. Given the public health importance of this decision, we will attempt to reach a decision on whether to grant priority review within the following timeframes:

- **Pre-submission Communications**[7] - When priority review is a consideration during Pre-Submission communications with companies, review divisions should make a prompt determination regarding device eligibility. Whenever possible, FDA expects the review divisions to make a determination within two (2) weeks of the request for, or discussion of, a particular device's eligibility for priority review status.

- **510(k)s and de novo classification actions** - The decision to apply priority review status should be made within two (2) weeks from the receipt date of the submission.

- **PMAs** - The decision to grant priority review status should be made as early as possible during the 45-day filing review.[8] For PMA supplements that are filed upon receipt (e.g., 180-day supplements), the decision should be reached within 30 days of receipt of the submission

- **BLAs and BLSs** – the decision to grant priority review status should be made at the IND stage or as early as possible during the filing review[9], i.e., within 60 days of receipt of the submission.

D. FDA Administrative Procedures

To document the determination that priority review is appropriate, the division should complete the *"Priority Review Checklist"* (Attachment 1) specifying the basis for its determination. A copy of this form, signed by the Division Director, is to be provided to the appropriate Office Director, and the 510(k) or PMA Staff, or in CBER, to the Regulatory Project Manager (RPM).

The *Priority Review Checklist* also includes certain information regarding resource utilization. In completing the form, review divisions should establish:

- **A Review Team** – The division should designate a team leader and review team, as well as identify resources from outside the division that may be needed to appropriately prioritize the review; and

- **A Tentative Timeline for Review of the Application** – The division should establish a timeline for review. Each division should use project management techniques to prioritize applications and monitor timeframes.

[7] For purposes of this guidance document, "pre-submission communications" includes meetings requested and conducted in accordance with CBER's meeting procedures for device INDs and BLAs/BLSs.
[8] See 21 CFR 814.42(a).
[9] See 21 CFR 601.12(a).

In CDRH, the division will prepare and issue a letter notifying the applicant of the priority review status. In CBER, the Office should prepare the letter notifying the applicant of the priority review status. The notification conveying priority review status may be incorporated into other outgoing correspondence between the applicant and FDA (e.g., a response to an IDE or a PMA filing letter). A copy of the notification letter should be included in the administrative file according to established procedures.

VII. Priority Review Procedures for FDA

The review division and all other FDA components that may be participating incur specific responsibilities upon granting priority review. The areas below warrant special consideration.

A. Resource Management

The Division Director should ensure that the application is reviewed in the most efficient manner, tracked as a priority review, and completed within the MDUFA timeframes. Implementation of this policy may have an impact on other review work of the division. Additional resources will likely be necessary for review of the marketing applications granted priority review. The following should be considered, when appropriate, to accommodate the priority review process:

- assignment of a team leader/project manager to manage the administrative activities (such as arranging internal and external meetings and teleconferences, taking meeting minutes, etc.);
- shift in a reviewer or branch workload within the affected reviewing division;
- scientific experts from outside the Center and/or FDA may need to be consulted to facilitate review of an priority application; and
- scientists from elsewhere in the Center may be needed to provide support in areas where the standard review queue is affected by the workload shift.

B. Advisory Panel Review

FDA takes most PMAs and BLAs that are granted priority review status to an advisory panel for review. While most 510(k)s are not taken to panel, the review division should discuss with the applicant whether a priority 510(k) submission will go to an advisory panel for review at the time that priority review status is granted.

C. Public Disclosure

The fact that FDA has determined a device is eligible for priority review procedures generally will not be disclosed to the public by FDA until the time that marketing

authorization has been granted, or until the materials are made available in connection with advisory panel meetings for those applications or submissions undergoing panel review.[10] Although FDA generally does not comment on the status of pending applications, it may release publicly disclosable information if it becomes necessary to correct misleading statements made by the applicant.

At the time of approval or clearance, FDA may provide notice to appropriate media outlets (through FDA's Press Office) and FDA information sources (CDRH web page, DSMICA, OCOD, etc.) depending on the significance of the approval or clearance. FDA may make public sufficient information to permit interested parties to monitor the agency's implementation of the priority review program, with the exception of information related to priority reviews granted for the special considerations described in Section III above.[11]

[10] See "Guidance for Industry: Advisory Committee Meetings – Preparation and Public Availability of Information Given to Advisory Committee Members" http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM125650.pdf.

[11] Any disclosures will be made in accordance with 21 CFR Part 20 and any other applicable laws protecting private, confidential commercial information, and trade secrets.

Attachment 1 - Priority Review Checklist

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:[1] 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: _____ Signature: _____
Lead reviewer & Date Supervisor & Date

Signature: _____
Division Director & Date

[1] FDA will verify the applicability of any justification proposed.