Guidance for Industry and FDA Staff

Expedited Review of Premarket Submissions for Devices

Document issued on: November 26, 2003

This document supersedes and replaces PMA/510(k) Expedited Review - Guidance for Industry and CDRH Staff (G98-4), issued March 20, 1998.

For questions regarding the use or interpretation of this guidance in the review of PMAs, PDPs and PMRs, please contact Thinh Nguyen at (301) 594-2186 or by email at txn@cdrh.fda.gov.

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, please contact Heather Rosecrans at (301) 594-1190 or by email at hsr@cdrh.fda.gov.

For questions regarding the use or interpretation of this guidance in the review of devices regulated by CBER, please contact Sayah Nedjar at (301) 827-3524 or by email at nedjar@cber.fda.gov.

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

Written comments and suggestions may be submitted 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. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. When submitting comments, please refer to Docket No. 98D-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 at: http://www.fda.gov/cdrh/mdufma/108.pdf or to receive this document via your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt, press 1 to order a document. Enter the document number (**108**) followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

Additional copies are also available: Office of Communication, Training and Manufacturers Assistance, HFM-40, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, Internet: http://www.fda.gov/cber/guidelines.htm or Voice information System: 800-835-4709 or 301-827-1800.

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Expedited 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. Purpose

The purpose of this document is to (1) develop a common understanding of the statutory criteria for granting expedited review and (2) outline standard procedures that should be followed to achieve an efficient expedited review process. Furthermore, the updated procedures outlined in this document have been developed to permit the agency to meet specific performance goals under the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) for a subset of device submissions eligible for expedited review.[1]

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 guidances means that something is suggested or recommended, but not required.

The Least Burdensome Approach

We believe we should consider the least burdensome approach in all areas of medical device regulation. This guidance reflects our careful review of the relevant scientific and legal requirements and what we believe is the least burdensome way for you to comply with those requirements. However, if you believe that an alternative approach would be less burdensome, please contact us so we can consider your point of view. You may send

[1] Refer to the letter from the Secretary of Health and Human Services to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate (hereafter referred to as the "Goals Letter") dated November 19, 2002, http://www.fda.gov/cdrh/mdufma/pgoals.html and referenced in Section 101(3) of MDUFMA.

your written comments to the contact person listed in the preface to this guidance or to the CDRH Ombudsman. Comprehensive information on CDRH's Ombudsman, including ways to contact him, can be found on the Internet at http://www.fda.gov/cdrh/resolvingdisputes/ombudsman.html.

II. Background

A. The History of Expedited Review of Device Premarket Submissions

An expedited review process for medical devices was first developed in 1994 and explained in a General Program Memorandum (G94-2) entitled, "PMA/510(k) Expedited Review." That document was revised and issued as a guidance document on March 20, 1998 to reflect the expedited review criteria in Section 515(d)(5) of the Federal Food, Drug, and Cosmetic Act (the act), as modified by Section 202 of the FDA Modernization Act of 1997 (FDAMA). The revised guidance document, known as "PMA/510(k) Expedited Review – Guidance for Industry and CDRH Staff" is superseded and replaced by this guidance document, which reflects the decade of experience from administering an expedited review program for medical devices, as well as the performance goals set forth in the Goals Letter.

Section 515(d)(5) of the act only applies to premarket approval applications (PMAs). However, because of the potential public health importance of devices warranting expedited review status, the agency also has applied the expedited review criteria to all premarket submissions, including devices evaluated under a product development protocol (PDP), the Evaluation of Automatic Class III Designation process (also known as the "*de novo*" or "risk based" classification process),[2] and premarket notification submissions (510(k)s).

B. Devices Appropriate for Expedited Review

FDA considers a device, or combination product containing a device,[3] appropriate for expedited review[4] if the device or combination product:

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

2. **addresses an unmet medical need, as demonstrated by one of the following:**

[2] Refer to Section 513(f)(2) of the act as amended by Section 207 of FDAMA and the guidance document on the Evaluation of Automatic Class III Designation classification process found at http://www.fda.gov/cdrh/modact/classiii.html.

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

[4] FDA is required by statute, section 515(d)(5), to review only PMAs meeting certain conditions on an expedited basis. FDA, however, is using these criteria as guidelines for expedited review of PDPs, 510(k)s and de novo classifications.

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; or

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

c. **The device offers significant, clinically meaningful advantages over existing approved alternative treatments.** The device should provide for 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 the current treatment, or ability to provide clinical benefit without the serious side effects associated with current treatments; or

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.

Manufacturers who are working with a federal agency in the development of devices to address a national security issue, should provide FDA with a letter from the 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. The letter should be on official agency letterhead, signed by an individual with authority to make the request, and be provided to FDA at the time that expedited review status is requested.

Please note that while all device submissions granted expedited review status are subject to priority review, there is no assurance that the devices will receive FDA marketing authorization, or actually get to market, in a more timely manner when compared with submissions not granted expedited status. Although FDA is committed to completing its evaluation of such submissions in the most expedient manner possible, incomplete submissions as well as unresolved scientific and regulatory issues can delay, or preclude, FDA clearance or approval.

Likewise, experience has shown that there are numerous obstacles that are not under FDA's control that may further delay market entry, e.g., manufacturing difficulties. In order to reap a benefit from the expedited review process, the commitment on behalf of the submitter to resolving all scientific and regulatory issues should match that of the agency. It will only be through effective communication and a total

commitment to fulfilling all regulatory and scientific requirements that FDA and the submitter can speed market authorization for safe and effective products.

FDA is committed to working interactively with manufacturers of expedited products in order to ensure that the review process is as efficient as possible. As part of the Goals Letter, FDA has committed, among other things, to apply user fees for more hiring, training, and outside consultation. The agency expects to use these additional resources to enhance the scientific expertise available for the review of expedited devices.

C. Expedited Review: Its Meaning and Impact

Granting expedited review status means that a marketing application that is determined to be appropriate for expedited review is placed at the beginning of the appropriate review queue and receives additional review resources, as needed. If multiple applications for the same type of device offering comparable advantage over existing approved alternatives have been granted expedited review, they are reviewed with priority assigned on a first-in-first-reviewed (FIFR) basis. Once one of the devices is granted market authorization, however, the remaining devices under review generally lose their expedited status, but retain their place in the review queue for the current cycle. Any subsequent review cycles are subject to the standard FIFR procedures applicable to non-expedited submissions.

Historically, devices evaluated in accordance with expedited review procedures have not always shown reduced review times when compared to their non-expedited review counterparts. The reasons for this outcome are varied. Many of the devices involve new technology or present complex scientific and regulatory issues, needing more in-depth review that takes more time. Additionally, a lack of interaction between the submitter and FDA staff, a failure of the manufacturing facility to be prepared for inspection, or an incomplete submission may contribute to a longer time to market.

To address the variety of problems that may delay expedited submissions, the Goals Letter that accompanied the authorization of medical device user fees committed the agency to meeting specific performance goals when a PMA submission is filed only when the applicant meets designated conditions. (Refer to Attachment 1). FDA, in accordance with the Goals Letter, tracks expedited applications against the MDUFMA performance goals when the PMA:

- has been the subject of a pre-filing meeting between the applicant and FDA;
- is substantively complete as defined at the pre-filing meeting; and
- identifies manufacturing facilities that are prepared for a good manufacturing practice (GMP) inspection at the time of submission.

Although all expedited PMAs are subject to the same review procedures, only those expedited PMAs meeting the conditions stated in the Goals Letter will be assessed against the MDUFMA performance goals. FDA intends to continue to assess its

review performance related to expedited review PMAs that do not satisfy the conditions of the Goals Letter as part of the overall PMA program goals. Although the Goals Letter did not include expedited review performance goals for other types of marketing applications (e.g., 510(k)s, PDPs, *de novos*), FDA intends to apply priority review to applications meeting the expedited review PMA criteria identified in the statute. We will assess review performance of these applications as a part of each program's goals.

D. Review Organizations Subject to this Guidance Document

There currently are two offices within CDRH with decision-making responsibilities for premarket submissions, the Office of Device Evaluation (ODE) and the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD). These offices should use this guidance in the review of incoming applications. In addition, this guidance also should be used by other CDRH and FDA organizational components with medical device review responsibilities, including the Center for Biologics Evaluation and Research (CBER).

III. PMA Expedited Review Performance Goals; Applicability

In order to be tracked against the PMA performance goals outlined in Attachment 1, the following conditions described in the Goals Letter should be met:

1. **The applicant should have a pre-filing meeting with FDA** (see "Pre-filing Meetings" below).[5] During such a meeting, FDA and the applicant should discuss the timeline for submission, the format of the PMA, the level of information necessary to permit a substantive review, pre-approval inspection issues, and issues related to advisory panel review, as appropriate. Other pre-submission meetings during which discussion of the above information took place may also satisfy this condition of the Goals Letter. That is, if FDA and the applicant have thoroughly discussed such information in a previous meeting, FDA may consider that meeting to be the pre-filing meeting and not ask the applicant to have an additional meeting to satisfy this condition of the Goals Letter. If, however, FDA or the applicant identifies new issues (e.g., design changes, data analysis questions, unexpected adverse events) since the applicant previously met with FDA, another meeting should occur before the PMA is submitted.

   Note: In addition to the pre-filing meeting, the agency encourages applicants to take advantage of opportunities to communicate with the Center during the development and submission process. These opportunities include pre-IDE

[5] Teleconferences or other convenient forms of interaction may substitute for face-to-face meetings between the applicant and the agency. Applicants are encouraged to discuss alternatives to face-to-face meetings with the individual review division.

discussions[6] to discuss the device development plan, including preclinical studies and clinical trial design, if appropriate. Multiple discussions may be appropriate depending on device development. For example, a meeting held prior to IDE submission would be appropriate for discussion of preclinical requirements or the design of the clinical study.

2. **The application should be substantively complete** (i.e., the application fulfills the PMA content requirements described in 21 CFR 814.20, is acceptable for filing,[7] and addresses any key issues identified during any pre-PMA submission meetings). Meeting minutes should reflect device-specific items identified by the agency as necessary to support filing. FDA may determine that applications that do not contain these items are not adequate for filing.

3. **PMA submissions should contain a complete manufacturing section and include a statement that the manufacturing facility is prepared for a GMP inspection.[8]**

IV. Requesting Expedited Review

The responsibility for identifying devices that are appropriate for expedited 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 submission may be granted expedited review status to facilitate an early recognition of devices that merit such review. (Refer to Attachment 2 for suggested timeframes for making expedited review determinations early in the device development process.)

A. Industry Responsibilities

Opportunities to identify a device as a candidate for expedited 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 expedited review status may be apparent during the early stage of development, while other factors that indicate a device should be granted expedited review status may not be apparent until there has been an actual assessment of the patient outcome. As an example, a device in the early design stage may qualify for expedited review if, for a certain life-threatening disease or condition, there exists no approved alternative treatment (i.e., see 1. and 2.b. in Section II. B. of this guidance). Alternatively, a device further along in the development process that has undergone clinical testing may be eligible

[6] Pre-IDE meetings may include formal determination and/or agreement meetings established under sections 513(a)(3)(D) and 520(g)(7) of the act, respectively. For information on early collaboration meetings, please refer to http://www.fda.gov/cdrh/ode/guidance/310.html.

[7] For information regarding the FDA filing decision (21 CFR 814.42), please refer to the guidance document at http://www.fda.gov/cdrh/ode/guidance/297.html.

[8] See "Quality System Information for Certain Premarket Application Reviews" at www.fda.gov/cdrh/comp/guidance/1140.pdf for guidance on the submission of manufacturing information for PMAs.

for expedited review based on significant advances in safety and effectiveness by satisfying conditions 1. and 2.c.

Regardless of the device's stage of development, we encourage industry to identify devices that may be appropriate for expedited review in correspondence with the Center as early as possible. The following milestones may be good opportunities to assess a device for eligibility for expedited review and to notify FDA of devices that appear to warrant expedited review status:

- Pre-IDE discussions with FDA, including formal agreement and determination meetings
- IDE meetings where significant findings are presented to the agency
- Pre-market submission meetings, such as those frequently scheduled with review divisions before submitting PMAs, PDPs, and select 510(k)s.

FDA recommends that industry requests for expedited review of a premarket submission be made in writing and accompany any materials submitted in preparation for an interaction with the agency or with the application that is to be expedited. The request for expedited review should cite the relevant expedited 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 expedited review status in advance of the submission of a marketing application, the submitter should include a copy of the FDA correspondence with the marketing application.

Once FDA grants expedited review status for a submission, industry responsibilities do not end. If the expedited review program is to have a meaningful benefit, 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 responding to FDA additional information requests in as timely a manner as possible. It will only be through a complete and total commitment by all parties involved that expedited review will result in safe and effective devices getting to market in as short a time as possible.

B. FDA Responsibilities

It is the responsibility of FDA staff to consider whether new devices are appropriate for expedited review, regardless of whether a company has identified its device as a potential candidate for this program.

The following represent opportunities for identifying devices that are eligible for expedited review:

- Pre-IDE discussions with companies, including formal agreement and determination meetings
- IDE meetings where significant findings may be being presented by a sponsor

- Pre-PMA, pre-PDP, and pre-510(k) meetings where scientific and regulatory requirements may be discussed
- The early phase of FDA review of marketing applications (refer to discussion of specific timeframes discussed below).

Timeframes for Agency Determinations

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

- **Pre-Submission Communications** - When expedited 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 weeks of the request for, or discussion of, a particular device's eligibility for expedited review status.

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

- **PMAs and PMA Supplements** – The decision to expedite the review should be made as early as possible during the 45-day filing review.[9] 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.

Note: When granting expedited review, the review divisions should consider other pending submissions for the same intended use that may also be appropriate for expedited review. Likewise, the review divisions need to monitor incoming submissions for devices of the same type that may also be appropriate for expedited review status. If more than one pending submission is appropriate for expedited review, both submissions should be granted expedited review status until one of the submissions is granted marketing authorization for that intended use.

Administrative Procedures

After FDA determines that expedited review is appropriate, the division should complete the *"Expedited Review Form"* (Attachment 3) specifying the basis for its determination along with its assessment as to whether the device meets the additional conditions in the Goals Letter and, therefore, should be tracked against the expedited performance goals for qualified expedited review submissions. A

[9] 21 CFR 814.42(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 Section of the Program Operations Staff (POS), or in CBER, to the Regulatory Project Management Branch.

The *Expedited Review Form* 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 expedite the review.

- **A Tentative Timeline for Review of the Application** – The division should establish a timeline for review. This is particularly critical for PMAs because they are subject to the expedited times outlined in the MDUFMA Goals Letter. Each division should use project management techniques to expedite the applications and monitor timeframes. CBER should use the structure of a Regulatory Project Manager (RPM) and Scientific Lead (SL) to achieve these goals.

In CDRH, the division will prepare and issue a letter, based upon the current boilerplate letter provided by POS, notifying the submitter of the expedited review status. Within CBER, the Office should prepare the letter notifying the submitter of the expedited review status. The notification conveying expedited review status may be incorporated into other outgoing correspondence between the submitter and the agency, e.g., a response to an IDE or a PMA filing letter. A copy of the letter should be included in the administrative file according to established procedures. Issuance of a letter should also prompt an update of the pertinent database to reflect FDA's granting of expedited review status.

V. PMA Pre-filing Meetings

As discussed previously, in order for an expedited PMA to be reviewed in accordance with the enhanced performance goals, the applicant should have a pre-filing meeting with FDA. Below, we offer some suggestions for the timing for the meeting as well as outline procedures and topics for discussion at the pre-filing meeting.

A. Suggested timing for the PMA pre-filing meeting

The proper timing for the PMA pre-filing meeting depends on whether there have been previous pre-submission meetings with FDA and on the types of questions the applicant may have for the agency. If FDA and the applicant have been meeting regularly throughout the clinical trial process and FDA and the applicant have addressed the major issues, it would be appropriate to have the pre-filing meeting closer to the submission of the PMA. If, however, there have not been any prior meetings to discuss the clinical trial or its progress or significant issues have arisen, it may prove more beneficial to have the pre-filing meeting early on during the applicant's PMA preparation rather than waiting until the PMA is almost ready to be

submitted. Similarly, if the applicant anticipates other issues needing FDA input such as changes to the device design or manufacturing process, the applicant should time the meeting to ensure that FDA's advice can be incorporated into the PMA.

B. Requesting a PMA pre-filing meeting

The applicant should contact the appropriate reviewing division or branch by e-mail or fax to request a pre-filing meeting. To make the most efficient use of agency resources, the meeting request should include adequate information for the division to identify the staff necessary to discuss the proposed agenda items. The meeting request should include the following information:

- Product name and application number (if applicable)
- Brief device description
- Proposed indication(s) for use
- A brief statement of the purpose of the meeting (i.e., pre-filing meeting for an expedited review application)
- A preliminary proposed agenda
- A draft list of topics for which the applicant/submitter is seeking agency feedback
- A list of individuals expected to attend representing the applicant or submitter
- The approximate date on which supporting information will be sent to the division/branch for review
- Suggested dates and times for the meeting.

Within 14 days of receipt of the request, the reviewing division/branch should respond to the requestor (via e-mail, fax, or telephone) with suggested dates and times for the meeting.

C. Suggested content for pre-meeting package

As mentioned above, during a pre-filing meeting, FDA and the applicant should discuss the timeline for submission, the format of the PMA, the level of information necessary to permit a substantive review, pre-approval inspection issues, and issues related to advisory panel review, as appropriate. To facilitate discussion at the pre-filing meeting, the pre-meeting package should be organized according to the proposed agenda. The requestor should provide hard copies of the package for each FDA participant. Please consult the lead reviewer or administrative project manager (if appropriate) for the appropriate number of copies.

If FDA and the applicant have had previous pre-submission meetings, the content of the pre-filing meeting package may vary. However, the package generally should include the following information:

- preclinical testing summary (if appropriate)
- clinical data summary (including any data collected from outside the US either in a clinical trial or as a part of marketing)

- proposed timeline for submission, taking into consideration the need for a complete manufacturing section and GMP-ready facilities for PMA products to qualify for expedited review[10]
- special issues (e.g., statistical questions, new data analysis proposal, etc.) that the firm would like to discuss with FDA or that should be resolved before the PMA is submitted.

The submission of a comprehensive pre-meeting package, with sufficient time to enable FDA staff to adequately review the information, is critical to achieving a productive meeting. **In CDRH, an applicant or submitter should submit the pre-meeting package *no less than 2 weeks* prior to the meeting date. In CBER, the pre-meeting package should be submitted *no less than 4 weeks* prior to the meeting date.**

D. Meeting documentation

A member of the FDA review team (e.g., the team leader, project manager) should prepare minutes of the meeting, incorporating the applicant's notes as appropriate. Meeting minutes should reflect those items discussed at the meeting that have been identified as necessary for the application/submission to be considered complete for substantive review. The meeting minutes should also document the understanding of both FDA and the PMA applicant that a PMA missing one or more of the specific items may not be filed. If the applicant identifies areas of dispute, these concerns should be raised with the team leader as quickly as possible. Further discussion to resolve these differences may be necessary.

VI. Expedited Review Procedures for FDA

The review division, along with all other CDRH components that may be participating, incur specific responsibilities upon granting expedited review. The following areas warrant special consideration:

- **Resource Management** –The director of the reviewing division should ensure that the application is reviewed in the most efficient manner, tracked as an expedited review and, as appropriate, completed within the time frames outlined in the MDUFMA Goals Letter. 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 expedited review. The following should be considered, when appropriate, to accommodate the expedited 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 the workload within the affected reviewing division;

[10] Refer to section 515(d)(5) of the act.

- scientific experts from outside the Center and/or the agency may need to be consulted to facilitate review of an expedited application;

- scientists from elsewhere in CDRH may be needed to provide support in areas where the standard review queue is affected by the workload shift; and

- **Monitoring** - On a quarterly basis, the Office of the Director should review the progress of submissions granted expedited review status. The purpose of this review will be to provide feedback to the review divisions and to offer suggestions for any difficulties that they may be encountering.

- **Withdrawal of expedited status** - If an application or submission that initially qualified for expedited review status no longer does, e.g., if an alternative device is approved or cleared, the agency generally should withdraw the applicant's or submitter's expedited review status.[11] To optimize the use of resources, the position of a submission losing expedited review status in the review queue should remain the same for the current cycle. The Division Director should issue a letter to the submitter stating that the submission is no longer subject to expedited review. A copy of the letter should be included in the administrative file of the submission. Additionally, the Office should adjust its database to reflect the change in status to ensure that any assessment of the expedited review program does not inappropriately reflect our review performance for submissions that have lost expedited status.

- **Public disclosure** - The fact that FDA has determined a device is eligible for expedited 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.[12] Although FDA generally does not comment on the status of pending applications, the agency may release information if it becomes necessary to correct misleading statements made by the applicant.

  At the time of approval or clearance, a publicly disclosable paragraph may be provided to appropriate media outlets (through FDA's Press Office) and FDA information sources (CDRH web page, DSMICA, etc.) depending on the significance of the approval or clearance. FDA may make public sufficient

[11] As discussed previously, there may be cases in which a manufacturer is working with a federal agency to develop a device to address a national security issue. In this situation, and there may be others, clearance/approval of the first device would not necessarily affect the expedited status of subsequent applications. FDA would need to determine if the factors warranting expedited review status still apply to the other products.

[12] See http://www.fda.gov/cdrh/ode/guidance/1341.html for information about the public availability of the advisory panel materials.

information to permit interested parties to monitor the agency's implementation of the expedited review program.[13]

VII. Advisory Panel Review

FDA takes most PMAs that are granted expedited review status to an advisory panel for review. The respective review division should make the decision whether a PMA will go to an advisory panel, in consultation with the sponsor, at the time of the filing decision. While most 510(k)s are not taken to panel, the review division should make the decision whether an expedited 510(k) submission will go to an advisory panel for review, in consultation with the sponsor, at the time that the expedited review is granted – usually within two weeks of receipt of the submission. It is the responsibility of the Director of the reviewing division to ensure that the decision to bring the application or submission to an advisory panel is made within the appropriate timeframe. The review team and the respective advisory panel Executive Secretary should be involved in this process. Information about the procedures for advisory panel review is available at http://www.fda.gov/cdrh/modact/amendpan.pdf.

VIII. Conclusion

Proper application of the principles and procedures outlined in this guidance document can promote public health by speeding the development of valuable medical device technology. FDA expects the combined commitment of its own staff and industry stakeholders to resolving all scientific and regulatory issues will enable the agency to meet its performance goals for rendering sound scientific decisions on expedited products in an efficient and timely manner.

[13] 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 Expedited Original PMA Submissions

The following performance goals apply to PMA submissions where (see also Table 1):

- FDA has granted the application expedited status;
- The applicant has requested and attended a pre-filing review meeting with FDA;
- The applicant's manufacturing facilities are prepared for inspection upon submission of the application; and
- The application is substantively complete, as defined at the pre-filing review meeting.

Table 1. When do PMA Performance Goals Apply?

PMA performance goals apply
If
You have a pre-filing meeting with FDA.
And
Your application:
• fulfills the PMA content requirements of 21 CFR §814.20
• is acceptable for filing
• addresses any key issues identified during any pre-PMA submission meetings
• contains a complete manufacturing section
And
• contains a statement that the manufacturing facility is prepared for a GMP inspection.

All other submissions (e.g., 510(k)s, *de novos*, PDPs) qualifying for priority review are placed at the top of the review queue and evaluated in a manner consistent with the submitter's commitment to achieving FDA marketing authorization. The agency's performance in reviewing these submissions is assessed against the regular performance goals rather than the enhanced expedited PMA MDUFMA goals as stated in the Goals Letter (see below).

As stated in the MDUFMA Goals Letter:

Cycle Goals for Expedited PMAs

The following cycle goals apply to: 70% of submissions received in fiscal year 2005; 80% of submissions received in fiscal year 2006; 90% of submissions received in fiscal year 2007:

- First action major deficiency letters will issue within 120 days
- All other first action letters (approval, approvable, approvable pending GMP inspection, not approvable, or denial) will issue within 170 days
- Second or later action major deficiency letters will issue within 100 days
- Amendments containing a complete response to major deficiency or not approvable letters will be acted on within 170 days.

Decision Goals for Expedited PMAs

The decision goals apply, as follows, to:

- 70% of submissions received in fiscal year 2005 will have an FDA decision in 300 days
- 80% of submissions received in fiscal year 2006 will have an FDA decision in 300 days
- 90% of submissions received in fiscal year 2007 will have an FDA decision in 300 days
- 90% of amendments containing a complete response to an approvable letter received in fiscal years 2003 through 2007 will be acted on within 30 days.

Attachment 2 Suggested Timeframes for Discussing Expedited Review with FDA

Table 2. Suggested Timeframes for Discussing Expedited Review Status (shown in solid shading)

Criteria					
1+ 2a				opportunities for discussion	
1+ 2b	opportunities for discussion				
1+2c			opportunities for discussion		
1+2d			opportunities for discussion		
	Concept	**Prototype**	**Pre-clinical**	**Clinical**	**Performance Assessment**

Pre-Submission Product Development Timeline

LEGEND FOR TABLE 2

Criteria for Expedited Review

1. Condition is life-threatening or irreversibly debilitating
   And
2. the device addresses an unmet medical need, demonstrated by **any one** of the following:
   - **a.** breakthrough technology
   - **b.** no approved alternative
   - **c.** significant clinically meaningful advantage
   - **d.** in the best interest of patients.

Pre-Submission Product Development Timeline

Phase	Primary Activity
Concept	Working up the abstract or generic idea
Prototype	Building first functional, full scale, preproduction model
Pre-clinical	Bench testing prototype and subsequent models
Clinical	Conducting human subject trials
Performance Assessment	Evaluating data from preclinical and clinical phases

Attachment 3 Expedited Review Form

Applicant: _____

Device: _____

Use/Indications: _____

Document #: _____

Justification for Expedited 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:[14]	
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 YES?	❑
If no, skip to 8.	
4. Is the submission an original PMA application?	❑
If no, skip to 9.	

Original PMA Performance Goals Criteria	
5. a. Did the applicant attend a pre-filing review meeting with FDA?	❑
b. Are the applicant's manufacturing facilities prepared for inspection (at the time the PMA was submitted)?	❑
c. Is the original PMA substantively complete, as defined at the pre-filing review meeting?	❑
6. Are the answers to 5a, b & c **all** YES?	❑
If no, skip to 9.	

Expedited Review Assessment (check only one)	
7. The original PMA qualifies for expedited review status and is subject to MDUFMA Performance Goals	❑
8. The submission does not qualify for expedited review status	❑
9. The submission qualifies for expedited review status, but it is not subject to MDUFMA Performance Goals	❑

Identify review team leader & members:
Attach tentative review timeline.

Signature:

Division Director date

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