Guidance for Industry and FDA Staff

FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals

Document Issued on: June 30, 2008

This document supersedes "FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Performance Assessment" dated October 8, 2003.

The information collection provisions in this guidance have been approved under OMB control numbers 0910-0120, 0910-0231, and 0910-0338. These approvals expire 8/31/2010, 09/30/2007, and 6/30/2010, respectively.

For questions regarding the use or interpretation of this guidance in the review of PMAs, please contact the PMA Staff at (240) 276-4040.

For questions regarding the use or interpretation of this guidance in the review of devices regulated by CBER, please contact Robert Yetter, Ph.D. at (301) 827-0373 or by email at robert.yetter@fda.hhs.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. Please identify your comments with the docket number listed in the notice of availability that publishes in the *Federal Register* announcing the availability of this guidance document. 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 Center for Devices and Radiological Health (CDRH) through the Internet at: http://www.fda.gov/cdrh/mdufma/guidance/1218.pdf or http://www.fda.gov/cdrh/mdufma/guidance/. You may also send an email request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance document or send a fax request to 240-276-3151 to receive a hard copy. Please use the document number (**1218**) to identify the guidance document you are requesting.

Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

Contains Nonbinding Recommendations

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Guidance for Industry and FDA Staff

FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals

This guidance document 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 document. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance document.

I. Introduction

This guidance document describes:

- the different FDA actions that may be taken on premarket approval applications (PMAs)[1];
- the effect each action has on goals under the Medical Device User Fee and Modernization Act (MDUFMA) of 2002 (Public Law 107-250) for PMAs filed in FY 2003-2007;
- the effect each action has on goals under the Food and Drug Administration Amendments Act (FDAAA) of 2007 (Public Law 110-85) for PMAs filed in FY 2008-2012; and
- the different industry actions that may be taken on PMAs.

In the 2003 version of this guidance, FDA identified certain applications filed[2] between FY 2003 and 2007 that were subject to cycle, decision, and performance goals under MDUFMA. As described in this updated version of the guidance document, the goals for these applications have not changed, with the exception that all cycle goals were abolished for applications filed in FY 2007.[3] Under FDAAA, the following changes apply to applications filed between FY 2008 and FY 2012:

[1] Refer to guidance document entitled, "Premarket Approval Application Filing Review" at http://www.fda.gov/cdrh/ode/guidance/297.html for detailed information on filing PMAs. In addition, although not specifically discussed, the information in this guidance document also pertains to premarket reports (PMRs), which are premarket applications for a reprocessed, single-use device.

[2] The filing date for a supplement is the receipt date, assuming any applicable user fee has been paid.

[3] Performance goals for PMA applications filed between FY 2008 and FY 2012 are defined in a September 27, 2007 letter from DHHS Secretary Michael O. Leavitt to Congress. This letter also abolished cycle goals for FY 2007 applications. See 153 CONG. REC. S12420-S12421 (daily ed. October 2, 2007) (Performance Goals for the Medical Device User Fee Amendments of 2007). In addition, refer to the summary of performance decision goals at http://www.fda.gov/cdrh/mdufma/mdufmaii-comparison.html.

- traditional PMAs and panel-track supplements,[4] 180-day supplements, and real-time supplements are subject to two-tier decision goals;

- PMA modules are subject to two-tier cycle goals;

- FDA now has the option of issuing major deficiency letters for 180-day supplements; and

- the performance goals do not vary from year to year as they did under MDUFMA but, instead, remain constant for the five-year duration.

In addition, we removed the discussion of abandonment from this guidance document.

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.

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 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 contact information, can be found on the Internet at http://www.fda.gov/cdrh/ombudsman/.

II. FDA's Actions

The PMA regulation outlines the various actions FDA may take on a traditional PMA or PMA supplement during the course of our review.[5] For traditional PMAs, panel-track supplements, 180-day supplements, and real-time supplements,[6] [7] the following responses are considered FDA actions:

- approval order;

[4] There are two distinct sets of goals for PMAs and panel-track supplements: expedited or non-expedited.
[5] See 21 CFR 814, Subpart C.
[6] For more detailed information, see FDA's guidance document, "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; Guidance for Industry and FDA" at www.fda.gov/cdrh/mdufma/guidance/1201.pdf or the draft guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" at http://www.fda.gov/cdrh/ode/guidance/1584.pdf.
[7] Although not discussed in 21 CFR 814, FDA takes these same actions on expedited traditional PMAs and expedited panel-track supplements under section 515(d)(5) of the Act and on PMRs submitted under section 515(c)(2) of the Act.

- approvable letter (including approvable pending GMP inspection);
- major deficiency letter;
- not approvable letter; and
- denial order.

Furthermore, of these FDA actions, all but a major deficiency letter are an "FDA decision" under FDA's commitment letters and are measured against a MDUFMA/FDAAA goal:[8]

These FDA actions are described below.

A. Approval Order

FDA will issue an approval order (letter) informing the applicant that the PMA is approved and that the applicant may begin commercial distribution of the device in accordance with any prescribed conditions of approval after we have completed our review and:

- none of the reasons listed in 21 CFR 814.45 for denying approval applies;
- there is reasonable assurance the device is safe and effective (using the criteria provided in 21 CFR 860.7) for its intended use as prescribed in the product labeling; and
- the device manufacturing facilities, methods, and controls were inspected and found to be in compliance with the Quality System regulation (21 CFR Part 820).

When FDA issues an approval order, we shut off the FDA review clock. An approval order marks the end of FDA's review, as this is a final action.

B. Approvable Letter

FDA will issue an approvable letter informing the applicant that we have completed our review of the application and determined that there needs to be:

- resolution of minor deficiencies[9], which are identified in the approvable letter (21 CFR 814.44(e)); and/or
- completion of an FDA inspection that finds the manufacturing facilities, methods, and controls in compliance with the Quality System (QS) regulation, 21 CFR Part 820, and, if applicable, verifies records pertinent to the PMA as per 21 CFR 814.44(e)(1)(ii). When this is the case, the approvable letter states that the device is "approvable subject to an FDA inspection."

When FDA issues an approvable letter pending resolution of minor deficiencies, we stop the FDA review clock and place the application on hold. When FDA receives a complete

[8] The definitions for the term "FDA decision" are provided in a September 27, 2007 letter from DHHS Secretary Michael O. Leavitt to Congress; see footnote 3.

[9] Minor deficiencies may include, for example, clarifications of previously submitted information, revisions to the labeling, and revisions/development of a postapproval study protocol.

response to an approvable letter, we will restart the clock with a new FDA response timeframe.

When FDA issues an approvable pending GMP inspection letter, we stop the FDA review clock. Once FDA determines that the GMP issues are resolved, we will issue an approval order.

C. Major Deficiency Letter

FDA will issue a major deficiency letter informing the applicant that the PMA lacks significant information necessary for FDA to complete our review and requests the applicant to amend the application to provide the necessary information regarding the device (21 CFR 814.37(b)), such as:

- a detailed re-analysis of previously submitted data (e.g., alternative statistical method);
- additional test data to demonstrate safety and effectiveness of the device (e.g., electromagnetic compatibility, electrical safety; biocompatibility, reliability, software, labeling, animal testing, sensitivity and specificity in a certain population);
- scientific rationale for test data provided in the submission; or
- new validation data and analyses (e.g., due to device modifications made during the course of the PMA review).

When FDA issues a major deficiency letter, we stop the FDA review clock and place the application on hold. Because a major deficiency letter is not a MDUFMA decision, when FDA receives a complete response to a major deficiency letter, we will resume the clock and our review with a goal of reaching a MDUFMA decision within the remaining time of the application's review track (e.g., 180 days).

D. Not Approvable Letter

FDA will issue a not approvable letter informing the applicant that we have completed our review and that we do not believe that the application can be approved because of significant deficiencies. The not approvable letter will describe the deficiencies in the application, including each applicable ground for denial and, where practical, will identify measures required to place the submission in approvable form. 21 CFR 814.44(f).

Generally, before FDA issues a not approvable letter, we will first issue a major deficiency letter to provide the applicant with an opportunity to address our concerns. However, if an applicant fails to provide an adequate response to a major deficiency letter, FDA intends to issue a not approvable letter rather than a subsequent major deficiency letter.

When FDA issues a not approvable letter, we stop the review clock and place the application on hold. When FDA receives a complete response to a not approvable letter, we will restart the clock with a new FDA response timeframe.

E. Denial Order

FDA will issue a denial order (letter) when we need to inform the applicant that we have decided not to approve the application. The denial order will identify all deficiencies in the application, including each applicable ground for denial under section 515(d)(2) of the Act and, where practical, will identify measures required to place the application in approvable form. The denial order will include a notice of an opportunity to request review under section 515(d)(3) of the Act. In addition, FDA may deny approval of a PMA for any of the reasons identified in 21 CFR 814.45(a). 21 CFR 814.45

When FDA issues a denial order, we shut off the FDA review clock if a prior action has not already done so.[10] A denial order marks the end of FDA's review, as this is considered a final action.

Under the PMA regulation, FDA considers a traditional PMA or PMA supplement to have been voluntarily withdrawn if an applicant fails to respond to an approvable, major deficiency, or not approvable letter within 180 days. (21 CFR 814.44(g)) However, upon request, FDA intends to allow one 180-day extension to respond to one of these three FDA action letters, increasing the time to provide a complete response to the FDA action letter to a total of 360 days. Any amendment submitted in response to an FDA action letter after 360 days will be considered a resubmission of the PMA. As such, it will be assigned a new PMA number, will be subject to the requirements of 21 CFR 814.20, and the applicant must pay a new user fee.

III. Cycle, Decision, and Performance Goal Definitions

A cycle goal measures FDA's performance by reference to the number of FDA review days required to complete a review cycle. A review cycle is defined as:

- the number of FDA review days between the filing date and the date of any FDA action letter; or

- the number of FDA review days between the receipt of a response to an action letter to the issuance of another FDA action letter.

A decision goal is the number of FDA review days from the filing date to the date of issuance of the first MDUFMA action/decision (i.e., approval, approvable, approvable pending GMP inspection, not approvable, denial).

A performance goal considers FDA's performance with cycle and decision goals for the entire pool of filed submissions of a particular type for a given fiscal year.[11]

[10] FDA expects that a denial will normally be preceded by another FDA action that stops the review clock, such as a not approvable letter. There is, however, no statutory requirement for any prior FDA action, and FDA may, in appropriate circumstances, proceed directly to issue a denial order.
[11] FDA frequently refers to a pool as a "receipt cohort."

IV. Goals for PMAs Filed in FY 2003-2007

The performance goals for traditional PMAs (expedited and non-expedited), panel-track supplements (expedited and non-expedited), and 180-day supplements filed from FY 2003 through FY 2007 were defined in a November 14, 2002 letter from DHHS Secretary Tommy G. Thompson to Congress.[12,13] In a September 27, 2007 letter from DHHS Secretary Michael O. Leavitt to Congress, all cycle goals for these PMA applications filed in FY 2007 were abolished.[14]

The following sections describe the cycle, decision, and performance goals in effect for traditional PMAs (expedited and non-expedited), panel-track supplements (expedited and non-expedited), and 180-day supplements filed from FY 2003 through FY 2007. Each section provides a table that shows, for each fiscal year, the maximum FDA review time permitted for an application to meet the cycle and decision goals and the percentage of actions that must be completed within that review time target in order to meet the performance goal. Under MDUFMA, FDA's performance goals were phased in over five years, with additional and more demanding performance goals going into effect each year. Where the table shows a dash (—), there is no performance goal in effect for that action and fiscal year.

A. Non-Expedited Traditional PMAs and All Panel-Track Supplements

Table 1 outlines the performance goals in effect for non-expedited PMAs and all panel-track supplements (whether expedited or not) filed from FY 2003 through FY 2007. All of the actions have only a single performance goal for any given fiscal year, except the FDA decision goal for FY 2007 which has two tiers (i.e., 50% of applications are to reach a MDUFMA decision within 180 days and 90% of applications are to reach a MDUFMA decision with 320 days).[15]

The following scenarios illustrate the goals shown in Table 1:

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 170, then we will have met both the cycle goal (180 days) and the decision goal (320 days).

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 250, then we will have missed the cycle goal (180 days), but we will have met the decision goal (320 days). FDA could successfully meet the second cycle goal by reviewing the complete response to the not approvable letter within 180 days.

[12] See 148 CONG. REC. S11549-S11551 (daily ed. November 18, 2002) (Performance Goals for the Medical Device User Fee and Modernization Act of 2002).
[13] Refer to the summary of performance decision goals at http://www.fda.gov/cdrh/mdufma/mdufmaii-comparison.html.
[14] See 153 CONG. REC. S12420-S12421 (daily ed. October 2, 2007) (Performance Goals for the Medical Device User Fee Amendments of 2007).
[15] The submission of an unsolicited major amendment will increase the number of FDA review days allotted to reach a MDUFMA decision.

- If FDA determines that a major deficiency letter is necessary as our first action, and we issue the letter on day 250, then we will have missed the cycle goal (we have 150 days to issue a major deficiency letter when we do so as a first action). If the applicant provides a complete response to our major deficiency letter, and we issue an approvable letter 175 days after receiving the response, we will have met the second or later action cycle goal (we have 180 days to act on a complete response to a major deficiency letter), but we will have missed the decision goal (250 days + 175 days = 425 days, which exceeds the 320 days allotted to reach a MDUFMA decision).

Table 1 - FDA Performance Goals for FY 2003 – FY 2007
Non-Expedited Traditional PMAs and all Panel-track Supplements

FDA Action Measured by Goal	FDA Review Time Goal	MDUFMA Performance Goals* (— indicates no MDUFMA goal)				
		2003	2004	2005	2006	2007
Decision Goals						
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)	180 days	—	—	—	—	50%
	320 days	—	—	—	80%	90%
Cycle Goals						
First action – major deficiency letter	150 days	—	—	75%	80%	—
First action – all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	180 days	—	—	75%	80%	—
Action on an amendment containing a complete response to a major deficiency letter	120 days	—	—	75%	80%	—
Action on an amendment containing a complete response to a major deficiency or not approvable letter	180 days	—	—	75%	80%	—
Action on an amendment containing a complete response to an approvable letter	30 days	90%	90%	90%	90%	—

*Review times for non-expedited, traditional PMAs and ALL panel-track supplements are compared to MDUFMA goals for non-expedited traditional PMAs.

B. Expedited Traditional PMAs

Table 2 outlines the FDA review time and MDUDMA performance goals in effect for expedited traditional PMAs filed from FY 2003 through FY 2007. The following scenarios illustrate the use of Table 2:

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 170, then we will have met both the cycle goal (170 days) and the decision goal (300 days).

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 250, then we will have missed the cycle goal (170 days), but we will have met the decision goal (300 days). FDA could successfully meet the second cycle goal by reviewing the complete response to the not approvable letter within 180 days.

- If FDA determines that a major deficiency letter is necessary as our first action, and we issue the letter on day 250, then we will have missed the cycle goal (120 days). If the applicant provides a complete response to our major deficiency letter, and we issue an approvable letter 150 days after receiving the response, we will have met the cycle goal (we have 170 days to act on a complete response to a major deficiency letter), but we will have missed the decision goal (250 days + 150 days = 400 days, which exceeds the 300 days allotted to reach a MDUFMA decision).

Table 2 - FDA Performance Goals for FY 2003 – FY 2007
Expedited Traditional PMAs

FDA Action Measured by Goal	**FDA Review Time Goal**	**MDUFMA Performance Goals*** (— indicates no MDUFMA goal)				
		2003	2004	2005	2006	2007
Decision Goal						
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)	300 days	—	—	70%	80%	90%
Cycle Goals						
First action – major deficiency letter	120 days	—	—	70%	80%	—
First action – all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	170 days	—	—	70%	80%	—
Action on an amendment containing a complete response to a major deficiency letter	100 days	—	—	70%	80%	—
Action on an amendment containing a complete response to a major deficiency or not approvable letter	170 days	—	—	70%	80%	—
Action on an amendment containing a complete response to an approvable letter	30 days	90%	90%	90%	90%	—

* Review times for expedited, traditional PMAs are compared to the MDUFMA goals for expedited traditional PMAs.

C. 180-Day Supplements

Table 3 outlines the FDA review time and MDUDMA performance goals in effect for 180-day supplements filed from FY 2003 through FY 2007. The following scenarios illustrate the use of Table 3:

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 110, then we will have met both the cycle goal (120 days) and the decision goal (180 days).

- If FDA determines that a not approvable letter is necessary as our first action, and we issue the letter on day 170, then we will have missed the cycle goal (120 days), but we will have met the decision goal (180 days). FDA could successfully meet the second cycle goal by reviewing the complete response to the not approvable letter within 160 days.

Table 3 — FDA Performance Goals for FY 2003 – FY 2007
180-Day Supplements

FDA Action Measured by Goal	**FDA Review Time Goal**	**MDUFMA Performance Goals** (— indicates no quantitative goal)				
		2003	2004	2005	2006	2007
Decision Goal						
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)	180 days	—	—	80%	80%	90%
Cycle Goals						
First action – not approvable letter	120 days	—	—	80%	85%	—
First action – all other first actions (approval, approvable, approvable pending GMP inspection, or denial)	180 days	—	—	80%	85%	—
Action on an amendment containing a complete response to a not approvable letter	160 days	—	—	80%	85%	—
Action on an amendment containing a complete response to an approvable letter	30 days	90%	90%	90%	90%	—

V. Goals for PMAs Filed in FY 2008-2012

The performance goals for PMA applications filed from FY 2008 through FY 2012 are defined in a September 27, 2007 letter from DHHS Secretary Michael O. Leavitt to Congress.[16] Under FDAAA, the differences between PMAs filed in FY 2008 through FY 2012 versus FY 2003 through FY 2007 are as follows:

- There are two-tier decision goals for traditional PMAs and panel-track supplements, 180-day supplements, and real-time supplements. A decision goal is the number of FDA review days allotted by MDUFMA from the filing date to the date of issuance of the first MDUFMA decision (i.e., approval, approvable, approvable pending GMP inspection, not approvable, denial). The submissions will be initially assigned a Tier 1 review track (i.e., shorter time allotted to reach MDUFMA decision) unless the circumstances warrant assigning a Tier 2 review track.[17]

- Cycle goals no longer apply to traditional PMAs, panel-track supplements, and 180-day supplements.

- There are two-tier cycle goals for PMA modules. The submissions will be initially assigned a Tier 1 review track (i.e., shorter time) unless the circumstances warrant assigning a Tier 2 review track.

- FDA now has the option of issuing major deficiency letters for 180-day supplements.

- The performance goals remain constant over the FY 2008 to 2012 period.

The following sections describe the cycle or decision, as well as the performance goals, in effect for traditional PMAs (expedited and non-expedited), panel-track supplements (expedited and non-expedited), 180-day supplements, real-time supplements, and PMA modules[18] filed from FY 2008 through FY 2012. Each section provides a table that shows the maximum FDA review time permitted for an application to meet each of the two-tier decision or cycle goals and the percentage of actions that must be completed within that review time target in order to meet the performance goal. Because the performance goal remains constant, this information is not stratified by fiscal year.

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[16] See 153 CONG. REC. S12420-S12421 (daily ed. October 2, 2007) (Performance Goals for the Medical Device User Fee Amendments of 2007).

[17] FDA will work to achieve the Tier 1 (faster) goal, unless special circumstances (e.g., the application is for a combination product that will require review by two FDA Centers) clearly show that the Tier 1 goal cannot be met within the bounds on an orderly and efficient review. When such special circumstances apply to a premarket application (PMA, PDP, or PMR) or to a panel-track PMA supplement, the Office Director may authorize the review to focus on achieving the Tier 2 goal without making a special effort to meet the Tier 1 goal. When such special circumstances apply to any other type of submission, the Division Director may authorize the review to focus on achieving the Tier 2 goal.

[18] PMA modules are not "filed" but, rather, are "accepted" for review following submission of a PMA shell and payment of the appropriate user fee. When the applicant submits the final module, then the modular PMA is processed the same as a traditional PMA.

A. Non-Expedited Traditional PMAs and Panel-Track Supplements

Table 4 outlines the FDA review time and MDUFMA performance goals in effect for non-expedited traditional PMAs and panel-track supplements filed from FY 2008 through FY 2012.

Although there are no cycle goals, FDA intends to review a complete response to an approvable letter within 30 days and a complete response to a not approvable letter within 180 days. In addition, if we issue a major deficiency letter as a first action, then we have the remaining number of days allotted (i.e., 180 or 295 days minus number of FDA review days used) to complete our review of a complete response to a major deficiency letter.

Table 4 - FDA Performance Goals for FY 2008 – FY 2012
Non-Expedited Traditional PMAs and Panel-Track Supplements

	FDA Review Time Goal	Performance Goal*
Decision Goal		
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)*	180 days	60%
	295 days	90%

* Review times for non-expedited, traditional PMAs and panel-track supplements are compared to MDUFMA goals for non-expedited, traditional PMAs and panel-track supplements.

B. Expedited Traditional PMAs and Panel-Track Supplements

Table 5 outlines the FDA review time and MDUFMA performance goals in effect for expedited traditional PMAs and panel-track supplements filed from FY 2008 through FY 2012. The guidance provided in Section A also applies here, except that, to meet the Tier 2 goal, FDA must make a decision on expedited applications more rapidly.

Although there are no cycle goals, FDA intends to review a complete response to an approvable letter within 30 days and a complete response to a not approvable letter within 180 days. In addition, if we issue a major deficiency letter as a first action, then we have the remaining number of days allotted (i.e., 180 or 280 days minus number of FDA review days used) to complete our review of a complete response to a major deficiency letter.

Table 5 - FDA Performance Goals for FY 2008 – FY 2012
Expedited Traditional PMAs and Panel-Track Supplements

	FDA Review Time Goal	Performance Goal*
Decision Goal		
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)*	180 days	50%
	280 days	90%

* Review times for expedited, traditional PMAs and panel-track supplements are compared to MDUFMA goals for expedited, traditional PMAs and panel-track supplements.

C. 180-Day Supplements

Table 6 outlines the two-tiered decision goals for 180-day supplements filed from FY 2008 through 2012. Although there are no cycle goals, FDA intends to review a complete response to an approvable letter within 30 days and a complete response to a not approvable letter within 180 days. In addition, if we issue a major deficiency letter as a first action, then we have the remaining number of days allotted (i.e., 180 or 210 days minus number of FDA review days used) to complete our review of a complete response to a major deficiency letter.

Table 6 - FDA Performance Goals for FY 2008 – FY 2012
180-Day Supplements

	FDA Review Time Goal	Performance Goal
Decision Goal		
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial)*	180 days	85%
	210 days	95%

D. Real-Time Supplements

Table 7 outlines the two-tiered decision goals for real-time supplements filed from FY 2008 through FY 2012. Although there are no cycle goals, FDA intends to review a complete response to an approvable letter within 30 days and a complete response to a not approvable letter within 180 days.

Table 7 – FDA Performance Goals for FY 2008 – FY 2012
Real-Time Supplements

	FDA Review Time Goal	Performance Goal
Decision Goal		
FDA decision (approval, approvable, not approvable, denial)	60 days	80%
	90 days	90%

E. PMA Modules

Table 8 outlines the two-tiered cycle goals for PMA modules received from FY 2008 through FY 2012. These are per cycle goals. The cycle goals for individual PMA modules do not apply once the final module is submitted. When the final module is submitted, all open modules (i.e., modules for which an acceptance letter was not issued) are no longer processed on an individual basis (that is, each module is no longer reviewed and tracked separately from other portions of the PMA). At that point, all open modules are considered closed and are assessed against their goals. The applicant should respond to any outstanding issues cited in deficiency letters for individual modules as part of the last module that is submitted. Then the modular PMA is assigned a PMA number (e.g., P080099) and we apply the performance goals for a traditional PMA.

Table 8 – FDA Performance Goals for FY 2008 – FY 2012 PMA Modules		
	FDA Review Time Goal	**Performance Goal**
Cycle Goal		
FDA action (acceptance, deficiency)	90 days	75%
	120 days	90%

VI. Applicant's Actions

Actions taken by an applicant may include the submission of an unsolicited major amendment, submission of a solicited major amendment, submission of a minor amendment, or withdrawal of the application (either by letter or by not responding to an FDA request). 21 CFR 814.37(a) & (d). The information below clarifies the basis for each action an applicant may take and the effect each action has on the FDA review clock and review goals.

A. Unsolicited Major Amendment

An unsolicited major amendment is a submission of substantial new data by the applicant, on an applicant's own initiative, to be added to a pending PMA submission. Typical situations that may prompt an applicant to submit an unsolicited major amendment include:

- the applicant obtains additional test data related to the safety or effectiveness of the device, or the applicant becomes aware of data that was omitted from the original application (e.g., electromagnetic compatibility, electrical safety, biocompatibility, reliability, software, labeling, animal testing);
- the applicant obtains significant new clinical data from a previously-unreported study, or obtains updated data from a previously-reported study; or
- the applicant obtains new validation data and analyses (e.g., concerning device modifications made by the applicant during the course of the PMA review).

The submission of an unsolicited major amendment by the applicant extends the time allotted to reach a FDA decision goal (i.e., MDUFMA decision) as follows:[19]

- if the applicant submits an unsolicited major amendment during the first review cycle, the FDA decision goal date is extended by the number of days equal to 75% of the difference between the filing date and the date of receipt of the amendment; or

[19] If the unsolicited major amendment is for an application that is subject to a cycle goal (i.e., the application was filed from FY 2003 through FY 2006), FDA considers the submission of an unsolicited major amendment to be the equivalent of an FDA action when we report on our progress against the first action or subsequent action performance goal.

- if the applicant submits an unsolicited major amendment during a second or subsequent review cycle, the FDA decision goal date is extended by the number of days equal to 75% of the difference between the date of the receipt of the complete response to FDA's latest action letter and the date of receipt of the amendment.

For a PMA module, the submission of an unsolicited major amendment starts a new cycle and, thus, restarts the review clock.

B. Solicited Major Amendment[20]

A solicited major amendment is the formal submission of information by the applicant, at the request of the FDA (i.e., in response to a major deficiency or not approvable letter), to be added to a pending PMA. The applicant should submit a major amendment to FDA when the applicant receives:

- a major deficiency letter requesting additional information; or
- a not approvable letter that identifies the deficiencies to which the applicant must satisfactorily respond in order to place the PMA in approvable form.

The submission of a solicited major amendment that is a complete response restarts the FDA review clock upon receipt. A partial response to an action letter does not restart the FDA review clock.

C. Minor Amendment[21]

A minor amendment is an amendment that contains clarification of previously submitted data or additional information of a minor nature. It is submitted by an applicant on its own initiative or at the request of FDA. The submission of a minor amendment has no effect on the review clock.

D. Withdrawal of an Application

An applicant may, on its own initiative, withdraw a PMA submission at any time prior to approval, and for any reason, by submitting an amendment informing FDA of its intent to remove the application from FDA's review. A withdrawal action will stop the review clock on the receipt date of the amendment. FDA will treat the withdrawal as a final FDA action that satisfies any applicable cycle goal and the decision goal for that submission.

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[20] Although a response to an approvable letter is not considered a major amendment because the issues are minor in nature, it will restart the FDA review clock upon receipt. A partial response to an approvable letter will not restart the review clock.

[21] FDA believes that many of the minor deficiencies can be resolved through the interactive review process as described in our guidance document entitled, "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements," dated February 28, 2008 and available at http://www.fda.gov/cdrh/ode/guidance/1655.pdf.

In addition, as stated in Section II above, FDA considers a traditional PMA or PMA supplement to have been voluntarily withdrawn if an applicant fails to respond to an approvable, major deficiency, or not approvable letter within a total of 360 days.