Guidance for Industry and FDA Staff

FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment

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

Center for Biologics Evaluation and Research

Contains Nonbinding Recommendations

Preface

Public Comment

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FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment

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 and Modernization Act of 2002 (MDUFMA), Public Law 107-250, amends the Federal Food, Drug, and Cosmetic Act (the act) to provide the Food and Drug Administration (FDA) new responsibilities and resources. A provision of MDUFMA authorizes FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2002, including premarket notification submissions (510(k)s). The additional funds obtained from user fees will enable FDA, with the cooperation of industry, to improve the device review process to meet the performance goals identified in the letter from the Secretary of Health and Human Services to Congress (Goals Letter)[1] and summarized below.

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.

[1] This letter can be found at http://www.fda.gov/cdrh/mdufma/pgoals.html)

II. Purpose

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the MDUFMA performance goals.

III. 510(k) Performance Goals

For 510(k) submissions, the performance goals contain both cycle (i.e., "first action" and "second and later action") goals and decision goals. A "cycle" (or review cycle) is the period of time (in FDA days[2]) beginning with the date FDA receives the 510(k)[3] and ending with the date FDA issues a letter requesting additional information or announcing a "decision" (e.g., substantially equivalent (SE) or not substantially equivalent (NSE) determination). More than one cycle may occur before FDA issues its decision on the 510(k) submission.

The table below summarizes the 510(k) performance goals under MDUFMA. FDA has committed to meeting the following action and decision goals for a specified percentage of submissions, depending on the fiscal year:

- an FDA decision (i.e., issuance of a SE or NSE determination letter) will issue within 90 days (cumulative FDA review time)
- first action additional information (AI) letters will issue within 75 days
- subsequent action additional information letters will issue within 60 days.

Table 1. 510(k) Performance Goals

Action	Review Time (FDA days)	Performance Level (by FY) (— indicates no quantitative goal)				
		2003	2004	2005	2006	2007
FDA decision	90	—	—	75%	75%	80%[A]
First AI letter	75	—	—	70%	80%	90%

[2] The term "FDA days" refers to the amount of time a submission is under review by FDA and does not include the time when the clock has been stopped.

[3] The recorded receipt date of a 510(k) submission is the date the submission is received by FDA or the date US Bank notifies FDA that payment of all fees due has been received, whichever is later. For additional information, see http://www.fda.gov/cdrh/devadvice/314a.html

Second or later AI letter	60	—	—	70%	80%	90%

[A]FY 2007 FDA decision goal (80% within 90 days) may be re-evaluated in consultation with industry to determine whether it is appropriate for FY 2007.

IV. FDA Actions

FDA may take any of the following actions on a 510(k) after FDA has conducted its review (21 CFR 807.100(a)):

- issue an order declaring a device SE (SE letter)
- issue an order declaring a device NSE (NSE letter)
- request AI[4]
- advise the submitter that the 510(k) submission is not required (i.e., product is not regulated as a device or device is exempt from the premarket notification requirements of the act)

Further, in accordance with 21 CFR 807.87(l), the agency may consider a 510(k) to be withdrawn if additional information is not provided within 30 days following issuance of a request for additional information. In this instance, FDA may issue a notice of withdrawal.[5]

The following sections describe the actions FDA may take on 510(k)s, explain when these actions may be appropriate, and discuss the effect that each action has on the review clock and on the MDUFMA performance goals.

A. Issue an Order Declaring a Device SE

An order declaring a device to be SE is a letter issued to the submitter of a 510(k) informing the submitter that FDA has determined that the device described in the 510(k) is substantially equivalent to a legally marketed device.[6] An order declaring a device to be SE authorizes marketing of the device in the United States (U.S.), subject to specific statutory and regulatory requirements of FDA.[7]

[4] Includes requests for a certification or disclosure statement as per 21 CFR 807.100(a)(4).
[5] A notice of withdrawal is sometimes referred to as a "deletion letter." The term "deletion" is used to differentiate a withdrawal under 21 CFR 807.87(l) from a request to withdraw a pending 510(k) by the submitter.
[6] See 21 CFR 807.92(a)(3) for the definition of "legally marketed device."
[7] See section 513(i) of the act.

1. Criteria

The criteria for determining a device to be SE are described in section 513(i) of the act and in 21 CFR 807.100(b). Additional information relating to determinations of SE can be found in the guidance documents entitled, *"Guidance on the Center for Devices and Radiological Health's Premarket Notification Review Program"* and "*Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff."*[8]

2. Effect on Review Clock

An SE decision is a decision that shuts off the review clock and marks the end of FDA review. The reported FDA review time for the 510(k) decision is the cumulative FDA days for all review cycles from the date the 510(k) is received to the date the SE letter is issued.

3. Effect on MDUFMA Goals

In accordance with the Goals Letter, to be counted as meeting the MDUFMA decision goals, the SE letter should issue within 90 FDA days from the date the 510(k) is received if it is the first action on the submission; or within 90 cumulative FDA days if the SE determination is a second or later action.

B. Issue an Order Declaring a Device NSE

An order declaring a device to be NSE is a letter issued to the submitter of a 510(k) informing the submitter that FDA has determined that the device described in the 510(k) is NSE to a legally marketed device and may not be introduced into commercial distribution in the U.S.[9]

1. Criteria

In general, FDA issues an NSE letter in the following situations:

- no predicate device exists
- the device has a new intended use compared to the predicate device
- the device has different technological characteristics that raise different questions of safety and effectiveness than the predicate device

[8] These two guidance documents are located at http://www.fda.gov/cdrh/k863.html and http://www.fda.gov/cdrh/ode/guidance/857.html, respectively.
[9] See section 513(i) of the act.

- the device has new indications for use or different technological characteristics than the predicate device and performance data[10] on the device do not demonstrate that the device is as safe and effective as a legally marketed device.

2. Effect on Review Clock

An NSE determination is a decision that shuts off the review clock and marks the end of FDA review. The reported FDA review time for the 510(k) decision is the cumulative FDA days for all review cycles from the date the 510(k) is received to the date the NSE letter is issued.

3. Effect on MDUFMA Goals

In accordance with the Goals Letter, to be counted as meeting the MDUFMA decision goals, the NSE letter should issue within 90 FDA days from the date the 510(k) is received if it is the first action on the submission; or within 90 cumulative FDA days from the date the 510(k) is received if the NSE determination is a second or later action.

C. Request Additional Information (AI)

FDA requests AI when the 510(k) lacks information necessary for the agency to begin, continue, or complete the review and make a determination as to whether the device is SE or NSE. Requests for additional information may be issued by letter, telephone, fax, or e-mail.[11]

a. Request AI by letter ("formal" AI request)

A request for AI by letter refers to a request made (1) directly by letter or (2) first by telephone, fax, or e-mail, and then followed-up with a letter informing the submitter that the 510(k) is being placed on "hold" pending receipt of a response to all of the identified deficiencies.

b. Request AI by means other than letter ("informal" AI request)

An informal request for AI refers to a request made by telephone, fax, or e-mail, and not followed-up with a letter. An informal AI request does not result in the 510(k) being placed on "hold."

[10] This may include data that are inadequate or inconclusive.

[11] For CDRH, refer to Blue Book memorandum entitled *"Fax & E-mail Communication with Industry about Premarket Files Under Review,"* located at http://www.fda.gov/cdrh/ode/a02-01.html; for CBER, request a secure e-mail account through the Regulatory Project Manager.

1. Criteria

FDA requests AI when the information identified in 21 CFR 807.87 is not contained in the 510(k) submission.

Note: FDA generally will utilize a maximum of three cycles of FDA review to reach a SE or NSE decision. The first review cycle begins upon receipt of the original 510(k) submission, and subsequent review cycles start when we receive responses to our requests for AI by letter. Thus, if there are multiple review cycles, FDA intends to issue a final decision following its review of industry's response to a second AI request. In general, if unresolved deficiencies exist following FDA's review of a response to a second AI request, FDA will issue an NSE letter.

a. Request AI by letter (formal AI request)

FDA generally requests AI by letter when the agency believes the additional information is not minor in nature and/or cannot be provided within a reasonable period of time (i.e., such that the review will not be delayed).

b. Informal AI request

FDA generally requests AI by means other than a letter when the agency believes the additional information is relatively minor in nature (e.g., a simple change to the device's proposed labeling) and can be provided quickly. Such requests are generally made when FDA believes the submitter can address all of the information requested within a reasonable period of time that will not delay the review and the reviewer receives the 510(k) submitter's commitment to providing the AI by the agreed upon time.

2. Effect on Review Clock

a. Request AI by letter (formal AI request)

A request for AI by letter is an interim action that stops the review clock and marks the end of an FDA review cycle. The FDA review time for this 510(k) action is the number of FDA days for the review cycle. The review cycle begins on the date FDA receives the original 510(k) submission (or supplemental submission in response to an AI request letter) and ends on the date FDA issues the AI letter.

b. Informal AI request

An informal request for additional information does not stop the FDA review clock because the 510(k) remains under review.

Note: If FDA does not receive industry's response to all of the deficiencies in the informal AI request within the agreed upon time, FDA may issue a letter placing the 510(k) on "hold" to stop the clock.

3. Effect on MDUFMA Goals

a. Request AI by letter (formal AI request)

In accordance with the Goals Letter, to meet the MDUFMA decision goals, requests for AI should issue as early as possible in the review cycle so that the cumulative number of FDA review days does not exceed 90. In accordance with the Goals Letter, to be counted as meeting the MDUFMA cycle goals, FDA should issue the first AI request letter within 75 days from the date the original 510(k) submission is received or, for a second AI request, within 60 FDA days from the date of receipt of the submitter's response to all of the deficiencies identified in the first AI request.

b. Informal AI request

This 510(k) action has no effect on the MDUFMA goals because this action does not affect the review clock.

D. Advise the Submitter that the 510(k) is Not Required

FDA believes that it is the responsibility of a manufacturer to initially determine whether a 510(k) submission is required based on the act, device regulations, and guidance documents. The Division of Small Manufactures Assistance, International, and Consumer Assistance, the Program Operations Staff, the review division, and product classification resources on the CDRH website at http://www.fda.gov/cdrh/devadvice/313.html can help you ascertain whether your device is exempt by regulation. You may also obtain information regarding the regulatory status of your device or product by submitting a 513(g) request.[12]

a. Not-a-Device Decision

[12] For products regulated by CDRH, requests for classification information under section 513(g) of the act should be submitted to the attention of the 513(g) Coordinator, Food and Drug Administration, Center for Devices and Radiological Health, 510(k) Document Mail Center (HFZ-401), 9200 Corporate Boulevard, Rockville, MD 20850. For products regulated by CBER, 513(g) requests should be submitted to the CBER Ombudsman, Center for Biologics Evaluations and Research, Suite 200 North, HFM-4, 1401 Rockville Pike, Rockville, MD 20852-1448.

A "not-a-device" letter informs the submitter that the product described in the 510(k) is not regulated as a device.

1. Criteria

FDA sends a "not-a-device" letter when FDA has determined that the product described in the 510(k) does not meet the definition of "device" in section 201(h) of the act.

2. Effect on Review Clock

The issuance of a "not-a-device" letter shuts off the review clock and marks the end of FDA review. The FDA review time for this 510(k) decision is the cumulative FDA days from the date the 510(k) is received to the date the not-a-device letter issues.

3. Effect on MDUFMA Goals

The MDUFMA goals do not include a performance goal for this action, so "not-a-device" decisions will not be counted towards the goals. Nevertheless, FDA intends to process 510(k)s with a not-a-device decision within a timely manner.

b. Exempt from 510(k) Decision

An "exempt" letter informs the 510(k) submitter that the device described in the 510(k) is classified as exempt from the premarket notification requirements of section 510(k) of the act.

1. Criteria

FDA sends an "exempt" letter when FDA determines that the device described in the 510(k) is exempt by regulation from the premarket notification requirements of section 510(k) of the act. Exemptions are found in 21 CFR 807.20(c), 807.65 and 807.85, as well as individual classification regulations (21 CFR Parts 862-892).

2. Effect on Review Clock

The issuance of an "exempt" letter is a decision that shuts off the review clock and marks the end of FDA review. The reported FDA review time for the 510(k) decision is the cumulative FDA days for all review cycles from the date the 510(k) is received to the date the exempt letter is issued.

3. Effect on MDUFMA Goals

The MDUFMA goals do not include a performance goal for this action, so "exempt" decisions will not be counted towards the goals. Nevertheless, FDA intends to process 510(k)s with an exempt decision within a timely manner.

E. Issue a Notice of Withdrawal

A notice of withdrawal informs the 510(k) submitter that FDA considers the 510(k) to be withdrawn (21 CFR 807.87(l)). The letter represents a final FDA decision to end its review of the 510(k) submission because the submitter failed to submit a timely response to an AI letter that placed the submission on hold.

1. Criteria

FDA may issue a notice of withdrawal for a 510(k) that is on hold for AI if the submitter fails to submit a timely response to all of the deficiencies identified in the AI letter. In accordance with 21 CFR 807.87(l), FDA may consider a 510(k) to be withdrawn if the submitter fails to provide additional information within 30 days of a request. In the past, FDA has not strictly enforced this timeframe and has allowed submitters additional time to respond to requests for AI. The agency intends to continue this practice of allowing additional time. In general, FDA intends to issue a notice of withdrawal in accordance with the following procedures:

- If the submitter **does not** submit a written request for an extension to the Document Mail Center, as per 21 CFR 807.90, and **does not** provide a response to all of the deficiencies in the AI request within 90 days of the request, FDA intends to consider the 510(k) to be withdrawn.

- If the submitter **does** submit a written request for an extension and the request is received within 90 days of the date of the AI request, FDA intends to permit the 510(k) to remain on hold for up to 180 days from the date of the AI request. FDA intends to consider the 510(k) to be withdrawn if the agency does not receive a complete response to all of the deficiencies in the AI request within 180 days of the date of the AI request.

2. Effect on Review Clock

Because the 510(k) is on hold at the time the agency issues a notice of withdrawal, an FDA notice of withdrawal does not affect the time clock. The

FDA review time for this action will be measured as the number of days from the beginning of the FDA review until the request for AI. If there are multiple requests for AI, subsequent cycles will begin when FDA receives a complete response to the AI and end when the agency sends out an additional request.

3. Effect on MDUFMA Goals

The MDUFMA goals do not include a decision goal for this action. However, the agency will report its performance on the cycle goals for those applications whose review ends with a notice of withdrawal. In accordance with the Goals Letter, to be counted as meeting the cycle goals, FDA should issue the first AI letter within 75 days from the date the agency receives the original 510(k) submission or, for a second AI request, within 60 days from the date FDA receives the submitter's response to all deficiencies identified in the first AI request.

V. Industry Actions

Industry actions after submitting a 510(k) are generally limited to providing AI to FDA. Submitters should provide information requested by FDA within the timeframes discussed below.

Industry actions include the following submissions to a pending 510(k):

- a response to an FDA letter requesting AI
- a response to an informal AI request
- a request to withdraw the 510(k)
- a request for an extension of time to respond to an FDA request for AI

All of the above industry actions, with the exception of the submission of a response to an informal AI request, must be submitted by letter to the appropriate Center within FDA, in accordance with 21 CFR 807.90.[13]

The following sections describe the industry actions, explain the basis for each industry action, and discuss the effect that each action has on the review clock and on the MDUFMA performance goals.

[13] See *"Fax & E-mail Communication with Industry about Premarket Files Under Review,"* http://www.fda.gov/cdrh/ode/a02-01.html for additional information about time frames and responsibilities.

A. Industry Submits a Response to an FDA Letter Requesting Additional Information

A response to an FDA AI letter is the submission of additional information, addressing identified deficiencies, that allows FDA to continue or complete the substantive review and make a decision on the 510(k).

1. Basis for Submission

The submitter should provide a complete response to a letter from FDA requesting AI. The response should address all of the deficiencies identified by the agency in its letter.

2. Effect on Review Clock

Industry's submission of a response to an FDA AI letter is an action that, upon receipt by FDA, restarts the FDA review clock, i.e., a new 90-day review clock starts upon receipt of the AI.

Note: If, however, FDA determines that the submitter has not addressed one or more of the deficiencies identified in the AI letter, the review cycle should be terminated until FDA receives a response addressing the remaining deficiencies. In such a case, FDA should inform the submitter by telephone, fax, or e-mail that the response is incomplete and, therefore, the clock has not restarted.

3. Effect on MDUFMA Goals

In accordance with the Goals Letter, to be counted as meeting the MDUFMA decision goals, a final decision letter should issue within 90 cumulative FDA days from the date the 510(k) is received. In accordance with the Goals Letters, to be counted as meeting the MDUFMA cycle goals, FDA should act on a submission containing a complete response to an FDA AI letter within 60 days of its receipt.

B. Industry Submits a Response to an Informal Request for Additional Information

A response to an informal request for AI is the submission to FDA of additional information, addressing previously identified deficiencies, by letter, telephone, fax, or e-mail, that allows the agency to continue or complete the substantive review and make a decision on the 510(k).

1. Basis for Submission

The submitter should provide a response to all of the deficiencies after receiving FDA's informal request for AI.

Note: As explained above in Section IV(C), FDA makes an informal request for AI when FDA believes the submitter can address all of the information requested within a reasonable period of time that will not adversely affect the review and the reviewer receives the submitter's commitment to providing the AI by the agreed upon time.

2. Effect on Review Clock

Industry's submission of a response to an informal FDA request for AI is an action that does not affect the review clock because the 510(k) remains under review while the request is pending.

Note: If the agency does not receive industry's response to all of the deficiencies within the agreed upon time, FDA may issue a letter placing the 510(k) on "hold" and stop the review clock.

3. Effect on MDUFMA Goals

Industry's submission of a response to a FDA informal request for AI has no effect on the MDUFMA goals because this action does not affect the review clock.

C. Industry Requests Withdrawal of the 510(k)

A request to withdraw a 510(k) informs the agency of the submitter's intention to discontinue its pursuit of FDA review of the device at this time.[14]

1. Basis for the Request

The 510(k) submitter may request withdrawal of the pending 510(k) at any time, and for any reason, after it is submitted for review but before FDA renders its final decision.

2. Effect on Review Clock

Industry's submission of a request to withdraw a pending 510(k) is an action that shuts off the review clock. If the 510(k) is under review at the time FDA receives

[14] See *"Fax & E-mail Communication with Industry about Premarket Files Under Review,"* http://www.fda.gov/cdrh/ode/a02-01.html for information on 510(k) withdrawal procedures.

the withdrawal request, the review clock should stop on that date. If the 510(k) is on hold at the time FDA receives the withdrawal request, the review clock should remain stopped as of the date the 510(k) was last placed on hold for AI. The reported FDA review time for the 510(k) is the cumulative FDA days for all review cycles from the date the submission is originally received to the date the withdrawal request is received, or the date the submission was last placed on hold, as applicable.

3. Effect on MDUFMA Goals

The MDUFMA goals do not include a decision goal for this action. However, the agency will report its performance on the cycle goals for applications whose review ends with a request for withdrawal. In accordance with the Goals Letter, to be counted as meeting the cycle goals, FDA should issue the first AI letter within 75 days from the date the agency receives the original 510(k) submission or, for a second AI request, within 60 days from the date of receipt of the submitter's response to all deficiencies identified in the first AI request.

D. Industry Requests an Extension of Time to Respond to an FDA Letter Requesting Additional Information

An industry request for an extension of time to respond to an AI letter informs the agency of the 510(k) submitter's wish to extend the response time identified in FDA's request.

1. Basis for the Request

In the past, FDA has not strictly enforced the 30 day timeframe identified in requests for AI and has allowed submitters additional time to respond to such requests. The agency intends to continue to allow additional time for responses. If the submitter needs more than 90 days to respond to the deficiencies in an AI letter, the submitter should send a letter requesting an extension to the Document Mail Center.

Note: FDA intends to issue a notice of withdrawal if it does not receive a request for additional time.[15] (Refer to section IV. E. *Issue a Notice of Withdrawal* for additional discussion of FDA actions regarding requests for extension.) Even in those situations where a submitter does request an extension, FDA does not intend to keep 510(k)s indefinitely on hold while

[15] In accordance with 21 CFR 807.87(l), FDA may consider a 510(k) to be withdrawn if the submitter fails to provide additional information within 30 days of a request. As explained in Section IV. E., FDA generally permits submitters additional time to respond to such requests.

awaiting the AI. Therefore, in general, FDA intends to issue a notice of withdrawal if the submitter, who has requested an extension, fails to provide a complete response within 180 days from the date of the AI request.

2. Effect on Review Clock

A request for an extension of time to respond to an AI request does not affect the FDA review clock because the 510(k) remains on hold.

3. Effect on MDUFMA Goals

Industry's submission of a request for an extension has no effect on the MDUFMA goals because this action does not affect the review clock.