On October 5, 2021, FDA issued a final rule on the De Novo Classification Process. The final rule added new regulations at 21 CFR Part 860, Subpart D--De Novo Classification, and is effective 90 days after publication. FDA has updated this guidance to reflect the De Novo final rule, including addition of references to 21 CFR Part 860. The references to 21 CFR Part 860 in this guidance are not in effect until the effective date of the final rule. This updated guidance includes minor updates from the version issued September 9, 2019.

Contains Nonbinding Recommendations

FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals

---

Guidance for Industry and Food and Drug Administration Staff

Document issued on October 5, 2021.

Document originally issued on October 2, 2017.

This document supersedes FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals issued September 9, 2019.

For questions about this document, contact CDRH's Division of Industry and Consumer Education (DICE) at 1-800-638-2041, 301-796-7100, or DICE@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development (OCOD) at 1-800-835-4709, 240-402-8010 or ocod@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

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov/. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2017-D-5712. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 16058 and complete title of the guidance in the request.

CBER

Additional copies are available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Room 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, by email, ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

Table of Contents

FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals

---

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The Medical Device User Fee Amendments of 2017[1] (MDUFA IV) amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to authorize FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2017, including De Novo classification requests (De Novo requests). The additional funds obtained from user fees will enable FDA, with the cooperation of industry, to improve the device review process to meet certain performance goals and implement improvements for the medical device review process.

Performance goals were negotiated and agreed to under MDUFA IV for De Novo requests received in FY 2018-2022. These performance goals and process improvements are outlined in the MDUFA IV Commitment Letter from the Secretary of Health and Human Services (the Secretary) to Congress[2] and are further described below.

[1] See Title II of the FDA Reauthorization Act of 2017 (Public Law 115-52).
[2] See 163 CONG. REC. S4729-S4736 (daily ed. August 2, 2017) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/102699/download.

On October 5, 2021, FDA issued a final rule on the De Novo Classification Process. This final rule will add new regulations at 21 CFR Part 860, Subpart D--De Novo Classification that describe the procedures and criteria FDA will use in assessing whether a request for an evaluation of automatic class III designation (De Novo classification request or De Novo request) contains the information necessary to permit a substantive review. FDA is updating this guidance to reflect the De Novo final rule.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required

II. Scope

This document describes:

- the different FDA actions that may be taken on De Novo requests;
- the effect each action has on goals under MDUFA IV for De Novo requests received in FY 2018-2022; and
- the different industry actions that may be taken on De Novo requests.

III. FDA Actions

FDA will begin substantive review of a De Novo request after the request is accepted under 21 CFR 860.230. After FDA conducts a substantive review of the submission, FDA may take any of the following actions (21 CFR Part 860, Subpart D):

- issue an order granting a De Novo request for classification (granting order);
- issue an order declining a De Novo request for classification (decline order); or
- issue a request for additional information (AI request).

Further, in accordance with 21 CFR 860.250(a), the Agency may consider a De Novo request to be withdrawn if additional information is not provided within 180 calendar days following issuance of an AI request. In this instance, FDA may issue a notice of withdrawal to the requester (21 CFR 860.250(b)). A notice of withdrawal is sometimes referred to as a "deletion letter." The term "deletion" is used to differentiate a lack of timely response from a request to withdraw a pending De Novo request by the requester.

Of these FDA actions, issuing a granting order and issuing a decline order are considered MDUFA decisions, as defined in the MDUFA IV Commitment Letter.

The following sections describe the actions FDA may take on an accepted De Novo request, explain when these actions may be appropriate, and discuss the effect that each action has on the review clock.

A. Issue an Order Granting the Request to Classify the Device

An order granting the De Novo request to classify the device (granting order) is a letter issued to the De Novo requester stating that FDA has determined that the device meets the criteria for classification into either class I or class II.[3] A granting order authorizes marketing of the device in the United States (U.S.), subject to specific statutory and regulatory requirements.

The criteria for granting a De Novo request are described in section 513(f)(2) of the FD&C Act and 21 CFR Part 860. The grounds on which FDA may decline a De Novo request are described in 21 CFR 860.260. If none of the reasons apply, then FDA will issue to the request an order granting a De Novo request. Such an order shuts off the review clock, marks the end of FDA review, and is considered a final action.

B. Issue an Order Declining the Request

An order declining the De Novo request (decline order) is a letter issued to a De Novo requester (21 CFR 860.260(b)) stating that FDA has determined that either: a) the device is not eligible for De Novo classification; or b) the device is eligible for De Novo classification, but the requester has not demonstrated that the device described in the De Novo request meets the criteria under section 513(a)(1) of the FD&C Act (21 U.S.C. 360c(a)(1)) and 21 CFR 860.260. Therefore, the request is declined and the device remains in class III (Premarket Approval).

FDA will issue a decline order in the following situations (21 CFR 860.260(c)):

- the device does not meet the criteria under section 513(a)(1) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 860.3 for classification into class I or II (21 CFR 860.260(c)(1));
- the De Novo request contains a false statement of material fact or there is a material omission (21 CFR 860.260(c)(2));
- the devices's labeling does not comply with the requirements in 21 CFR parts 801 or 809, as applicable (21 CFR 860.260(c)(3));

[3] See section 513(f)(2) of the FD&C Act (21 U.S.C. 360c(f)(2)).

- the product does not meet the definition of a device under section 201(h) of the FD&C Act (21 U.S.C. 321(h)) and is not a combination product as defined at 21 CFR 3.2(e) (21 CFR 860.260(c)(4));

- the device is of a type which has already been approved in existing applications for PMAs (21 CFR 860.260(c)(5));

- the device is of a type which has already been classified into class I, class II, or class III (e.g., it is probable that the device could be determined to be substantially equivalent (SE) to a predicate device (i.e., a device that has already been classified within an existing class I or class II classification regulation or an unclassified preamendments device) (21 CFR 860.260(c)(6));

- an inspection of a relevant facility under 21 CFR 860.240(c) results in a determination that general or general and special controls would not provide reasonable assurance of safety and effectiveness (21 CFR 860.260(c)(7));

- a nonclinical study subject to 21 CFR part 58 that is described in the De Novo request, and that is essential to show there is reasonable assurance of safety, was not conducted in compliance with 21 CFR part 58 and no reason for the noncompliance is provided or, if a reason is provided, the practices used in conducting the study do not support the validity of the study (21 CFR 860.260(c)(8));

- a clinical investigation described in the De Novo request involving human subjects that is subject to the institutional review board regulations in 21 CFR part 56, informed consent regulations in 21 CFR part 50, or GCP described in 21 CFR 812.28(a), was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected or the supporting data were determined to be otherwise unreliable (21 CFR 860.260(c)(9));

- a clinical or nonclinical study necessary to demonstrate that general controls or general and special controls provide reasonable assurance of safety and effectiveness: (i) has not been completed per the study protocol, or (ii) deficiencies related to the investigation and identified in any request for additional information under 21 CFR 860.240(b)(1) have not been adequately addressed (21 CFR 860.260(c)(10)); or

- After the De Novo request is accepted for review under 21 CFR 860.230(b), the requester makes significant unsolicited changes to the device's indications for use or technological characteristics (21 CFR 860.260(c)(11)).

FDA's decision to decline a De Novo request will be based on review of the totality of the information provided to support the De Novo request, and may therefore be a combination of multiple situations outlined above. A device that is eligible for De Novo classification will be declined if the totality of the information provided, including performance data, is insufficient (e.g., data that were inadequate or inconclusive) to demonstrate that the device is

of low to moderate risk. A De Novo request will also be declined if, based on the totality of the information provided, including performance data, FDA determines that general controls would be inadequate to control the risks and special controls to mitigate the risks cannot be developed.

A decline order will inform the requester of the deficiencies in the De Novo request, including each applicable ground for declining (21 CFR 860.260(d)). A decline order shuts off the review clock, marks the end of FDA review, and is considered a final action.

C. Request for Additional Information

FDA issues a request for additional information (AI request) when the De Novo request lacks information necessary for the Agency to complete its review and determine whether to grant or decline the De Novo request (21 CFR 860.240(b)(1)). AI requests are issued by email with an attachment document identifying deficiencies.[4] These requests inform the requester that the De Novo is being placed on hold pending receipt of a complete response to all of the identified deficiencies. The hold starts on the issue date of the AI request.

FDA generally issues an AI request when FDA believes the additional information needed from the requester is not suitable for interactive review and/or cannot be provided within a reasonable period of time (i.e., such that the review would be unduly delayed if the submission were not placed on hold).

An AI request is an interim action that stops the review clock and marks the end of an FDA review cycle. The review clock will resume upon the receipt of a complete response to the AI request in the appropriate Document Control Center (DCC). Any additional information submitted to FDA must include the reference number assigned to the original De Novo request and, if submitted on the requester's own initiative, the reason for submitting the additional information (21 CFR 860.240(b)(2)).

D. Issue a Notice of Withdrawal

A notice of withdrawal informs the De Novo requester that FDA considers the De Novo request to be withdrawn. The notice of withdrawal represents an FDA decision to discontinue its review of the De Novo request.

In accordance with 21 CFR 860.250(a), FDA considers a De Novo request to have been withdrawn if:

- FDA does not receive, in a submission to the appropriate Center's Document Control Center, a complete response to a request for additional information pursuant to 21

[4] Please note that AI requests from CBER will be issued according to SOPP 8119: Use of Email for Regulatory Communications.

CFR 860.240(b)(1) within 180 calendar days after the date FDA issues such request (21 CFR 860.250(a)(1));

- FDA does not receive a response, after refusing to accept the De Novo request, within 180 calendar days of the date notification was issued by FDA (21 CFR 860.250(a)(2));

- FDA is not permitted an opportunity to inspect relevant facilities, pursuant to 21 CFR 860.240(c), at a reasonable time and in a reasonable manner, and to have access to copy and verify all records pertinent to the De Novo request (21 CFR 860.250(a)(3)); or

- The requester submits a written notice to FDA that the De Novo request has been withdrawn (21 CFR 860.250(a)(4)).

If a De Novo request is withdrawn while the submission is on hold, an FDA notice of withdrawal does not affect the review clock. Issuance of a notice of withdrawal shuts off the review clock, marks the end of FDA review, and is considered a final action. The notice will include the De Novo request reference number and the date FDA considered the De Novo request withdrawn (21 CFR 860.250(b)).

IV. De Novo Performance Goals for MDUFA IV

The performance goals for De Novo requests received from FY 2018 through FY 2022 (the time frame defined for MDUFA IV) are defined in the MDUFA IV Commitment Letter. Performance goals and associated changes to be implemented in MDUFA IV include:

- most De Novo requests are subject to a user fee;

- FDA will issue draft and final guidance that includes a submission checklist to facilitate a more efficient and timely review process;

- De Novo requests are subject to a one-tier MDUFA decision goal (there are no "cycle" (or review cycle) goals for interim actions); and

- for De Novo requests for which a MDUFA decision has not been rendered within 180 FDA days, at the requester's request and resources permitting, but not to the detriment of meeting the quantitative review timelines, FDA will discuss with the requester all outstanding issues with the submission preventing FDA from reaching a decision.

A. Submission

Most De Novo requests will be subject to a user fee as described in the guidance document entitled "User Fees and Refunds for De Novo Classification Requests,"[5] and all De Novo requests will be subject to the requirement for an eCopy. FDA is authorized by section 745A(b)(1) of the FD&C Act (21 U.S.C. 379k-1(b)(1)) to implement eCopy requirements for De Novo requests after the issuance of final guidance. Please see the guidance entitled "eCopy Program for Medical Device Submissions,"[6] for more information about eCopy requirements.

De Novo requests will not be processed and distributed to the appropriate Office for review without confirmation of user fee payment (or applicability of a user fee exception), and a valid eCopy.

B. Acceptance Review

In accordance with 21 CFR 860.230, within 15 calendar days of receipt, FDA intends to conduct an acceptance review to make a threshold determination that the De Novo request contains the information necessary to permit a substantive review.[7] If FDA refuses to accept a De Novo request, FDA will notify the requester within 15 calendar days that the submission has not been accepted. The notification will identify those items that are the basis for the refuse to accept (RTA) decision and are therefore necessary for the submission to be considered accepted. The submission will be placed on hold and the review clock will not start until the missing elements are provided. For additional information, please refer to the guidance, "Acceptance Review for De Novo Classification Requests."[8]

This communication represents an administrative review of the submission and is not indicative of deficiencies that may be identified later in the review cycle.

C. Substantive Review

Once the submission has been accepted for review (i.e., after the acceptance phase of review), FDA will conduct a substantive review (21 CFR 860.240(a)). During the substantive review, FDA will generally communicate with the requester through a Substantive Interaction. The Substantive Interaction communication can be an AI request (which stops

[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/user-fees-and-refunds-de-novo-classification-requests

[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions

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

[8] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-review-de-novo-classification-requests

the clock) or an email stating that FDA will attempt to resolve any outstanding deficiencies interactively in real-time, without stopping the FDA review clock (Interactive Review).

Following a Substantive Interaction, FDA intends to work with the requester via Interactive Review to reach a MDUFA decision.

D. MDUFA IV Goals

MDUFA IV includes a goal for a MDUFA decision (see Table 1 below), defined in terms of FDA Days, which are calendar days when a submission is considered to be under review at the Agency. FDA Days begin on the date of receipt of the submission (i.e., user fee is paid and a validated eCopy is provided).

Table 1. De Novo Performance Goals

Action	Review Time (FDA days)	Performance Level (by Fiscal Year)				
		FY2018	FY2019	FY2020	FY2021	FY2022
MDUFA Decision (grant/decline)	150	50%	55%	60%	65%	70%

E. Missed MDUFA Decision Communication

At Industry's request and as resources permit, but not to the detriment of meeting the quantitative review timelines, if a final decision has not been rendered within 180 FDA days, FDA will discuss with the requester, in a meeting or teleconference, all outstanding issues with the submission preventing FDA from reaching a decision. This discussion will reflect appropriate management input and approval, and will include action items for FDA and/or the requester, as appropriate, with an estimated date of completion for each party to complete their respective tasks.

V. Requester Actions

Actions taken by the requester of a pending De Novo request may include submission of a response to FDA's AI request (i.e., not a request made via interactive review) or withdrawal of the De Novo request (either by submission of a request for withdrawal to the respective Center's DCC or by not responding to an FDA AI request within 180 calendar days) (see 21 CFR 860.250(a)). The information below describes the actions a requester may take and the effect each action has on the FDA review clock.

As with the original De Novo request, any amendment or supplement to a De Novo request or a request to withdraw a De Novo request will need to include an eCopy as part of the submission to the appropriate DCC for the submission to be processed as described in the guidance document entitled "eCopy Program for Medical Device Submissions."[9]

[9] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions

A. Response to an AI Request

A response to an FDA AI request is the submission of additional information, addressing all of the deficiencies identified in that AI request, that allows FDA to continue or complete the substantive review and reach a decision on the De Novo request (21 CFR 860.240(b)).

The requester should provide a complete response to an AI request from FDA. The response should address all of the deficiencies identified by FDA in its AI request to be considered a complete response.

The requester's submission of a response to an AI request is an action that, upon receipt by FDA, resumes the FDA review clock (i.e., the 150-day review clock resumes upon receipt of the additional information).

Note: If FDA determines that the requester has not addressed one or more of the deficiencies identified in the AI request, the review cycle will be terminated until FDA receives a response addressing the remaining deficiencies. In such a case, FDA informs the requester by letter or e-mail that the response is incomplete and the De Novo request will be placed back on hold as of the date of the original AI request; therefore, the review clock has not resumed. The requester will have 180 calendar days from the date of the original AI request in which to submit a complete response, or the De Novo request will be considered to be withdrawn (21 CFR 860.250(a)(1)).

B. Request for Withdrawal of the De Novo Request

A request to withdraw a De Novo request informs FDA of the requester's intent to discontinue its pursuit of FDA review of the De Novo request (21 CFR 860.250(a)(4)).

The De Novo requester may request withdrawal of the pending De Novo request at any time, and for any reason, after it is submitted for review but before FDA renders its final decision. FDA does not consider requests for withdrawal after a final decision has been rendered.

The requester's request to withdraw a pending De Novo request shuts off the review clock, marks the end of FDA review, and is considered a final action. If the De Novo request is under review at the time FDA receives the withdrawal request, the review clock will stop on that date. If the De Novo request is on hold at the time FDA receives the withdrawal request, the review clock will remain stopped as of the date the De Novo request was last placed on hold.