It's De Novo All Over Again: FDA Issues a Proposed Rule to Implement the De Novo Classification Process

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In December 2018, the Food and Drug Administration issued a proposed rule that would amend the medical device classification regulation to implement the De Novo classification process.[1] In short, the notice explains FDA's thinking, and the rule, if finalized as proposed, would formally implement the law on the submission and withdrawal of requests for De Novo classification. Furthermore, the rule would set the criteria used by the agency when reviewing, approving, rejecting, or withdrawing these requests. FDA will accept comments submitted by March 7, 2019.

This Bulletin summarizes some of the key provisions of the proposed rule.

Current De Novo Classification Process – High-Level Overview

- The De Novo classification process is authorized by statute and allows a pathway for sponsors of certain new or novel types of medical devices to obtain marketing authorization for those devices as class I or class II devices, rather than the devices remaining automatically designated as class III devices, which require premarket approval, i.e., a Premarket Approval Application (PMA).[2]
- When FDA classifies a device type as class I or II through the De Novo classification process, other manufacturers generally are not required to submit a De Novo request or PMA in order to legally market a device of the same type.[3] Manufacturers can instead use the less burdensome pathway of premarket notification (i.e., submit a 510(k) premarket notification application, when applicable) to legally market the device, because the device that was the subject of the original De Novo request can serve as a predicate device for a substantial equivalence determination.[4]
- The agency has, at times, issued written guidance on different parts of the De Novo program, but has not previously promulgated any De Novo classification process regulations, as it is proposing now.[5]

Proposed Rule

- **Content Requirements**
  - The proposed rule's De Novo request content requirements are intended to provide more clarity and predictability as to FDA's expectations.
  - The content should include, among other things: requester contact information; a statement on the device's regulatory history; a summary of each study used in support of the request (which can include those conducted overseas); and a

1 83 Fed. Reg. 63127 (Dec. 7, 2018).
2 21 U.S.C. § 360c (f)(2).
3 If a device has a new intended use or technological characteristics that raise different questions of safety or effectiveness as compared to the predicate device, a De Novo request or PMA may likely be required. Even if a PMA or a De Novo request is not required, other medical device requirements may apply (e.g., establishment registration, product listing, Medical Device Reporting, and Quality System Regulation compliance).
4 We will not discuss the device classification criteria in this Bulletin.
5 See, e.g., FDA, Guidance for Industry and FDA Staff, *De Novo Classification Process (Evaluation of Automatic Class III Designation)* (Oct. 2017), available at: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm080197.pdf.

discussion of observed device failures, if any.

- In October 2017, FDA issued a draft guidance, "Acceptance Review for De Novo Classification Requests."[6] The proposed rule requirements are similar, but would require De Novo sponsors to submit additional information in the requests, such as:
  - a bibliography of all published and unpublished reports on the device and any other information relevant to a device's safety or effectiveness;
  - non-clinical data;
  - samples of the device and its components (if requested by FDA); and
  - advertisements for the device.

- **Submission Process**
  - A person may submit a De Novo request after submitting a 510(k) and receiving a not substantially equivalent (NSE) determination.
  - A person may also submit a De Novo request without first submitting a 510(k), if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence; that is, the company does not have to wait for FDA to issue an NSE.
  - In order to be accepted for substantive review, a De Novo request must include all required information (i.e., meet the content requirements).

- **Criteria**
  - FDA describes the criteria for acceptance of a request in the proposed rule.
  - The primary purpose of these criteria is to enable the agency to determine if the request contains the information necessary to permit a substantive review.
  - FDA will evaluate whether the request: contains each required item or a justification for the omission; is in the required format; is for more than one device type; is for a device that is also the subject of other pending pre-market submissions or reclassification requests; and includes a complete response to FDA requests for additional information, if any.
  - In the proposed rule, FDA also describes the criteria for review of an accepted request, and for the withdrawal, granting, or denial of a request.
  - FDA proposes the following grounds, among others, for declining a De Novo request: the device does not meet criteria for Class I or II classification; the request contains a false statement of material fact or material omission; proposed labeling does not meet applicable requirements; the product does not meet the definition of a device and is not an eligible combination product; the device type has already been approved in existing PMAs; the device type has already been classified; certain inspection-related results raise concern; FDA finds certain deficiencies in essential nonclinical or clinical studies; or significant device changes not solicited by FDA have been made either to the device's indications for use or to the device's technological characteristics.

- **FDA Action**
  - FDA may refuse to accept a De Novo request that is "ineligible or is incomplete on its face"; if this happens, FDA will notify the requester of the deficiency.
  - After a De Novo request is accepted for review, FDA will begin a substantive review that may result in requesting additional information, issuing an order granting the request, or declining to grant the De Novo request.
  - FDA proposes that the agency will substantially review and grant or decline a De Novo request within 120 days after the De Novo request is received or additional information is received that results in acceptance of the De Novo request.
    - A deadline is already in the Federal Food, Drug, and Cosmetic Act (although industry experience to date has been that it is frequently missed).
  - FDA proposes that a De Novo requester be permitted to supplement or amend a pending request to revise existing information or provide additional information.

6 FDA, Draft Guidance for Industry and FDA Staff, *Acceptance Review for De Novo Classification Requests* (Oct. 2017), available at: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM582251.pdf.

- If requested information is not received within the timeframe specified by FDA, or is incomplete, the agency will place the request on hold until it receives the information.
- FDA proposes that it may inspect relevant facilities prior to granting or declining a De Novo request: The agency states that an inspection is intended to assist in determining whether a reasonable assurance of safety and effectiveness can be provided.
- Once a De Novo request has been withdrawn by the requester or deemed withdrawn by FDA, the requester will be required to submit a new De Novo request to restart the De Novo review process.
- A De Novo request will be considered withdrawn if the De Novo requester:
  - does not permit an authorized FDA employee an opportunity to inspect the facilities and to have access to copy and verify relevant records;
  - submits a written notice to FDA that the De Novo request has been withdrawn;
  - fails to provide a complete response to any deficiencies within 180 days of the date FDA notifies the requester of such deficiencies; or
  - fails to provide a complete response to a request for additional information within 180 days.
  - FDA will publish a notice in the *Federal Register* announcing the new device classification and codifying it in the Code of Federal Regulations.

AGG Observations

- As FDA is proposing to issue a rule formalizing the De Novo classification request process and adding additional requirements, this is a key time to submit a comment to FDA if a company has concerns, objections, or possible improvements to the De Novo process.
- The potential effect of inspections on the 120-day timeline is not adequately addressed in the proposed rule, and this may be opportunity to request clarification.
- Firms planning to submit De Novo classification requests in the near future may want to consult the proposed rule as they are preparing their request (even if the request will be submitted under current draft guidance), as the preamble and rule may be helpful in understanding FDA's expectations and reasoning.
- Even if not yet required, a company might consider submitting much of what FDA has suggested in a De Novo request; it could possibly speed review by anticipating agency inquiries.

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