AdvaMed Accel | Regulatory Best Practices Guide

INTRODUCTION & OVERVIEW

A De Novo Classification Request is a type of premarket submission that uses a risk-based approach to classify novel medical devices. It is intended for low- to moderate-risk devices that do not have suitable predicate devices and would otherwise be identified as Class III. When the FDA issues a De Novo order to a Class I device, it is subject to general controls only. Class II devices require both general and special controls because they are moderate risk products.

The De Novo regulatory pathway was established in the Food and Drug Administration Modernization Act (FDAMA) of 1997. At that time, FDA regulations required companies to submit 510(k) applications before determining whether their products were eligible for De Novo classification. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) added the direct De Novo option to federal law due to the complexity and timeliness of the De Novo process. The FDA has seen a steady increase in the number of De Novo submissions since this change.

De Novo Application Contents

- ☐ **Cover sheet**
- ☐ **Administrative Information** *(including all appropriate contact information)*
- ☐ **Regulatory History:** Indicate whether previous submissions exist
- ☐ **Device Description**
- ☐ **Indications for Use**
- ☐ **Classification Summary:** Explain why the device is eligible for a De Novo order using classification regulations from similar devices.
- ☐ **Classification Recommendation:** low risk **(Class I)** or moderate risk **(Class II)**.
- ☐ **Performance Information**
  - **Clinical** *(if required)*
  - **Shelf-Life**
  - **Non-clinical** *(bench testing)*
  - **Biocompatibility**
- ☐ **Sterilization** *(if applicable)*
- ☐ **Summary of Benefits and Risks to Health**
- ☐ **Benefit-Risk Consideration and Mitigation Information:** Sponsors must include measures to mitigate each risk.
- ☐ **Device Labeling**

De Novo Pathways

510(k) to De Novo

Applicant submits 510(k) application

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FDA reviews 510(k) submission

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FDA issues NSE determination to applicant

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Applicant submits De Novo request

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FDA reviews De Novo submission

↓

FDA grants De Novo classification order to applicant

Direct De Novo

Applicant submits De Novo request

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FDA reviews De Novo submission

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FDA grants De Novo classification order to applicant

FDA and industry experts recommend that companies request an in-person Pre-Submission meeting or phone call to gain useful feedback about whether the Direct De Novo process is most appropriate for their novel technologies and how to prepare their applications.

De Novo Submission Process

1. After submitting a De Novo request, FDA sends a **submission receipt** to company sponsors if the following two criteria are met: **(1) user fees have been paid and (2) the Agency received an electronic copy (eCopy) of the submission.**

2. The review clock starts from the date of the submission receipt, and at this point, applications undergo **Acceptance Review**. The Agency issues a **Refuse to Accept (RTA) designation** if applications are missing critical information. If company sponsors do not respond within 180 days to the issues present in their RTA designations, their applications are **withdrawn**.*

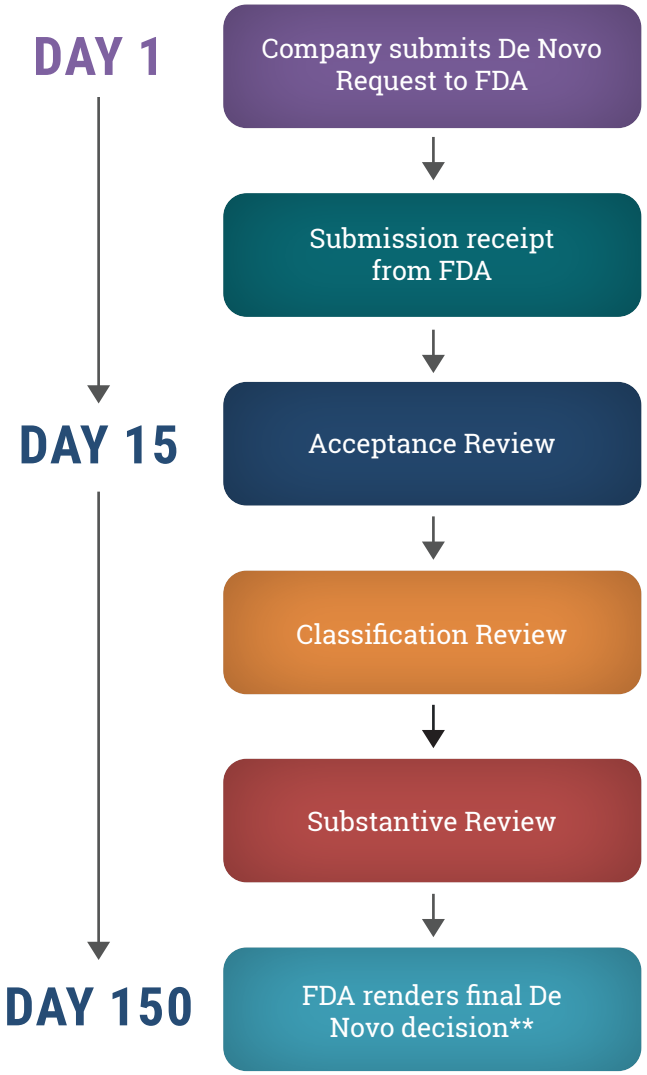
3. If applications are accepted, they move on to **Classification Review**, where FDA determines whether products are eligible for De Novo classification based on two criteria: **(1) the device must be low to moderate risk and (2) the first of its kind.** FDA **declines** all applications that **do not** meet these criteria.

4. If applications are eligible for De Novo classification, they undergo **Substantive Review**; the FDA reviews all submissions to search for deficiencies. If any are found, applications are placed on hold, and the review clock stops. FDA then issues **Additional Information (AI) letters** to companies with specific details about such deficiencies, and company sponsors are required to respond with additional information and/or clarifications in a timely manner. Once FDA receives responses to deficiency letters, the review clock restarts.

5. After further interactions between company sponsors and Lead Reviewers from FDA, **the Agency will either grant or decline De Novo classification**.

Company sponsors have **180 days to respond to deficiencies found in their De Novo applications. If they do not provide complete responses to the Agency within this time period, then their applications are deleted, and they must resubmit their applications and start the process from the beginning.*

MDUFA Time Commitments



***Based on MDUFA IV time commitments, the total review time for De Novo submissions is **150 review days**, not including time periods during which applications are placed on hold.*

Additional Resources

FDA Presentation: De Novo Program (November 4, 2014)

FDA Webinar: Acceptance Review for De Novo Classification Requests (September 18, 2019)

AdvaMed Accel Weekly Policy Call Presentation: MDUFA IV Overview (August 27, 2019)

AdvaMed Working Groups

FDA Strategy Working Group
Staff Lead: **Janet Trunzo**, *Senior Executive Vice President*, Technology and Regulatory Affairs
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510(k) Working Group
Staff Lead: **Ruey Dempsey**, *Vice President*, Technology and Regulatory Affairs
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De Novo Decisions

De Novo Request GRANTED:

- A **product classification** is made based on risk level.
- **Class I device** *(low risk)*: subject to general controls
- **Class II device** *(moderate risk)*: subject to both general controls and special controls
- FDA publishes an **order and decision summary**.
  - The **order** declares the device's new classification and regulatory controls.
  - The **decision summary** highlights the scientific evidence used to grant the De Novo Request.
- Once a De Novo is granted, **the device can serve as a predicate for future 510(k) submissions**. This is available for both the company that submitted the De Novo (for modifications) and companies with similar devices.

De Novo Request DECLINED:

- A request is **declined** due to at **least one** of the following:
  - The application **did not pass** Classification Review.
  - FDA needs **additional information** to grant a De Novo classification
  - After completing a benefit-risk profile, FDA determined that **the device's benefits do not outweigh its risks**.
- **The device remains in Class III,** and a PMA must be approved before marketing.

Tips from the Experts

1. **Make sure your product is eligible** for De Novo before submitting a request. This can often be accomplished via a phone call to FDA.
2. **Hold an informational meeting with FDA in the early stages of product development and request an in-person Pre-Submission meeting at a later stage.** The device design should be finalized and suitable for testing that can be submitted to FDA before requesting a Pre-Submission meeting.
3. **Include a detailed device description and intended use** with the De Novo Request.
4. **Make sure you can identify a potential mitigation for each health risk.**
5. **Include performance testing in De Novo submissions.** Many De Novo devices require clinical data; be sure to follow applicable Investigation Device Exemption (IDE) requirements to gather the data.

FDA GUIDANCE DOCUMENTS

Acceptance Review for De Novo Classification Requests

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

User Fees and Refunds for De Novo Classification Requests

De Novo Classification Process (Evaluation of Automatic Class III Designation)

Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions

Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications