Welcome To Today's Webinar

Thanks for joining us!
We'll get started in a few minutes.

Today's Topic: De Novo Final Rule: Overview and Guidance Updates
December 14, 2021, 1-2 pm EST

De Novo Final Rule: Overview and Guidance Updates

Peter J. Yang, PhD
De Novo Policy Analyst and Program Lead
Division of Submission Support

Office of Regulatory Programs
Office of Product Evaluation and Quality
Center for Devices and Radiological Health
U.S. Food and Drug Administration

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Learning Objectives

- Describe the background and history of the De Novo Program
- Describe the new De Novo regulations and changes to the De Novo review process
- Describe what the updated De Novo guidances cover
- Identify the contents of the updated De Novo Refuse-to-Accept (RTA) checklist and what is required for acceptance of a De Novo request

Keep in mind…

- Final rule, updated guidances, and RTA checklist are not for implementation until **January 3, 2022.**
- For any De Novo request received prior to January 3, 2022, FDA will review under existing policies, including the current RTA guidance.

What Is a De Novo Request?

- A type of premarket submission (marketing authorization)
- Intended for devices that are automatically classified into class III by virtue of not yet being classified
- Request to classify the device into class I or class II based on a determination of **reasonable assurance of safety and effectiveness** (RASE)
- If the De Novo request is granted:
  - FDA **creates a new classification regulation**
  - the new device type is now regulated through 510(k), if class II
  - the De Novo device can serve as the first predicate device of its kind

A De Novo Request is Not:

- A type of premarket notification [510(k)]
- A substantial equivalence (SE) determination
- A premarket approval application (PMA)
- A 513(g) Request for Information

Classification Process – Goals

- Determine if probable benefits outweigh probable risks
- Identify probable risks to health for the device/product
- Determine level of regulatory controls needed:
  - general controls only = class I
  - general controls + special controls = class II

Together, these provide reasonable assurance of safety and effectiveness.

History and Evolution

- FDAMA (1997) — *Created De Novo pathway*
- FDASIA (2012) — *Added Direct De Novo option*
- 21st Century Cures (2016) — *Added combination products (21 CFR 3.2(e))*
- FDARA (2017) — *Added user fees; resulted in new guidances*
- De Novo RTA — *Final guidance issued September 2019*
- De Novo Final Rule — *Published October 5, 2021*

MDUFA IV User Fees and Performance

User Fees

- Standard fee = 30% of PMA user fee
- Small business fee = 25% of standard fee

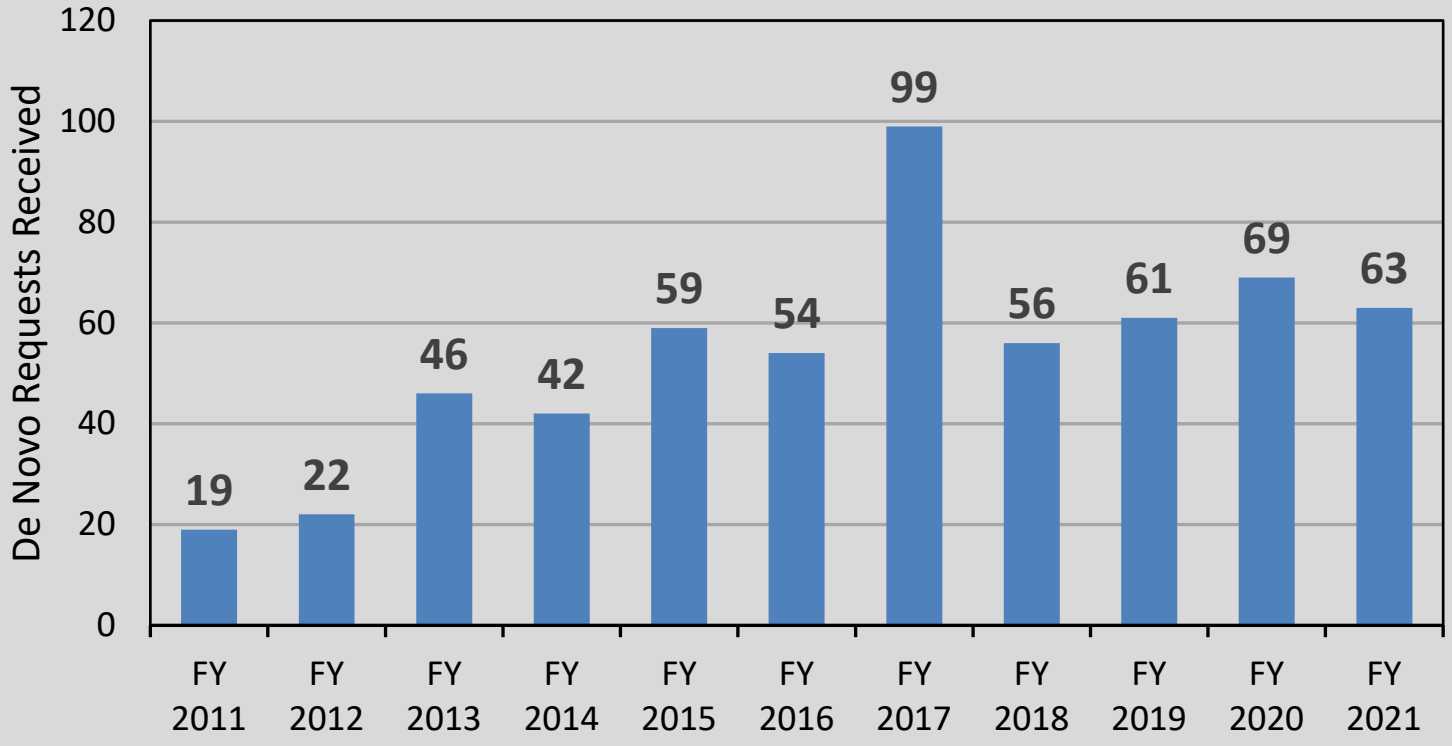
Performance Goals

- Based on 150 FDA days
  - Different than statutory deadline of 120 FDA days
- Based on % of De Novo requests reaching final decision (grant, decline, withdraw)

	Final Decision by Day 150	User Fee	Small Business Fee
FY 2018	50%	$93,229	$23,307
FY 2019	55%	$96,644	$24,161
FY 2020	60%	$102,299	$25,575
FY 2021	65%	$109,697	$27,424
FY 2022	70%	$112,457	$28,114

MDUFA: Medical Device User Fee Amendments

De Novos Received In CDRH



De Novo Program Support

What we have (had)

- Statute – section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)
- Guidances
  - De Novo Program
  - De Novo User Fees (MDUFA IV)
  - De Novo Actions/Clock (MDUFA IV)
  - De Novo RTA (MDUFA IV, guidance issued in 2019)

What we need(ed)

- Regulations
  - De Novo program and review process implemented entirely through non-binding guidance
  - Provides clarity in the review procedures for De Novo requests
  - Provides regulatory framework for De Novo program, similar to 510(k) and PMA regulations

What's in the De Novo Final Rule?

What is the De Novo Final Rule?

- Adds new regulations to the Code of Federal Regulations (CFR) that govern the De Novo review process
- 21 CFR 860: Medical device classification procedures
- De Novo regulations placed at **21 CFR 860 Subpart D**

21 CFR 860 Subpart D Overview

- **21 CFR 860 Subpart D: 860.200 – 860.260**
  - 860.200: Purpose and applicability.
  - 860.210: De Novo request format.
  - 860.220: De Novo request content.
  - 860.230: Accepting a De Novo request.
  - 860.240: Procedures for review of a De Novo request.
  - 860.250: Withdrawal of a De Novo request.
  - 860.260: Granting or declining a De Novo request.

21 CFR 860.200 and 21 CFR 860.210

- **21 CFR 860.200: Purpose and applicability**
  - Explains the purpose of the De Novo classification process
  - Distinguishes between post-Not Substantially Equivalent (NSE) and direct De Novos
- **21 CFR 860.210: De Novo request format**
  - Specifies electronic format
  - Specifies where to send the De Novo request
  - Requires De Novo request to be submitted in English

21 CFR 860.220:
De Novo request content.

- Table of contents
- Administrative information
- Regulatory history
- Device name
- Indications for use
- Device description
- Alternative practices and procedures
- Classification summary
- Summary of risks and mitigations
- Proposed special controls
- Classification recommendation
- Standards
- Summary of studies
- Benefit and risk considerations
- Technical sections:
  - Non-clinical testing
  - Software
  - Clinical testing
- Other information
  - Bibliography
  - Other information reasonably known to the requester
  - Other information to support reasonable assurance of safety and effectiveness
- Samples (if requested)
- Labeling

Blue text: De Novo classification-specific elements

21 CFR 860.230:
Accepting a De Novo request.

- Codifies acceptance review process
  - **Aligns with current Refuse-to-Accept (RTA) guidance for De Novo requests and RTA policies for other programs**
  - Acceptance means the De Novo request contains the information necessary to permit a substantive review.
  - FDA will perform an acceptance review within 15 days of receipt.
  - If acceptance review not performed, the file is automatically accepted.

21 CFR 860.230:
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  - If acceptance review not performed, the file is automatically accepted.

21 CFR 860.230(c):
Accepting a De Novo request.

- FDA may **refuse to accept** a De Novo if:
  - Existing open or pending submission (510(k), PMA, etc.) or reclassification petition for the same device and indication
  - De Novo request is incomplete or does not follow proper format
  - De Novo request is for more than one type of device
  - Requester has not responded (or provided a justification for not responding) to a previous deficiency

21 CFR 860.240:
Procedures for review of a De Novo request.

- Review takes place in 120 days (statutory requirement, but 150 days per MDUFA IV)
- Outlines additional information request process
- Outlines inspection authority
  - Data integrity
  - Quality System Regulation inspection for critical and/or novel manufacturing processes

21 CFR 860.250:
Withdrawal of a De Novo request.

- De Novo requests are considered withdrawn when:
  - Requester voluntarily withdraws De Novo request
  - Requester does not respond to RTA decision within 180 days
  - Requester does not respond to additional information request within 180 days
  - Requester does not permit FDA to inspect facilities at a reasonable time and in a reasonable manner

21 CFR 860.260:
Granting or declining a De Novo request.

- **Granting** decisions
  - Grant De Novo request unless there is a reason to decline
  - Within 30 days of granting, a notice will be published in the Federal Register to update the CFR with the new regulation and special controls (if class II)
  - Device can be used as a predicate for future 510(k)s, when necessary
- **Decline** decisions
  - Sent by written order to the requester
  - Include all outstanding deficiencies
- Specifies that final decisions are always based on the classification criteria explained in 21 CFR 860.7

Reasons for Declining
per 21 CFR 860.260(c):

Ineligibility

- Not a device or combination product
- Device type has already been approved in existing PMAs
- Device type is already classified into class I, class II, or class III (including unclassified devices)

General

- Device does not meet criteria in section 513(a)(1) of the FD&C Act for classification into class I or II
- False statement of material fact or a material omission
- Labeling does not comply with 21 CFR 801 or 809 (*in vitro* diagnostics)

Reasons for Declining
per 21 CFR 860.260(c):

Data

- Inspection results in determination that general or general & special controls would not provide reasonable assurance of safety and effectiveness (RASE)
- Nonclinical study was not performed according to 21 CFR 58 and the practices used in conducting the study do not support the validity of the study
- Clinical study was not performed in accordance with 21 CFR 50, 21 CFR 56, or 21 CFR 812.28(a) (good clinical practices) such that subject rights or safety were not adequately protected or the supporting data was found to be otherwise unreliable
- A clinical or nonclinical study was either (i) not completed per the study protocol or (ii) deficiencies related to the study have not been adequately addressed
- After a De Novo request has been accepted for review, the requester makes significant unsolicited changes to the device's (i) indications for use or (ii) technological characteristics

De Novo Final Rule: Other Updates

- Minor editorial changes to 21 CFR 860
  - scope, definitions
- Addition of confidentiality provisions for De Novo requests
  - De Novo files are not available for public disclosure (including their existence) until De Novo request is granted

De Novo Regulation Distinctives

- Specifies submission content requirements
- Codifies acceptance review process
- Adds specific inspection authority
- Outlines specific reasons for declining a De Novo, including reasons related to eligibility, inspections, and non-clinical and clinical data deficiencies

De Novo Guidance Updates

Updated De Novo Guidances

- De Novo Program: De Novo Classification Process (Evaluation of Automatic Class III Designation)
- De Novo User Fees: User Fees and Refunds for De Novo Classification Requests
- De Novo Actions/Clock: FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals
- De Novo RTA: Acceptance Review for De Novo Classification Requests

Summary of Changes

- Guidances updated to reflect changes for consistency with the final rule.
- De Novo final rule largely reflects the existing process as implemented through guidance. Therefore, changes to the guidances are generally not substantive.
- Minor updates to guidances to reflect the final rule include:
  - Adding references to 21 CFR 860
  - An updated acceptance checklist based on 21 CFR 860

De Novo Program Guidance

- **Purpose: Provide overview of De Novo classification pathway and FDA review process**
- Explains when De Novo classification is and is not appropriate (eligibility)
- Emphasizes the importance of early interaction with the Agency (Pre-Submission)
- Outlines the De Novo request review process
- Explains what happens when De Novo is granted

De Novo User Fees Guidance

- **Purpose: Provide overview of user fee policy for De Novo requests**
- Explains when and how to pay a user fee for a De Novo request
- Explains circumstances under which FDA will or will not refund a user fee
- Adding minor clarifications in refunds policy

De Novo Actions/Clock Guidance

- **Purpose: Describe actions that FDA and industry may take on De Novo requests, and how those actions affect the FDA review clock**
- Describes FDA actions (grant, decline, request information)
  - Enumeration of each reason why a De Novo may be declined, referencing 21 CFR 860.260(c)
- Describes industry actions (submitting or withdrawing De Novo requests, or submitting additional information)
- Describes De Novo performance goals for MDUFA IV

De Novo RTA Guidance

- **Purpose: Ensure De Novo request is acceptable for substantive review**
- Facilitates efficient and timely review
- Similar to RTA policies for 510(k) and PMA
  - Intend to complete RTA review within 15 calendar days of receiving De Novo
  - De Novo is considered accepted if RTA review is not completed within 15 calendar days
- Fulfills MDUFA IV commitment (“submission checklist”)

Specific Changes – RTA Guidance

Background

- Current RTA checklist is split into two:
  - Appendix A – Acceptance Checklist (**required**)
  - Appendix B – Recommended Checklist (**not required**)
- New RTA checklist requires all content described in 21 CFR 860.220 and essentially combines both Required and Recommended checklists, **so all elements are now Required**

Changes

- Current RTA checklist includes items such as:
  - Intended use
  - Device description
  - Proposed special controls (if proposing class II)
- New RTA checklist adds items such as:
  - Prior submissions
  - Classification summary (eligibility analysis)
  - Device labeling

Keep in mind…

- Final rule, updated guidances, and RTA checklist are not for implementation until **January 3, 2022.**
- For any file received prior to January 3, 2022, FDA will review under existing policies.
- Both current and updated RTA guidances are published on FDA's website so you can prepare for the change.

What's Ahead

- Electronic Submission Template And Resource (eSTAR)
  - Official De Novo eSTAR anticipated to be available to use after January 3, 2022
  - eSTAR will reflect items required by the updated RTA checklist
  - See the voluntary eSTAR Program webpage

De Novo Resources

- De Novo Final Rule in the Federal Register
- De Novo Classification Requests (includes guidance links at the bottom of the webpage)
- Other resources
  - De Novo Transparency Web Page
  - De Novo Searchable Database

Resources

De Novo Final Rule	www.federalregister.gov/documents/2021/10/05/2021-21677/medical-device-de-novo-classification-process
De Novo Classification Requests	www.fda.gov/medical-devices/premarket-submissions/de-novo-classification-request
De Novo Classification Process (Evaluation of Automatic Class III Designation) ("De Novo Program Guidance")	www.fda.gov/regulatory-information/search-fda-guidance-documents/de-novo-classification-process-evaluation-automatic-class-iii-designation
User Fees and Refunds for De Novo Classification Requests ("De Novo User Fees")	www.fda.gov/regulatory-information/search-fda-guidance-documents/user-fees-and-refunds-de-novo-classification-requests
FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals ("De Novo Actions/Clock")	www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-de-novo-classification-requests-effect-fda-review-clock-and-goals
Acceptance Review for De Novo Classification Requests ("De Novo RTA Guidance", both current and new)	www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-review-de-novo-classification-requests
Voluntary eSTAR Program	www.fda.gov/medical-devices/premarket-notification-510k/voluntary-estar-program
CDRH Transparency – De Novo Summaries	www.fda.gov/about-fda/cdrh-transparency/evaluation-automatic-class-iii-designation-de-novo-summaries
De Novo Searchable Database	www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm

Peter J. Yang

De Novo Program Lead

FDA/CDRH/OPEQ/Office of Regulatory Programs

Peter.Yang@fda.hhs.gov

Summary

- The De Novo review process has evolved since its creation in 1997.
- The De Novo regulations codify the processes for De Novo request review, which largely reflect current review practices.
- The De Novo program guidance documents have been updated to reflect the final rule, including a new RTA checklist that essentially combines the Recommended and Required checklists from the current RTA guidance.
- The De Novo final rule and associated guidances are for implementation on January 3, 2022.


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Let's Take Your Questions

- **To Ask a Question:**
  1. Please "Raise Your Hand" 

  2. Moderator will Announce Your Name to Invite You to Ask Your Question
  3. Unmute yourself when called

- **When Asking a Question:**
  - Ask 1 question only
  - Keep question short
  - No questions about specific submissions or data-specific

- **After Question is Answered:**
  - Please mute yourself again
  - If you have more questions - raise your hand again

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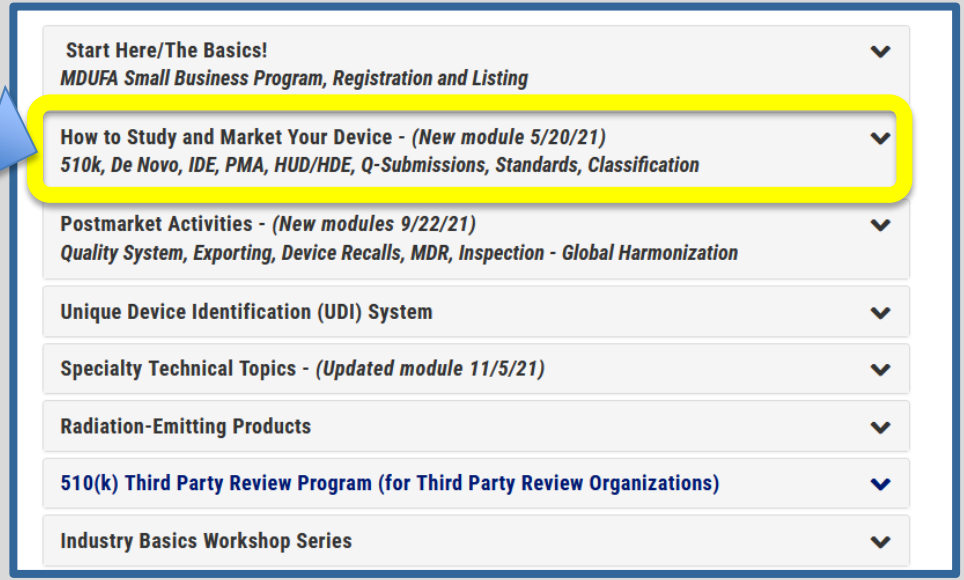

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