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510(k) Premarket Notification and De Novo Requests

Ryan Michael Fournier

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Agenda

- 510(k) Premarket Notification
- De Novo Requests
- Questions?

510(k) Premarket Notification

What is a 510(k) Premarket Notification?

A 510(k) is a premarket submission that is required for all Class I and Class II devices that are not 510(k)-exempt

Must demonstrate the device is ***substantially equivalent*** to a ***predicate device***

User Fee's required: $12,745 ($3,186 for small businesses)

Device Classification

- Degree of FDA regulation and the type of submission required depends on the applicable ***device classification***

Device Classification	Risk Level	FDA Requirements	Premarket Review
Class I	Low Risk Devices	General Controls	None (for most)
Class II	Moderate Risk Devices	General and Special Controls	510(k) Premarket Notification
Class III	High Risk and Novel Devices	General Controls	Premarket Approval (PMA) or *de novo* Request

When is 510(k) Required/Not Required?

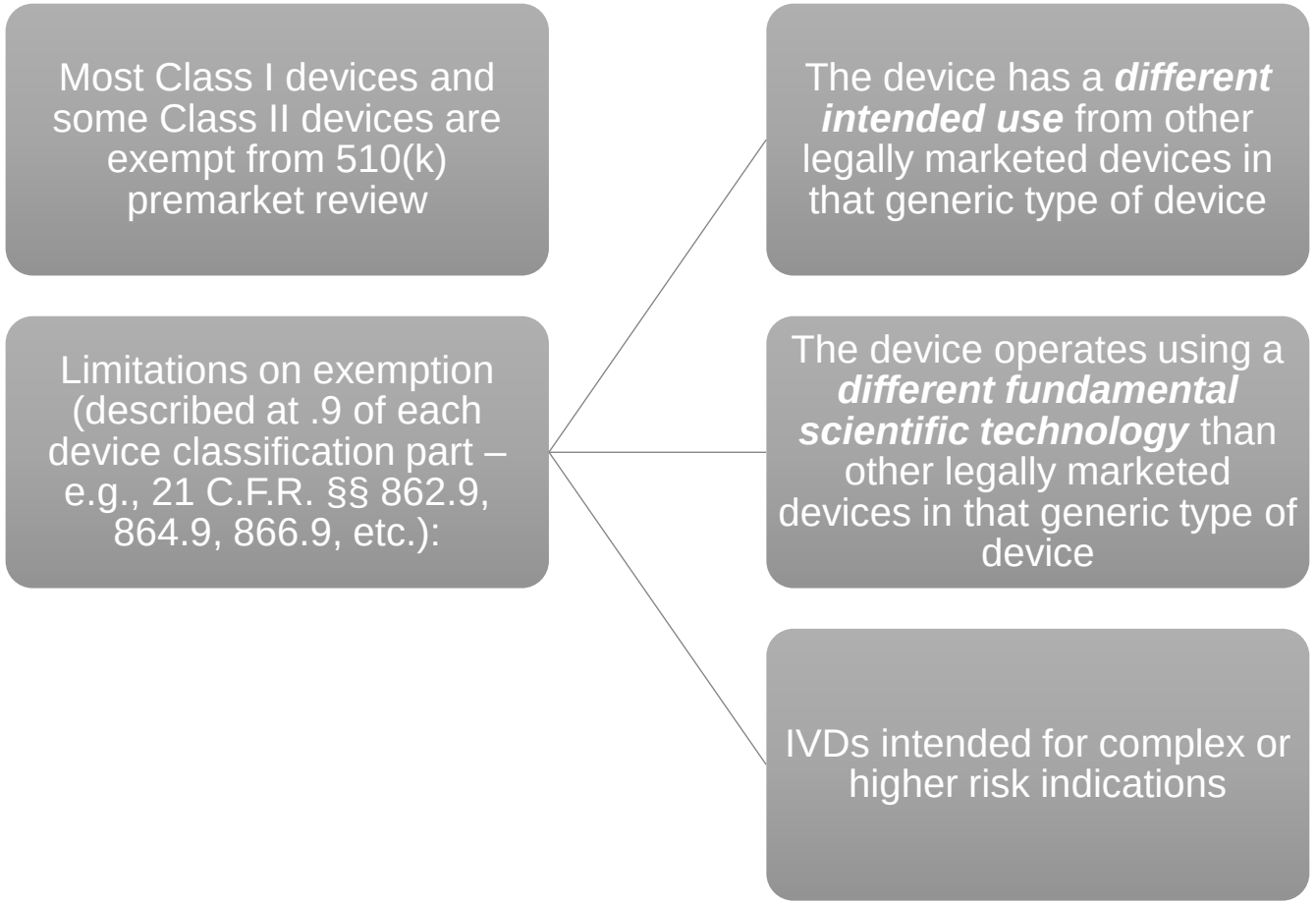
When is a 510(k) required?

- Commercial distribution (marketing) for the first time
- For certain device changes/modifications

When is a 510(k) not required?

- For devices in distribution before May 28, 1976 (i.e., grandfathered)
- Devices in development stage only (not for commercial marketing)
- For device components (i.e., not finished devices or finished device accessories).

510(k) Premarket Notification Exemptions



What is a Predicate Device?

Predicate Device:

- A pre-1976 device that did not require a PMA; or
- A device that has been reclassified from Class III to Class II or I (e.g., via the *de novo* process); or
- **A device previously cleared via the 510(k) process**

Multiple predicates can be used when seeking 510(k) clearance for a device, if the device:

- Combines features from two or more predicate devices with the same intended use
- Has more than one intended use
- Has more than one **indication for use** under the same **intended use**

What is Substantial Equivalence?

Substantial Equivalence – the subject device must:

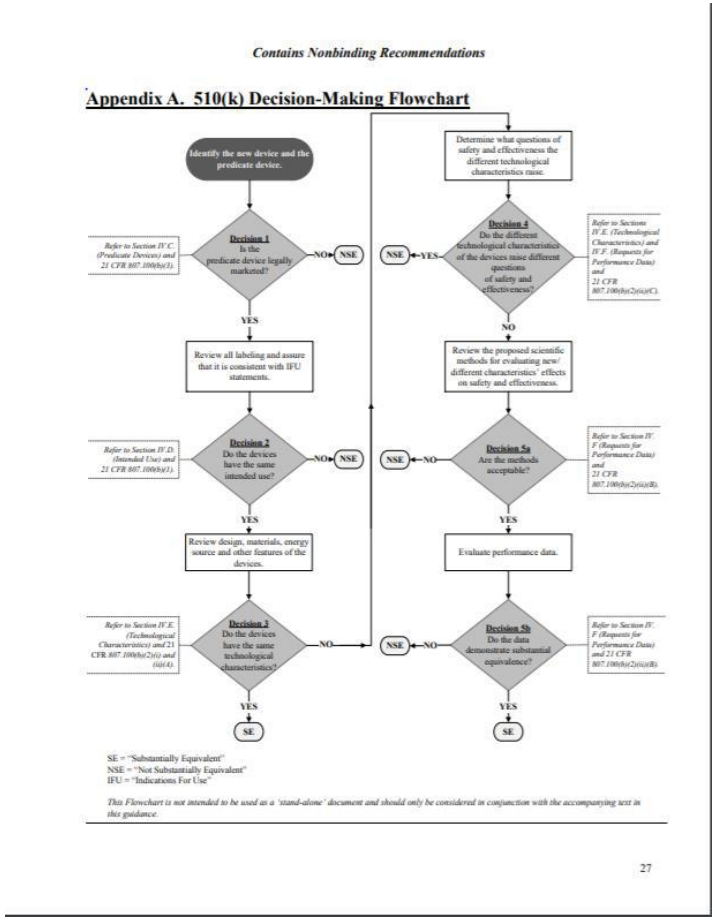
- Have the **same intended use** as the predicate, and
- Either:
  - Have the **same technological characteristics** as the predicate, **or**
  - Have **different technological characteristics**, and
    - Have data to establish that the subject device is as safe and as effective as the predicate, and
    - Does not raise different questions of safety and effectiveness than the predicate device

Significant changes in technology or new intended use can result in a **not substantially equivalent (NSE) determination**

- Could trigger PMA or *de novo* requiremrent

What is Substantial Equivalence

- Check out FDA Guidance – The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (July 2014)
  - Appendix A Flowchart
  - https://www.fda.gov/media/82395/download



Contains Nonbinding Recommendations

Appendix A. 510(k) Decision-Making Flowchart

Identify the new device and the predicate device.

Decision 1 Is the predicate device legally marketed? — NO → NSE

YES

Review all labeling and assure that it is consistent with IFU statements.

Decision 2 Do the devices have the same intended use? — NO → NSE

YES

Review design, materials, energy source and other features of the devices.

Decision 3 Do the devices have the same technological characteristics? — NO → Determine what questions of safety and effectiveness the different technological characteristics raise.

YES → SE

Decision 4 Do the different technological characteristics of the devices raise different questions of safety and effectiveness? — YES → NSE

NO

Review the proposed scientific methods for evaluating new/different characteristics' effects on safety and effectiveness.

Decision 5a Are the methods acceptable? — NO → NSE

YES

Evaluate performance data.

Decision 5b Do the data demonstrate substantial equivalence? — NO → NSE

YES → SE

SE = "Substantially Equivalent"
NSE = "Not Substantially Equivalent"
IFU = "Indications For Use"

This Flowchart is not intended to be used as a 'stand-alone' document and should only be considered in conjunction with the accompanying text in this guidance.

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Question

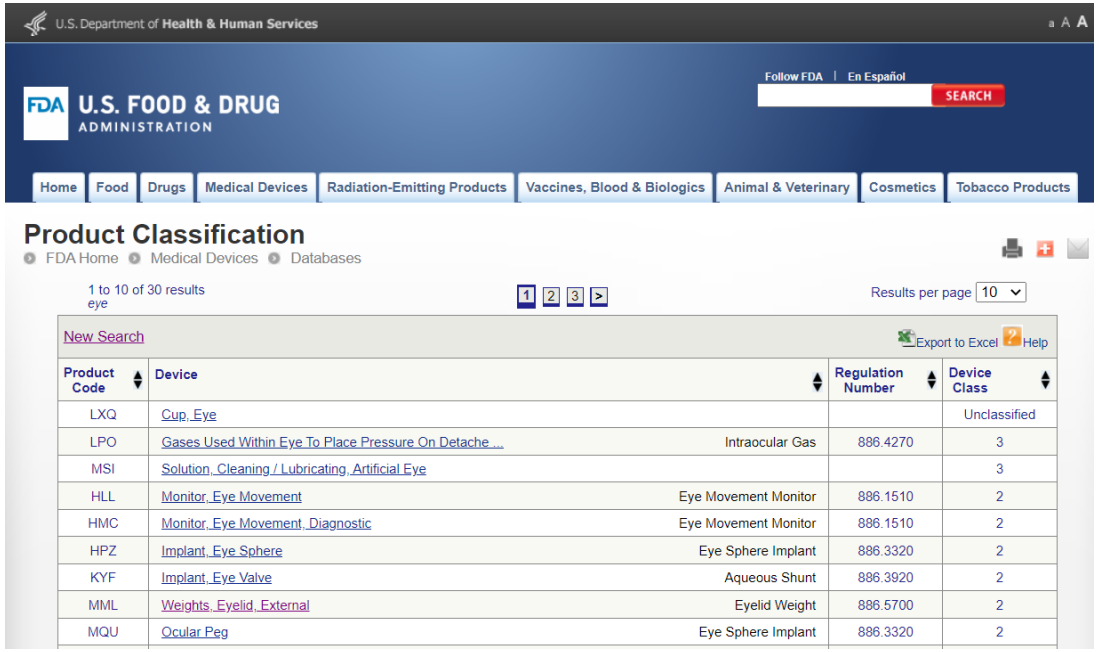
- What question(s) should you ask when determining substantial equivalence?
  - Is the predicate device legally marketed?
  - Do the devices have the same intended use?
  - Do the devices have the same technological characteristics?
  - Do the different technological characteristics of the devices raise different questions of safety and effectiveness?
  - All the above.

Strategizing for a 510(k) Submission

Strategizing for a 510(k) Submission

1. Identify predicate device(s)
2. Compare subject device with predicate
3. Identify what testing is needed to support substantial equivalence
4. Consider pre-submission meeting with FDA

Strategizing for a 510(k) Submission – Identify Product Classification

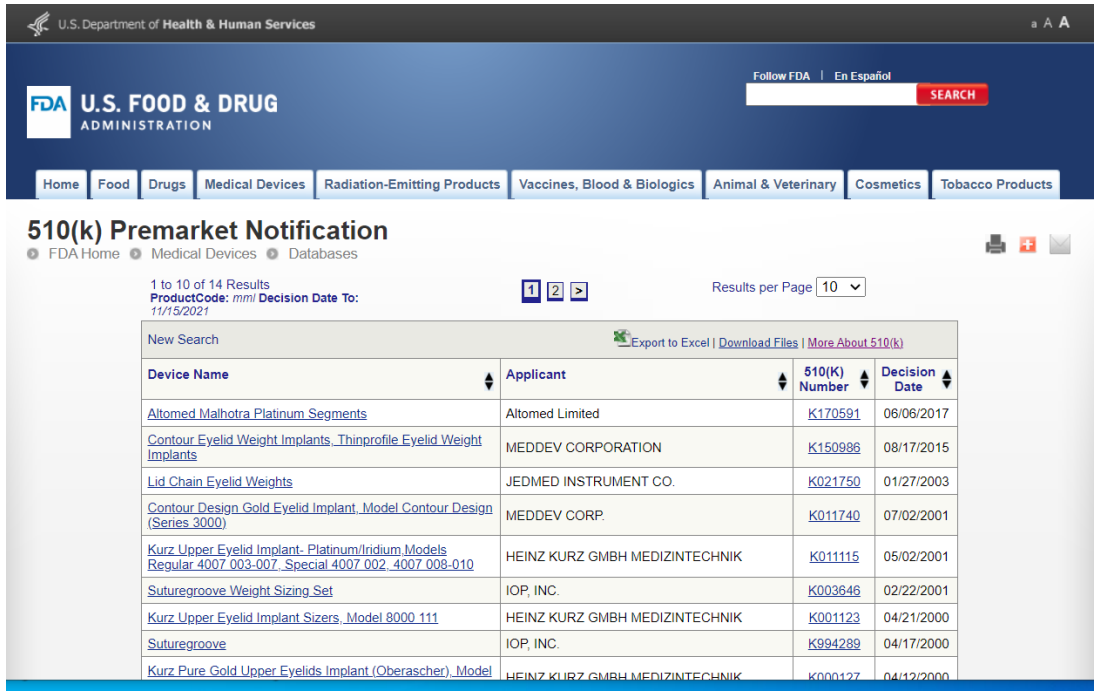


Product Code	Device		Regulation Number	Device Class
LXQ	Cup, Eye			Unclassified
LPO	Gases Used Within Eye To Place Pressure On Detache ...	Intraocular Gas	886.4270	3
MSI	Solution, Cleaning / Lubricating, Artificial Eye			3
HLL	Monitor, Eye Movement	Eye Movement Monitor	886.1510	2
HMC	Monitor, Eye Movement, Diagnostic	Eye Movement Monitor	886.1510	2
HPZ	Implant, Eye Sphere	Eye Sphere Implant	886.3320	2
KYF	Implant, Eye Valve	Aqueous Shunt	886.3920	2
MML	Weights, Eyelid, External	Eyelid Weight	886.5700	2
MQU	Ocular Peg	Eye Sphere Implant	886.3320	2

- FDA Product Classification Database:
  - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm

Strategizing for a 510(k) Submission – Identify Potential Predicates

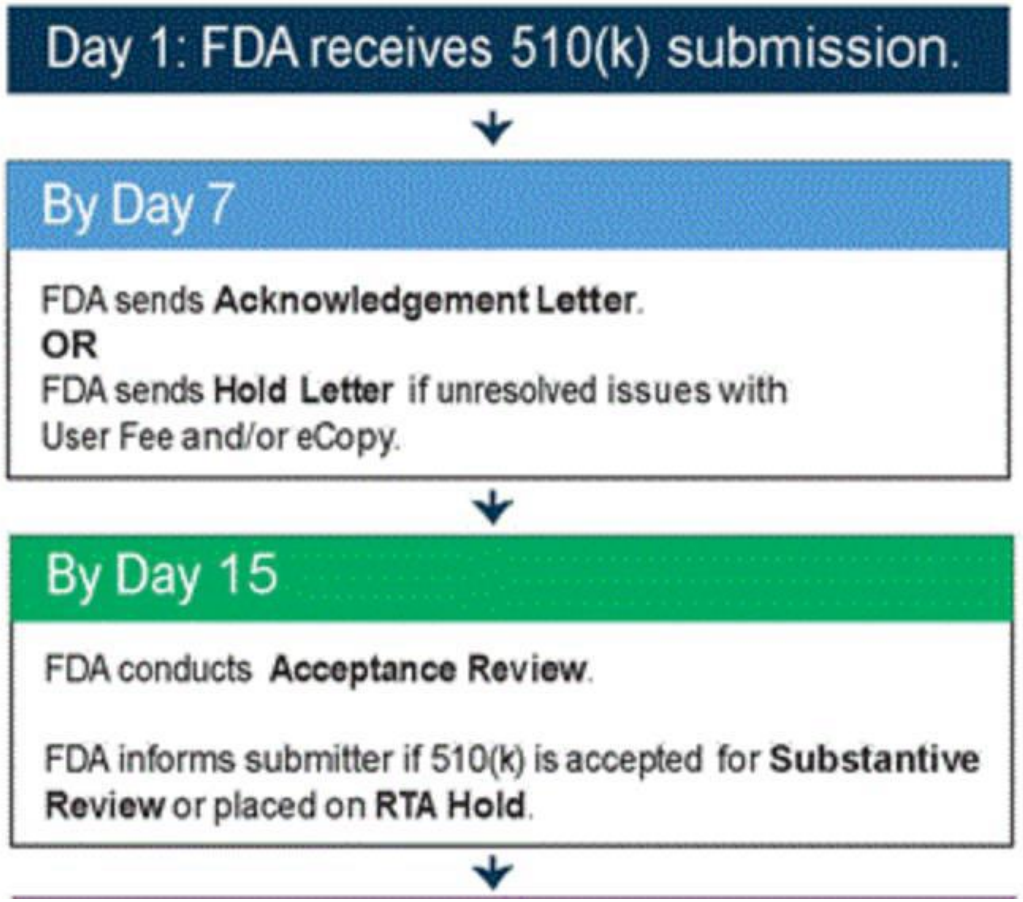
- FDA 510(k) Premarket Notification Database:
  - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm



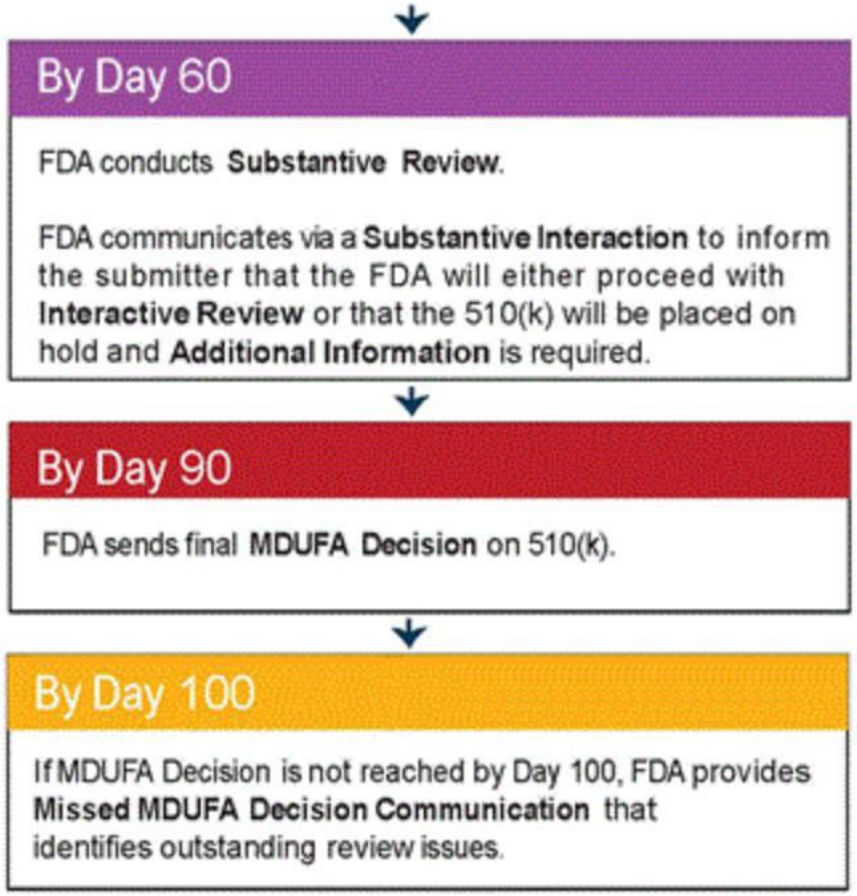
Contents of a 510(k)

- Device name
- Sponsor identification
- Classification
- Description
- Indications for Use
- Substantial Equivalence Comparison
- Software
- Standards
- Performance Testing
- Biocompatibility
- Sterility
- Electromagnetic Compatibility and Electrical, Mechanical, and Thermal Safety
- Labeling
- 510(k) Summary of Statement
- Truthful and Accuracy Statement
- Form FDA 3674 (clinicaltrials.gov compliance)
- Form FDA 3601 (user fees)

510(k) Review Process



510(k) Review Process (cont'd)

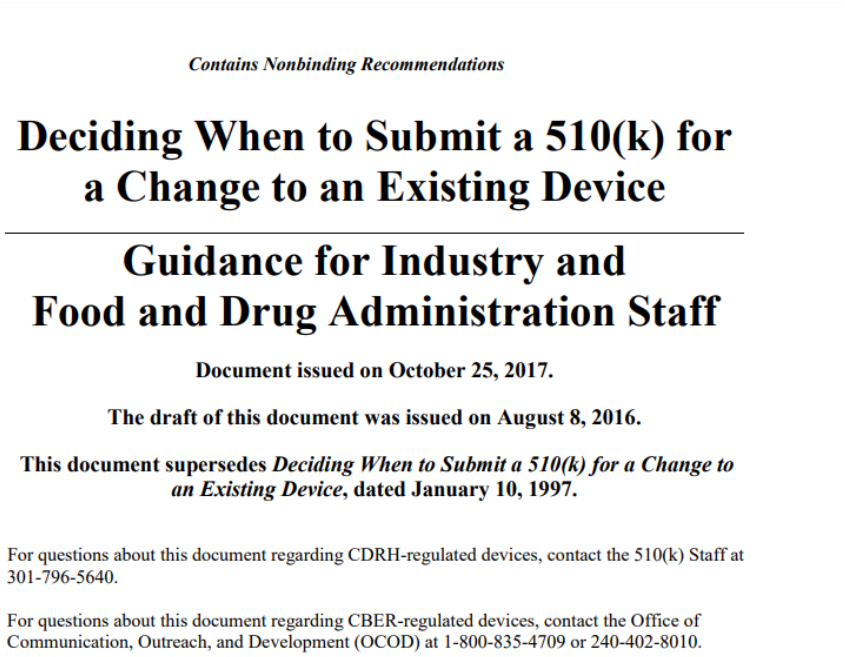


Question

- At least how many days prior to marketing a device must a manufacturer submit its 510(k) notice?
  - 30 days
  - 60 days
  - 90 days
  - 120 days
  - No set requirement

Changes to a 510(k) Cleared Device

- **A new 510(k) is required for each type of changes to a previously cleared device**
  - A change or modification that could significantly impact the safety or efficacy of the device
  - A major change or modification to the intended use of the device
- **FDA Guidance**
  - Labeling Changes
  - Technology, engineering, and performance changes
  - Material changes
- https://www.fda.gov/media/99812/download



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Deciding When to Submit a 510(k) for a Change to an Existing Device

Guidance for Industry and Food and Drug Administration Staff

Document issued on October 25, 2017.

The draft of this document was issued on August 8, 2016.

This document supersedes *Deciding When to Submit a 510(k) for a Change to an Existing Device*, dated January 10, 1997.

For questions about this document regarding CDRH-regulated devices, contact the 510(k) Staff at 301-796-5640.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

De Novo Requests

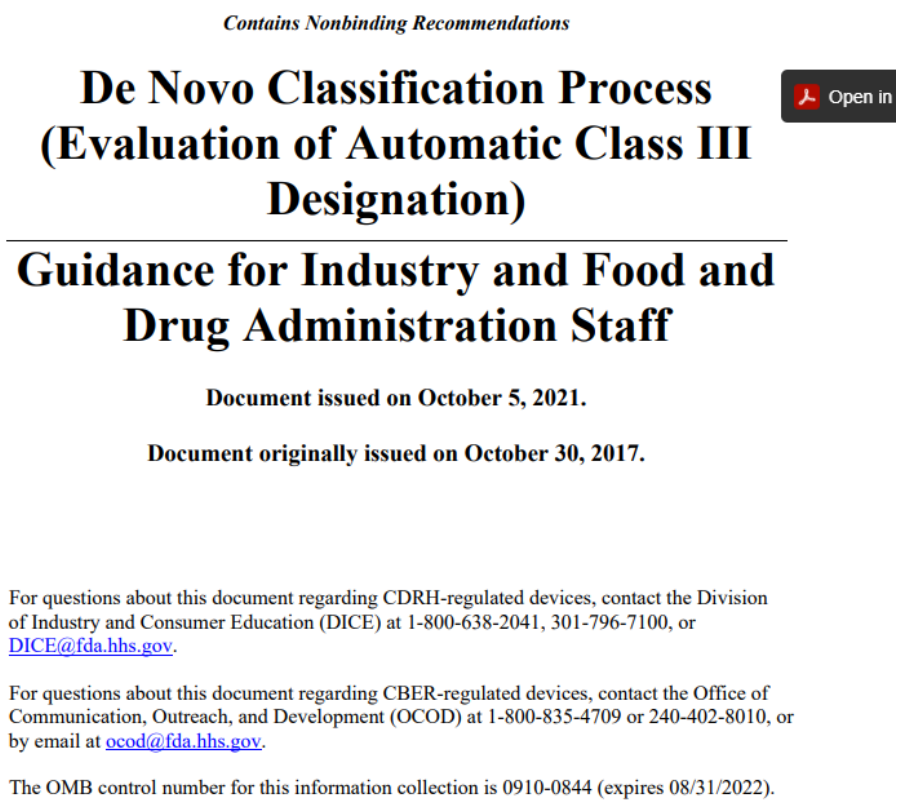
What is a *De Novo* Request?

- "*De Novo*" pathway – Established by the Food and Drug Administration Modernization Act of 1997 (FDAMA) to provide a new mechanism for reclassification of certain lower risk devices from Class III to Class I or II.

Background

- Before and After
  - Before
    - Burdensome, lengthy process
    - Required a 510(k) submission and an NSE decision due to a lack of a predicate device before *de novo* classification could be sought
  - After
    - The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), created a more streamlined alternative
    - Submission of a 510(k) and an NSE decision prior to submission of a *de novo* **not** required

FDA Guidance



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

Open in

Guidance for Industry and Food and Drug Administration Staff

Document issued on October 5, 2021.

Document originally issued on October 30, 2017.

For questions about this document regarding CDRH-regulated devices, contact the Division of Industry and Consumer Education (DICE) at 1-800-638-2041, 301-796-7100, or DICE@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.

The OMB control number for this information collection is 0910-0844 (expires 08/31/2022).

- ***De Novo* FDA Guidance** – issued on October 5, 2021
- https://www.fda.gov/media/72674/download

FDA Review Process

- Pre-Submission (optional)
- Submission of De Novo Request
- FDA Acceptance Review
- FDA Substantive Review
- Any Additional Information Needed
- Target 120 days

Recommended Content for a *De Novo* Request

- Administrative information
- Regulatory history
- Device information and summary
- Indications for use
- Change summary (if appropriate)
- Classification summary and recommendation
- Supporting protocols and/or data
- Summary of benefits
- **Summary of identified risks to health**
- **Risk and mitigation information**
- **Benefit-risk considerations**
- Device labeling

FDA Benefit-Risk Determination

- Extent of probable benefit
- Assessment of the Risks
- Uncertainty
- Patient-reported outcomes
- Characterization of disease/condition
- Patient perspectives
- Availability of alternative treatments/diagnostics

De Novo Pathway Not Limited to Low-Risk Devices

- Examples of *de novos* granted for devices presenting more than low risk:
  - Active implantable bone conduction hearing system (DEN 170009)
  - Radiological computer-assisted diagnostic software for lesions suspicious for cancer (DEN 170022)
  - High intensity ultrasound for prostate tissue ablation (DEN 150011)
  - See FDA *De Novo* Database
    - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm

Pros of the *De Novo* Process

- Enables companies to bring more innovative low risk products to market, or to make new claims for existing Class I or II products, without having to go through the more rigorous PMA process
- Can establish limit barrier to entry to competitors through special controls and classification regulation
- Not a PMA
- May be the only alternative

Cons of the *De Novo* Process

Statute says *de novo* classifications must occur within 120 days – this does not happen

Uncertainty and variability of data requirements

Establishment of a new product code can facilitate 510(k) filings by competitors, and more expeditious market clearance

User fee is significant – $112,457 ($28,114 for small business)

What Happens After a *De Novo* is Granted?

- Device may be legally marketed subject to the applicable general and special controls established
- FDA will post an order announcing the new classification and controls, and will subsequently publish this in the Federal Register
- FDA will post summary online

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Thank you!

Ryan Michael Fournier

Rfournier@wiley.law