Premarket Notification (510(k)) and De Novo Requests

Introduction to Medical Device Law and Regulation
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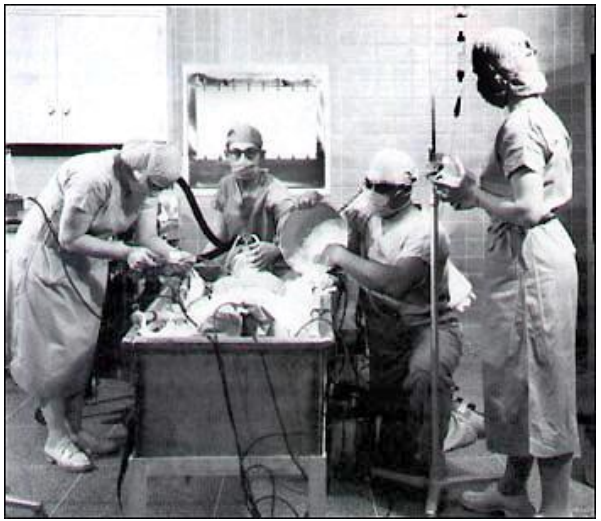
Agenda

- **Overview of the 510(k) Program**
- What Is 510(k)?
- What Is a Predicate Device?
- What Does “Substantial Equivalence” Mean?
- FDA 510(k) Review Process
- How to Strategize for a 510(k) Submission
- Other Types of 510(k)s
- Confidential, Proprietary, and Trade Secret Information
- User Fees for 510(k) Submissions
- Modifications to a Legally Marketed Device
- What Is a De Novo Petition?

Overview of the 510(k) Program

- The 510(k) Program was established over 45 years ago as part of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) in 1976.
- Devices were much simpler in 1976:
  - The electronics revolution and trend towards miniaturization had not yet begun.
  - There was no internet.
  - There were few combination products.



Overview of the 510(k) Program

- 510(k) is the largest premarket program at CDRH, addressing a great diversity of device types.
  - 510(k) is the regulatory pathway by which most medical devices go to market in the United States.
  - Most new indications for use and most new technologies go to market via the 510(k) pathway.
- Approximately 50% of devices go to market as “510(k)-exempt.”
- Many significant-risk devices go to market via 510(k) route, including several implants and life-sustaining and life-supporting devices.

Overview of the 510(k) Program

- There are approximately 3,000 to 4,000 510(k) submissions per year, compared to 30-40 premarket approval applications (PMAs) (several hundred PMA supplements).
- The 510(k) Program is supported in part by user fees.
- The 510(k) Program allows for innovation and flexibility to provide for reasonable assurance of the safety and effectiveness of a device to demonstrate substantial equivalence.

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What Is 510(k)?

- Premarket notification
- Section 510(k) of the FDCA
- 21 C.F.R. Part 807, subpart E
- Allows FDA to make a determination regarding substantial equivalence (SE) or not substantial equivalence (NSE)
- “Clearance” of a device—not an “approval”
- The classification process for devices

What 510(k) Is Not

- A form
- Establishment registration
- Device listing
- Premarket approval (PMA)
- De novo classification request (de novo petition)

Relevant Statutory Provisions

- Under Section 510(k) of the FDCA, a person proposing to market a medical device for the first time must submit a notification to FDA at least 90 days before introducing the device into commercial distribution, unless the device has been exempted from the premarket notification requirement. 21 U.S.C. § 360(k).
- Section 513(f)(1) provides that a postamendment device is automatically Class III (and subject to the PMA approval requirement), unless the device is "substantially equivalent" to an already marketed Class I or Class II device. 21 U.S.C. § 360c(f)(1).

510(k) Classification of Postamendments Devices

- A 510(k) classifies postamendments devices by:
  - Finding the individual device substantially equivalent (SE) to the type in the classification regulation; or
  - Finding the individual device not substantially equivalent (NSE) to the type in the classification regulation.
    - If it is NSE, the device is automatically placed into Class III and requires: (1) PMA; (2) de novo review to be placed in Class I or Class II; or (3) reclassification.

Devices Eligible for 510(k) Review

- **Class I – *Most are exempt from 510(k)***
  - Most Class I devices have been exempted from 510(k) review.
  - Class I devices are generally subject only to "general controls," because the risks are well understood and general controls are sufficient to provide reasonable assurance of safety and effectiveness.
- **Class II – *Most are subject to 510(k)***
  - Most Class II devices may be put into commerce only after submission of a premarket notification submitted pursuant to Section 510(k) of the FDCA and **if** a "substantial equivalence" determination from FDA.
  - Class II devices are moderate risk devices for which general controls alone are insufficient to provide reasonable assurance of their safety and effectiveness, but special controls can be identified to address the risks—in addition to the general controls of the FDCA.
- **Class III – *Most are subject to PMA***
  - Most Class III devices are subject to FDA approval of a premarket approval application (PMA) as a precondition of commercial distribution.
  - FDA may, however, clear a 510(k) for a Class III device if the 510(k) demonstrates that the device is substantially equivalent to a preamendments Class III device on which the FDA had not yet imposed the PMA requirement.

510(k)-Exempt Devices

- The Medical Device Amendments of 1976 required manufacturers to submit a 510(k) for every device not requiring a PMA. Through rulemaking, FDA could exempt generic types of device from the 510(k) requirement. FDCA § 513(d)(2)(A), 21 U.S.C. § 360c(d)(2)(A).
  - FDA exempted through rulemaking 574 generic types of Class I devices from the 510(k) requirement.
- In 1997, Congress made the decision to exempt all Class I devices from the 510(k) requirement, unless a device is intended for a use that is of substantial importance in preventing impairment to human health or presents a potential unreasonable risk of illness or injury. FDCA § 510(l), 21 U.S.C. § 360(l).
  - Class I devices that meet the "reserved" criteria are referred to as "reserved" devices. See 63 Fed. Reg. 5,387 (Feb. 2, 1998) (listing Class I reserved devices).
  - The 1997 Act also permitted FDA to exempt Class II device types for which a 510(k) is not necessary. FDCA § 510(m), 21 U.S.C. § 360(m).

510(k)-Exempt Devices

- Manufacturers of 510(k)-exempt devices are thus permitted to make substantial equivalence decisions themselves.
- Even though a 510(k) is not required, a manufacturer must still comply with other requirements for marketing, such as registration and listing and labeling requirements.

FDCA Section 510(l) for Class I Device Types

(1) A report under subsection (k) is **not required** for a device intended for human use that is exempted from the requirements of this subsection under subsection (m) or is within a type that has been classified into class I under section 513. **The exception established in the preceding sentence does not apply to any class I device that is intended for a use which is of substantial importance in preventing impairment of human health, or to any class I device that presents a potential unreasonable risk of illness or injury.**

(2) Not later than 120 calendar days after the date of enactment of the 21st Century Cures Act [December 13, 2016] and at least **once every 5 years thereafter**, as the Secretary determines appropriate, the Secretary shall identify, through publication in the Federal Register, any type of class I device that the Secretary determines no longer requires a report under subsection (k) to provide reasonable assurance of safety and effectiveness. Upon such publication-

(A) each type of class I device so identified shall be exempt from the requirement for a report under subsection (k); and

(B) the classification regulation applicable to each such type of device shall be deemed amended to incorporate such exemption.

FDCA Section 510(m) for Class II Device Types

(1) The Secretary shall-

(A) not later than 90 days after the date of enactment of the 21st Century Cures Act [December 13, 2016] and at least **once every 5 years** thereafter, as the Secretary determines appropriate-

(i) publish in the Federal Register a notice that contains a list of each type of class II device that the Secretary determines no longer requires a report under subsection (k) to provide reasonable assurance of safety and effectiveness; and

(ii) provide for a period of not less than 60 calendar days for public comment beginning on the date of the publication of such notice; and

(B) not later than 210 calendar days after the date of enactment of the 21st Century Cures Act [December 13, 2016], publish in the Federal Register a list representing the Secretary's final determination with respect to the devices contained in the list published under subparagraph (A).

FDCA Section 510(m) for Class II Device Types (continued)

(2) Beginning on the date that is 1 calendar day after the date of publication of the final list under paragraph (1)(B), the Secretary may exempt a class II device from the requirement to submit a report under subsection (k), upon the Secretary's own initiative **or a petition of an interested person**, **if the Secretary determines that such report is not necessary to assure the safety and effectiveness of the devi**ce. The Secretary shall publish in the Federal Register notice of the intent of the Secretary to exempt the device, or of the petition, and provide a 60-calendar-day period for public comment. Within 120 days after the issuance of the notice in the Federal Register, the Secretary shall publish an order in the Federal Register, that sets forth the final determination of the Secretary regarding the exemption of the device that was the subject of the notice. **If the Secretary fails to respond to a petition within 180 days of receiving it, the petition shall be deemed to be granted.**

(3) Upon publication of the final list under paragraph (1)(B)-

(A) each type of class II device so listed shall be exempt from the requirement for a report under subsection (k); and

(B) the classification regulation applicable to each such type of device shall be deemed amended to incorporate such exemption.

Limitations on Exemption

- The 510(k) exemption has certain limitations, which are so noted in the ".9" regulation of each chapter. See, e.g., 21 C.F.R. § 878.9.
- The ".9" regulation states that the exemption from premarket notification is "only to the extent that the device has existing or reasonably foreseeable characteristics of commercially distributed devices within that generic type or, in the case of in vitro diagnostic devices, only to the extent that misdiagnosis as a result of using the device would not be associated with high morbidity or mortality."
- As a result, manufacturers must still submit a 510(k) when:
  - The device has a different intended use than the legally marketed device in that generic type
  - The device operates using a different fundamental scientific technology than the legally marketed device in that generic type
  - The device is an in vitro device and has certain, specified intended uses

Other Devices Not Subject to the 510(k) Requirement

- Preamendments Devices
- Unfinished Devices
- Finished Devices Not Sold in U.S.
- Devices Covered Under Another 510(k), e.g., Private Labeled Device
- Custom Devices
- General Purpose Articles
- Veterinary Devices
- Devices Exempt by Statute or Regulation from 510(k)

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What Is a Predicate Device?

"An identification of the legally marketed device to which the submitter claims equivalence. A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from class III to class II or I (the predicate), or a device which has been found to be substantially equivalent through the 510(k) premarket notification process."

21 C.F.R. § 807.92(a)(3)

What Can Be a Predicate for Purposes of Establishing Substantial Equivalence?

- A legally marketed device that does not require a PMA, including:
  - A preamendments device
  - A device found by FDA to be substantially equivalent
  - A 510(k)-exempt device
  - A device marketed pursuant to a granted de novo classification request
- May be legally marketed by your firm or another
- Should be chosen early in the development process in order to collect all necessary information for the 510(k) submission
  - Obtaining specifications
  - Comparative testing

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What Does "Substantial Equivalence" Mean?

- "Substantial equivalence" to a lawfully marketed predicate device is the review standard for 510(k) devices. FDCA § 513(i)(1)(A), U.S.C. § 360c(i)(1)(A); 21 C.F.R. § 807.81.
- A "substantially equivalent" device:

  (1) must have the same intended use as the predicate device, and
  (2)

  (i) must have the same technological characteristics as the predicate device, or

  (ii) if it has different technological characteristics, must be supported by information and data demonstrating that the device is as safe and effective as a legally marketed device and does not present different questions of safety or effectiveness.

  FDCA § 513(i), 21 U.S.C. § 360c(i); 21 C.F.R. § 807.100(b).
- "Different technological characteristics" means "a significant change in the materials, design, energy source, or other features of the device from those of the predicate device." FDCA § 513(i)(1)(B), 21 U.S.C. § 360c(i)(1)(B); 21 C.F.R. § 807.100(b)(2)(ii).

What Does “Substantial Equivalence” Mean?

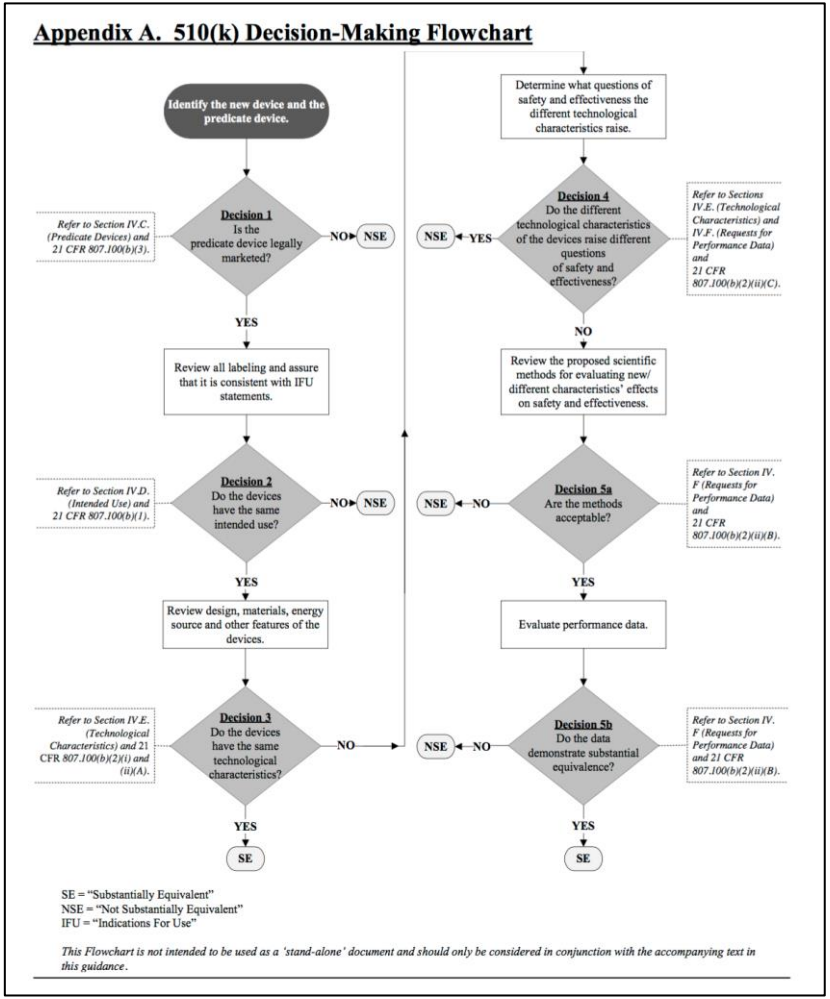
The term “substantially equivalent” is not intended to be so narrow as to refer only to devices that are identical to marketed devices nor so broad as to refer to devices which are intended to be used for the same purposes as marketed products. The Committee believes that the term should be construed narrowly where necessary to assure the safety and effectiveness of a device but not so narrowly where differences between a new device and a marketed device do not relate to safety and effectiveness.

House Report No. 853, 94th Congress, 2d Session 36-37 (1976)

What Does “Substantial Equivalence” Mean?

- Four parts to substantial equivalence decision-making process (first three prior to review of data):
  - Predicate
  - Intended use
  - Technology
  - Data

Guidance for Industry and FDA Staff: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)] (July 2014), available at https://www.fda.gov/media/82395/download.



Intended Use

- The general purpose or function of the device
  - 21 C.F.R. § 801.4
    - Regulation recently revised
    - 86 Fed. Reg. 41,383 (Aug. 2, 2021), available at https://www.govinfo.gov/content/pkg/FR-2021-08-02/pdf/2021-15980.pdf.
  - FDA determines the intended use by evaluating the device labeling (including promotional material—including the web)
  - Encompasses indications for use
  - Subject and predicate device(s) must share the same intended use

Indications for Use

- The disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including the patient population for which the device is intended.
- Indications for use is stated explicitly in the 510(k) submission on a standard form
- Indications for use is what appears in the labeling for the user

Indications for Use – Examples

- Percutaneous Vascular Catheter
  - Indications for Use – provide access to neurovasculature for diagnosis/therapy
  - Intended Use – provide access to vasculature for diagnosis/therapy

- CO_2 Laser
  - Indications for Use – skin resurfacing for wrinkle removal
  - Intended Use – skin resurfacing

Indications for Use Make a Difference

- "Scrubbing and cleaning the human body as a washcloth."
  - Not a device
- "For use as a dust particle mask."
  - Not a device, but regulated by Consumer Product Safety Commission (CPSC) and Occupational Safety and Health Administration (OSHA)
- "For use as a tourniquet."
  - Class I-exempt device under 21 C.F.R. § 878.5900
- "As a bandage for treating psoriasis."
  - Exceeds exemption for elastic bandage under 21 C.F.R. § 880.5075
  - A 510(k) is required

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Content of a 510(k) Submission

- FDA regulations detail the specific information that each 510(k) submission must contain, including, among other things:
  - Proposed labeling (21 C.F.R. § 807.87(e))
  - A statement regarding the similarities and differences between the device and others of comparable type (21 C.F.R. § 807.87(f))
  - Supporting data (21 C.F.R. § § 807.87(f) & 807.100(b)(2)(ii)(B))
  - Any additional information regarding the device requested by FDA that is necessary for FDA to make a finding as to whether or not the device is substantially equivalent to a device in commercial distribution (21 C.F.R. § 807.87(l))

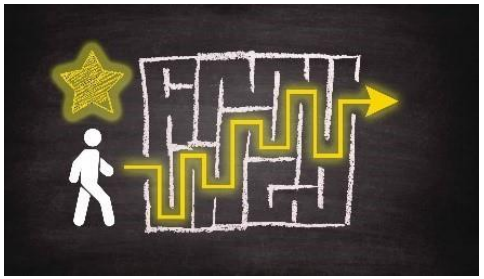
Refuse to Accept Policy for 510(k)s

- To focus FDA's review resources on complete 510(k) submissions and provide for a more efficient review process, FDA adopted a Refuse to Accept (RTA) policy for 510(k)s.
- The policy includes an early review against specific acceptance criteria.
- The submitter is informed within the first 15 calendar days after receipt of a submission if the submission is complete, and, if not, FDA identifies the missing elements.
- The 510(k) submitter may respond to an RTA notification by providing the missing information. A new submission and new user fee are not required.
- If a response to the RTA notification is not received within 180 days of the date of the notification, FDA will consider the 510(k) to be withdrawn.

See Guidance for Industry and FDA Staff: Refuse to Accept Policy for 510(k)s (Sept. 13, 2019), available at https://www.fda.gov/media/83888/download.

Refuse to Accept Policy for 510(k)s

- eSTAR Program
  - The eSTAR is a voluntary and interactive PDF form that guides submitters through the process of preparing a comprehensive medical device submission.
  - With a standardized format, submitters can ensure their submissions are complete, and CDRH can conduct premarket reviews more efficiently to help promote timely access to safe, effective, and high-quality medical devices.
  - Due to the use of automatic verification, the CDRH does not conduct a Refuse to Accept (RTA) review for submissions submitted as an eSTAR.
  - See https://www.fda.gov/medical-devices/how-study-and-market-your-device/voluntary-estar-program.



Data Requirements

- In 1990, Congress specifically authorized FDA to require clinical data in 510(k)s. Many 510(k)s include such data.
  - "[I]f deemed necessary," FDA may request "appropriate clinical or scientific data" that demonstrate that the device is as safe and effective as predicate device.

  FDCA § 513(i)(1)(A)(ii)(I), 21 U.S.C. § 360c(i)(1)(A)(ii)(I); see also 21 C.F.R. § § 807.87(l) and 807.100(b)(2)(ii)(B).
- When making such requests, FDA is required to "only request information that is necessary to making substantial equivalence determinations" and must "consider the least burdensome means of demonstrating substantial equivalence and request information accordingly."
- Data must be collected under IDE regulations. See 21 C.F.R. Part 812.

Performance Data in 510(k)s

- Bench, animal, and/or clinical data
- Most 510(k)s have performance data unless **identical** to the predicate
- Must demonstrate, using valid scientific evidence (21 C.F.R. § 860.7), that the new device is **at least** as safe and effective as the predicate

Clinical Data in 510(k)s

- Clinical data is provided in at least 10% of all 510(k)s
- Important difference with the predicate device—almost always for a new indications for use
- Must be collected under investigational device exemption (IDE) regulations (21 C.F.R. Part 812)

Valid Scientific Evidence

- All premarket review pathways, including 510(k), require valid scientific evidence. 21 C.F.R. § 860.7.
- "The valid scientific evidence used to determine the effectiveness of a device shall consist principally of well-controlled investigations . . . ." 21 C.F.R. § 860.7

Valid Scientific Evidence (continued)

- Also evidence from:
  - partially controlled studies,
  - studies and objective trials without matched controls,
  - well-documented case histories conducted by qualified experts,
  - and reports of significant human experience with a marketed device from which it can be fairly and responsibly concluded by qualified experts that there is a reasonable assurance of safety and effectiveness

21 C.F.R. § 860.7

Additional Information (AI) Request

- FDA requests AI when a 510(k) submission lacks the information necessary for the agency to continue or complete its review and to determine whether the device is SE or NSE. See 21 C.F.R. § § 807.87(l), 807.100(a)(3).
- An AI request places the 510(k) review 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 resumes upon the receipt of a complete response to the AI request in the appropriate Document Control Center.
- Under the regulations, if the AI is not submitted within 30 days following the date of the request, FDA will consider the premarket notification to be withdrawn. However, FDA automatically grants an extension of a maximum of 180 days from the date of the AI request.

See 21 C.F.R. § 807.100; see also Guidance for Industry and FDA Staff: FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals (Oct. 2, 2017), available at https://www.fda.gov/media/73507/download.

FDA Decision Regarding a 510(k)

- After review of a 510(k) submission, FDA will:
  - Issue an order declaring the device substantially equivalent (SE)
  - Issue an order declaring the device not substantially equivalent (NSE)
  - Request additional information (AI)
  - Advise that a 510(k) is not required
- An applicant may not proceed to market until receiving an order declaring the device SE

See 21 C.F.R. § 807.100; see also Guidance for Industry and FDA Staff: FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals (Oct. 2, 2017), available at https://www.fda.gov/media/73507/download.

Regulatory Options After an NSE Decision

- If FDA determines that a device is NSE, the applicant may:
  - Submit another 510(k) with new data;
  - Submit a PMA;
  - Request a Class I or Class II designation through the de novo review process; or
  - File a reclassification petition.
- Consider appealing the decision. See Guidance for Industry and FDA Staff: CDRH Appeals Process (Mar. 2, 2022), available at https://www.fda.gov/media/128444/download.

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How to Strategize for a 510(k) Submission

- ***Tip 1:*** When calling FDA to ask questions, make sure you ask the right person at the right level. The "person" responding is not "FDA."
- ***Tip 2:*** Ask questions from FDA officials who are contacts on guidance documents and regulations, if necessary.
- ***Tip 3:*** When emailing your reviewer, always copy the immediate supervisor.

How to Strategize for a 510(k) Submission

- ***Tip 4:*** A Pre-Submission (Pre-Sub) may not always be the best start.
  - Try not to ask questions in any pre-sub, but rather provide your plan and your answers.
  - If you do ask questions, carefully plan what you will ask.
- ***Tip 5:*** Be aware of the political dynamics in the room among the FDA/CDRH officials present.

How to Strategize for a 510(k) Submission

- ***Tip 6:*** Try not to withdraw your 510(k).
- ***Tip 7:*** Make your “device case” for a combination product, unless you are required to submit a Request for Designation (RFD).
- ***Tip 8:*** Try not to submit anything “off” the FDA review clock.

How to Strategize for a 510(k) Submission

- ***Tip 9:*** A 510(k) statement requires you to always fulfill that requirement. The 510(k) summary is the way to go! Once you have a "statement," you cannot switch to a "summary."
- ***Tip 10:*** 510(k) summaries receive full reviews.

How to Strategize for a 510(k) Submission

- ***Tip 11:*** FDA will review whatever 510(k) you submit--even if the 510(k) was not needed. The burden is initially on you to determine if the 510(k) is needed.
- ***Tip 12:*** The Freedom of Information backlog is down. Always request a copy of the review team reviews for every submission.
- ***Tip 13:*** Try to avoid filing a 510(k) between December 5 to January 5.

How to Strategize for a 510(k) Submission

- ***Tip 14:*** If there is a device-specific guidance for your device type, address every section of the guidance – even if it obviously does not apply to your device . . . and say why.
- ***Tip 15:*** Compare every change you make to your predicate. (As part of its final decision, FDA will determine the predicate.)

How to Strategize for a 510(k) Submission

- ***Tip 16:*** When multiple changes have been made to your device, the guidance requests that you tell the FDA of the change(s) made to the predicate.
- ***Tip 17:*** FDA will work with you on "catch-up" 510(k)s when one is needed.
- ***Tip 18:*** Changes to "make it better" require you to file a 510(k). The regulation states that the change "could significantly affect safety and effectiveness"
  - Does not say "does significantly affect . . . "
  - The effect can be positive. No one ever changes their device to try to make it worse!

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Special 510(k)s

- ONLY when modifying your own legally marketed device (not PMA)
- Same indications for use
- Same fundamental technology
- Include summary of risk analysis and declaration of conformity with design controls (21 C.F.R. § 820.30) in lieu of raw data in 510(k)
- Subject to expedited review (30 days)
- Guidance for Industry and FDA Staff: The Special 510(k) Program (September 13, 2019), available at https://www.fda.gov/media/116418/download

Abbreviated 510(k)s

- Relies on the use of guidance documents, special controls, and recognized standards to facilitate review
- Manufacturers may choose to submit an abbreviated 510(k) when:
  - A guidance document exists;
  - A special control is established; or
  - FDA recognizes a relevant consensus standard
- Manufacturers have the option to use a third party to assess conformance with the recognized standard
- Guidance for Industry and FDA Staff: The Abbreviated 510(k) Program (September 13, 2019), available at https://www.fda.gov/media/72646/download.

Other Considerations

- Breakthrough Devices Program
  - Guidance for Industry and FDA Staff: Breakthrough Devices Program (Dec. 18, 2018), available at https://www.fda.gov/media/108135/download.
- Safer Technologies Program (STeP)
  - Guidance for Industry and FDA Staff: Safer Technologies Program for Medical Devices (Jan. 6, 2021), available at https://www.fda.gov/media/130815/download
- Accessories
  - Guidance for Industry and FDA Staff: Medical Device Accessories—Describing Accessories and Classification Pathways (Dec. 20, 2017), available at https://www.fda.gov/media/90647/download.

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Confidential, Proprietary, and Trade Secret Information

- FDA regulations address the confidentiality of information submitted to FDA. See, e.g., 21 C.F.R. § 807.95 and Part 20.
- 21 C.F.R. § 807.95
  - In certain, specified instances, FDA will disclose the existence of a 510(k) submission. 21 C.F.R. § 807.95(a)
  - In certain, specified instances, FDA will not disclose the existence of a 510(k) submission for a device that is not on the market and where the intent to market the device has not been disclosed for 90 days from the receipt of the submission. 21 C.F.R. § 807.95(b) & (c)
  - FDA will make a 510(k) summary available to the public within 30 days of an SE determination. 21 C.F.R. § 807.95(d)
  - Data or information submitted in a 510(k) submission are subject to disclosure, unless exempt from disclosure under 21 C.F.R. Part 20. 21 C.F.R. § 807.95(e)

Confidential, Proprietary, and Trade Secret Information

- 21 C.F.R. Part 20
  - Part 20 specifies FDA's policies and procedures governing the disclosure of FDA records
    - General policy
    - Procedures and fees
    - Exemptions
    - Limitations on exemptions
    - Availability of specific categories of records

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- Overview of the 510(k) Program
- What Is 510(k)?
- What Is a Predicate Device?
- What Does “Substantial Equivalence” Mean?
- FDA 510(k) Review Process
- How to Strategize for a 510(k) Submission
- Other Types of 510(k)s
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- **User Fees for 510(k) Submissions**
- Modifications to a Legally Marketed Device
- What Is a De Novo Petition?

User Fees for 510(k) Submissions

- Under the authority granted to it by the Medical Device User Fee Act, FDA collects user fees for its review of 510(k)s.
- The standard user fee for a 510(k) submission in FY2022 is ***$12,745***.
- The small business fee for a 510(k) submission in FY2022 is ***$3,186***.

Review Times for 510(k) Submissions

- Under the FDCA, the standard review time for a 510(k) is 90 calendar days. FDCA § 510(n), 21 U.S.C. § 360(n).
- CDRH performance data shows the following:

Performance Metric	FY 2019	FY 2020	FY 2021
510(k)s Accepted	3,463	3,495	3,578
Average Review Cycles	1.62	1.63	1.52
Non-MDUFA IV Decision	423	325	97
Number with MDUFA IV Decisions	3,035	3,036	2,273
510(k)s Pending MDUFA IV Decision	5	134	1,208
Average FDA Days to MDUFA IV Decision	73.52	77.05	74.31
Average Industry Days to MDUFA IV Decision	60.09	65.31	35.79
Average Total Days to MDUFA IV Decision	133.61	142.36	110.10

See https://www.fda.gov/media/156515/download.

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Modifications to a Legally Marketed Device

- A 510(k) notification is required when a device that is legally marketed pursuant to a cleared 510(k) (or subject to exemption) **could** be significantly changed or modified in design, components, method of manufacture, or intended use. Such a change or modification includes:
  - A change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process
  - A major change or modification in the intended use

    21 C.F.R. § 807.81(a)(3)

  Guidance for Industry and FDA Staff: Deciding When to Submit a 510(k) for a Change to an Existing Device (October 25, 2017), available at https://www.fda.gov/media/99812/download.

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What Is a De Novo Petition?

- Devices not otherwise classified by regulation, by default, are Class III devices. FDCA § 513(f)(1), 21 U.S.C. § 360c(f)(1).
- In 1997, Congress gave FDA the authority to automatically down classify a device that would otherwise be Class III by default if:
  - The device is low to moderate risk; and
  - General controls in combination with special controls (where appropriate) are sufficient to provide a reasonable assurance of safety and effectiveness.

  FDCA § 513(f)(2), 21 U.S.C. § 360c(f)(2).

Devices Eligible for De Novo Review

- To be eligible for de novo review:
  - A device must not be of a type that has been classified as Class I or Class II
    - Therefore, no predicate exists for the device, and the device is automatically a Class III device.
  - A device must be low to moderate risk and should appear, based on what is known about the device, to meet the statutory standards for classification into Class I or Class II
    - i.e., general controls or general and special controls would provide reasonable assurance of the safety and effectiveness of the device
  - The applicant should sufficiently understand and be able to explain all of the known risks and benefits of the device and how known risks can be mitigated and device effectiveness can be assured through controls.

See Guidance for Industry and FDA Staff: De Novo Classification Process (Evaluation of Automatic Class III Designation) (Aug. 2014), available at https://www.fda.gov/media/72674/download.

Two Possible Pathways for De Novo Review

- There are two possible pathways for de novo review:

(1) Submission of a 510(k), Followed by De Novo Petition	(2) Direct De Novo Pathway
A person may first submit a 510(k) notice resulting in a Not Substantially Equivalent (NSE) determination and then submit a de novo petition.	A person may skip the 510(k) submission and immediately file a de novo petition.

User Fees for De Novo Classification Requests

- Under the authority granted to it by the Medical Device User Fee Act, FDA collects user fees for its review of de novo classification requests.
- The standard user fee for a de novo classification request in FY2022 is ***$112,457***.
- The small business fee for de novo classification request in FY2022 is ***$28,114***.

Review Times for De Novo Classification Requests

- Under the FDCA, the standard review time for a de novo classification request is 120 calendar days. FDCA § 513(f)(2)(A)(iii), 21 U.S.C. § 360c(f)(2)(A)(iii).
- CDRH performance data shows the following:

Performance Metric	FY 2019	FY 2020	FY 2021
De Novos Accepted	61	64	53
Average Review Cycles	1.61	1.77	1.81
Non-MDUFA IV Decision	0	0	0
Number with MDUFA IV Decisions	61	57	16
De Novos Pending MDUFA IV Decision	0	7	37
Average FDA Days to MDUFA IV Decision	143.57	169.58	148.88
Average Industry Days to MDUFA IV Decision	117.44	165.93	69.63
Average Total Days to MDUFA IV Decision	261.02	335.51	218.50

See https://www.fda.gov/media/156515/download.


Thank You!