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MEDICAL DEVICES

FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process



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Highlights of [GAO-09-190](#), a report to congressional addressees

MEDICAL DEVICES

FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process

Why GAO Did This Study

The Food and Drug Administration (FDA) within the Department of Health and Human Services (HHS) is responsible for oversight of medical devices sold in the United States. Regulations place devices into three classes, with class III including those with the greatest risk to patients. Unless exempt by regulation, new devices must clear FDA premarket review via either the 510(k) premarket notification process, which determines if a new device is substantially equivalent to another legally marketed device, or the more stringent premarket approval (PMA) process, which requires the manufacturer to supply evidence providing reasonable assurance that the device is safe and effective. Class III devices must generally obtain an approved PMA, but until FDA issues regulations requiring submission of PMAs, certain types of class III devices may be cleared via the 510(k) process. The FDA Amendments Act of 2007 mandated that GAO study the 510(k) process. GAO examined which premarket review process—510(k) or PMA—FDA used to review selected types of device submissions in fiscal years 2003 through 2007. GAO reviewed FDA data and regulations, and interviewed FDA officials.

What GAO Recommends

GAO recommends that FDA expeditiously take steps to issue regulations for class III device types currently allowed to enter the market via the 510(k) process by requiring PMAs or reclassifying them to a lower class. HHS agreed with GAO's recommendation.

To view the full product, including the scope and methodology, click on [GAO-09-190](#). For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

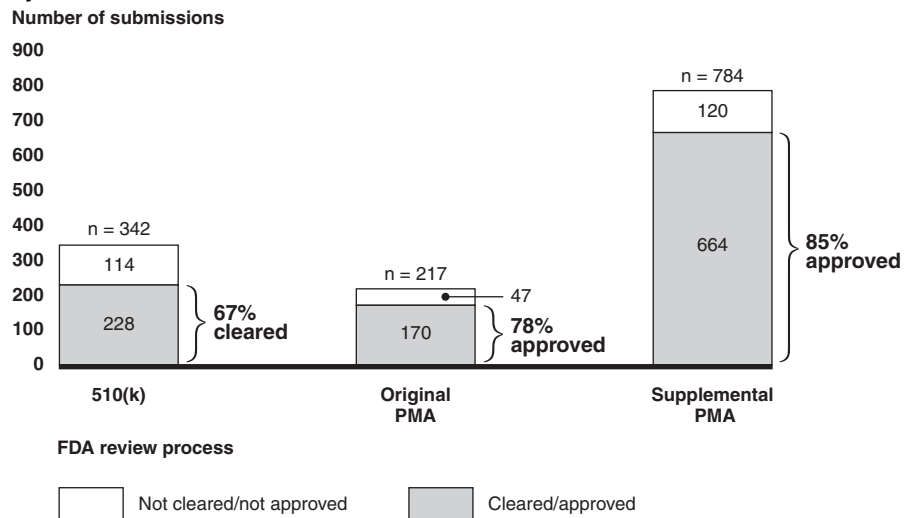
What GAO Found

In fiscal years 2003 through 2007, as part of its premarket review to determine whether devices should be permitted to be marketed in the United States, FDA

- reviewed 13,199 submissions for class I and II devices via the 510(k) process, clearing 11,935 (90 percent) of these submissions;
- reviewed 342 submissions for class III devices through the 510(k) process, clearing 228 (67 percent) of these submissions; and
- reviewed 217 original and 784 supplemental PMA submissions for class III devices and approved 78 percent and 85 percent, respectively, of these submissions.

Although Congress envisioned that class III devices would be approved through the more stringent PMA process, and the Safe Medical Devices Act of 1990 required that FDA either reclassify or establish a schedule for requiring PMAs for class III device types, this process remains incomplete. GAO found that in fiscal years 2003 through 2007 FDA cleared submissions for 24 types of class III devices through the 510(k) process. As of October 2008, 4 of these device types had been reclassified to class II, but 20 device types could still be cleared through the 510(k) process. FDA officials said that the agency is committed to issuing regulations either reclassifying or requiring PMAs for the class III devices currently allowed to receive clearance for marketing via the 510(k) process, but did not provide a time frame for doing so.

Class III Device Submissions with FDA Review Decisions in Fiscal Years 2003 through 2007, by FDA Review Process and Review Decision



Source: GAO analysis of FDA data.

Notes: 510(k) includes traditional and abbreviated 510(k) submissions. Supplemental PMA includes certain types of submissions for changes to devices that were previously approved through the PMA process. Not cleared/not approved includes 510(k) submissions that were denied or other (e.g., withdrawn) and PMAs that were withdrawn or otherwise not approved.

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Abbreviations

FDA	Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act
HHS	Department of Health and Human Services
NSE	not substantially equivalent
PMA	premarket approval
SE	substantially equivalent
SMDA	Safe Medical Devices Act of 1990

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United States Government Accountability Office
Washington, DC 20548

January 15, 2009

The Honorable Edward M. Kennedy
Chairman
The Honorable Michael B. Enzi
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Henry A. Waxman
Chairman
The Honorable Joe Barton
Ranking Member
Committee on Energy and Commerce
House of Representatives

The Honorable Charles E. Grassley
United States Senate

The Honorable John D. Dingell
House of Representatives

The federal government, through the Food and Drug Administration (FDA) within the Department of Health and Human Services (HHS), is responsible for ensuring that medical devices sold in the United States provide reasonable assurance of safety and effectiveness and do not pose a threat to public health.¹ These devices range from simple tools like bandages and surgical clamps to complicated devices like pacemakers.

FDA classifies each device type into one of three classes—class I, II, or III—based on the level of risk it poses and the controls necessary to

¹Generally, medical devices include items used for the diagnosis, cure, mitigation, treatment, or prevention of a disease. See 21 U.S.C. § 321(h). Throughout this report, the term *device* refers to a medical device that is not being regulated as a drug or a biological product.

reasonably ensure its safety and effectiveness.² According to FDA, the risk the type of device poses to the patient or the user is a major factor in the class it is assigned: class I includes devices with the lowest risk, and class III includes devices with the highest risk. Examples of types of devices in each class include the following:

- class I: tongue depressors, elastic bandages, reading glasses, and forceps;
- class II: electrocardiographs, powered bone drills, and mercury thermometers; and
- class III: pacemakers and replacement heart valves.

In general, unless exempt under FDA regulations, devices are subject to one of two types of FDA premarket review before they may be legally marketed in the United States.³

- **Premarket approval (PMA):** The manufacturer must provide evidence, typically including clinical data, providing reasonable assurance that the new device is safe and effective. The PMA process is the most stringent type of premarket review. A successful submission results in FDA approval.

²Throughout this report we refer to *type of device* or *device type* to indicate a generic category of device, which has a particular intended use (for example, a scalpel is intended to cut tissue) and which may include a variety of models made by different manufacturers. FDA's classifications of device types are codified in parts 862 through 892 of title 21 of the *Code of Federal Regulations*; in addition, FDA's Web site provides searchable databases at www.fda.gov/cdrh/databases.html. Class I devices are those for which compliance with general controls, such as good manufacturing practices specified in FDA's quality system regulation, are sufficient to provide reasonable assurance of their safety and effectiveness. Class II devices are subject to general controls and may also be subject to special controls, such as postmarket surveillance. Class II devices may support or sustain human life. For class II devices that are represented or purported to be used for those purposes, FDA must examine, identify, and describe the special controls necessary to provide assurance of their safety and effectiveness. Class III devices are those (1) for which insufficient information exists to determine whether general and special controls are sufficient to provide a reasonable assurance of the safety and effectiveness of the devices *and* (2) that support or sustain human life or are of substantial importance in preventing impairment of human health, or that present a potential unreasonable risk of illness or injury. See 21 U.S.C. § 360c.

³A small percentage of devices enter the market by other means, such as through the humanitarian device exemption process that allows market entry, without adherence to certain requirements, for devices benefiting patients with rare diseases or conditions. See 21 U.S.C. § 360j(m), 21 C.F.R. pt. 814, subpart H (2008).

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- **Premarket notification (510(k)):** The manufacturer must demonstrate to FDA that the new device is *substantially equivalent* to a device already legally on the market that does not require a PMA.⁴ A successful submission results in FDA clearance.⁵

In general, class I and II device types subject to premarket review are required to obtain FDA clearance through the 510(k) process, and class III device types are required to obtain FDA approval through the more stringent PMA process. However, certain types of class III devices that were in commercial distribution in the United States before May 28, 1976⁶ (called preamendment device types) and those determined to be substantially equivalent to them may be cleared through the less stringent 510(k) process until FDA publishes regulations requiring them to go through the PMA process or reclassifies them into a lower class.⁷ The Safe Medical Devices Act of 1990 (SMDA) required FDA (1) to reexamine the preamendment class III device types for which PMAs were not yet required to determine if they should be reclassified to class I or II or remain in class III and (2) to establish a schedule to promulgate regulations requiring those preamendment device types that remain in class III to obtain FDA approval through the PMA process.⁸ Accordingly, all class III devices are eventually to be reviewed through the PMA process.

⁴*Substantial equivalence* or *substantially equivalent* means that the device has the same intended use as another legally marketed device and the same technological characteristics, or different technological characteristics and submitted information demonstrates that the device is as safe and effective as the legally marketed device and does not raise different questions of safety or effectiveness. See 21 U.S.C. § 360c(i)(1)(A).

⁵Some devices are exempt from premarket notification requirements. Most class I and some class II device types are in this exempt category. In these cases, the manufacturers must still register and list the devices with FDA.

⁶May 28, 1976, is the date of enactment of the Medical Device Amendments of 1976, which established the three device classes. See Pub. L. No. 94-295, 90 Stat. 539.

⁷Based on new information respecting a device, FDA may, upon its initiative or upon petition of an interested person, by regulation change the classification of a device from class III to (1) class II if it determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls alone would not provide reasonable assurance of the safety and effectiveness of the device or (2) class I if FDA determines that general controls alone would provide reasonable assurance of the safety and effectiveness of the device. See 21 U.S.C. § 360c(e).

⁸Pub. L. No. 101-629, § 4(b), 104 Stat. 4511, 4515-17 (codified at 21 U.S.C. § 360c(i)).

The FDA Amendments Act of 2007⁹ mandated that GAO study FDA’s premarket review of devices under section 510(k) of the Federal Food, Drug, and Cosmetic Act (FDCA).¹⁰ This report discusses (1) the premarket review process—510(k) or PMA—FDA used to review class I, II, and III device submissions in fiscal years 2003 through 2007 and (2) the extent to which FDA has determined that devices reviewed through the 510(k) process had new intended uses or new technological characteristics.

To determine the premarket review process FDA used to review class I, II, and III device submissions, as well as the number of submissions reviewed and cleared in fiscal years 2003 through 2007, we obtained and analyzed data from FDA’s 510(k) and PMA databases. These databases contain information on 510(k) and PMA submissions,¹¹ respectively, including the name of the device, the FDA-assigned product code,¹² the status of the submission, and any FDA decisions related to the submission and the dates of those decisions. We also used data from FDA’s Device Nomenclature Management System to determine other attributes of the device types covered by the 510(k) and PMA submissions. We obtained and analyzed data on submissions for which FDA made review decisions in fiscal years 2003 through 2007.¹³ Our analysis included traditional and abbreviated 510(k) submissions, original PMA submissions, and submissions for certain types of PMA supplements (panel-track and

⁹Pub. L. No. 110-85, § 225, 121 Stat. 823, 854.

¹⁰21 U.S.C. § 360(k).

¹¹Throughout this report, we refer to both submissions to FDA through the 510(k) process and applications to FDA through the PMA process as device submissions. Because related devices can be “bundled” together in a single submission, one submission may include one or more devices.

¹²The FDA-assigned product code for a device is based on the classification designated under the relevant classification regulations.

¹³For the purposes of this report, submissions for which FDA made *review decisions* include cases in which FDA made a determination to allow or disallow marketing of a device and cases in which FDA decided to discontinue consideration for other reasons such as if the manufacturer withdrew its submission. See app. I for additional information on our scope and methodology.

180-day user-fee supplements).¹⁴ To assess the reliability of these data, we interviewed FDA officials knowledgeable about these databases, performed electronic testing for accuracy and completeness, and where applicable compared our results to aggregate information from other sources, such as published FDA reports and the FDA Web site. We determined that the data were sufficiently reliable for the purposes of this report.¹⁵

To examine the extent to which FDA has determined that devices reviewed through the 510(k) process had new intended uses or new technological characteristics, we used FDA's 510(k) database to select and review all class III 510(k) submission files and a stratified random sample of class II 510(k) submission files for which FDA reached a determination of substantially equivalent (SE) or not substantially equivalent (NSE) in fiscal years 2005 through 2007. The sample totaled 459 submissions to the Office of Device Evaluation within FDA's Center for Devices and Radiological Health and did not include submissions to other FDA offices or centers.¹⁶ In each case, we collected data primarily from the FDA reviewer's memo, which outlined the decisions that FDA made to reach its determination and summarized FDA's rationale for finding the submission SE or NSE. Because our sample of class II device submissions is representative of all class II device submissions meeting our selection criteria, in reporting the results of our analysis we provide estimates for the universe of all 4,900 traditional and abbreviated 510(k) submissions for class II devices for which FDA made determinations of SE or NSE in fiscal years 2005 through 2007. To assess the reliability of the data we obtained from FDA's files, we compared our results with information from FDA's 510(k) database. In addition, we discussed cases where the determination path or rationale was unclear with knowledgeable FDA officials. We

¹⁴Our analysis did not include certain types of device submissions, for example, special 510(k) submissions, which are requests for clearance of modifications to devices that have already been cleared through the 510(k) process. Panel-track PMA supplements are requests for approval for a significant change in design, performance, or use of a device, for which clinical data are generally necessary to provide a reasonable assurance of safety and effectiveness; 180-day PMA supplements are requests for approval for a significant change in components, materials, design, specification, software, color additive, or labeling.

¹⁵See app. I for additional information on our scope and methodology.

¹⁶See app. I for additional information on our scope and methodology. Some 510(k) submissions may be reviewed by third parties. For additional information on third-party review of 510(k) submissions, see app. II.

determined that the data were sufficiently reliable for the purposes of this report.

In addition to our data analysis, we reviewed relevant laws, regulations, and FDA guidance, and interviewed FDA officials, representatives of professional associations representing device manufacturers, and consumer advocates. We conducted this performance audit from March 2008 to January 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Results in Brief

In fiscal years 2003 through 2007, FDA reviewed all class I and II device submissions through the 510(k) process, and reviewed some types of class III device submissions through the 510(k) process and others through the PMA process.

- FDA reviewed all 13,199 submissions for class I and class II devices through the 510(k) process, clearing 90 percent (11,935 submissions) for marketing.
- FDA reviewed 342 submissions for class III devices through the 510(k) process, clearing 67 percent (228 submissions) for marketing.
- FDA also reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices, approving 78 percent and 85 percent, respectively, of these submissions for marketing.

Although Congress envisioned that class III devices would be approved through the more stringent PMA process, and the SMDA required that FDA establish a schedule for doing so, this process remains incomplete. We found that in the 5-year period we examined FDA cleared submissions for 24 class III device types through the 510(k) process. These submissions were more likely than class I or class II submissions to be implantable or life sustaining, or to pose a significant risk to the health, safety, or welfare of a patient. As of October 2008, 4 of the 24 device types had been reclassified and 20 class III device types could still be cleared through the 510(k) process. FDA officials have acknowledged the importance of publishing regulations requiring PMA submissions or reclassifying

preamendment class III device types. When asked for their time frame for doing so, however, the officials did not provide one.

In fiscal years 2005 through 2007, FDA determined that relatively few class II and III devices reviewed through the 510(k) process had a new intended use or new technological characteristics. Of the 5,063 class II or class III 510(k) submissions with SE or NSE determinations in this time period, we estimate that about 1 percent had a new intended use and about 15 percent had new technological characteristics. Among devices FDA determined SE (and therefore cleared for marketing), all of the submissions had the same intended use and 86 percent had the same technological characteristics as a device already on the market. In contrast, among the 248 510(k) submissions found NSE, FDA determined that more than half of the devices had a new intended use or new technological characteristics.

We are recommending that FDA expeditiously take steps to issue regulations for each class III device type currently allowed to enter the market through the 510(k) process, including (1) reclassifying each device type into a lower class or requiring it to remain in class III and (2) for those device types remaining in class III, requiring approval for marketing through the PMA process. HHS commented that the draft report fairly and accurately describes the FDA's medical device 510(k) program and the department agreed with our conclusions and recommendation.

Background

The Medical Device Amendments of 1976 established three classes of medical devices.¹⁷ Under current law, these three device classes are defined as follows:

- Class I devices are those for which compliance with general controls, such as good manufacturing practices specified in FDA's quality system regulation, are sufficient to provide reasonable assurance of their safety and effectiveness.
- Class II devices are subject to general controls and may also be subject to special controls, such as postmarket surveillance, patient registries, or

¹⁷Pub L. No. 94-295, § 2, 90 Stat. 539-41 (codified as amended at 21 U.S.C. § 360c(a)(1)).

specific FDA guidelines, if general controls alone are insufficient to provide reasonable assurance of the device’s safety and effectiveness.¹⁸

- Class III devices are subject to general controls, but are distinguished from class I and II devices because class III devices are those (1) for which insufficient information exists to determine whether general and special controls are sufficient to provide a reasonable assurance of the safety and effectiveness of the device and (2) that support or sustain human life or are of substantial importance in preventing impairment of human health, or that present a potential unreasonable risk of illness or injury.

Devices Exempt from FDA Premarket Review

Under federal regulations, many types of devices are exempt from FDA premarket review.¹⁹ Although FDA does not track the number of devices that are actually sold or marketed in the United States, manufacturers are required to register with FDA and provide a list of devices intended for commercial distribution, including device types that are exempt from premarket review.²⁰ As shown in figure 1, about 67 percent of the more than 50,000 separate devices that manufacturers listed with FDA during

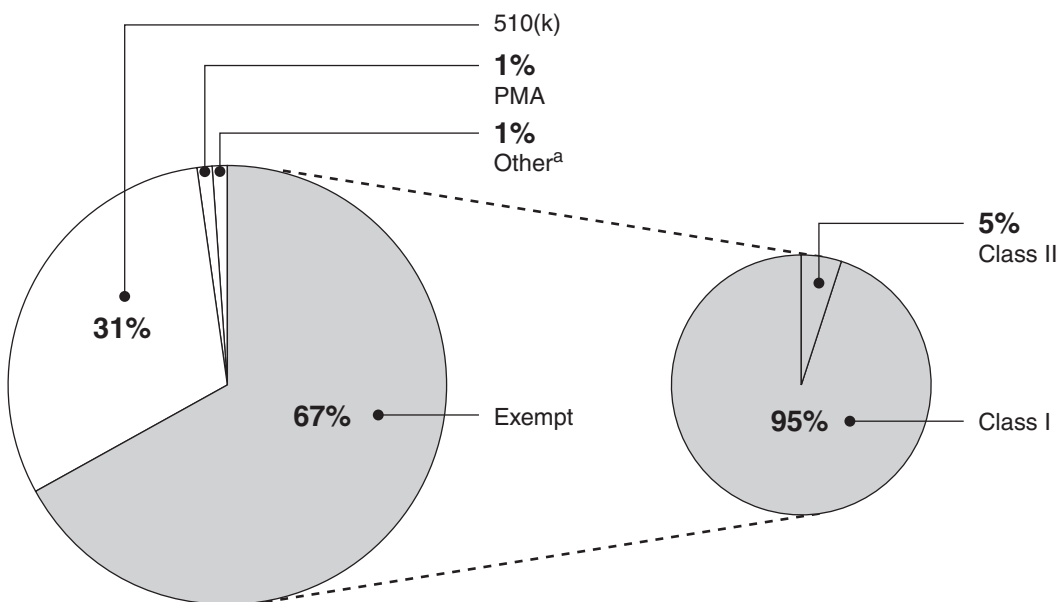
¹⁸Before 1990, class II devices were defined as those for which general controls alone were insufficient to provide reasonable assurance of safety and effectiveness, but for which sufficient information existed for FDA to establish a “performance standard” to provide such assurance. Under the SMDA, this definition was revised to include those devices for which sufficient information existed for FDA to establish “special controls”—such as performance standards, postmarket surveillance, patient registries, guidelines, and FDA recommendations—to provide such assurance.

¹⁹Each manufacturer that wants to market a class I, II, or III device intended for human use for which premarket approval is not required must obtain marketing clearance by a 510(k) submission unless FDA issues a regulation stating that the device type is exempt from the 510(k) premarket notification requirements of the FDCA.

²⁰Manufacturers are required to register with FDA within 30 days after operations begin and provide it with a list at that time of their devices intended for commercial distribution. Registrations and device listings must be updated annually. 21 U.S.C. § 360(j)(2)(A); 21 C.F.R. § 807.21 (2008).

fiscal years 2003 through 2007 were exempt from premarket review.²¹ Of the exempt devices that manufacturers listed with FDA, about 95 percent were class I devices, for example reading glasses and forceps. About 5 percent were class II devices, for example wheeled stretchers and mercury thermometers.

Figure 1: Devices That Manufacturers Listed with FDA during Fiscal Years 2003 through 2007, by Review Process and Device Class



Source: GAO analysis of FDA data.

Notes: Data are for the 50,189 devices listed with FDA by device manufacturers during the period October 1, 2002, through September 30, 2007. Even if their devices are exempt from premarket notification requirements, manufacturers must still comply with other FDA requirements, such as good manufacturing practice requirements specified in FDA's quality system regulation. See 21 C.F.R. pt. 820 (2008).

²¹Regarding the devices listed with FDA that were not exempt from premarket review, about 31 percent (15,472) of the listed devices were allowed to enter the U.S. market through the 510(k) premarket notification process, and about 1 percent (529) of the listed devices were required to enter the U.S. market through the more stringent PMA process. Approximately 1 percent (389) were allowed to enter the market via other means, such as through the humanitarian device exemption process. A humanitarian device exemption requires a submission that is similar to a PMA submission, but does not include effectiveness requirements. FDA approval of a humanitarian device exemption authorizes the manufacturer to market a device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects fewer than 4,000 individuals in the United States per year. See 21 U.S.C. § 360j(m); 21 C.F.R. pt. 814, subpart H.

^a*Other* includes devices that were allowed to enter the market via other means, such as through the humanitarian device exemption process that allows market entry, without adherence to certain requirements, for devices benefiting patients with rare diseases or conditions.

Premarket Review Process for Class III Devices

With the enactment of the Medical Device Amendments of 1976, Congress imposed requirements under which all class III devices would be approved through the PMA process before being marketed in the United States.²² However, when it passed the 1976 amendments, Congress distinguished between those devices in commercial distribution before the date of enactment and those entering the market on or after enactment.

- **Preamendment devices.** Class III devices that were in commercial distribution prior to May 28, 1976 (referred to as preamendment devices) were allowed to be reviewed and cleared for the U.S. market without PMA approval until FDA published final regulations requiring each device type to obtain approval for the U.S. market through the PMA process.²³
- **Postamendment devices.** Devices that were not in commercial distribution prior to May 28, 1976 (referred to as postamendment devices) were classified automatically into class III and required to go through the PMA process unless FDA either (1) determined they were substantially equivalent to a preamendment device type for which premarket approval is not required²⁴ or (2) reclassified the device type into class I or class II.²⁵

Within this framework, Congress thus envisioned that class III devices would be approved through the more stringent PMA process and that the premarket review of class I and class II devices would entail a lesser degree of scrutiny.

²²Pub. L. No. 94-295, 90 Stat. 539, 552-53 (codified at 21 U.S.C. § 360e).

²³The act required FDA to promulgate regulations providing for the premarket approval of preamendment class III devices.

²⁴For both preamendment and postamendment class III devices, after FDA issues a regulation setting an effective date requiring PMAs for a particular device type, all devices of that type must obtain an approved PMA to remain on the market. In addition, any new devices of the same type subsequently entering the market must also go through the PMA process—that is, they are no longer allowed to be cleared through the 510(k) process.

²⁵After FDA reclassifies the device type into a lower class, the class I or class II device type would require clearance for the U.S. market through the 510(k) process unless FDA also exempted the device type from premarket notification requirements.

By the late 1980s, FDA had not acted to require PMAs for many preamendment class III device types.²⁶ In 1990, the SMDA required FDA to

1. before December 1, 1995, order industry submission of safety and effectiveness information for preamendment class III device types that were not yet required to go through the PMA process;
2. after ordering industry submission of safety and effectiveness information but before December 1, 1995, publish regulations for each such device either revising its classification into class I or class II or requiring it to remain in class III;²⁷ and
3. as promptly as is reasonably achievable, but not later than 12 months after the effective date of a regulation requiring a device to remain in class III, establish a schedule for the promulgation of regulations requiring the submission of PMAs for the preamendment class III device types required to remain in class III.²⁸

The House of Representatives report accompanying the SMDA stated that “In formulating these schedules, the FDA should take into account its priorities and limited resources, together with the Committee’s intention that the evaluation process be expeditious.”²⁹

²⁶For example, in 1988, GAO reported that FDA had called for premarket approval applications for only 9 of approximately 150 types of preamendment class III devices. See GAO, *Medical Devices: FDA’s 510(k) Operations Could Be Improved*, [GAO/PEMD-88-14](#) (Washington, D.C.: Aug. 17, 1988).

²⁷The SMDA required that (1) FDA publish a proposed regulation regarding the classification of the device and provide reasonable opportunity for the submission of comments and (2) the final regulations regarding classification could not take effect until 90 days after the publication of a proposed regulation in the *Federal Register*.

²⁸21 U.S.C. § 360e(i)(3). The SMDA required the schedule to be established within 12 months of the effective date of the regulation requiring a device to remain in class III. Under the FDCA, in order to require PMAs for preamendment class III devices, FDA must take a number of steps, including publishing a notice of proposed rule making, allowing comments on the proposed rule, providing an opportunity to request reclassification of the device based on new information, and then publishing a final regulation requiring the submission of PMAs. 21 U.S.C. § 360e(b).

²⁹H.R. Rep. No. 101-808, at 6320 (1990).

In May 1994, FDA published a notice in the *Federal Register* announcing a strategy for implementation of the SMDA.³⁰ According to the FDA memorandum outlining this strategy, the agency planned the following:

- To publish proposed regulations by 1996 requiring PMAs for 15 device types that FDA had determined to present an unreasonably high risk to public health because significant issues of safety or effectiveness or both were not being resolved or, to the best of FDA's knowledge, had little probability of being resolved. According to FDA, the timetable for publication of each final regulation would be based on specific data needs, comments received (in response to the proposed rule), and the existence, if any, of petitions received to reclassify the devices.
- To order manufacturers to submit information on safety and effectiveness by 1998 for 58 device types. FDA identified 27 of these device types as not presenting as great a risk to the public health in light of FDA's knowledge and experience with the devices. FDA identified the other 31 device types as strong candidates for reclassification. FDA's strategy stated that after receipt of the safety and effectiveness information, the agency would proceed with rule making to either reclassify the devices or retain them in class III.
- To issue one proposed regulation in 1994 requiring PMAs for 44 device types in limited use.

The agency's strategy established a plan to start addressing the class III device types that were allowed to go through the 510(k) process, but it did not establish completion dates for doing so. See appendix III for additional information on the FDA strategy.

FDA's 510(k) Review Process

As a general rule, devices are subject to 510(k) premarket review unless exempt or required to go through the PMA process. Specifically, the 510(k) process, established in 1976, requires a device manufacturer to notify FDA 90 days before it intends to market a device and to establish that the device is substantially equivalent to a legally marketed device that does not require a PMA. The legally marketed device is referred to as a predicate device. Under federal regulations, a predicate device can be a device that

³⁰59 *Fed. Reg.* 23731 (May 6, 1994).

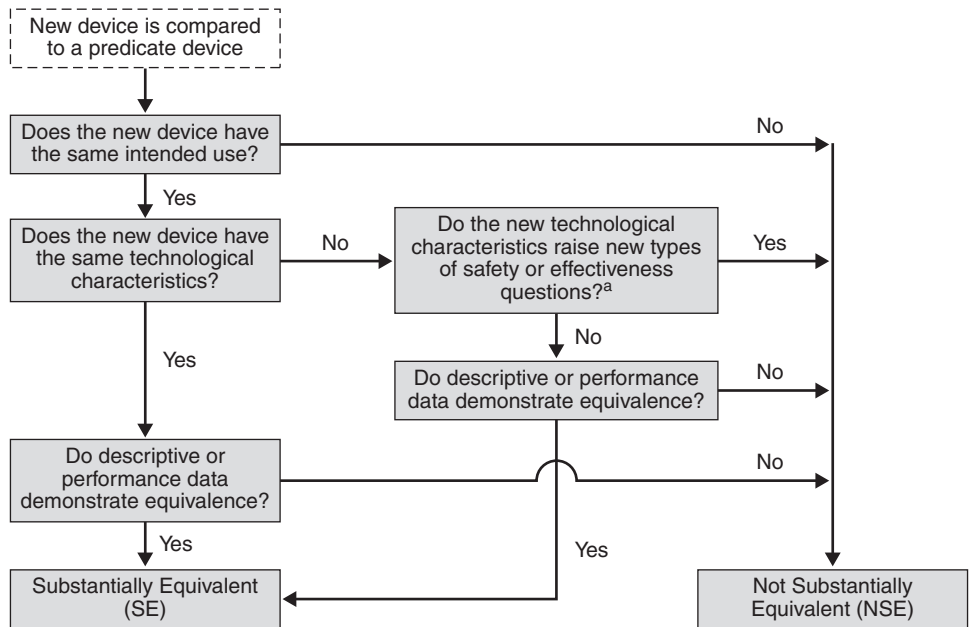
-
- was legally marketed prior to May 28, 1976, for which a PMA is not required; or
 - was marketed on or after May 28, 1976, and was found to be substantially equivalent to a legally marketed device through the 510(k) process; or
 - was reclassified by FDA from class III to class II or I.³¹

FDA reviews each 510(k) submission to determine whether the device in question is SE or NSE to a predicate device.³² To be SE, a device must (1) have the same intended use as the predicate device and (2) have the same technological characteristics as the predicate device or have different technological characteristics and submitted information demonstrates that the device is as safe and effective as the marketed device and does not raise different questions of safety or effectiveness. Because the predicate device may be a device that was marketed on or after May 28, 1976, that was found SE when compared to another legally marketed device through the 510(k) process, there could be multiple iterations of a given device type cleared through the 510(k) process. As a result, a 510(k) submission for a new device in 2008 could be compared to the 20th iteration of a device type that was on the market before 1976. Figure 2 shows FDA's 510(k) decision-making process.

³¹21 C.F.R. § 807.92 (a)(3) (2008). Anyone submitting a 510(k) for a device type that has not been previously classified and which FDA subsequently classifies into class III, may, within 30 days after receiving notice of such classification, request that FDA reclassify the device under the statutory criteria for class I and class II devices. This process, known as the de novo classification process, permits FDA to establish a class I or II designation for devices that do not have a predicate and to allow them to enter the U.S. market and to serve as a predicate device for subsequent 510(k) submissions. 21 U.S.C. § 360c(f)(2).

³²In addition to an FDA determination of SE or NSE, FDA may decide to discontinue its review for other reasons, for example, if the manufacturer withdraws its submission.

Figure 2: FDA's 510(k) Decision-Making Process



Source: GAO.

Notes: In cases where FDA determines that a new device has new technological characteristics that could not affect safety and effectiveness, the device may be determined SE if descriptive characteristics alone are precise enough to ensure equivalence. In cases where FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence. For cases in which descriptive or performance information is insufficient, FDA requests additional information.

^aFor devices with new technological characteristics, FDA first examines whether the new technological characteristics could affect safety or effectiveness.

Relative to the PMA process, the 510(k) premarket review process is generally:

- **Less stringent.** For most 510(k) submissions, clinical data are not required and substantial equivalence will normally be determined based on comparative device descriptions, including performance data.³³ In contrast, in order to meet the PMA approval requirement of providing

³³According to FDA, performance testing should be submitted if there are important descriptive differences between the device and other devices of the same type or if the descriptive characteristics for the new device are not precise enough to ensure comparability. In these instances, the most appropriate bench testing, animal testing, or both to address the performance issue should be provided, and summary information regarding the testing should generally suffice.

reasonable assurance that a new device is safe and effective, most original PMAs and some PMA supplements require clinical data.³⁴ In addition, other aspects of FDA's premarket review are less stringent for 510(k) submissions than for PMA submissions. For example, FDA generally does not inspect manufacturing establishments as part of the 510(k) premarket review process—the 510(k) review process focuses primarily on the end product of the manufacturing process rather than the manufacturing process itself. In contrast, the agency does inspect manufacturing establishments as part of its review of original PMA submissions.³⁵ Manufacturing establishments that produce devices cleared through the 510(k) process, as well as those that produce devices approved through the PMA process, are subject to periodic inspections under FDA's normal inspection program.³⁶

- **Faster.** FDA generally makes decisions on 510(k) submissions faster than it makes decisions on PMA submissions. FDA's fiscal year 2009 goal is to review and decide on 90 percent of 510(k) submissions within 90 days and 98 percent of them within 150 days. The comparable goal for PMAs is to review and decide upon 60 percent of original PMA submissions in 180 days and 90 percent of them within 295 days.³⁷
- **Less expensive.** The estimated cost to FDA for reviewing submissions is substantially lower for 510(k) submissions than for PMA submissions. For fiscal year 2005, for example, according to FDA the estimated average cost for the agency to review a 510(k) submission was about \$18,200, while the estimate for a PMA submission was about \$870,000. For the applicant, the standard fee provided to FDA at the time of submission is also significantly lower for a 510(k) submission than for a PMA submission. In

³⁴When clinical outcome can be reliably predicted from nonclinical data, well-designed bench testing or animal testing or both can be the basis for PMA approval.

³⁵In addition to inspecting manufacturing establishments as part of its premarket review of original PMA submissions, FDA may also conduct inspections as part of the approval process for certain types of PMA supplements.

³⁶For additional information on FDA's inspection of device manufacturing establishments, see GAO, *Medical Devices: Challenges for FDA in Conducting Manufacturer Inspections*, [GAO-08-428T](#) (Washington, D.C.: Jan. 29, 2008), and "Related GAO Products" at the end of this report.

³⁷FDA's goals for original PMAs included panel-track PMA supplements. For 180-day PMA supplements, FDA's fiscal year 2009 goal is to review and decide upon 85 percent of submission within 180 days and 95 percent of them within 210 days.

fiscal year 2009, for example, the standard fee for 510(k) submissions is \$3,693, while the standard fee for original PMA submissions is \$200,725.³⁸

Consumer advocates have raised questions regarding the number of devices, particularly class III devices, that are cleared through the 510(k) process and regarding the use of the 510(k) process to clear devices that may utilize new technologies that are different than those in the marketed devices to which they are compared. Officials of associations representing medical device manufacturers, however, have asserted that the 510(k) premarket review is an important tool for reviewing device submissions, saying that it is a rigorous process that gives FDA the flexibility to identify and request the information it needs to assess the safety and effectiveness of medical devices.

FDA Used the 510(k) Process to Review Class I and II Device Submissions, and Used Both the 510(k) and PMA Processes to Review Class III Device Submissions

In fiscal years 2003 through 2007, FDA reviewed all submissions for class I and II devices through the 510(k) process, and reviewed submissions for some types of class III devices through the 510(k) process and others through the PMA process. Specifically, FDA reviewed all 13,199 submissions for class I and class II devices through the 510(k) process, clearing 11,935 (90 percent) of these submissions. FDA also reviewed 342 submissions for class III devices through the 510(k) process, clearing 228 (67 percent) of these submissions. In addition, the agency reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices and approved 78 percent and 85 percent, respectively, of these submissions. Although Congress envisioned that class III devices would be approved through the more stringent PMA process, we found that FDA has not published regulations requiring PMA submissions for some types of preamendment class III devices nor has it reclassified them. As a result, some types of class III devices have been cleared for the U.S. market through the 510(k) process.

Table 1 summarizes the FDA review decisions, by class of device, in fiscal years 2003 through 2007 for 510(k) and PMA submissions.

³⁸In fiscal year 2009, the standard fee for a panel-track supplement is \$150,544 and the standard fee for a 180-day supplement is \$30,109.

Table 1: FDA 510(k) and PMA Decisions by Class, Fiscal Years 2003 through 2007

Submission type	Device class	SE or approved (percentage of row)	NSE or denied (percentage of row)	Other decision ^a (percentage of row)	Total (percentage of row)
510(k)	Class I	1,265 (84)	40 (3)	204 (14)	1,509 (100)
	Class II	10,670 (91)	373 (3)	647 (6)	11,690 (100)
	Class III	228 (67)	100 (29)	14 (4)	342 (100)
	Other ^b	476 (33)	27 (2)	955 (66)	1,458 (100)
PMA					
Original	Class III	170 (78)	— ^c	47 (22) ^c	217 (100)
Supplemental ^d	Class III	664 (85)	— ^c	120 (15) ^c	784 (100)

Source: GAO analysis of FDA data.

Notes: Data represent 14,999 traditional and abbreviated 510(k) submissions, 217 original PMA submissions, and 784 supplemental PMA submissions for which FDA made review decisions in fiscal years 2003 through 2007. Percentages may not sum to 100 because of rounding.

^aOther decisions include submissions that were withdrawn, were exempted by regulation, were not responsive to FDA's requests within a specified time frame, were forwarded to another FDA center (e.g., drugs or biologics), were duplicates, or were for products determined not to be devices.

^bOther device class includes submissions for which a device class was not recorded in FDA's 510(k) database.

^cAccording to FDA data, all PMA decisions during fiscal years 2003 through 2007 were approved or withdrawn. FDA did not deny approval of any PMA submissions during this period. According to FDA officials, when a PMA was seriously deficient, FDA issued a "not approvable" letter under 21 C.F.R. § 814.44(f) and placed the submission on hold. A company may withdraw a submission voluntarily. FDA also considers submissions to be withdrawn voluntarily if the applicant is unable to provide the information necessary to support approval within 180 days.

^dSupplemental PMA submissions include 180-day (user-fee) and panel-track PMA supplements. The numbers in this row do not include other types of PMA supplements.

FDA Reviewed All Submissions for Class I and Class II Devices through the 510(k) Process

FDA reviewed all class I and class II device submissions in fiscal years 2003 through 2007 through the 510(k) process. As shown in table 2, FDA cleared approximately 9 out of every 10 of the 510(k) submissions for class I and class II devices for which FDA made review decisions during this time period.

Table 2: FDA Review Decisions for 510(k) Submissions for Class I and Class II Devices, by Fiscal Year (2003-2007)

Fiscal year	FDA decision			Total (percentage of row)
	SE (percentage of row)	NSE (percentage of row)	Other decision ^a (percentage of row)	
2003	2,519 (90)	72 (3)	215 (8)	2,806 (100)
2004	2,484 (92)	86 (3)	119 (4)	2,689 (100)
2005	2,395 (90)	89 (3)	164 (6)	2,648 (100)
2006	2,325 (91)	78 (3)	156 (6)	2,559 (100)
2007	2,212 (89)	88 (4)	197 (8)	2,497 (100)
Total	11,935 (90)	413 (3)	851 (6)	13,199 (100)

Source: GAO analysis of FDA data.

Note: Percentages may not sum to 100 because of rounding.

^aOther decisions include submissions that were withdrawn, exempted by regulation, not responsive to FDA's requests within a specified time frame, forwarded to another FDA center or office, duplicates, or for products determined not to be devices or not actively regulated by FDA.

Of the 10,670 510(k) submissions for class II devices that FDA cleared in fiscal years 2003 through 2007, FDA's databases identified one-quarter as being for devices that were implantable; were life sustaining; or presented significant risk to the health, safety, or welfare of a patient (see table 3). Of these characteristics, implantable was the most frequently identified characteristic. In terms of 510(k) submissions for class I devices, according to FDA, none of the more than 1,200 510(k) submissions for class I devices that FDA cleared during the same time period were for devices that were implantable; were life sustaining; or presented significant risk to the health, safety, or welfare of a patient.

Table 3: 510(k) Submissions for Class I and Class II Devices Cleared in Fiscal Years 2003 through 2007

	Flag					Total (percentage of row)
	Implantable only (percentage of row)	Life sustaining only (percentage of row)	Significant risk only (percentage of row)	More than one flag (percentage of row)	No flag (percentage of row)	
Class I	0 (0)	0 (0)	0 (0)	0 (0)	1,265 (100)	1,265 (100)
Class II	1,957 (18)	266 (3)	159 (1)	235 (2)	8,053 (75)	10,670 (100)
Total	1,957 (16)	266 (2)	159 (1)	235 (2)	9,318 (78)	11,935 (100)

Source: GAO analysis of FDA data.

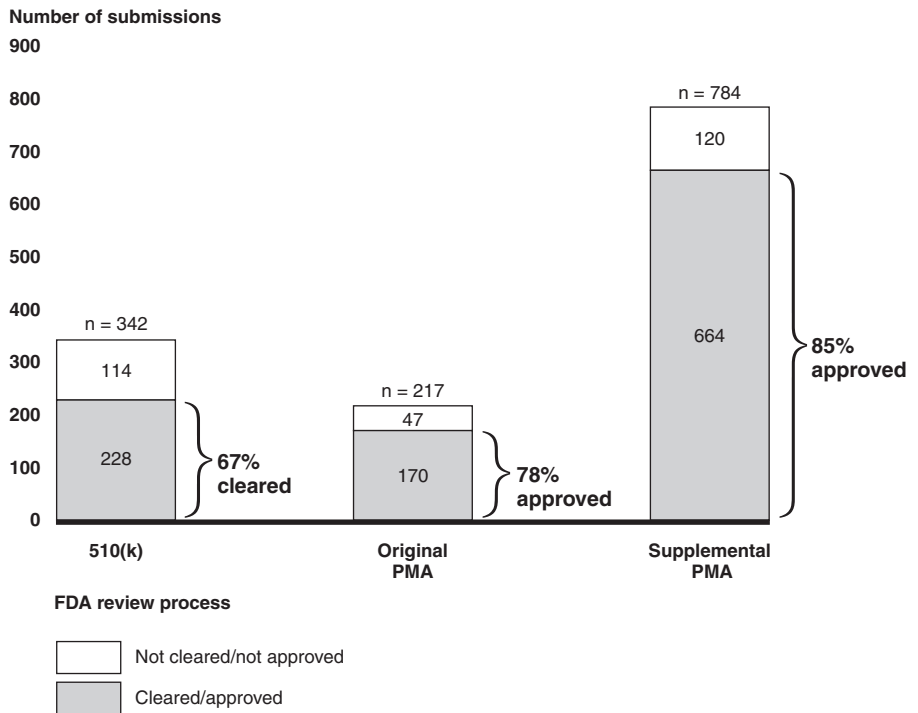
Note: Percentages may not sum to 100 because of rounding.

FDA Reviewed Submissions for Some Class III Devices Types through the 510(k) Process and Others through the PMA Process

In fiscal years 2003 through 2007, FDA reviewed submissions for some types of class III devices through the 510(k) process, and other types of class III devices through the PMA process. Specifically, FDA reviewed 342 submissions for new class III devices through the 510(k) process, determining 228 (67 percent) of these submissions to be SE to a predicate device.³⁹ During the same time period, FDA reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices and approved 78 percent and 85 percent of them, respectively. (See fig. 3.)

³⁹See app. IV for additional information on 510(k) submissions for class III devices reviewed by FDA.

Figure 3: Class III Device Submissions with FDA Review Decisions in Fiscal Years 2003 through 2007, by FDA Review Process and Review Decision



Source: GAO analysis of FDA data.

Notes: Figure represents FDA review decisions made between October 1, 2002, and September 30, 2007, for class III device submissions reviewed through the 510(k) and PMA processes. *510(k)* includes traditional and abbreviated 510(k) submissions; *supplemental PMA* includes panel-track supplements and 180-day (user-fee) supplements.

Not cleared/not approved includes (1) for 510(k) submissions, those submissions FDA found to be NSE or withdrawn and (2) for PMA submissions, those submissions that were withdrawn. According to FDA data, all PMA decisions during fiscal years 2003 through 2007 were approved or withdrawn. FDA did not deny approval of any PMA submissions during this period. According to FDA officials, when a PMA is seriously deficient, FDA issues a “not approvable” letter and places the submission on hold. An applicant may then withdraw a submission voluntarily. FDA also considers submissions to be withdrawn voluntarily if the applicant is unable to provide the information necessary to support approval within 180 days.

FDA Has Not Issued Regulations Requiring PMA Submissions for Some Types of Class III Devices

Although Congress envisioned that class III devices would be approved through the more stringent PMA process, and the SMDA required that FDA establish a schedule for doing so, this process remains incomplete. The 228 class III submissions that FDA cleared through the 510(k) process in fiscal years 2003 through 2007 were allowed to undergo premarket review through the 510(k) process because they were for preamendment class III device types, or those substantially equivalent to them, for which FDA had

not yet issued regulations either requiring PMA submissions or reclassifying them. These 228 510(k) submissions involved 24 device types (see table 4).⁴⁰ Of these types, 16 were included in one of the priority groups in FDA's 1994 strategy for reclassifying or requiring PMAs for class III device types, and in particular 4 device types—accounting for 39 of the 228 submissions—were among those that FDA identified as presenting an unreasonably high risk to public health.

Table 4: Number of Submissions for Class III Devices Cleared through the 510(k) Process in Fiscal Years 2003 through 2007

Group	Number of device types	Number of submissions cleared in FYs 2003-2007	Examples
Included in a priority group in FDA's 1994 strategy	16	123	Certain types of hip joints, implanted blood access devices
Other ^a	8	105	Pedicle screws for certain types of spinal surgeries, dental implants, automated external defibrillator
Total	24	228	

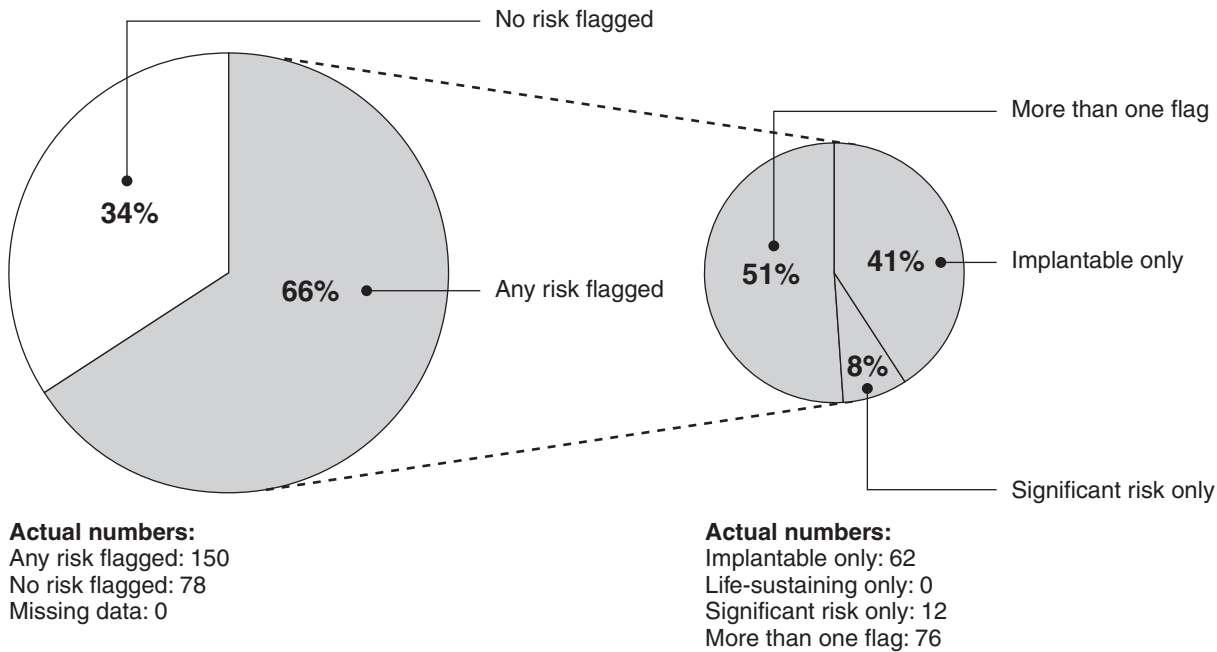
Source: GAO analysis of FDA data.

^aOther includes device types for which FDA had already taken some action by 1994 (for example, FDA indicated that it had reclassification petitions pending for some device types in 1994) as well as new device types that FDA established after 1994 (for example, FDA issued a new regulation for a subset of one device type).

The class III submissions FDA cleared through the 510(k) process were more likely than other 510(k) submissions to be for device types that were implantable; were life sustaining; or pose a significant risk to the health, safety, or welfare of a patient. Of the 228 510(k) submissions for class III devices that FDA cleared in fiscal years 2003 through 2007, FDA's databases flagged 66 percent as being for device types that are implantable, life sustaining, or of significant risk (see fig. 4). This compares to no 510(k) submissions for class I devices and 25 percent of 510(k) submissions for class II devices.

⁴⁰See app. IV for additional information on 510(k) submissions for class III devices reviewed by FDA.

Figure 4: Proportion of Cleared 510(k) Submissions for Class III Devices Flagged as Implantable, Life Sustaining, or of Significant Risk, Review Decisions Made in Fiscal Years 2003 through 2007



Source: GAO analysis of FDA data.

Notes: Figure represents data for 228 510(k) submissions for class III devices that FDA determined to be SE in fiscal years 2003 through 2007. FDA's database flagged 150 of these submissions as device types that were implantable; were life sustaining; presented significant risk to the health, safety, or welfare of a patient; or a combination of those flags.

Four of the 24 class III device types for which FDA cleared 510(k) submissions in fiscal years 2003 through 2007 have since been reclassified by FDA as class II device types.⁴¹ Twenty of the 24 device types, however, may still be cleared through the 510(k) process.⁴² Further, there are other preamendment class III device types that did not happen to have any

⁴¹For these device types, FDA determined that general controls alone were insufficient to provide reasonable assurance of safety and effectiveness and that sufficient information existed to establish special controls to provide such assurance.

⁴²This includes two device types that FDA reclassified to class II under certain conditions, but retained the device type as class III that may be cleared through the 510(k) process for other conditions. For example, FDA reclassified endosseous dental implants to class II for root-form implants, but retained the blade-form implants as class III devices that may be cleared through the 510(k) process.

510(k) submissions cleared in fiscal years 2003 through 2007 that are also still eligible to be cleared through the 510(k) process.

FDA officials have acknowledged the importance of publishing regulations requiring PMA submissions or reclassifying preamendment class III device types. When asked for their time frame for doing so, the officials did not provide one. Rather, they responded that the agency is committed to addressing this issue as resources and priorities permit.

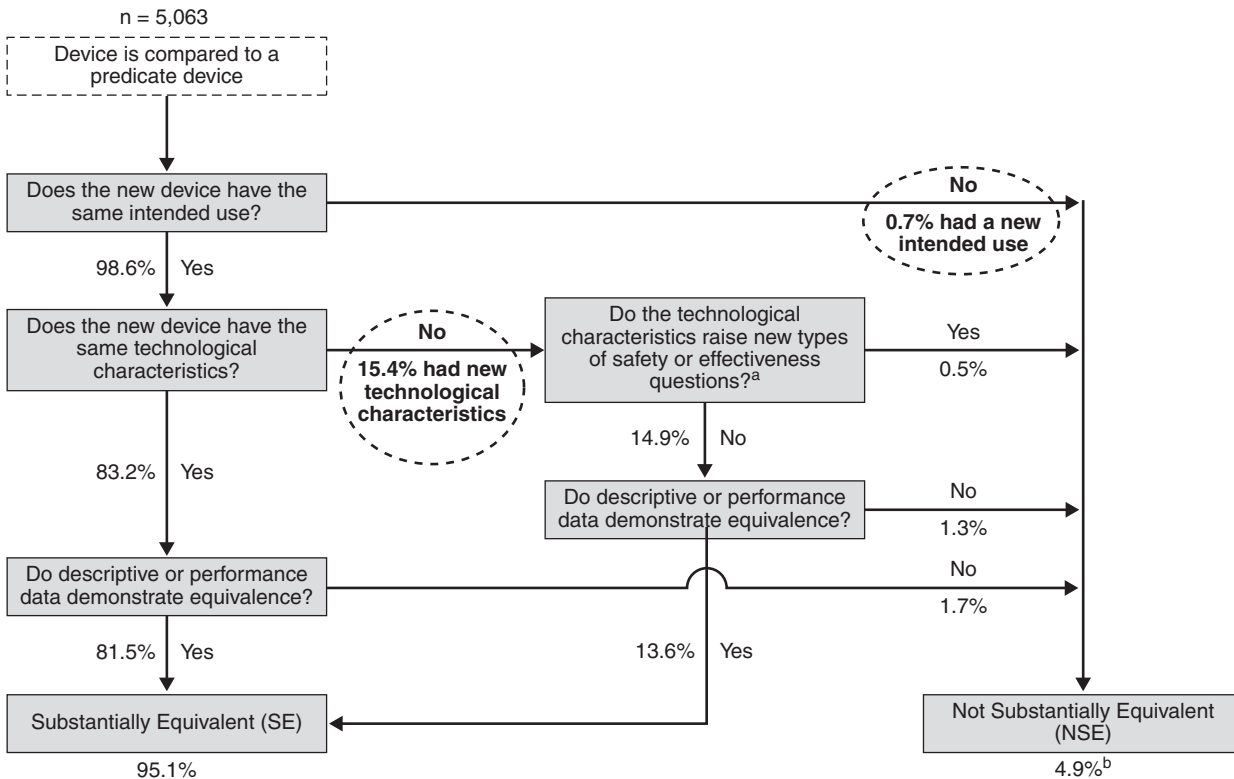
Relatively Few Class II and Class III 510(k) Submissions Had a New Intended Use or New Technological Characteristics

In our review of 510(k) submission files for which FDA reached a determination of SE or NSE in fiscal years 2005 through 2007, we found that FDA determined that relatively few devices had a new intended use or new technological characteristics. Overall, we found that FDA determined about 1 percent of class II and III submissions had a new intended use and about 15 percent had new technological characteristics.⁴³ For the 510(k) submissions that FDA cleared, FDA found that all of the devices had the same intended use as their predicate devices, and 86 percent also had the same technological characteristics. In contrast, of the 510(k) submissions that FDA determined to be NSE, more than half were for devices that had a new intended use or new technological characteristics.

Figure 5 shows the estimated percentage of 510(k) submissions reaching each step in the review process. See appendix V for additional information on FDA's decision-making process.

⁴³All figures are estimates based on our sample of 510(k) submissions. Our analysis of FDA files did not include submissions for class I devices or submissions that did not receive a final determination, such as submissions that were withdrawn. See app. I for additional information on the scope of our review.

Figure 5: Projected Percentages of 510(k) Submissions for Class II and Class III Devices in Fiscal Years 2005 through 2007 Reaching Each Point in FDA’s Decision-Making Process



Source: GAO analysis of FDA files.

Notes: Estimates based on GAO review of all class III and a sample of class II 510(k) submissions. This figure includes data for 510(k) submissions for class II and class III devices that FDA determined to be SE and NSE in fiscal years 2005 through 2007. The sampling errors of the estimated percentages of 510(k) submissions reaching SE or NSE in FDA’s decision-making process are within plus or minus 1 percentage point at the 95 percent confidence level.

In cases where FDA determines that a new device has new technological characteristics that could not affect safety and effectiveness, the device may be determined SE if descriptive characteristics alone are precise enough to ensure equivalence. In cases where FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence. For cases in which descriptive or performance information is insufficient, FDA requests additional information.

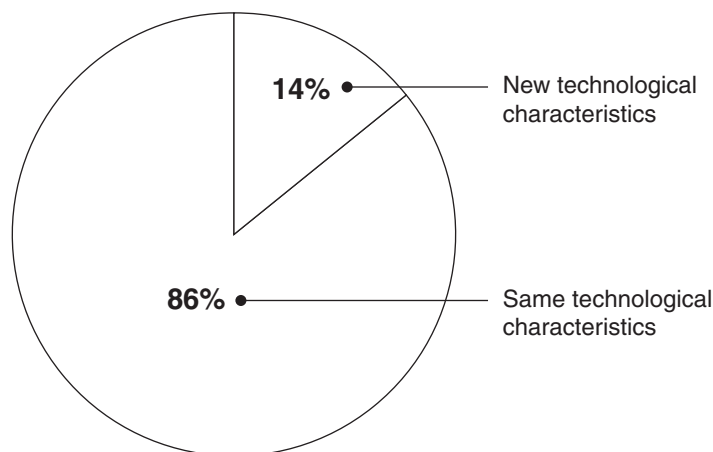
^aFor devices with new technological characteristics, FDA first examines whether the new technological characteristics could affect safety or effectiveness.

^bIncludes some submissions (0.6% of the 5,063 510(k) submissions) in which FDA made a determination of NSE but for which the determination path is not represented in this figure. Reasons that these cases were found NSE include the applicant failing to respond to an FDA data request and a PMA already being required for the device.

All 510(k) Submissions That FDA Cleared Had the Same Intended Use and Most Had the Same Technological Characteristics as Predicate Devices

All 510(k) submissions for class II and class III devices that FDA cleared in fiscal years 2005 through 2007 had the same intended use and most had the same technological characteristics as predicate devices. In all 4,815 class II and class III submissions cleared through the 510(k) process during this time period, FDA determined that the new devices had the same intended use as their predicate devices. In 86 percent of these submissions, we found that FDA determined that the new devices also had the same technological characteristics as their predicate devices. (See fig. 6.)

Figure 6: 510(k) Submissions Cleared in Fiscal Years 2005 through 2007, by Technological Characteristics



Source: GAO analysis of FDA files.

Notes: Data are estimated results for 4,815 submissions based on a sample of submissions for class II and class III devices cleared by FDA during fiscal years 2005 through 2007. The sampling errors of the estimated percentages in this chart are within plus or minus 5 percentage points at the 95 percent confidence level.

In 14 percent of the class II and class III submissions cleared through the 510(k) process in fiscal years 2005 through 2007, FDA determined that the new device had new technological characteristics. For the cleared submissions with new technological characteristics, FDA determined, among other things, that either

1. the new technological characteristics could not affect safety or effectiveness—for example, FDA determined that software modifications to a defibrillator allowing physicians greater control over the device’s CPR (cardiopulmonary resuscitation) settings could not affect the safety or effectiveness of the defibrillator—or

2. the new characteristics do not raise new types of safety or effectiveness questions—for example, FDA determined that a digital electrocardiograph did not raise new types of effectiveness questions relative to the predicate device, an analog electrocardiograph.

Table 5 shows the distribution of cleared submissions by class and characteristics of the determination.

Table 5: Characteristics of Cleared 510(k) Submissions, Fiscal Years 2005 through 2007

Characteristics of cleared submissions	Class II (percentage)	Class III (percentage)	Total (percentage)
Same technological characteristics	4,052 (86)	75 (77)	4,127 (86)
New technological characteristics that could not affect safety or effectiveness	323 (7)	12 (12)	335 (7)
New technological characteristics that do not raise new types of safety or effectiveness questions	342 (7)	11 (11)	353 (7)
Total	4,717 (100)	98 (100)	4,815 (100)

Source: GAO analysis of FDA files.

Note: Data are estimated for 4,815 510(k) submissions based on a sample of submissions for class II and class III devices cleared by FDA in fiscal years 2005 through 2007. The sampling errors of the estimates of class II 510(k) submissions and total 510(k) submissions are within plus or minus 5 percentage points at the 95 percent confidence level.

More Than Half of the 510(k) Submissions FDA Determined Not Substantially Equivalent Were for Devices That Had a New Intended Use or New Technological Characteristics

We found that of the 248 class II and III submissions that FDA determined to be NSE in fiscal years 2005 through 2007, slightly more than half

- had a new intended use,
- had a new technological characteristic that raised new types of safety or effectiveness questions, or
- had a new technological characteristic that could affect safety or effectiveness and did not have performance data to demonstrate equivalence to the predicate device.

We also found that about one in every three 510(k) submissions FDA determined to be NSE had the same intended use and the same technological characteristics as the predicate device, but FDA determined the submissions NSE because of a lack of performance data. An additional 13 percent of submissions were determined NSE for other reasons, such as

not providing adequate data early in the review or not having a predicate device (see table 6).

Table 6: Characteristics of 510(k) Submissions for Devices FDA Determined NSE in Fiscal Years 2005 through 2007

Characteristics	Class II (percentage)	Class III (percentage)	Total (percentage)
New intended use	15 (8)	22 (34)	37 (15)
New technological characteristics that raise new types of safety or effectiveness questions	19 (10)	22 (34)	41 (17)
New technological characteristics and insufficient performance data	42 (23)	7 (11)	49 (20)
Same technological characteristics, but insufficient performance data	88 (48)	1 (2)	89 (36)
Other ^a	19 (10)	13 (20)	32 (13)
Total	183 (100)	65 (100)	248 (100)

Source: GAO analysis of FDA files.

Notes: Data are estimated for 248 510(k) submissions for class II and class III devices that FDA determined NSE in fiscal years 2005 through 2007. The sampling errors of the estimates of class II 510(k) submissions and total 510(k) submissions are within plus or minus 10 percentage points at the 95 percent confidence level.

Percentages may not add to 100 because of rounding.

^aOther includes 510(k) submissions for devices that were required to go through the PMA process, devices that did not have a predicate, and those that were determined to be NSE because of a lack of data early in the 510(k) process.

Conclusions

The 510(k) process plays a major role in FDA's oversight of medical devices. During fiscal years 2003 through 2007, FDA reviewed over 2,400 510(k) submissions annually and cleared about 90 percent of these submissions for the U.S. market. These included 228 cleared submissions for class III devices. In establishing device classes in 1976, Congress envisioned that all class III devices would eventually be required to undergo premarket review through the more stringent PMA process, which requires the manufacturer to provide evidence, which may include clinical data, providing reasonable assurance that the new device is safe and effective. However, certain preamendment class III device types may be reviewed through the 510(k) process until such time as FDA publishes regulations requiring them to go through the PMA process. In 1990 the SMDA directed FDA to take action on the remaining preamendment class III device types by reclassifying them to a lower class or requiring them to remain in class III and go through the PMA process, but we found

that more than 14 years after FDA published its strategy and plans for doing so, a significant number of class III devices—including device types that FDA has identified as implantable; life sustaining; or posing a significant risk to the health, safety, or welfare of a patient—still enter the market through the less stringent 510(k) process.

FDA has stated that eventually all class III devices will require FDA approval through the PMA process and FDA officials reported that the agency is committed to addressing this issue, but the agency has not specified time frames for doing so. Without FDA action, the remaining preamendment class III device types—including device types that FDA identified in 1994 as presenting an unreasonably high risk to public health—may enter the U.S. market through FDA's less stringent premarket notification process.

Recommendation for Executive Action

We are recommending that the Secretary of Health and Human Services direct the FDA Commissioner to expeditiously take steps to issue regulations for each class III device type currently allowed to enter the market through the 510(k) process. These steps should include issuing regulations to (1) reclassify each device type into class I or class II, or requiring it to remain in class III, and (2) for those device types remaining in class III, require approval for marketing through the PMA process.

Agency Comments

We received comments on a draft of this report from HHS. (See app. VI.) The department commented that the draft report fairly and accurately describes FDA's 510(k) program and the department agreed with our conclusions and recommendation.


HHS agreed with our recommendation that FDA expeditiously take steps to reclassify or require PMAs for each class III device type currently allowed to enter the market through the 510(k) process, noting that since 1994 (when FDA announced its strategy to implement provisions of the Safe Medical Devices Act of 1990) FDA has called for PMAs or reclassified the majority of class III devices that did not require PMAs at that time. The department's comments, however, do not specify time frames in which FDA will address the remaining class III device types allowed to enter the market via the 510(k) process, stating instead that the agency is considering its legal and procedural options for completing this task as expeditiously as possible, consistent with available resources and competing time frames. Given that more than 3 decades have passed since Congress envisioned that all class III devices would eventually be required

to undergo premarket review through the more stringent PMA process, it is imperative that FDA take immediate steps to address the remaining class III device types that may still enter the market through the less stringent 510(k) process by requiring PMAs for or reclassifying them.

The department also provided technical comments, which we incorporated as appropriate.

We are sending copies of this report to the Secretary of Health and Human Services and other interested parties. The report is also available at no charge on the GAO Web site at <http://www.gao.gov>.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix VII.



Marcia Crosse
Director, Health Care

Appendix I: Scope and Methodology

To review the Food and Drug Administration's (FDA) use of the 510(k) and premarket approval (PMA) processes to review class I, II, and III device submissions in fiscal years 2003 through 2007, we used FDA's 510(k) and PMA databases. These databases contain information on device submissions,¹ including the name of the device, the FDA-assigned product code,² the status of the submission, and any FDA decisions related to the submission and the dates of those decisions. In both cases, we obtained and analyzed data on submissions for which FDA made a review decision in fiscal years 2003 through 2007.³ We also used FDA's Device Nomenclature Management System to determine other attributes of the device types covered by the device submissions.

The 510(k) submissions we analyzed included traditional and abbreviated 510(k) submissions. We did not include special 510(k) submissions, which are requests for clearance of modifications to devices that have already been cleared through the 510(k) process (see table 7). The PMA submissions we analyzed included original PMA submissions and some supplemental PMA submissions. Specifically, we included supplemental PMA submissions that represented requests for approval for a significant change in a device: *panel-track supplements*, which are requests for approval for a significant change in design, performance, or use of a device for which clinical data are necessary to provide a reasonable assurance of safety and effectiveness; and *180-day (user-fee) supplements*, which are requests for approval for a significant change in components, materials, design, specification, software, color additives, or labeling. We did not include other types of PMA supplements, such as *real-time supplements*, which are requests for approval for a minor change to a

¹In this report, we refer to both 510(k) submissions and PMA applications as *device submissions*. Because related devices can be "bundled" together in a single submission, one submission may include one or more devices.

²The FDA-assigned product code for a device is based on the relevant classification regulation.

³For the purposes of this report, *review decisions* include cases where FDA made a determination to allow or disallow marketing of a device and cases where FDA decided to discontinue consideration for other reasons.

device, such as a minor change in design, sterilization, software, or labeling.⁴

To assess the reliability of these data, we interviewed FDA officials knowledgeable about these databases, performed electronic testing for accuracy and completeness, and where applicable compared our results to aggregate information from other sources, such as published FDA reports and the FDA Web site. We determined that the data were sufficiently reliable for the purposes of this report.

In order to examine the extent to which FDA has determined that devices reviewed through the 510(k) process had new intended uses or new technological characteristics, we used FDA's 510(k) database to select and review a stratified random sample of class II and all class III 510(k) submission files from fiscal years 2005 through 2007. See table 7 for the scope of our file review.

⁴Our analysis also excluded de novo submissions. De novo submissions are for first-of-a-kind devices lacking a legally marketed predicate. Anyone submitting a 510(k) for a device type that has not been previously classified and which FDA subsequently classifies into class III may, within 30 days after receiving notice of such classification, request that FDA reclassify the device under the statutory criteria for class I and class II devices. The de novo classification process permits FDA to establish a class I or II designation for devices that do not have a predicate and allow them to enter the U.S. market. See 21 U.S.C. § 360c(f)(2).

Table 7: Scope of File Review by 510(k) Submission Type, Review Decision, and FDA Office or Center

Characteristic of 510(k) submission	Included in file review?	Reason
Submission type		
Traditional	Yes	Traditional 510(k) submissions are the conventional 510(k) submission type used to clear new devices for market. Traditional submissions constituted the majority of 510(k) submissions made to FDA during the time of our review.
Abbreviated	Yes	Abbreviated 510(k) submissions are a streamlined version of the traditional 510(k) process. In an abbreviated 510(k) submission, applicants use guidance documents, special controls, or performance standards to assess and then report on the performance of their new device to expedite review.
Special	No	Special 510(k) submissions are submitted for a modification to a device that has been cleared through the 510(k) process. We excluded them from our review because this type of submission is only used for modifications to a device which has already cleared the 510(k) process.
Review decision		
Substantially equivalent (SE)	Yes	The submissions completed the 510(k) review process and were cleared for market.
Not substantially equivalent (NSE)	Yes	The submissions completed the 510(k) review process and were not cleared for market.
Withdrawn	No	Withdrawn submissions did not complete the 510(k) review process.
Deleted	No	Deleted submissions did not complete the 510(k) review process.
FDA office or center		
Center for Devices and Radiological Health, Office of Device Evaluation	Yes	This office administers the 510(k), PMA, Humanitarian Device Exemption, and Investigational Device Exemption programs. It processes the majority of 510(k) submissions each year: for example, in FY 2007, it processed 85 percent of all 510(k) submissions.
Center for Devices and Radiological Health, Office of In Vitro Diagnostic Device Evaluation and Safety	No	This office oversees the regulation of devices such as in-home and laboratory diagnostic tests, and processes relatively few 510(k) submissions each year. In FY 2007, it processed 13 percent of all 510(k) submissions.
Center for Biologics Evaluation and Research	No	This office oversees devices such as those used for licensed blood collection and processing, and processes relatively few 510(k) submissions each year. In FY 2007, it processed 2 percent of all 510(k) submissions.

Source: GAO.

Note: The scope of the file review also excluded de novo submissions, which are submissions for first-of-a-kind devices lacking a legally marketed predicate. See 21 U.S.C. § 360c(f)(2).

All 163 class III submissions that met the inclusion criteria were included in the sample. The 296 class II cases included in the sample constituted a random sample of the 4,900 class II submissions that met the inclusion criteria. The class II submissions included in the sample were stratified by

decision, meaning that class II submissions determined not substantially equivalent (NSE) were oversampled so that the results could be generalizable to the universe of all class II submissions, to class II submissions determined NSE, or to class II submissions determined substantially equivalent (SE). The sample contained a total of 459 submissions. See tables 8 and 9 for the number of submissions by fiscal year, class, and decision.

Table 8: Cases Reviewed, by Fiscal Year

Fiscal year	Count	Percentage
2005	167	36
2006	141	31
2007	151	33
Total	459	100

Source: GAO.

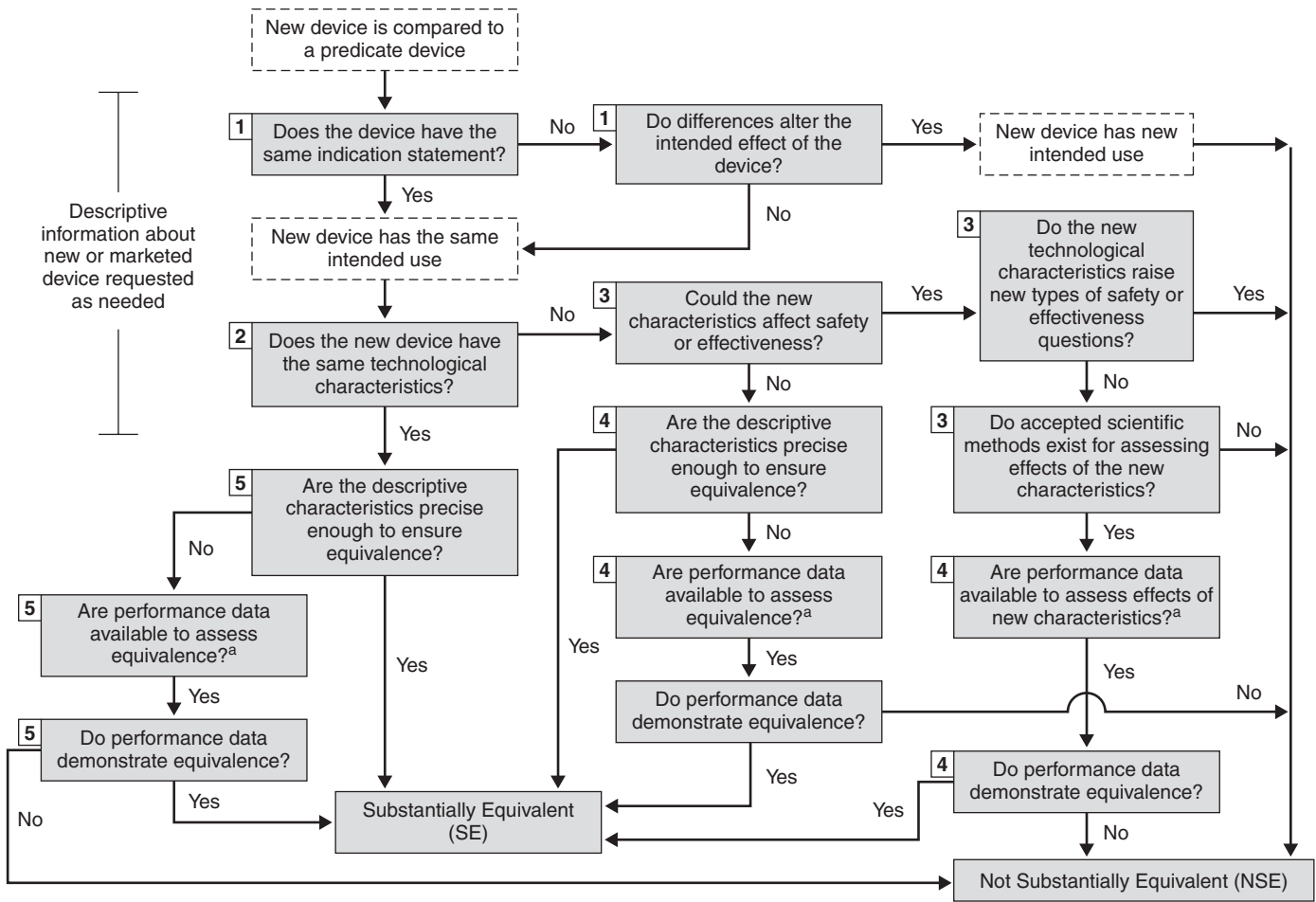
Table 9: Cases Reviewed, by Class and SE/NSE Determination

FDA decision	Class II	Class III	Total
SE	195	102	297
NSE	101	61	162
Total	296	163	459

Source: GAO.

We conducted our file review in June 2008. We collected data primarily from the FDA reviewer memo, which contained information concerning the steps FDA took to reach its determination of SE or NSE. This information included the incremental decisions FDA made concerning the use and technological characteristics of the new device, and in sum, defined the path through an FDA decision tree the reviewer took to reach a determination of SE or NSE. See figures 7 and 8 for detailed and simplified versions, respectively, of FDA’s decision tree. We recorded the individual decisions made in each case, and analyzed the results with respect to the path the FDA reviewer took to reach the final determination of SE or NSE.

Figure 7: Detailed Version of FDA's 510(k) Decision-Making Process

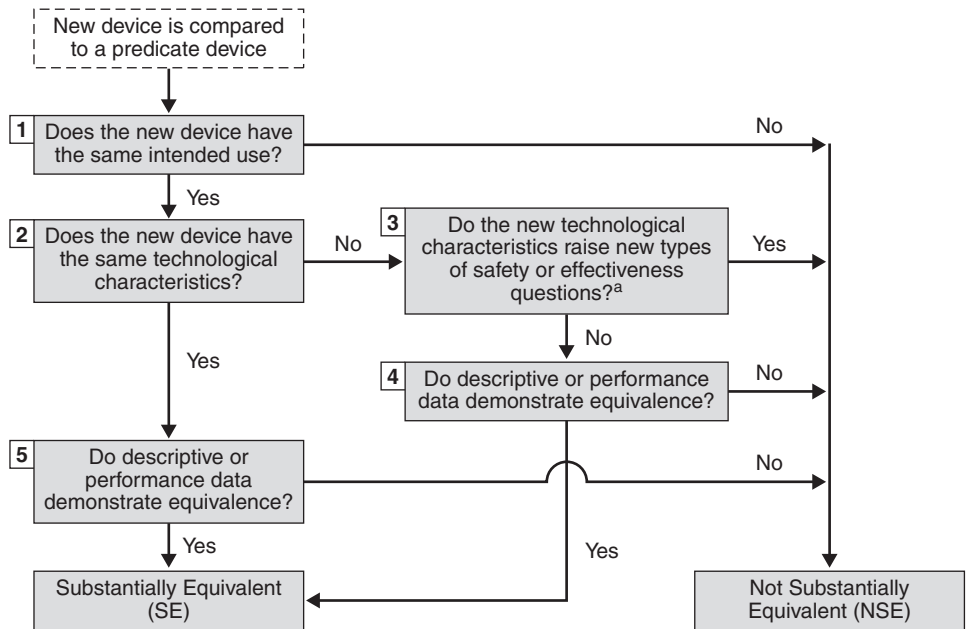


Source: GAO.

Notes: Numbered boxes correspond to numbered boxes on the simplified FDA decision-making process in fig. 8.

^aData may be in the 510(k), other 510(k)s, the center's classification files, or the literature. In cases where FDA determines that performance data are not available, FDA requests data from the applicant.

Figure 8: Simplified Version of FDA’s 510(k) Decision-Making Process



Source: GAO.

Notes: Numbered boxes correspond to numbered boxes on the detailed decision tree in figure 7.

In cases where FDA determines that a new device has new technological characteristics that could not affect safety and effectiveness, the device may be determined SE if descriptive characteristics alone are precise enough to ensure equivalence. If not, FDA will look at performance data. In cases where FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence. For cases in which descriptive or performance information is insufficient, FDA requests additional information.

^aFor devices with new technological characteristics, FDA first examines whether the new technological characteristics could affect safety or effectiveness.

In the 10 cases where we could not determine the steps FDA took to reach its determination during our file review, we requested additional information from FDA officials. Officials from the Office of Device Evaluation in FDA’s Center for Devices and Radiological Health reviewed the files in question and provided us with the information we requested.

To assess the reliability of these data, we compared our results with information from FDA’s 510(k) database and Device Nomenclature Management System. In addition, FDA officials stated that the data in the files were accurate and reliable and provided input in the development of our data collection instrument.

In addition to our data analysis, we reviewed relevant laws and regulations concerning the premarket review process. We also interviewed FDA officials from the FDA centers and offices that process device submissions (Center for Biologics Evaluation and Research, Office of Device Evaluation, and Office of In Vitro Diagnostic Device Evaluation and Safety). Finally, we interviewed representatives from professional associations representing device manufacturers (the Advanced Medical Technology Association, the ECRI Institute, the Medical Device Manufacturers Association, and the Medical Imaging and Technology Alliance) and consumer advocates (the National Research Center for Women & Families and Public Citizen).

We conducted this performance audit from March 2008 to January 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Third-Party Review of 510(k) Submissions

The FDA Modernization Act of 1997 directed FDA to accredit third parties (called accredited persons) in the private sector to conduct the initial review of 510(k) submissions for low- to moderate-risk devices.¹ Under FDA's Accredited Persons Program, device manufacturers may contract with accredited organizations (third parties)² to review certain 510(k) submissions for a negotiated fee.³ The third party uses the same statutory and regulatory criteria as FDA to determine substantial equivalence, documents its review and recommendation, and forwards the 510(k) submission and documentation to FDA's Center for Devices and Radiological Health. At the center, a third-party 510(k) submission is assessed by an FDA supervisor, who may accept or change the substantial equivalence recommendation of the third party. After completing the supervisory assessment, FDA issues a letter to the 510(k) applicant via the third-party reviewer with a final determination on the 510(k) submission. During the third-party review, the FDA supervisor can request additional information from the third party and the third party can request additional information from the 510(k) applicant.

FDA expanded the program to include more than 670 class I and class II device types to be eligible for 510(k) review by a third party.⁴ These include device types for diagnostic ultrasound systems, computed tomography X-ray systems, and surgical lasers. However, not all of the accredited third parties are authorized to review all device types eligible for third-party review. For example, in October 2008 FDA's Web site listed 7 of 11 accredited third parties as authorized to review 510(k) submissions for hearing aids.

¹Pub. L. No. 105-115, § 210, 111 Stat. 2296, 2342 (1997).

²As of August 6, 2008, FDA listed 11 accredited third parties that can conduct third-party reviews of 510(k) submissions: (1) British Standards Institution; (2) Center for Measurement Standards of Industrial; (3) Cheiron BV; (4) Citech; (5) Intertek Testing Services; (6) Kema Quality B.V.; (7) Niom-Scandinavian Institute of Dental Materials; (8) Regulatory Technology Services, LLC; (9) TUV Rheinland of North America, Inc.; (10) TUV SUD America, Inc.; and (11) Underwriters Laboratories, Inc.

³FDA does not maintain data on the amount of these fees, which are negotiated between the 510(k) submitter and the third-party reviewer. However, FDA officials estimate the fee to generally be in the \$5,000 to \$10,000 range.

⁴FDA initially identified 154 device types that were eligible for third-party review. In March 2001, FDA expanded the program to allow third parties to review 510(k) submissions for many class II device types that were not previously eligible.

Device types that are not eligible for third-party review include all class III devices; class II devices intended to be permanently implantable, life sustaining, or life supporting; and class II devices requiring clinical data to support their 510(k) clearance.⁵ During our review of FDA's 510(k) database, we found three instances of 510(k) submissions in which class II devices that were life sustaining were cleared for market through the third-party review program during fiscal years 2003 through 2007. FDA officials explained that about five life-sustaining, class II device types, hemodialysis devices, had inadvertently been added to the list of devices eligible for third-party review when the list was expanded in 2001, and that in May 2003, FDA removed the life-sustaining class II device types from the list of devices eligible for third-party review on FDA's Web site. The FDA officials said that while the three 510(k) submissions for class II life-sustaining device submissions had been submitted through the third-party review program, FDA also conducted its own review of the three 510(k) submissions before they were cleared for marketing.

During fiscal years 2003 through 2007, FDA reviewed and made final determinations on 1,082 third-party 510(k) submissions (see table 10). According to FDA, the number of third-party submissions increased as the result of (1) increased familiarity with the third-party review program among potential applicants, (2) the increase in the number of device types eligible for the program, and (3) less financial disincentives to use the third-party review program as FDA instituted device user fees.⁶ An FDA official familiar with the program stated that the third-party review program may be more attractive to device manufacturers because third-party review 510(k) submissions are processed faster than traditional 510(k) submissions. The official noted, however, that as FDA's review of traditional 510(k) submissions becomes more efficient, the advantages of

⁵21 U.S.C. § 360m(a)(3)(A). In addition, in February 2001, FDA issued guidance stating that third parties may not review 510(k) submissions that require multiple FDA centers to review the device—for example, for drug-device combination products—or if a center other than the Center for Devices and Radiological Health, for example, the Center for Biologics Evaluation and Research, has the primary responsibility for the 510(k) review.

⁶FDA user fees for FDA review of medical device applications took effect at the beginning of fiscal year 2003.

Appendix II: Third-Party Review of 510(k) Submissions

the third-party review program in terms of timeliness may diminish, which could lead to fewer third-party review 510(k) submissions.⁷

Table 10: Third-Party Review 510(k) Submissions with FDA Decisions, Fiscal Years 2003 through 2007

Fiscal year	FDA decision		Total (percentage)
	SE (percentage)	NSE (percentage)	
2003	157 (15)	2 (10)	159 (15)
2004	227 (21)	9 (43)	236 (22)
2005	226 (21)	3 (14)	229 (21)
2006	242 (23)	6 (29)	248 (23)
2007	209 (20)	1 (5)	210 (19)
Total	1,061 (100)	21 (100)	1,082 (100)

Source: GAO analysis of FDA data.

Note: Percentages may not sum to 100 because of rounding.

Table 11 shows the third-party review 510(k) submissions by medical specialty.

⁷According to FDA, in fiscal year 2005 the difference in average review times between 510(k) submissions reviewed by third parties and 510(k) submissions reviewed entirely by FDA was 13 days, versus 45 days in fiscal year 2000.

Table 11: Third-Party Review 510(k) Submissions by Medical Specialty, Fiscal Years 2003 through 2007

Medical specialty	Frequency	Percentage
Radiology	411	38.7
General and plastic surgery	120	11.3
Cardiovascular	116	10.9
General hospital	98	9.2
Dental	52	4.9
Gastroenterology and urology	49	4.6
Anesthesiology	45	4.2
Neurology	45	4.2
Physical medicine	43	4.1
Ophthalmic	25	2.4
Obstetrics and gynecology	22	2.1
Clinical chemistry	13	1.2
Ear, nose, and throat	7	0.7
Clinical toxicology	4	0.4
Microbiology	4	0.4
Hematology	3	0.3
Orthopedic	3	0.3
Immunology	1	0.1
Total	1,061	100

Source: GAO analysis of FDA data.

Note: Percentages may not sum to 100 because of rounding.

Appendix III: FDA's Implementation of Safe Medical Devices Act Provisions

The Safe Medical Devices Act of 1990 (SMDA) amended the definition of class II devices¹ and required FDA, for each preamendment class III device type and before December 1, 1995, to (1) order manufacturers to submit information on safety and effectiveness to FDA and (2) publish proposed and final regulations to reclassify each device type into class II or class I or to require it to remain in class III. For those devices for which FDA published a regulation requiring the device to remain in class III, the SMDA further directed FDA to, as promptly as reasonably achievable but not later than 12 months after the effective date of the regulation requiring the device to remain in class III, establish a schedule for the promulgation of regulations requiring the submission of PMAs.

In an April 19, 1994, memorandum from the Acting Director of the FDA Center for Devices and Radiological Health's Office of Device Evaluation, FDA outlined its strategy for implementation of the SMDA. Specifically, FDA grouped 117 preamendment class III device types for which FDA had not yet initiated any action to require the submission of PMAs into three groups and prioritized the devices to facilitate the SMDA activities. (See table 12.) The agency's proposed strategy established a plan for beginning to address the class III device types that were continuing to be reviewed through the 510(k) process, but did not establish completion dates for doing so.

¹Before enactment of the SMDA, class II devices were defined as devices for which general controls alone were insufficient to provide reasonable assurance of safety and effectiveness, but for which sufficient information existed to establish a performance standard to provide such assurance. Under the SMDA, the definition was revised to include those devices for which sufficient information existed to establish special controls to provide such assurance. In addition to performance standards, special controls include postmarket surveillance, patient registries, guidelines and recommendations, and other appropriate actions as determined by FDA. The SMDA also stated that for class II devices that purported or represented to be used for supporting or sustaining human life, FDA was required to examine and identify the necessary special controls and describe how they would provide adequate assurance of safety and effectiveness.

Appendix III: FDA's Implementation of Safe Medical Devices Act Provisions

Table 12: FDA Groupings and Time Frames for Implementation of SMDA Provisions for Class III Device Types in 1994 and Status as of October 2008

Group 3 (device types designated high priority)	
Number of device types	15
Description	<p>Group 3 contains devices that were not considered candidates for reclassification and that FDA believed were in commercial distribution and would require submission of PMAs in the near future.</p> <p>The high-priority subgroup of group 3 contains devices FDA determined presented an unreasonably high risk to public health because significant issues of safety, effectiveness, or both were not being resolved or, to the best of FDA's knowledge, had little probability of being resolved.</p>
Examples	Certain types of hip joints and shoulder joints, ultrasound and muscle stimulator.
Planned schedule	FDA planned to publish proposed rules related to these 15 device types by 1996. In its 1994 strategy memorandum, FDA noted that the timetable for publication of each final rule would be based upon specific data needs, comments received, and the existence, if any, of any petitions to reclassify the devices that FDA needed to review.
Status as of October 2008	Of the 15 device types designated high priority in group 3, 5 were reclassified, 6 now require PMAs, and 4 may still be cleared through the 510(k) process.
Group 3 (other device types)	
Number of device types	27
Description	<p>Group 3 contains devices that were not considered candidates for reclassification and that FDA believed were in commercial distribution and would require submission of PMAs in the near future.</p> <p>The devices in group 3 that were not designated high priority were not considered candidates for reclassification, but FDA planned to assess whether these devices should be moved to group 2. FDA stated that the continued marketing of these group 3 devices did not present as great a risk to the public health, in light of FDA's knowledge and experience with the devices, as the device types designated high priority.</p>
Examples	External pacemaker pulse generator, stairclimbing wheelchair.
Planned schedule	FDA planned to pursue the same course of evaluation and prioritization as used for group 2 device types.
Status as of October 2008	Of the 27 other device types in group 3 that were not designated high priority, 13 were reclassified, 7 now require PMAs, and 7 may still be cleared through the 510(k) process.
Group 2	
Number of device types	31
Description	Group 2 contains devices that FDA believed had a high potential for reclassification into class II and for which existing questions of safety, effectiveness, or both had been or could be answered by information already obtained or being obtained by manufacturers. According to FDA, the SMDA-modified definition of class II devices together with increased experience with these device types might provide grounds for reclassification of group 2 devices.
Examples	Tweezer-type epilator, cardiovascular permanent pacemaker electrodes, implanted blood access device.

Appendix III: FDA's Implementation of Safe Medical Devices Act Provisions

Group 3 (device types designated high priority)	
Planned schedule	FDA planned to issue an order requiring manufacturers to submit all safety and effectiveness information available or known to them, including adverse information, for all group 2 device types, to complete a review and evaluation of this safety and effectiveness information, and to proceed with rule making to reclassify these device types or retain them in class III by 1998. The 1994 memorandum did not specify any dates for publication of final regulations reclassifying devices or requiring them to remain in class III.
Status as of October 2008	Of the 31 device types in group 2, 23 were reclassified, 1 now requires a PMA, and 7 may still be cleared through the 510(k) process (this includes 1 case in which the device type was reclassified for some purposes but remains class III for others).
Group 1	
Number of device types	44
Description	Group 1 contains device types that FDA identified as having fallen into disuse or limited use. FDA determined that these device types raise significant questions of safety, effectiveness, or both but are rarely in current use. FDA believed that rule making requiring PMAs for these device types would be unlikely to result in viable PMAs or reclassification petitions.
Examples	Catheter balloon repair kit; certain types of hip joints, finger joints, and shoulder joints.
Planned schedule	FDA planned to publish one proposed regulation in 1994 requiring PMAs for all group 1 devices. The 1994 memorandum did not specify any dates for publication of final regulations.
Status as of October 2008	Of the 44 device types in group 1, 4 were reclassified, 39 now require PMAs, and 1 may still be cleared through the 510(k) process.
All groups	
Number of device types	117
Status as of October 2008	Of the 117 device types contained in FDA's strategy document, 45 have been reclassified, 53 now require PMAs, and 19 may still be cleared through the 510(k) process.

Source: GAO.

Note: In addition, the 1994 memorandum listed additional device types for which some action had been taken toward reclassification or requiring PMA submissions. For example, the memorandum listed device types, including endosseous (dental) implants, with reclassification petitions pending.

As of October 2008, FDA had reclassified 45 device types and published regulations requiring PMAs for 53 device types. Therefore, of the 117 preamendment class III device types covered by FDA's strategy, 19 device types remain in class III and may be cleared through the 510(k) process.² Four of those 19 device types are types that FDA had placed in group 3 and designated high priority—that is, they are device types that FDA had determined to present an unreasonably high risk to public health because significant issues of safety or effectiveness were not being resolved or, to the best of FDA's knowledge, had little probability of being resolved.

²See app. IV for information on class III device types that were cleared through the 510(k) process in fiscal years 2003 through 2007.

Appendix IV: Additional Information on 510(k) Submissions for Class III Devices Reviewed by FDA

This appendix summarizes the results from GAO analysis of FDA’s data for class III 510(k) submissions with FDA review decisions in fiscal years 2003 through 2007. The following tables show FDA’s final decisions for submissions for class III devices for each fiscal year through the 510(k) process (table 13); the primary medical specialties for submissions for class III devices cleared through the 510(k) process (table 14); and a detailed list of all device types covered by the class III devices cleared through the 510(k) process, including the status of these device types as of October 2008 (table 15).

Table 13: FDA Review Decisions for Class III 510(k) Submissions by Fiscal Year, Fiscal Years 2003 through 2007

Fiscal Year	FDA Decision			Total (percentage of row)
	SE (percentage of row)	NSE (percentage of row)	Other ^a (percentage of row)	
2003	58 (80)	12 (16)	3 (4)	73 (100)
2004	68 (80)	13 (15)	4 (5)	85 (100)
2005	31 (52)	27 (45)	2 (3)	60 (100)
2006	32 (50)	31 (48)	1 (2)	64 (100)
2007	39 (65)	17 (28)	4 (7)	60 (100)
Total	228 (67)	100 (29)	14 (4)	342 (100)

Source: GAO analysis of FDA data.

^aOther decisions include submissions that were withdrawn, exempted by regulation, not responsive to FDA’s requests within a specified time frame, forwarded to another FDA center or office, duplicates, determined not to be a device, or not actively regulated by FDA.

**Appendix IV: Additional Information on
510(k) Submissions for Class III Devices
Reviewed by FDA**

**Table 14: Primary Medical Specialties of Class III 510(k) Submissions Cleared in
Fiscal Years 2003 through 2007**

Medical specialty	Frequency	Percentage
Cardiovascular	64	28
Orthopedic	54	24
Gastroenterology and urology	36	16
Dental	31	14
Physical medicine	19	8
Neurology	14	6
Microbiology	7	3
General and plastic surgery	2	1
Obstetrics and gynecology	1	1
Total	228	100

Source: GAO analysis of FDA data.

Note: Totals may not sum to 100 because of rounding.

**Appendix IV: Additional Information on
510(k) Submissions for Class III Devices
Reviewed by FDA**

Table 15: Device Types with Class III 510(k) Submissions Cleared in Fiscal Years 2003 through 2007 and Their Status as of October 2008

Device type (regulation number)	Number of submissions cleared in FYs 2003-2007	Actions taken as of October 2008
Device types included in group 3 and designated high priority in FDA's 1994 strategy^a		
Iontophoresis device ^b (21 C.F.R. § 890.5525(b))	18	FDA published a notice of intent to reclassify this device type in 2000. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Hip joint metal/metal semiconstrained, with an uncemented acetabular component, prosthesis (21 C.F.R. § 888.3330)	18	FDA rejected one petition to reclassify this device type in 2002 and received another classification petition in 2005. According to FDA officials, the agency is reviewing the reclassification petition that it received in 2005. While it is doing so, this remains a class III device type that may be cleared through the 510(k) process.
Hip joint metal/metal semi-constrained, with a cemented acetabular component, prosthesis (21 C.F.R. § 888.3320)	2	FDA rejected one petition to reclassify this device type in 2002 and received another classification petition in 2005. According to FDA officials, the agency is reviewing the petition that it received in 2005. While it is doing so, this remains a class III device type that may be cleared through the 510(k) process.
Shortwave diathermy ^c (21 C.F.R. § 890.5290)	1	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Device types included in group 3 (but not designated high priority) in FDA's 1994 strategy^a		
Neurovascular embolization device ^d (21 C.F.R. § 882.5950)	11	FDA reclassified this device type to class II effective January 28, 2005.
External counter-pulsating device (21 C.F.R. § 870.5225)	9	FDA requested that manufacturers submit safety and effectiveness information by February 14, 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Arrhythmia detector and alarm (21 C.F.R. § 870.1025)	7	FDA reclassified this device type to class II effective November 28, 2003.
Vascular embolization device ^d (21 C.F.R. § 870.3300)	4	FDA reclassified this device type to class II effective January 28, 2005.
Intra-aortic balloon and control system (21 C.F.R. § 870.3535)	2	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Sorbent hemoperfusion system (21 C.F.R. § 876.5870)	1	FDA requested that manufacturers submit safety and effectiveness information by February 14, 1998. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.

**Appendix IV: Additional Information on
510(k) Submissions for Class III Devices
Reviewed by FDA**

Device type (regulation number)	Number of submissions cleared in FYs 2003-2007	Actions taken as of October 2008
External pacemaker pulse generator (21 C.F.R. § 870.3600)	1	FDA that requested manufacturers submit safety and effectiveness information by August 14, 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Device types included in group 2 in FDA's 1994 strategy^a		
Blood access device (implanted) (21 C.F.R. § 876.5540(b)(1))	35	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1998. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Herpes simplex virus serological assays ^d (21 C.F.R. § 866.3305)	7	FDA reclassified this device type to class II for type 1 and/or type 2 serological assays effective May 3, 2007; all other assays remain class III and may be cleared through the 510(k) process. According to FDA, the seven class III 510(k) submissions for herpes simplex virus serological assays cleared in fiscal years 2003 through 2007 were for type 1 and/or type 2 serological assays.
External cardiac compressor (21 C.F.R. § 870.5200)	4	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1998. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Topical oxygen chamber for extremities (21 C.F.R. § 878.5650)	2	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1997; FDA published a proposal to reclassify in 2006. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Cardiovascular pacemaker electrodes (permanent) (21 C.F.R. § 870.3680)	1	FDA requested that manufacturers submit safety and effectiveness information by August 14, 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Other^e		
Pedicle screw spinal system ^f (21 C.F.R. § 888.3070(b)(2))	34	In 2001, FDA stated that it intended to initiate the call for PMAs for the device when intended for certain uses in a future <i>Federal Register</i> notice. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Automated external defibrillator (21 C.F.R. § 870.5310)	30	In 2003, FDA began to regulate automated external defibrillators separately from arrhythmia detectors and alarms; at that time, the agency published a notice of intent to initiate a proceeding to reclassify. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.

**Appendix IV: Additional Information on
510(k) Submissions for Class III Devices
Reviewed by FDA**

Device type (regulation number)	Number of submissions cleared in FYs 2003-2007	Actions taken as of October 2008
Endosseous dental implant (blade form) (21 C.F.R. § 872.3640(b)(2))	26	FDA reclassified this device type to class II for root-form endosseous dental implants effective June 11, 2004; blade-form endosseous dental implants remain class III and may be cleared through the 510(k) process.
Endosseous dental implant abutment (21 C.F.R. § 872.3630)	4	FDA reclassified this device type to class II effective June 11, 2004.
Nonroller-type cardiopulmonary bypass blood pump (21 C.F.R. § 870.4360)	5	FDA had published a proposal to reclassify the device in 1993 and withdrew that proposal in 2004. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Cranial electrotherapy stimulator (21 C.F.R. § 882.5800)	3	FDA had required PMA submissions for this device type in 1995 but revoked that regulation in 1997. FDA requested safety and effectiveness information from manufacturers in 1997. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Mandibular condyle prosthesis (temporary) ^g (21 C.F.R. § 872.3960)	1	FDA amended the regulation in 1998 stating that no effective date had been established for the submission of PMAs for the implanted version of the device used for temporary reconstruction. In the applicable <i>Federal Register</i> notice, FDA added that at a later date, it would propose reclassifying from class III to class II the generic type of temporary mandibular condyle prosthesis intended for temporary reconstruction following surgical ablation of malignant and benign tumors. FDA has not issued a regulation reclassifying or requiring PMA submissions for this device type. It remains a class III type that may be cleared through the 510(k) process.
Pericardial patch	2	According to agency officials, FDA is in the process of determining how to address the situation under which FDA cleared two submissions for this type of class III device through the 510(k) process).

Source: GAO.

Notes: No submissions with device types included in group 1 of FDA's 1994 strategy were cleared in fiscal years 2003 through 2007. Generally, the name of the device type is the title of the relevant provision in the 2008 edition of title 21 of the *Code of Federal Regulations*.

^aFor a detailed description of the device types covered by FDA's 1994 strategy, see app. III.

^bFor uses other than (1) the diagnosis of cystic fibrosis or (2) those indicated on the label of the drug used with the device if the label includes adequate directions for the device's use with the drug.

^cFor uses other than (1) the treatment of malignancies or (2) the generation of deep heat within body tissues to treat conditions such as pain, muscle spasms, and joint contractures.

^dDuring the period of our review, FDA renamed these devices: the neurovascular embolization device, vascular embolization device, and herpes simplex virus serological assays were previously know as the artificial embolization device, arterial embolization device, and herpes simplex virus serological reagents, respectively.

**Appendix IV: Additional Information on
510(k) Submissions for Class III Devices
Reviewed by FDA**

⁶Other includes device types for which FDA had already taken some action by 1994 (for example, FDA indicated that it had reclassification petitions pending for some device types in 1994) as well as new device types that FDA established after 1994 (for example, FDA added a regulation for a subset of one device type).

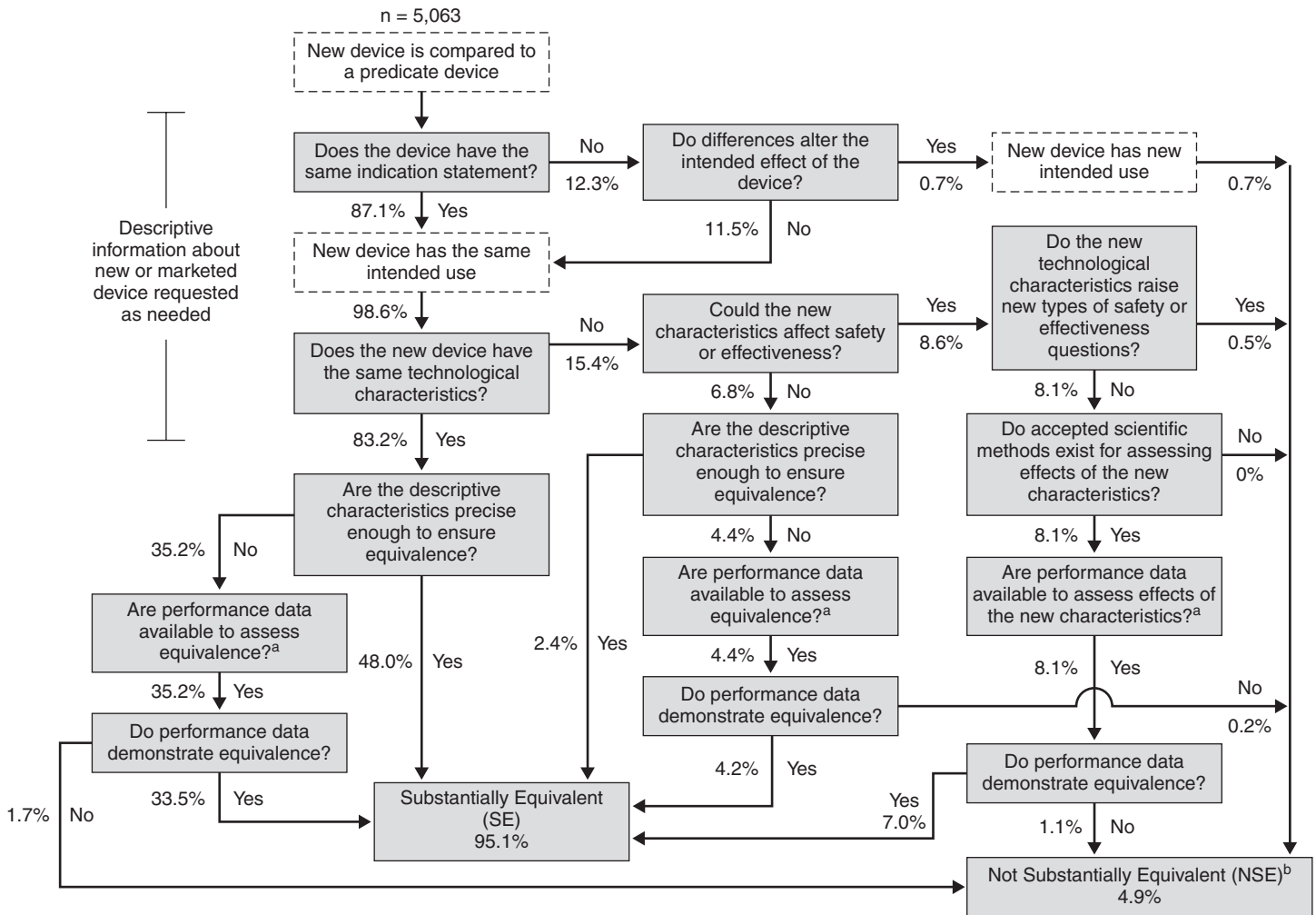
⁷When intended to provide immobilization and stabilization of spinal segments in the thoracic, lumbar, and sacral spine as an adjunct to fusion in the treatment of degenerative disc disease and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1 or degenerative spondylolisthesis with objective evidence of a neurologic impairment.

⁸In 1998 FDA issued a regulation requiring PMAs for mandibular condyle prostheses intended for permanent reconstruction.

Appendix V: FDA's 510(k) Decision-Making Process

This appendix presents the additional information from GAO analysis of FDA's 510(k) submission files for which FDA reached a determination of SE or NSE in fiscal years 2005 through 2007. The following figures show FDA's detailed decision-making process for class II and class III submissions (fig. 9); the decision-making process for class II devices alone (fig. 10); and the decision-making process for class III devices alone (fig. 11).

Figure 9: Projected Percentages of 510(k) Submissions for Class II and Class III Devices in Fiscal Years 2005 through 2007 Reaching Each Point in FDA's Detailed Decision-Making Process



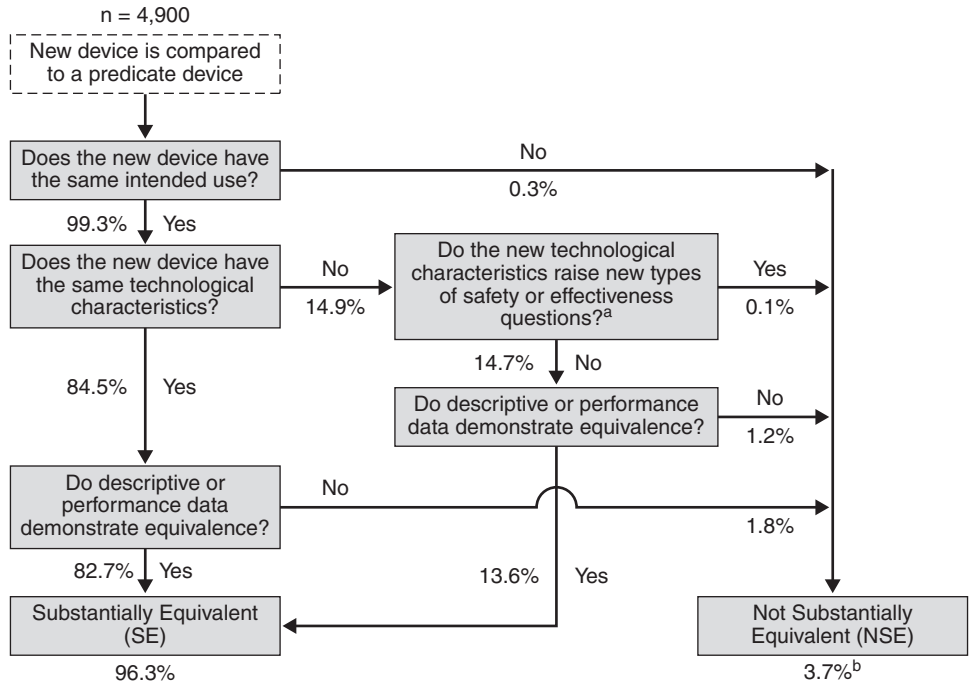
Source: GAO analysis of FDA files.

Note: The sampling errors of the estimated percentages of 510(k) submissions reaching SE or NSE in FDA's decision-making process are within plus or minus 1 percentage point at the 95 percent confidence level.

^aPerformance data may be contained in the 510(k) submission, other 510(k) submissions, the center's classification files, or academic literature. In cases where FDA determines that performance data are not available, FDA requests data from the applicant.

^bIn 0.6 percent of the 5,063 cases, FDA made a determination of NSE, but the determination path is not represented in this flowchart. Reasons that these cases were found NSE include: the applicant failing to respond to an FDA data request and a PMA already being required for the device type.

Figure 10: Projected Percentages of 510(k) Submissions for Class II Devices in Fiscal Years 2005 through 2007 Reaching Each Point in FDA's Decision-Making Process



Source: GAO analysis of FDA files.

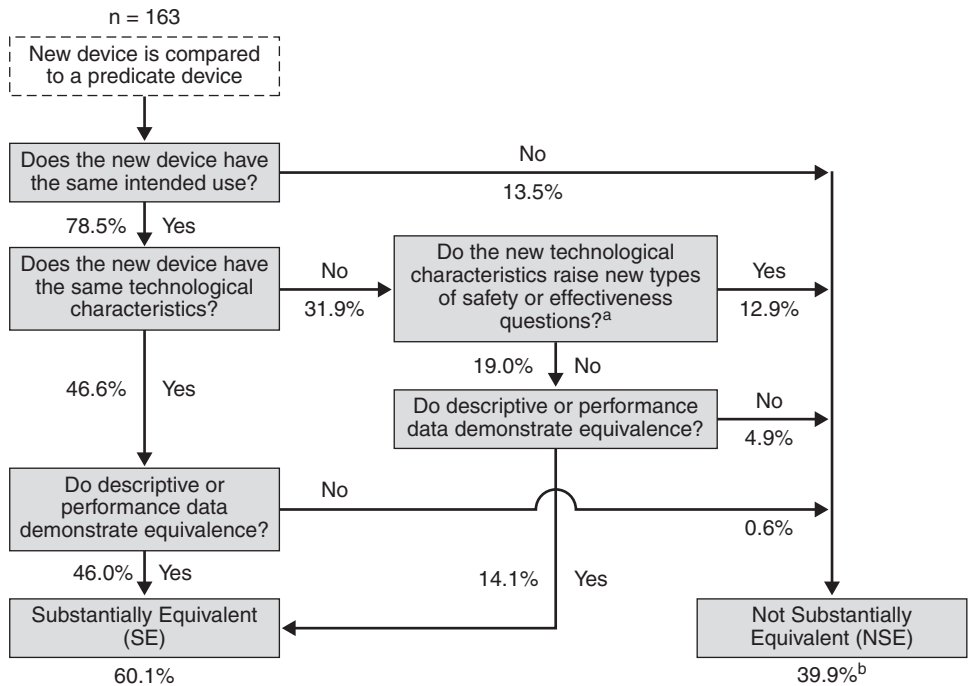
Notes: In cases where FDA determines that a new device has new technological characteristics that could not affect safety and effectiveness, the device may be determined SE if descriptive characteristics alone are precise enough to ensure equivalence. In cases where FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence. For cases in which descriptive or performance information is insufficient, FDA requests additional information.

The sampling errors of the estimated percentages of 510(k) submissions for class II devices reaching SE or NSE in FDA's decision-making process are within plus or minus 1 percentage point at the 95 percent confidence level.

^aFor devices with new technological characteristics, FDA first examines whether the new technological characteristics could affect safety or effectiveness.

^bIn 0.4 percent of the 4,900 class II cases, FDA made a determination of NSE, but the determination path is not represented in this flowchart. Reasons that these cases were found NSE include the applicant failing to respond to an FDA data request and a PMA already being required for the device type.

Figure 11: Percentages of 510(k) Submissions for Class III Devices in Fiscal Years 2005 through 2007 Reaching Each Point in FDA's Decision-Making Process



Source: GAO analysis of FDA files.

Notes: In cases where FDA determines that a new device has new technological characteristics that could not affect safety and effectiveness, the device may be determined SE if descriptive characteristics alone are precise enough to ensure equivalence. In cases where FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence. For cases in which descriptive or performance information is insufficient, FDA requests additional information.

Totals may not sum to 100 because of rounding.

^aFor devices with new technological characteristics, FDA first examines whether the new technological characteristics could affect safety or effectiveness.

^bIn 7.9 percent of the 163 class III cases, FDA made a determination of NSE, but the determination path is not represented in this flowchart. Reasons that these cases were found NSE include: the applicant failing to respond to an FDA data request and a PMA already being required for the device type.

Appendix VI: Comments from the Department of Health and Human Services



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

DEC 23 2008

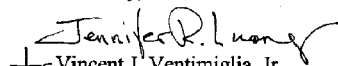
Marcia Crosse
Director, Health Care
Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Ms. Crosse:

Enclosed are the Department's comments on the U.S. Government Accountability Office's (GAO) draft report entitled: "MEDICAL DEVICES: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process" (GAO-09-190).

The Department appreciates the opportunity to review and comment on this report before its publication.

Sincerely,


for Vincent J. Ventimiglia, Jr.
Assistant Secretary for Legislation

Attachment

**GENERAL COMMENTS OF THE U.S. DEPARTMENT OF HEALTH AND
HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY
OFFICE'S (GAO) DRAFT REPORT ENTITLED: MEDICAL DEVICES: FDA
SHOULD TAKE STEPS TO ENSURE THAT HIGH RISK DEVICE TYPES ARE
APPROVED THROUGH THE MOST STRINGENT PREMARKET REVIEW
PROCESS (GAO 09-190)**

In general, we believe GAO's draft report fairly and accurately describes the Food and Drug Administration's (FDA) medical device premarket notification (510(k)) program. We agree with GAO's conclusions and recommendation to expeditiously take steps to either reclassify or call for PMAs for each class III device type currently allowed to enter the market through the premarket notification process.

FDA is committed to resolving the classification and premarket submission type for the remaining preamendment class III devices currently subject to 510(k). Since 1994, FDA has called for premarket approval applications (PMAs) or reclassified the majority of class III device types not requiring PMA at that time. In recent months, prior to the issuance of this report, FDA officials have met internally to discuss the most appropriate and expeditious method to require all class III device types to be approved through the PMA process. FDA is considering its legal and procedural options for completing this task as expeditiously as possible, consistent with available resources and competing priorities.

Appendix VII: GAO Contact and Staff Acknowledgments

GAO Contact

Marcia Crosse, (202) 512-7114 or crossem@gao.gov

Acknowledgments

In addition to the contact named above, Kim Yamane, Assistant Director; Susannah Bloch; Matt Byer; Sean DeBlieck; Linda Galib; Julian Klazkin; and Dan Ries made key contributions to this report.

Related GAO Products

Medical Devices: FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments. [GAO-08-780T](#). Washington, D.C.: May 14, 2008.

Reprocessed Single-Use Medical Devices: FDA Oversight Has Increased, and Available Information Does Not Indicate That Use Presents an Elevated Health Risk. [GAO-08-147](#). Washington, D.C.: January 31, 2008.

Medical Devices: Challenges for FDA in Conducting Manufacturer Inspections. [GAO-08-428T](#). Washington, D.C.: January 29, 2008.

Medical Devices: FDA's Approval of Four Temporomandibular Joint Implants. [GAO-07-996](#). Washington, D.C.: September 17, 2007.

Medical Devices: Status of FDA's Program for Inspections by Accredited Organizations. [GAO-07-157](#). Washington, D.C.: January 5, 2007.

Food and Drug Administration: Limited Available Data Indicate That FDA Has Been Meeting Some Goals for Review of Medical Device Applications. [GAO-05-1042](#). Washington, D.C.: September 30, 2005.

Food and Drug Administration: Data to Measure the Timeliness of Reviews of Medical Device Applications Are Limited. [GAO-04-1022](#). Washington, D.C.: August 30, 2004.

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