



Report to the Ranking Member,  
Subcommittee on Labor, Health and  
Human Services, Education, and Related  
Agencies, Committee on Appropriations,  
House of Representatives

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September 2015

# MEDICAL DEVICES

## FDA Ordered Postmarket Studies to Better Understand Safety Issues, and Many Studies Are Ongoing

Accessible Version

# GAO Highlights

Highlights of [GAO-15-815](#), a report to the Ranking Member, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives

## Why GAO Did This Study

Americans depend on FDA—an agency within the Department of Health and Human Services (HHS)—to oversee the safety and effectiveness of medical devices sold in the United States. FDA’s responsibilities begin before a new device is brought to market and continue after a device is on the market. As part of its postmarket efforts, FDA may order manufacturers to conduct two types of studies: (1) postapproval studies, ordered at the time of device approval, and (2) postmarket surveillance studies, generally ordered after a device is on the market.

GAO was asked to report on the characteristics and status of postmarket studies. This report describes (1) the types of devices for which FDA has ordered a postapproval study and the status of these studies, and (2) the types of devices for which FDA has ordered a postmarket surveillance study and the status of these studies. GAO analyzed FDA data—including data on medical specialty and study status as of February 2015—for (1) postapproval studies ordered from January 1, 2007, through February 23, 2015, and (2) postmarket surveillance studies ordered from May 1, 2008, through February 24, 2015. These represent the time periods for which FDA reported consistently tracking study data. GAO also reviewed documents, such as FDA guidance, and interviewed FDA officials.

HHS provided technical comments that were incorporated, as appropriate.

View [GAO-15-815](#). For more information, contact Marcia Crosse at (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov).

September 2015

## MEDICAL DEVICES

### FDA Ordered Postmarket Studies to Better Understand Safety Issues, and Many Studies Are Ongoing

#### What GAO Found

Fifty-six percent of the 313 medical device postapproval studies—studies that are ordered at the time of device approval—the Food and Drug Administration (FDA) ordered from January 1, 2007, through February 23, 2015, were for cardiovascular devices and most were making adequate progress. Postapproval studies are ordered to obtain additional information not available before devices are marketed, such as a device’s performance over the course of long-term use. In terms of study design, 69 percent of the 313 postapproval studies ordered were prospective cohort studies—that is, studies in which a group using a particular device was compared to a second group not using that device, over a long period of time. Most (72 percent) of the postapproval studies were ongoing as of February 2015, 20 percent of studies were completed, and 8 percent were inactive because, for example, the device is no longer marketed. Ongoing postapproval studies that GAO reviewed had been ongoing for an average of a little more than 3 years; FDA considered most of them (182 studies) to be progressing adequately and the rest (43 studies) to have inadequate progress or to otherwise be delayed. According to FDA officials, a key reason for a study’s delay may be limited patient enrollment in the postapproval study. On average, manufacturers completed postapproval studies in about 3 years, with the longest study taking almost 7 years, for the studies that GAO reviewed.

Ninety percent of the 392 medical device postmarket surveillance studies FDA ordered from May 1, 2008, through February 24, 2015, were for orthopedic devices and devices such as certain kinds of implantable surgical mesh following concerns with these types of devices, and many were consolidated into ongoing studies. Unlike postapproval studies, FDA may order postmarket surveillance studies at the time or after a device is approved or cleared for marketing—for example, if FDA becomes aware of a potential safety issue. Safety concerns about metal-on-metal hip implants, including potential bone and tissue damage from metal particles, led to an increase in such studies ordered in 2011. Forty percent of the 392 ordered studies were for implanted surgical mesh and other devices used in general and plastic surgery and obstetrics and gynecology procedures. FDA ordered most of these studies in 2012, following safety concerns associated with implanted surgical mesh, such as severe pain. Eighty-eight percent of the postmarket surveillance studies GAO analyzed were inactive as of February 2015. Inactive studies include those that were consolidated (108 studies), meaning that a manufacturer was able to combine an order for a postmarket surveillance study with other related study orders into a single study, such as combining studies of multiple device models into a single study; and those that were inactive for other reasons, such as if the order was for a device that is no longer marketed. The remaining 12 percent of the postmarket surveillance studies were either still ongoing (40 studies) or completed (8 studies). Of the 40 ongoing studies, more than half were progressing adequately, according to FDA, and had been ongoing for an average of a little less than 3 years; the rest were delayed and had been ongoing for an average of about 4 years as of February 2015. According to FDA, postmarket surveillance studies may be delayed for reasons similar to postapproval studies, such as difficulty enrolling patients into the study.

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### Abbreviations

FDA	Food and Drug Administration
HDE	humanitarian device exemption
HHS	Department of Health and Human Services
PMA	premarket approval

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September 30, 2015

The Honorable Rosa L. DeLauro  
Ranking Member  
Subcommittee on Labor, Health and Human Services,  
Education, and Related Agencies  
Committee on Appropriations  
House of Representatives

Dear Ms. DeLauro:

Americans depend on the Food and Drug Administration (FDA)—an agency within the Department of Health and Human Services (HHS)—to oversee the safety and effectiveness of medical devices sold in the United States.<sup>1</sup> FDA’s responsibilities for medical devices begin before a new device is brought to market and continue after a device is on the market. As part of its premarket efforts, FDA reviews submissions for thousands of new medical devices filed each year to decide whether they should be allowed to be marketed in the United States. As a part of its postmarket efforts, FDA may use a variety of tools to monitor marketed devices, including ordering manufacturers to conduct postmarket studies of medical devices.

FDA may order two types of postmarket studies for medical devices: (1) postapproval studies and (2) postmarket surveillance studies.<sup>2</sup> Postapproval studies may be ordered at the time of approval and are designed to obtain additional information about devices not available before they are marketed, such as the performance of those devices over

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<sup>1</sup>Medical devices include instruments, apparatuses, machines, and implants that are intended for use to diagnose, cure, treat, or prevent disease, or to affect the structure or any function of the body. See 21 U.S.C. § 321(h). These devices range from simple tools such as bandages and surgical clamps to complicated devices such as pacemakers.

<sup>2</sup>Section 522 of the Federal Food, Drug, and Cosmetic Act authorizes FDA to require a manufacturer to conduct postmarket surveillance of certain medical devices. See 21 U.S.C. § 360l. For this report, we refer to the studies required under this authority as postmarket surveillance studies.

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the course of long-term use.<sup>3</sup> In contrast, postmarket surveillance studies are designed to obtain additional information about devices and are generally ordered after they are on the market.<sup>4</sup> For example, if FDA receives reports of potential safety concerns related to a marketed device, the agency may order a manufacturer to conduct a postmarket surveillance study.

According to FDA, the agency has made it a priority to assure the appropriate balance between premarket and postmarket data requirements, balancing the possible benefits of earlier patient access to a device and the possible risks of patient harm from exposure to an unsafe or ineffective device.<sup>5</sup> For instance, patients could have earlier access to medical devices if some premarket data requirements are shifted to the postmarket phase, such as in the form of postapproval studies, while still requiring that devices meet the statutory standard of a reasonable assurance of safety and effectiveness. However, researchers have reported challenges, which can potentially delay the progress of a postmarket study.<sup>6</sup> For example, postmarket studies lack incentives for patients and clinicians to participate because they involve already marketed devices and additional reporting requirements. FDA has also cautioned that patient safety could be undermined if necessary postmarket data are not collected in a timely manner. Additionally, researchers and others have raised questions about FDA's oversight of

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<sup>3</sup>FDA may order postapproval studies for devices approved through certain premarket review processes, including the premarket approval (PMA) process used for the highest risk devices and the humanitarian device exemption (HDE) process for devices for rare disorders; the agency does not have authority to order postapproval studies for other devices on the U.S. market.

<sup>4</sup>FDA may order postmarket surveillance studies for certain device types, whether they are subject to premarket approval or cleared through the more frequently used 510(k) premarket notification process—also known as the 510(k) process.

<sup>5</sup>The agency identified as a priority achieving the following goal: assure the appropriate balance between premarket and postmarket data requirements to facilitate and expedite the development and review of medical devices, particularly high-risk devices of public health importance. Department of Health and Human Services, Food and Drug Administration, *2014-2015 Strategic Priorities: Center for Devices and Radiological Health*, accessed August 4, 2015, <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM384576.pdf>.

<sup>6</sup>The Brookings Institution, Engelberg Center for Health Care Reform at Brookings, *Strengthening Patient Care: Building an Effective National Medical Device Surveillance System* (Washington, D.C.: 2015).

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these studies, including whether FDA ensures that these studies are completed.<sup>7</sup>

You asked us to report on the postmarket studies of medical devices ordered by FDA. This report examines

1. the types of devices for which FDA has ordered a postapproval study and the status of these studies, and
2. types of devices for which FDA has ordered a postmarket surveillance study and the status of these studies.

To examine the types of devices for which FDA has ordered a postapproval study and the status of these studies, we analyzed data provided by FDA from its Center Tracking System for postapproval studies ordered from January 1, 2007, through February 23, 2015.<sup>8</sup> Specifically, we analyzed the number of postapproval studies ordered by FDA, the characteristics of the studies ordered during this time frame, including the medical specialty in which the device is used (e.g., cardiovascular), the study design (e.g., randomized clinical trials), the data source (e.g., newly collected data), and the premarket review process through which the device was approved.<sup>9</sup> We also analyzed these data for the status of postapproval studies as of February 23, 2015, and determined how long these studies had been ongoing or how long it took to complete them.

To examine the types of devices for which FDA has ordered a postmarket surveillance study and the status of these studies, we conducted a similar analysis as we did for postapproval studies, except that we analyzed FDA's data for postmarket surveillance studies ordered from May 1, 2008,

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<sup>7</sup>Reynolds, I.S., *et al*, "Assessing the Safety and Effectiveness of Devices after U.S. Food and Drug Administration Approval: FDA-Mandated Postapproval Studies," *Journal of the American Medical Association Internal Medicine*, vol. 174, no. 11 (2014).

<sup>8</sup>We reviewed studies ordered for medical devices reviewed by FDA's Center for Devices and Radiological Health and data from its Center Tracking System. According to FDA officials, data were not consistently tracked in the Center Tracking System for postapproval studies before January 1, 2007. February 23, 2015, was the date FDA retrieved data for GAO.

<sup>9</sup>Because of limitations in FDA's data, our analysis did not include orders for one postapproval study that was ordered for a device gaining marketing approval through the product development protocol method.



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through February 24, 2015. We did not analyze study design and data source for postmarket surveillance studies because FDA had not completed updating its database with data on these characteristics at the time of our review.<sup>10</sup>

For both objectives, we reviewed relevant laws and regulations and FDA policy and guidance documents, and we interviewed knowledgeable FDA officials about how the agency maintains data on postmarket studies for medical devices. We also assessed the reliability of the data by, for example, comparing data provided to us by FDA with the agency's publicly available data on study status. We determined that these data were sufficiently reliable for our purposes.

We conducted this performance audit from May 2015 to September 2015 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.

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## Background

FDA may order a postapproval study for a device at the time FDA approves that device for marketing through its premarket approval (PMA) process or its humanitarian device exemption (HDE) process (for devices that treat rare diseases or conditions).<sup>11</sup> There are no statutory limits on the length of a postapproval study, but according to FDA guidance, the

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<sup>10</sup>According to FDA, data were not consistently tracked in the Center Tracking System for postmarket surveillance studies before May 1, 2008. February 24, 2015, was the date FDA retrieved data for GAO, and we analyzed study status and the length of time ongoing studies had taken as of February 24, 2015. We did not analyze data on study design or data source because it was not available from the Center Tracking System for analysis at the time of our review. According to FDA officials, the agency has updated its postmarket surveillance studies database to populate data fields with information captured electronically, and posted information on study design and other characteristics of postmarket surveillance studies on its public website on August 3, 2015.

<sup>11</sup>21 C.F.R. §§ 814.82, 814.126 (2014). The PMA process is the more stringent of FDA's premarket review processes and requires the manufacturer to supply evidence providing reasonable assurance that the device is safe and effective. The HDE process for devices that treat rare diseases or conditions requires manufacturers to show that the probable benefit to health from the device outweighs the risk of using it. In 2014, FDA approved about 25 devices through the PMA process and 4 devices through the HDE process.

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device manufacturer and FDA agree on the study plan, which includes a study design (e.g., randomized clinical trial or other study design), the study's data source, and time frame for when the manufacturer will complete required reports.

In contrast, FDA may order a postmarket surveillance study at the time of approval or clearance for certain devices or any time thereafter as long as certain criteria are met.<sup>12</sup> (See table 1.) FDA may order a postmarket surveillance study not only for PMA and HDE devices, but also for devices that are cleared through the less stringent 510(k) premarket notification process—also known as the 510(k) process.<sup>13</sup> FDA may order postmarket surveillance studies if failure of the device would be reasonably likely to have serious adverse health consequences, and such studies may be ordered when FDA officials identify an issue with a device through adverse advent reports or reviews of scientific literature.<sup>14</sup> FDA is authorized to order postmarket surveillance studies for a duration of up to 36 months, but the time frame may be extended if the manufacturer and

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<sup>12</sup>This authority applies with respect to class II and class III devices. Class II devices, such as electrocardiographs, power bone drills, and mercury thermometers are subject to general and special controls. Class III devices, most of which are subject to the PMA process, include the highest-risk devices; for example, implantable pacemakers and other devices that support or sustain human life or are of substantial importance in preventing impairment of human health. In addition to the agency's authority to order a postmarket surveillance study at the time of approval or clearance for certain devices, FDA may also order a postmarket surveillance study as a condition to approval or clearance of a device that is expected to have significant use in pediatric populations. 21 U.S.C. § 360l(a)(1)(B).

<sup>13</sup>The 510(k) premarket notification process requires that a manufacturer demonstrate that a new device is substantially equivalent to a device already legally marketed in the United States that is not subject to a PMA. 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). In 2014, FDA cleared more than 2,500 devices through the 510(k) premarket notification process. FDA may also order postmarket surveillance studies for devices classified and marketed under the de novo process, which are devices of a new type that FDA has not previously classified and for which the manufacturer requested reclassification into class I or II. See 21 U.S.C. § 360c(f)(2). In this report, devices classified to class II through the de novo process for which postmarket surveillance studies were ordered are counted with devices cleared through the 510(k) process.

<sup>14</sup>Department of Health and Human Services, Food and Drug Administration, *Postmarket Surveillance Under Section 522 of the Federal Food, Drug and Cosmetic Act: Guidance for Industry and FDA Staff* (Rockville, Md.: April 2006).

FDA are in agreement. Additionally, FDA may order a study with a longer duration if the device is expected to have significant use in pediatric populations and an extended period is necessary to assess issues like the impact of the device on children’s growth or development.<sup>15</sup>

**Table 1: Characteristics of the Food and Drug Administration’s (FDA) Postapproval and Postmarket Surveillance Studies for Medical Devices**

Characteristic	Postapproval study	Postmarket surveillance study
When the study may be ordered	As a condition of approval of the medical device.	At or after approval or clearance of the medical device, if the device <ul style="list-style-type: none"> <li>would be reasonably likely to have serious adverse health consequences if it fails;</li> <li>is expected to be used significantly in pediatric populations;</li> <li>is intended to be implanted in the body for more than 1 year; or</li> <li>is intended to be a life-sustaining or life-supporting device used outside of a facility (e.g., oxygen tanks).</li> </ul> As a condition to approval or clearance if the device is expected to have significant use in pediatric populations.
Primary objective of study	To provide continuing evaluation and periodic reporting of device safety, effectiveness, and reliability.	To collect data that can reveal unforeseen adverse events, the actual rate of anticipated adverse events, or other information necessary to protect the public health.
Study duration	Time frame agreed to by FDA and the manufacturer.	Up to 36 months, or longer if <ul style="list-style-type: none"> <li>the device manufacturer agrees to extend the study time frame, or</li> <li>the device is expected to have significant use in pediatric populations and it is necessary to assess issues such as the device’s impact on development or growth.</li> </ul>
Types of devices for which FDA may order a study	<ul style="list-style-type: none"> <li>Devices approved through the premarket approval (PMA) process.</li> <li>Devices approved through the humanitarian device exemption (HDE) process.</li> </ul>	Class II and class III devices, <sup>a</sup> including <ul style="list-style-type: none"> <li>devices cleared through the 510(k) premarket notification process.<sup>b</sup></li> <li>devices approved through the PMA process.</li> <li>devices approved through the HDE process.</li> </ul>

Source: GAO analysis of FDA information. | GAO-15-815

<sup>a</sup>Class II devices, such as electrocardiographs, powered bone drills, and mercury thermometers are subject to general and special controls, such as postmarket surveillance. Class III devices, most of which are subject to the PMA process, include the highest-risk devices; for example, devices such as implantable pacemakers that support or sustain human life or devices that are of substantial importance in preventing impairment of human health.

<sup>b</sup>Includes devices classified and marketed under the de novo process. See 21 U.S.C. § 360c(f)(2).

<sup>15</sup>21 U.S.C. § 360l(b)(1),(2).

Manufacturers must periodically report to FDA information on these postmarket studies such as the progress of the study. Table 2 describes the various status categories that apply to postmarket studies.

**Table 2: Status Categories for Postapproval and Postmarket Surveillance Studies for Medical Devices**

Status category	Subcategory	Definition
Completed	Completed	Studies for which FDA has determined that the manufacturer has fulfilled the study order and closed the study.
Ongoing - Progress Adequate	Protocol/plan pending	Studies for which FDA has not approved the protocol or plan and it has been less than 6 months since the study was ordered.
	Study pending	Postapproval studies for which the protocol has been approved but the first interim report has not yet been reviewed by FDA. Postmarket surveillance studies for which FDA has approved the protocol or plan and it has been less than 6 months since that approval.
	Progress adequate	Studies have begun, and progress is consistent with the plan (e.g., meeting patient-enrollment schedule, rates of patient follow-up, endpoints evaluated).
Ongoing - Delayed	Protocol/plan overdue	Studies for which FDA has not approved the protocol or plan, and it has been 6 months or more since the study was ordered.
	Progress inadequate	Studies have begun, but progress is inconsistent with the plan (e.g., not meeting enrollment schedule, poor follow-up rates, not all endpoints evaluated); or it has been more than 15 months since the study was ordered and the study has not commenced.
Ongoing - Inactive	Consolidated	Studies for which the manufacturer has requested and FDA has agreed to combine multiple orders for postmarket surveillance studies for similar devices into a single study that covers all of the devices.
	Terminated	Postapproval studies that were terminated by FDA when the PMA or HDE submission was withdrawn, or when the HDE submission was converted to a PMA. Postmarket surveillance studies that were terminated by FDA because they were no longer relevant (e.g., the manufacturer changed the indication for use that was the subject of the postmarket surveillance study).
	Revised/replaced	Studies where the original study has been revised and subsequently replaced with a new study.
	Withdrawn	Postmarket surveillance studies that were withdrawn because the manufacturer demonstrated the objective of the study using publicly available data and FDA agreed with the results.
	Other	Studies that do not meet the characteristics of the other status categories and have an interim status, such as the manufacturer is awaiting FDA approval for a redesigned device, the manufacturer is no longer marketing the device, or a separate study on the same study question and device is pending.

Source: GAO analysis of FDA information. | GAO-15-815

## FDA Ordered Most Postapproval Studies for Cardiovascular Devices and Most Were Making Adequate Progress

### FDA Ordered Most Postapproval Studies for Cardiovascular Devices and Most Were Designed as Prospective Cohort Studies

Cardiovascular devices, such as stents and heart valves, accounted for 56 percent of the 313 postapproval studies ordered from January 1, 2007, through February 23, 2015. Orthopedic and general and plastic surgery devices were the second and third most common subjects of postapproval studies, respectively. FDA also ordered postapproval studies for another 11 medical specialties, which are included in the other category.<sup>16</sup> (See table 3.)

**Table 3: Medical Device Postapproval Studies by Medical Specialty, Ordered from January 1, 2007, through February 23, 2015**

Medical specialty of device	Examples	Number of studies (percentage)
Cardiovascular devices	Heart valves and stents	175 (56)
Orthopedic devices	Cervical disc systems	35 (11)
General and plastic surgery devices	Silicone breast implants	27 (9)
Other <sup>a</sup>	Devices for ophthalmic (e.g., intraocular lens), obstetrics and gynecology (e.g., permanent birth control system), and gastroenterology-urology (e.g., gastric banding system)	76 (24)
<b>Total</b>	<b>na</b>	<b>313 (100)</b>

Source: GAO analysis of FDA data. | GAO-15-815

<sup>a</sup>Other medical specialties include anesthesiology; clinical chemistry; dental; ear, nose, and throat; gastroenterology-urology; general hospital; microbiology; neurology; ophthalmic; obstetrics and gynecology; and pathology.

<sup>16</sup>Postapproval studies were ordered for medical devices in other medical specialties of anesthesiology (e.g., computer-assisted personalized sedation system); clinical chemistry (e.g., artificial pancreas device system); dental (e.g., bone grafting material); ear, nose, and throat (e.g., implantable hearing system); gastroenterology-urology (e.g., gastric banding system); general hospital (e.g., infusion pump); microbiology (e.g., human papillomavirus test); neurology (e.g., intracranial aneurysm flow diverter); ophthalmic (e.g., intraocular lenses); obstetrics and gynecology (e.g., permanent birth control system); and pathology (e.g., breast cancer detection test).

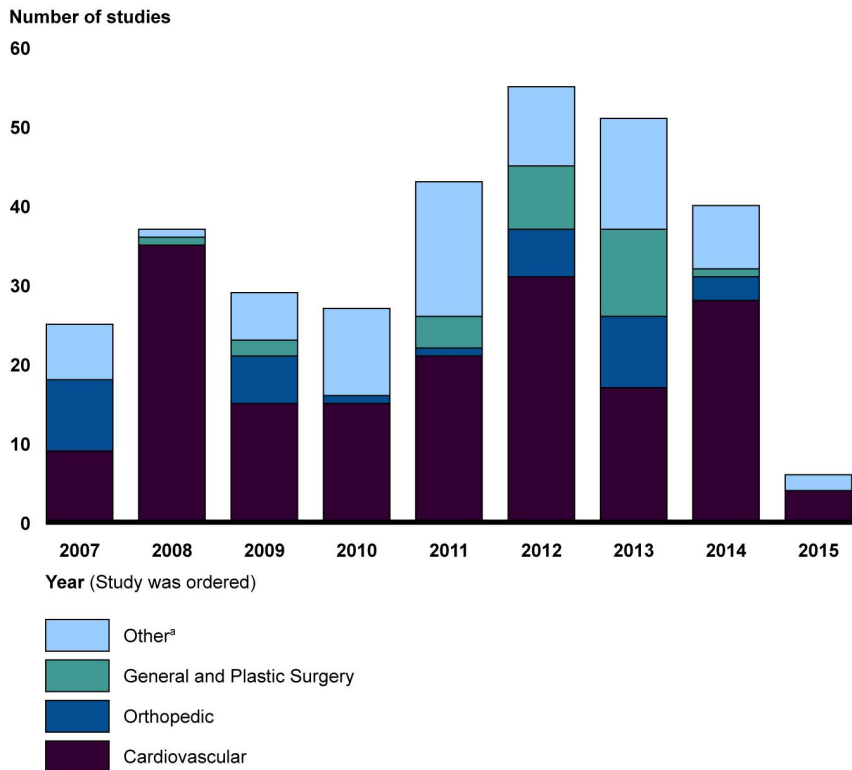
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The number of postapproval studies for cardiovascular devices varied from year to year, with the most cardiovascular device studies ordered in 2008 and 2012. (See fig. 1.) In general, FDA orders a postapproval study to obtain specific information on the postmarket performance of or experience with an approved device. For example, the increase in the number of postapproval studies ordered for cardiovascular devices in 2008 reflects that FDA has required that each new implantable cardioverter defibrillator lead undergo a postapproval study.<sup>17</sup>

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<sup>17</sup>Since 2008, FDA has required that these postapproval studies collect data on device performance in at least 1,000 patients for 5 years after implantation. The move resulted from growing concerns regarding these implanted devices, which can detect life-threatening heart rhythms and deliver an electrical shock through the lead to the heart. In December 2011, FDA classified the recall of one of these devices as a class I recall, the most serious type of recall; and that the manufacturer ceased sales of this device in late 2010.

**Fig. 1: Medical Device Postapproval Studies by Medical Specialty, Ordered from January 1, 2007, through February 23, 2015**



Source: GAO analysis of FDA data. | GAO-15-815

<sup>a</sup>Other includes devices for ophthalmic (e.g., intraocular lens); obstetrics and gynecology (e.g., permanent birth control system); gastroenterology-urology (e.g., gastric banding system); anesthesiology (e.g., computer assisted personalized sedation system); clinical chemistry (e.g., artificial pancreas device system); dental (e.g., bone grafting material); ear, nose, and throat (e.g., implantable hearing system); general hospital (e.g., infusion pump); microbiology (e.g., human papillomavirus test); neurology (e.g., intracranial aneurysm flow diverter); and pathology (e.g., breast cancer detection test).

FDA ordered nearly all of the postapproval studies for devices approved through the PMA process—the agency’s more stringent premarket review process—according to FDA data we analyzed.<sup>18</sup> Specifically, 94 percent of postapproval studies ordered between January 1, 2007, and

<sup>18</sup>The PMA process is the more stringent of FDA’s premarket review processes and requires the manufacturer to supply evidence providing reasonable assurance that the device is safe and effective before the device is legally available on the U.S. market.

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February 23, 2015, were for devices approved through the PMA process.<sup>19</sup>

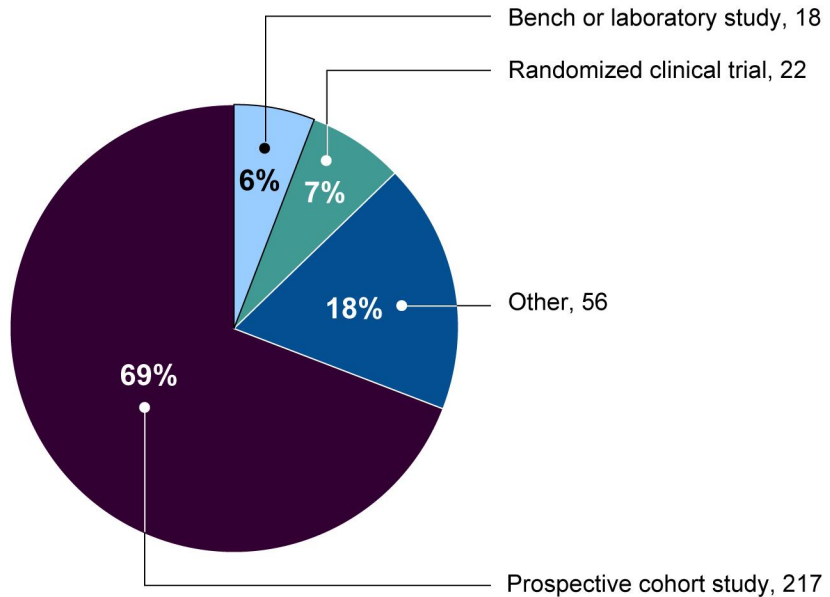
In terms of study design, more than two-thirds (69 percent) of the 313 postapproval studies ordered during the timeframe we examined were prospective cohort studies—that is, studies in which a group using a particular device was compared to a second group not using that device, over a long period of time. (See fig. 2.) For example, one postapproval prospective cohort study was designed to follow patients who received a certain type of breast implant over a 10-year period and to collect information on complications as they occur.

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<sup>19</sup>The remaining 6 percent of postapproval studies were ordered for devices approved through the HDE process—that is, the process for devices to treat rare conditions. The HDE process requires manufacturers to show that the probable benefit of the device outweighs the risk of using it. 21 U.S.C. § 360j(m). FDA may require postapproval studies for devices that were approved for the U.S. market through the PMA and HDE processes. 21 C.F.R. §§ 814.82, 814.126 (2014).



**Fig. 2: Medical Device Postapproval Studies by Study Design, Ordered from January 1, 2007, through February 23, 2015**



Source: GAO analysis of FDA data. | GAO-15-815

Notes: Prospective cohort studies include studies in which a group using a particular device was compared to a second group not using that device, over a long period of time. Randomized clinical trials include studies that compare the effects of an intervention against a control group. Bench or laboratory studies include studies conducted in a laboratory and may test the wear of a device, for example. Other includes active surveillance, animal studies, case-control studies, cross-sectional studies, enhanced surveillance, and retrospective cohort studies, as well as postapproval studies for which a type of study design was not available because no study protocol has been approved yet.

Additionally, postapproval studies were conducted using a variety of data sources, including newly collected data and medical device registries. Nearly two-thirds (196 studies) of the postapproval studies we examined relied upon new data collected by the manufacturer; and about one-third (98 studies) used data collected from registries—that is, a data system to collect and maintain structured records on devices for a specified time frame and population.<sup>20</sup> (See table 4.) Registries may be created and maintained by the manufacturer or another organization, such as a

<sup>20</sup>Studies that used new data collection used data that were collected by the manufacturer for the postapproval study and were not extracted from a registry or administrative database.

medical specialty’s professional association.<sup>21</sup> For example, FDA has established a National Medical Device Registry Task Force to further examine the implementation of registries in postmarket surveillance. According to FDA, registries play a unique role in the postmarket surveillance of medical devices because they can provide additional detailed information about patients, procedures, and devices. For example, registries can help assess device performance by collecting information on patients with similar medical conditions.

**Table 4: Data Sources for Medical Device Postapproval Studies, Ordered from January 1, 2007, through February 23, 2015**

<b>Data source</b>	<b>Number of studies (percent)</b>
New data collection <sup>a</sup>	196 (63)
Registry <sup>b</sup>	98 (31)
Other <sup>c</sup>	19 (6)
<b>Total</b>	<b>313 (100)</b>

Source: GAO analysis of FDA data. | GAO-15-815

<sup>a</sup>Data are collected for the specific study.

<sup>b</sup>Data are obtained from a registry that is created and maintained by the manufacturer or another organization such as a professional organization.

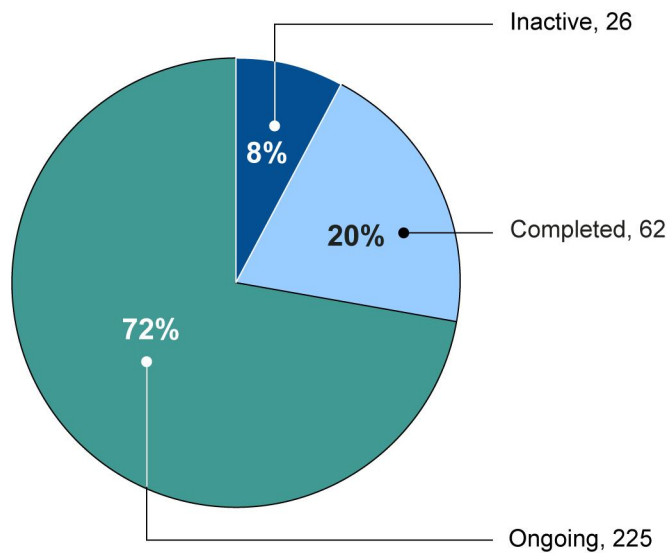
<sup>c</sup>Other data sources include an administrative database such as claims data from private health insurance companies, and studies for which a study protocol has not been approved.

<sup>21</sup>For example, the Society of Thoracic Surgeons and the American College of Cardiology run a patient registry launched in 2012 that captures clinical information on patients in the United States undergoing transcatheter valve treatments.

Most of the Postapproval Studies FDA Ordered Were Ongoing and Making Adequate Progress, According to FDA

About 72 percent of the postapproval studies we examined (or 225 of the 313 studies ordered) were categorized as ongoing as of February 2015. An additional 20 percent were completed and the remaining 8 percent were inactive.<sup>22</sup> (See fig. 3.)

**Fig. 3: Status of Medical Device Postapproval Studies Ordered from January 1, 2007, through February 23, 2015**



Source: GAO analysis of FDA data. | GAO-15-815

Note: Data are as of February 23, 2015.

Further analysis of FDA data on the 225 ongoing postapproval studies showed 81 percent (or 182 studies) to be progressing adequately, while the remaining 19 percent (43 studies) were delayed as of February 2015. The 182 ongoing postapproval studies considered to be progressing adequately—that is, the study was pending, the protocol or plan was

<sup>22</sup>The inactive category for postapproval studies includes studies with one of three FDA study sub-category statuses: (1) 3 studies where the original study was revised and replaced with a subsequent study; (2) 14 studies where the study was terminated by FDA because the PMA or HDE submission was withdrawn, or the HDE submission was converted to a PMA; and (3) 9 studies categorized as other—that is, these studies do not meet the characteristics of the other status categories and have an interim status, such as the manufacturer is awaiting FDA approval for a redesigned device, the manufacturer is no longer marketing the device, or a separate study on the same study question is pending.

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pending, or progress was adequate—had been ongoing for an average of 37 months, or a little over 3 years.

Similarly, the 43 ongoing postapproval studies considered to be delayed—that is protocol/plan overdue, or progress inadequate—had been ongoing for an average of 39 months or a little over 3 years. Delayed studies include studies for which FDA had not approved a study plan within 6 months of the PMA approval date (3 studies) or studies which had begun, but had not progressed as intended (40 studies).<sup>23</sup> According to FDA officials, a key reason for a study’s delay may be limited patient enrollment into the postapproval study. FDA officials said they work with manufacturers to address manufacturers’ inability to enroll patients, in part, by suggesting different strategies to improve enrollment, such as hiring a dedicated person for recruitment or reducing the cost of the study device to make it competitive with conventional treatments.

Twenty percent (or 62 studies) of the 313 postapproval studies were categorized as completed as of February 23, 2015—that is, FDA determined that the manufacturer had fulfilled the study order and had closed the study. As table 5 shows, on average, these completed postapproval studies took about 36 months, or 3 years, with the longest study taking almost 7 years. The remaining 8 percent (or 26 studies) were categorized as inactive. Postapproval studies that are considered inactive include studies that, for example, involve a device that is no longer being marketed or the study’s research questions are no longer relevant.

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<sup>23</sup>According to FDA guidance, the agency recommends manufacturers include, at a minimum, plans for the postapproval study in the original PMA submission and that development of the study occur concurrently with FDA’s review of premarket data. See Department of Health and Human Services, Food and Drug Administration, *Procedures for Handling Postapproval Studies Imposed by PMA Order: Guidance for Industry and FDA Staff* (Rockville, Md.: August 2007).

**Table 5: Length of Ongoing and Completed Medical Device Postapproval Studies Ordered from January 1, 2007, through February 23, 2015**

Study status	Number	In months (years)		
		Minimum	Maximum	Mean
Ongoing - Progress adequate	182	0.9 (0.1)	93.1 (7.6)	36.8 (3.0)
Ongoing - Delayed	43	7.1 (0.6)	93.0 (7.6)	38.9 (3.2)
Completed <sup>a</sup>	62	8.1 (0.7)	82.6 (6.8)	36.1 (3.0)
<b>Total</b>	<b>287</b>	<b>N/A</b>	<b>N/A</b>	<b>N/A</b>

Source: GAO analysis of FDA information. | GAO-15-815

Note: Data are as of February 23, 2015.

<sup>a</sup>For completed studies, this shows the length of time from the date of the study order to the date that FDA determined that the manufacturer had fulfilled the study order and had closed the study.

FDA Ordered Most Postmarket Surveillance Studies for Orthopedic, General/Plastic Surgery, and Obstetrics/Gynecology Devices and Many Were Consolidated into Ongoing Studies

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FDA Ordered Most Postmarket Surveillance Studies for Orthopedic, General/Plastic Surgery, and Obstetrics/Gynecology Devices Resulting from Concerns about Metal-on-Metal Implants and Certain Kinds of Implantable Surgical Mesh

FDA ordered 392 postmarket surveillance studies, half of which (196 studies) were for orthopedic medical devices, from May 1, 2008, through February 24, 2015. In 2011 alone, FDA ordered 176 studies for orthopedic devices following safety concerns about metal-on-metal hip implants, including potential bone or tissue damage from metal particles.<sup>24</sup> (See fig. 4.) An additional 40 percent (or 158 studies) of the postmarket surveillance studies FDA ordered were for devices used in general and plastic surgery and obstetrics and gynecology procedures. FDA ordered 121 postmarket surveillance studies for devices in these medical specialties in 2012, following safety concerns about the use of implanted surgical mesh used for urogynecologic procedures, such as severe pain.<sup>25</sup> About 10 percent of the postmarket surveillance studies were for devices in other medical specialties.<sup>26</sup>

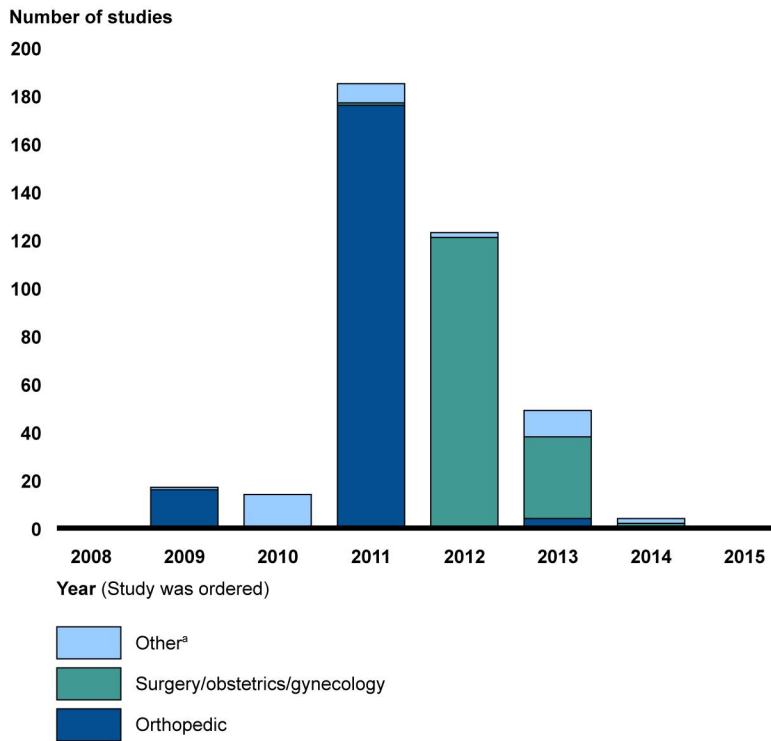
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<sup>24</sup>In May 2011, FDA required manufacturers of metal-on-metal hip implants to conduct postmarket surveillance studies of these devices due to safety concerns.

<sup>25</sup>According to FDA officials, in January 2012, FDA required manufacturers of surgical mesh to conduct postmarket surveillance studies, in part, based on feedback from a medical device advisory committee convened by FDA in September 2011, to discuss safety issues of these devices. Concerns were related to transvaginal placement of surgical mesh, which is permanently implanted in patients to treat pelvic disorders, such as stress urinary incontinence. Ninety percent (109) of the 121 studies ordered in 2012 for devices used in general and plastic surgery and obstetrics and gynecology procedures were ordered on January 3, 2012, for surgical mesh.

<sup>26</sup>Postmarket surveillance studies were ordered for medical devices in other medical specialties of cardiovascular (e.g., vena cava filter), dental (e.g., temporomandibular joint implant), general hospital (e.g., intravascular administration set), immunology (e.g., ovarian/adnexal mass assessment score test system), neurology (e.g., neurovascular embolization device), ophthalmic (e.g., contact lens), and physical medicine (e.g., powered exoskeleton).

**Fig. 4: Medical Device Postmarket Surveillance Studies by Medical Specialty, Ordered from May 1, 2008, through February 24, 2015**



Source: GAO analysis of FDA data. | GAO-15-815

<sup>a</sup>Other includes general hospital (e.g., intravascular administration set), cardiovascular (e.g., vena cava filter), dental (e.g., temporomandibular joint implant), immunology, neurology, ophthalmic, and physical medicine devices.

Between May 1, 2008, and February 24, 2015, about 94 percent of the postmarket surveillance studies ordered were for devices cleared through the 510(k) premarket notification process.<sup>27</sup> This reflects safety concerns regarding metal-on-metal implants and implantable surgical mesh used for urogynecologic procedures that arose after the devices were cleared through the 510(k) process, according to FDA officials.

<sup>27</sup>Includes devices cleared through the 510(k) premarket notification process and devices classified and marketed under the de novo process. See 21 U.S.C. § 360c(f)(2). The remaining devices were approved through FDA's more stringent PMA process (2 percent) or the HDE process (4 percent).

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## Most of the Postmarket Surveillance Studies FDA Ordered Were Inactive, and Many of Those Had Been Consolidated into Ongoing Studies

About 88 percent of the postmarket surveillance studies we examined (or 344 out of 392 studies) were categorized as inactive. (See fig. 5.) A study might be categorized as inactive, for example, because it had been consolidated, meaning that a manufacturer was able to combine an order for a postmarket surveillance study with other related study orders into a single study. For example, if FDA issued 22 orders for postmarket surveillance studies for different models of metal-on-metal implants from a single manufacturer, the manufacturer could combine all of the orders into a single study covering all of the devices, and the other 21 orders for postmarket surveillance studies would be categorized as consolidated and considered inactive. About 31 percent (or 108 studies) were inactive because they had been consolidated into another study.<sup>28</sup>

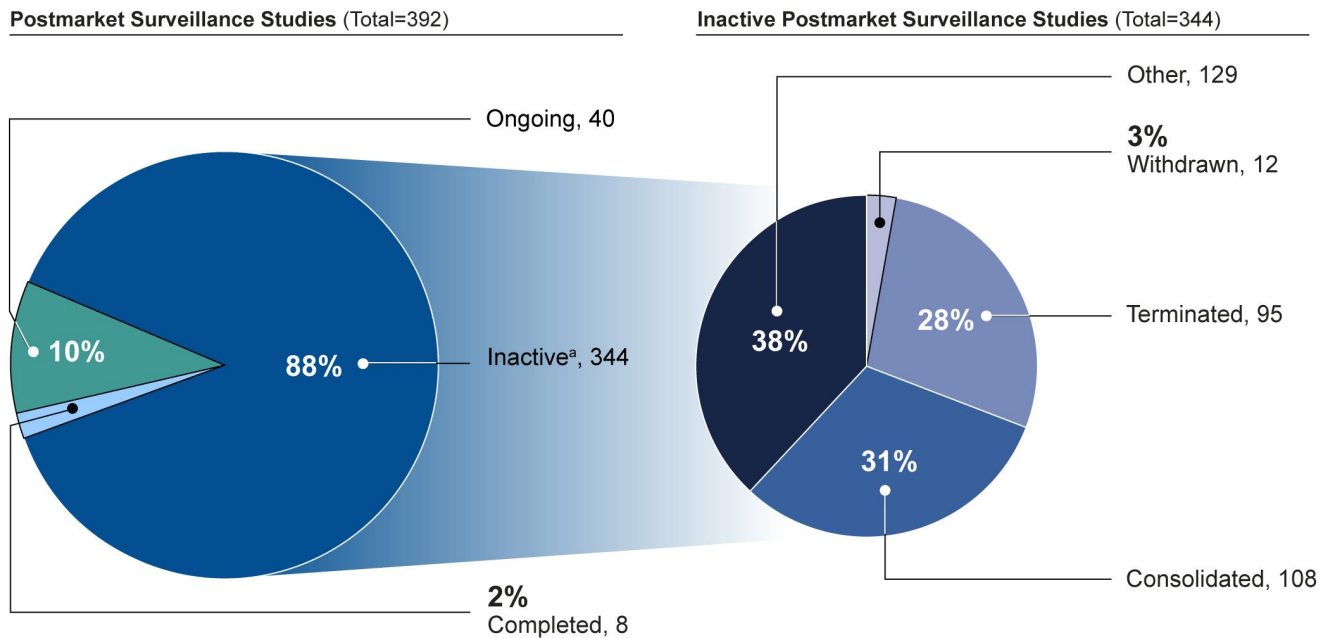
Another 31 percent of the inactive studies (or 107 studies) were categorized by FDA as either terminated, meaning the study was no longer relevant because, for example, the manufacturer changed the indication for use that was the subject of the postmarket surveillance study, or withdrawn by FDA because the manufacturer demonstrated the objective of the study using publicly available data and FDA agreed with the results. The remaining 38 percent (or 129 studies) were categorized as other—that is, the status does not fit in another category because, for example the device is no longer being marketed. However, according to FDA officials, if the manufacturer does begin marketing the device again, then it will have to conduct the study.

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<sup>28</sup>According to FDA data, 108 studies were consolidated into 13 remaining studies.



**Fig. 5: Status of Medical Device Postmarket Surveillance Studies Ordered from May 1, 2008, through February 24, 2015**



Source: GAO analysis of FDA data. | GAO-15-815

Note: Data are as of February 24, 2015.

<sup>a</sup>The inactive category for postmarket surveillance studies includes studies with one of four FDA study statuses: (1) other—that is, the study status does not fit another category, because, for example, the device is no longer being marketed or is being redesigned; (2) consolidated—that is, the study was one of many postmarket surveillance studies ordered and the manufacturer, with the approval of FDA, consolidated these multiple studies into a single study; (3) terminated—that is, studies that were terminated by FDA because they were no longer relevant (e.g., the manufacturer changed the indication for use that was the subject of the postmarket surveillance study); or (4) withdrawn—that is, studies that were withdrawn because the manufacturer demonstrated the objective of the study using publicly available data and FDA agreed with the results.

While 88 percent of the postmarket surveillance studies in our analysis were inactive, the remaining 12 percent (or 48 studies) were either still ongoing or completed as of February 24, 2015. Specifically, 10 percent (or 40 studies) were categorized as ongoing, while 2 percent (or 8 studies) were completed. Of the 40 ongoing postmarket surveillance studies, more than half were progressing adequately, while the rest were delayed. Further analysis showed the following:

- The 21 ongoing postmarket surveillance studies that FDA considered to be progressing adequately had been ongoing for an average of 33 months, or about 2.7 years. (See table 6.)
- The 19 ongoing postmarket surveillance studies that FDA considered to be delayed had been ongoing for an average of 49 months or about

4 years. Delayed studies included studies for which FDA had not approved a study plan within 6 months of ordering the study or studies that had begun but were not progressing as intended.<sup>29</sup> According to FDA, postmarket surveillance studies may be delayed for reasons similar to postapproval studies, such as difficulty enrolling patients into the study.

Regarding the eight completed postmarket surveillance studies, the average length of time to complete the study—that is, the time from the study order to the date FDA determined that the manufacturer had fulfilled the study order and had closed the study—was about 29 months or 2.4 years. FDA generally may order a manufacturer to conduct a postmarket surveillance study for up to 36 months unless the manufacturer and FDA agree to an extended time frame.<sup>30</sup>

**Table 6: Length of Ongoing and Completed Medical Device Postmarket Surveillance Studies, Ordered from May 1, 2008, through February 24, 2015**

Study status	Number	In months (years)		
		Minimum	Maximum	Mean
Ongoing - Progress adequate	21	2.5 (0.2)	59.2 (4.9)	32.9 (2.7)
Ongoing - Delayed	19	8.1 (0.7)	65.6 (5.4)	48.6 (4.0)
Completed <sup>a</sup>	8	11.6 (1.0)	50.2 (4.1)	28.6 (2.4)
<b>Total</b>	<b>48</b>	<b>N/A</b>	<b>N/A</b>	<b>N/A</b>

Source: GAO analysis of FDA information. | GAO-15-815

Note: Data are as of February 24, 2015.

<sup>a</sup>For completed studies, this shows the length of time from the date of the study order to the date that FDA determined that the manufacturer had fulfilled the study order and had closed the study.

<sup>29</sup>FDA draft guidance, which, if finalized, will represent FDA’s current thinking on postmarket surveillance studies, states that the study status will be categorized as “plan overdue” on FDA’s website if a manufacturer does not have an approved study plan within 6 months of the issuance of the postmarket surveillance study order. FDA also proposes to consider a manufacturer’s failure to have a study plan approval within 12 months of the issuance of the study order as a failure to comply, which could render the device as misbranded. See HHS/FDA, *Draft Guidance: Procedures for Handling Section 522 Postmarket Surveillance Studies*.

<sup>30</sup>FDA may order postmarket surveillance lasting longer than 36 months for specific devices expected to have a significant use in pediatric populations. 21 U.S.C. § 360I(b)(2).

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## Agency Comments

We provided a draft of this report to the Secretary of Health and Human Services. HHS provided technical comments that were incorporated, as appropriate.

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As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time we will send copies to the Secretary of Health and Human Services, appropriate congressional committees, and other interested parties. In addition, the report will be available at no charge on the GAO website at <http://www.gao.gov>.

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Sincerely yours,



Marcia Crosse  
Director, Health Care

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# Appendix I: GAO Contact and Staff Acknowledgments

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## GAO Contact

Marcia Crosse, (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov)

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## Staff Acknowledgments

In addition to the contact named above, Kim Yamane, Assistant Director; Britt Carlson; Carolyn Fitzgerald; Sandra George; Cathleen Hamann; and Gay Hee Lee were major contributors to this report.

# Appendix II: Accessible Data

## Data Tables for Charts

**Data Table for Fig. 1: Medical Device Postapproval Studies by Medical Specialty, Ordered from January 1, 2007, through February 23, 2015**

Medical Specialty	2007	2008	2009	2010	2011	2012	2013	2014	2015
Cardiovascular	9	35	15	15	21	31	17	28	4
Orthopedic	9	0	6	1	1	6	9	3	0
General and Plastic Surgery	0	1	2	0	4	8	11	1	0
Other <sup>a</sup>	7	1	6	11	17	10	14	8	2

**Data Table for Fig. 2: Medical Device Postapproval Studies by Study Design, Ordered from January 1, 2007, through February 23, 2015**

Study Design	Postapproval Studies by Study Design n=313	Percent of Postapproval studies by study design
Prospective Cohort Study	217	69
Randomized Clinical Trial	22	7
Bench or Laboratory Study	18	6
Other	56	18

**Data Table for Fig. 3: Status of Medical Device Postapproval Studies Ordered from January 1, 2007, through February 23, 2015**

Status	Status of All Postapproval Studies n=313	
Ongoing	225	72
Completed	62	20
Inactive	26	8

**Data Table for Fig. 4: Medical Device Postmarket Surveillance Studies by Medical Specialty, Ordered from May 1, 2008, through February 24, 2015**

Medical Specialty	2008	2009	2010	2011	2012	2013	2014	2015
Orthopedic	0	16	0	176	0	4	0	0
Surgery/Ob/Gyn	0	0	0	1	121	34	2	0
Other <sup>a</sup>	0	1	14	8	2	11	2	0

**Data Table for Fig. 5: Status of Medical Device Postmarket Surveillance Studies Ordered from May 1, 2008, through February 24, 2015**

PostMarket Surveillance Studies (Total 392)

Status	Number of Studies	Percent of Studies
Ongoing	40	10
Completed	8	2
Inactive <sup>a</sup>	344	88

Inactive Postmarket Surveillance Studies (Total 344)

Status	Number of Studies	Percent of Inactive Studies
Consolidated	108	31
Terminated	95	28
Withdrawn	12	3
Other	129	38

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