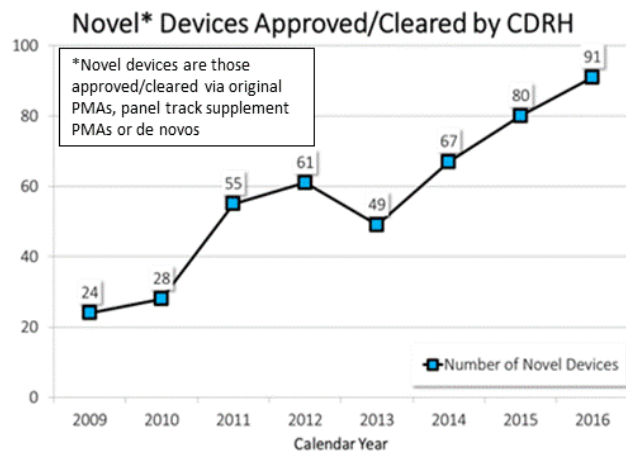


U.S. Food and Drug Administration Center for Devices and Radiological Health: Progress in Achieving Our Vision of Patients First

In the early part of this decade, industry argued that FDA regulation hindered innovation and contributed to the growing number of device companies seeking marketing authorization for their devices abroad before introducing them in the United States, and the increasing gap between when a device is approved in another country and when it is approved in the US. This reality, its adverse impact on patients, plus CDRH’s own awareness of our declining performance over almost a decade, led CDRH to implement new programmatic changes. These changes, along with increased user fee funding and changes in Federal law have helped us strengthen our performance and better address the rapidly-evolving field of medical device innovation. To guide us in our mission to improve the health and quality of life of patients, in 2012 we adopted a [new vision](#)¹ to reflect this change in mindset, that: **Patients in the US have access to high-quality, safe and effective medical devices of public health importance first in the world.**

DOING BUSINESS BETTER

Since late 2009, CDRH has continuously improved the way we do business through a series of culture, policy and process changes. This can be seen through our commitment to providing excellent customer service, new patient-centered paradigms, and our strong performance across a range of objective measures, including the time it takes to review several types of medical device submissions. These improvements are reflected by the nearly four-fold increase in the annual number of novel medical device approvals.

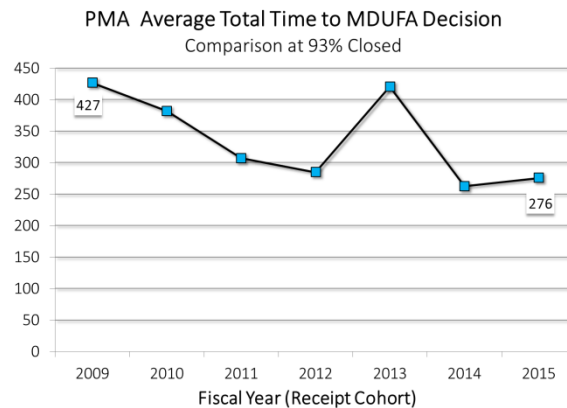


Fast Facts CDRH oversees approximately **175,000 medical devices** on the US market, more than **18,000 medical device manufacturers**, and more than **25,000 medical device facilities worldwide**. Each year we receive some **22,000 premarket submissions** (includes supplements and amendments) and more than **1.4 million reports on medical device adverse events and malfunctions**.

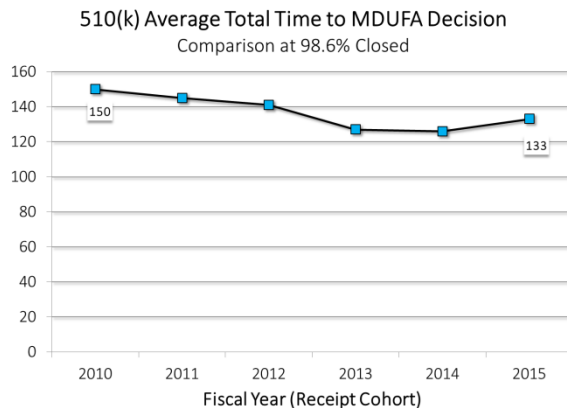
¹ [CDRH Mission, Vision and Shared Values](#)

Time Time, with its cost implications, plays a critical role in an innovator’s decision as to whether and when to bring a new technology to the US. What good is a new technology if patients do not have timely access to it? How helpful is a new technology that doesn’t benefit patients or poses unacceptable risks? By reducing the time of every regulatory stage of the total product life cycle, including the review of medical device submissions, while still assuring robust but appropriate (least burdensome) evidence generation and high-quality decision making, we help patients get access to safe and effective medical technologies and foster innovation. After steadily worsening performance from 2002 to 2010 on a variety of measures, including premarket review times, CDRH has reduced the decision time on all key premarket submission types.

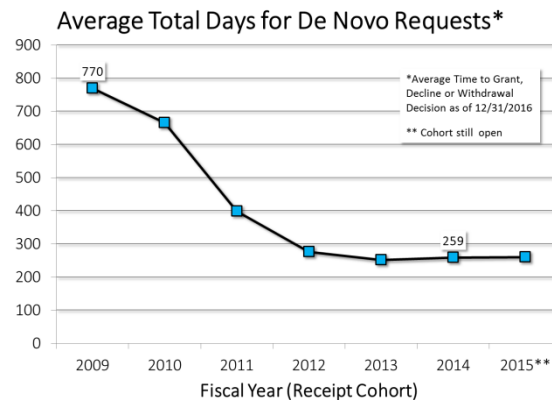
PMA While premarket approval applications (PMAs) only account for approximately one percent of all premarket medical device submissions, they represent medical devices with the highest risk to patients (Class III devices) and, therefore, require more data and a more rigorous review by CDRH. In 2009, it took an average of 427 total days to reach a decision on a PMA. **By 2015, we had reduced the total decision time by 35 percent.**



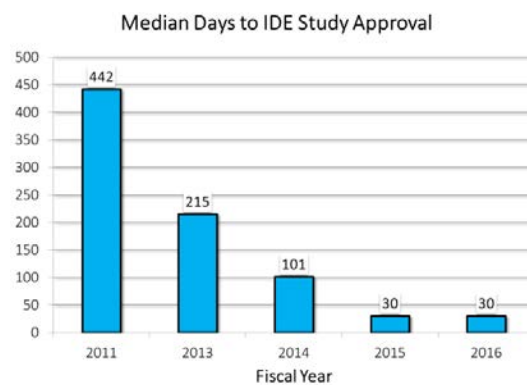
510(k) Named after its section number in federal law, this category represents the bulk of premarket submissions for medical devices. Manufacturers submit 510(k)s to CDRH for devices with low to moderate risk to patients (Class II), and our review standard is based on substantial equivalence (whether a device is at least as safe and effective as a device already on the market). In 2010, it took an average of 150 total days to reach a decision on a 510(k). **By 2015, we had reduced the total decision time by 11 percent.**



De Novo *De novo* classification is a pathway that enables manufacturers of certain low to moderate risk novel devices for which there are no similar marketed devices to come to market, instead of having to submit a PMA. In 2009, it took an average of 770 total days to reach a *de novo* decision. **By 2014, we had reduced the total decision time by 66 percent.**



IDE Manufacturers submit Investigational Device Exemptions (IDEs) for certain devices they want to study via a clinical trial. CDRH reviews an IDE submission before a manufacturer can begin to collect clinical data that may be necessary for future approval. **CDRH slashed median review times for IDE full approvals by more than a year between 2011 and 2015.**



DOING BUSINESS DIFFERENT

Since 2009, CDRH has been evaluating all of our programs to address concerns from patients, industry, health care providers, our own staff, and other customers about issues including review times, backlogs, and our expertise in increasingly complex technology. We have sought to address these concerns by **changing our culture** to put **patients first** and recognizing that **advancing innovation and assuring patient safety are not mutually exclusive**, revising or eliminating old policies, and developing new policies and approaches with an eye on meeting measurable objectives. Increased medical device user fees have supported these efforts so that we are better positioned to respond to the needs of patients.

•**Clinical Trials** In addition to [dramatically improved performance](#)² in reviewing IDEs, CDRH has encouraged the use of **innovative methodologies and study designs in clinical trials**. We recognize that manufacturers need CDRH input early and often so that the ultimate **device review process moves as quickly and smoothly as possible**. In 2013, CDRH issued final guidance for manufacturers on early feasibility studies to encourage conducting these studies in the US. Innovators tend to market their technologies sooner in countries where they elect to conduct their early clinical studies. Since 2013, **the number of early feasibility studies approved has more than doubled—from 17 in FY 2013 to 40 in FY 2016.**

² [CDRH Clinical Trial Enterprise Targets and Performance](#)

CDRH encourages the use of innovative clinical trial designs and statistical methods such as [adaptive clinical trials](#)³ and [Bayesian statistics](#)⁴ because, where appropriate to use, they can reduce the time and cost of a clinical study. In recent years, many devices have come to market based on the results of clinical trials using adaptive trial designs. **For the period from 2007 to May of 2013, CDRH received 201 submissions that were adaptive.**

CDRH continues to develop computational models that can, in some instances, supplement or replace data from clinical investigations, such as the [Virtual Family \(VF\)](#)⁵—a set of highly detailed, anatomically correct, computational whole-body models, designed to mimic humans of both sexes at various stages of growth. **Since 2007, more than 160 submissions have included Virtual Family research.**

● **Flexible, Risk-Based Regulatory Approaches** CDRH continues to adapt our oversight policies to emerging new technologies. In a manner consistent with our statutory mission, we now approach a medical technology by first asking whether active CDRH oversight will be value-added. If not, we take a less active regulatory approach. If it would, we focus on assuring timely patient access to technologies that will benefit patients by considering the device’s innovation cycles and evidence generation needs.

For example, widespread adoption and use of digital health technologies is creating new and innovative ways to improve health and health care delivery. In **one of the biggest de-regulatory actions for CDRH in decades**, to foster greater innovation in the digital health space while promoting public health, we have exercised our enforcement discretion to cease subjecting certain lower-risk medical devices (such as apps for patient care management and medication reminders) to medical device requirements.

Additionally, balancing data needs between what’s collected before the device comes on the market (premarket) and what’s collected after it is on the market (postmarket) reflects our approach to best assure timely patient access to safe and effective devices.

In 2015, CDRH completed a [retrospective review](#)⁶ of the benefit-risk profile of all types of high-risk devices to determine if we could reduce premarket data collection requirements for at least some devices. As a result, for 30 percent of high-risk medical devices, **CDRH determined, based on the current body of evidence and experience, we could consider some devices candidates for down-classification, eliminate some data requirements or shift some premarket data requirements to the postmarket setting.** In 2016, CDRH reached out to stakeholders for input on the results of the retrospective reviews, in order to determine next steps.

● **Patient-Centered Benefit-Risk** For the past 5 years, CDRH has encouraged the use of **a more flexible, patient-centric, and transparent benefit-risk framework** to evaluate medical devices, starting with a 2012 guidance on the factors to consider when making benefit-risk determinations in

³ [Guidance Document: Adaptive Designs for Medical Device Clinical Studies Issued July 27, 2016](#)

⁴ [Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials](#)

⁵ [Virtual Family](#)

⁶ [CDRH Strategic Priorities and Updates](#)

support of device premarket approval decisions, which includes patient perspectives on potential benefits and risks. We are focusing more on what matters to patients.

In 2016 and 2017, CDRH expanded this approach by revising the 2012 guidance to [include additional patient-centric factors](#)⁷, and issuing two additional benefit-risk guidance documents: one which outlines the principal factors CDRH considers when making benefit-risk determinations during the premarket review process for [IDEs](#)⁸, and one which outlines factors to consider when determining whether and what [postmarket actions](#)⁹ we may take to address a problem, such as a recall, based on the benefits and risks of that action to patients.

● **Patients as Partners** CDRH had traditionally determined whether the benefits of a device outweighed its risks based on the trade-offs we thought were acceptable. However, patients who live with a disease or condition often have their own perspectives on what benefits and risks related to medical devices they are willing to accept. CDRH collaborates with patient scientists and other experts outside the FDA to help us advance the scientific field of assessing patient preferences and incorporate the patient perspective into our benefit-risk assessments and decision-making.

For example, in 2014, CDRH funded a collaborative study on patient preferences that led to changes in our review paradigm for obesity devices, and used the results to inform our decision to approve the first medical device for treating obesity since 2007. Better understanding of patient preferences can also help **rejuvenate development pipelines**; since then, CDRH has approved or granted marketing applications for five more medical devices that address obesity or weight loss.

In 2016, CDRH issued a final guidance that outlined [patient preference information \(PPI\)](#)¹⁰ that CDRH may use in decision making. Since then manufacturers have begun to submit—and we have approved—IDEs with patient preference studies.

CDRH’s efforts to incorporate the voice of patients in our decision making also are reflected in medical device clinical studies, which have been increasingly assessing what matters most to patients. Between 2009 and 2014, the number of **premarket submissions that included clinical studies with patient reported outcomes (PROs) increased by more than 500 percent** and half of IDE pivotal clinical studies now include PROs.

In 2015, CDRH established the first FDA advisory committee focused on the interests and needs of patients, and recruited potential new members in 2016. [The Patient Engagement Advisory Committee](#)¹¹ will hold its first meeting in 2017.

⁷ [Guidance Document: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and DeNova Classification \(Aug. 24, 2016\)](#)

⁸ [Guidance Document: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Investigational Device Exemptions](#)

⁹ [Guidance Document: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Product Availability, Compliance, and Enforcement Decisions](#)

¹⁰ [Guidance Document: Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling](#)

¹¹ [The Patient Engagement Advisory Committee](#)

•National Evaluation System for health Technology (NEST)

Despite rigorous premarket evaluation, we cannot fully understand how well a medical device works until it is used day-to-day by patients, caregivers, and clinicians. Premarket clinical trials provide critically important information but we don't understand the long-term benefit-risk profile until it is used in routine clinical practice. Currently our nation is limited in its ability to make widespread use of real-world evidence (RWE) to best inform all members of the medical device ecosystem.

CDRH intends for NEST to increase the quality and use of real-world data (RWD) collected as part of routine clinical care, which should also help reduce the time and cost of evidence generation. Ongoing implementation of the Unique Device Identification (UDI) system also will enable NEST to perform enhanced analyses of devices on the market, providing a clear and standard way to identify devices in electronic medical records.

CDRH is already relying on RWE to approve new devices, expand the indications for already marketed devices, and reduce the time and cost for device makers to meet their postmarket study requirements. In 2016, CDRH documented access to more than 28 million electronic patient records (from national and international clinical registries, claims data, and electronic health records) that included device identification and awarded \$3 million to the Medical Device Innovation Consortium to establish the NEST Coordinating Center.

•Streamlining the Pathway from FDA Approval to Payer Coverage

Timely access to innovative medical technologies has been identified as a significant issue in the delivery of high quality health care. Manufacturers of innovative medical products have said that after undergoing the FDA approval process the availability of their products to consumers is often slow because, in order to obtain coverage and payment from third-party payers, the manufacturers must go through a second review process by such payers. Therefore, CDRH established the Payer Communication Task Force (PCTF) to facilitate communication between device manufacturers and payers to shorten the time between FDA approval or clearance and coverage decisions. By communicating earlier, manufacturers may design their pivotal clinical trials to produce both the data required for regulatory approval or clearance, and positive coverage determinations.

To support these efforts, CDRH and the Centers for Medicare & Medicaid Services (CMS) began to pilot an approach in 2011 called Parallel Review that would give eligible device makers the voluntary option for CMS to start their national coverage determination process while the device is under review by CDRH. This process serves the public interest by reducing the time between FDA marketing approval or clearance decisions and CMS national coverage determinations. In 2016, CDRH and CMS established Parallel Review as a permanent program. Last year, CDRH also established an additional opportunity for device manufacturers to invite CMS, private payers, or health technology assessment groups (HTAs) to join FDA pre-submission meetings to provide early feedback on clinical trial design.

EVIDENCE OF IMPACT

Our investments are starting to pay off. For example, in 2016, CDRH approved 91 novel medical devices—the highest number since the advent of the user fee program in 2003. This followed the second highest number from 2015, and continued a 7-year trend that has resulted in a marked increase in the annual number of novel device approvals since 2009. These novel technologies, which can help improve the quality of life of patients, especially those that require day-to-day maintenance and ongoing attention, are yielding promising results. In addition, several of these devices are reaching US patients much earlier than they would have in previous years.

- **“Artificial Pancreas”** Approximately five percent of diabetics have Type 1 diabetes, also known as juvenile-onset diabetes. People with type 1 diabetes have to constantly monitor their glucose levels throughout the day and have insulin therapy through injection with a syringe, an insulin pen, or an insulin pump, to avoid becoming hyperglycemic (high glucose levels). Working interactively with the sponsor from the earliest stages of development to assist in making this technology available as quickly as possible while assuring it is safe and effective, **CDRH, in 2016, approved the first automated insulin delivery (AID) device in the world that is intended to automatically monitor glucose (sugar) and provide appropriate basal insulin doses—what some have called a first-generation “[artificial pancreas¹²](#).”**

- **Transcatheter Aortic Valve Replacement (TAVR) Therapy**

About 80,000 surgical aortic valve replacements (SAVR) are performed in the US annually. One-third of these patients are at intermediate surgical risk for death or complications. An aortic valve replacement that can be inserted through the blood vessels or, in some cases, through the tip of the heart by a catheter, rather than through open surgery, could avoid the risks of surgery and provide an alternative effective treatment to patients who are in the “intermediate surgical risk” category.

In 2011, CDRH approved the first TAVR device in the US for patients who are not surgical candidates for SAVR, more than four years after the device entered the European Union (EU) market. When, in 2016, CDRH [approved the expanded indication¹³](#) for use for a TAVR device in patients at intermediate surgical risk for death or complications, the positive impact of CDRH initiatives was evident. The gap between EU and US approval for the expanded indication for use was reduced from over four years to only 18 days. US Medicare coverage is also a factor in patients’ access to devices. For TAVR devices, access to real-world evidence—what NEST hopes to expand—proved to be a valuable asset. The US Medicare program immediately covered TAVR devices due to the ongoing collection of real-world evidence on these devices in a national registry—there was no delay between US approval and access to this technology. **As a result, more than 25,000 additional patients each year are now eligible for this life-saving procedure.**

¹² [The Artificial Pancreas Device System](#)

¹³ [Press Release: FDA approves expanded indication for two transcatheter heart valves for patients at intermediate risk for death or complications associated with open-heart surgery – Aug. 2016](#)

•**Diagnostics for National Emergencies** Accurate detection and diagnostics are critical to addressing national public health threats. For example, in 2016, CDRH authorized the use of fourteen diagnostic tests for [Zika](#)¹⁴ virus under our Emergency Use Authorization (EUA) authority—twelve tests to diagnose active infection and two tests to assess whether individuals who may have recently been exposed to Zika were actually infected. This rapid action provided timely patient access to Zika tests before the summer of 2016, when officials detected the virus in the U.S. **Since 2009, CDRH has granted 50 EUAs, reauthorized 19 EUAs, and granted 30 amendments for tests to help meet the country’s needs during a national public health emergency, such as outbreaks from Zika, Ebola, and H1N1.**

¹⁴ [Zika Virus Response Updates from FDA](#)