

Report to Congress
BREAKTHROUGH DEVICES PROGRAM

Submitted Pursuant to
Section 3051 of the 21st Century Cures Act

U.S. Department of Health and Human Services
Food and Drug Administration

Date _____

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Executive Summary

Section 3051 of the 21st Century Cures Act (Public Law 114-255) and section 901 of the FDA Reauthorization Act of 2017 (Public Law 115-52) codified section 515B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), granting FDA authority to establish a program referred to as the Breakthrough Devices Program. The program is intended to expedite the development and prioritize the review of certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. Section 3051 of the 21st Century Cures Act further required the Secretary of Health and Human Services to issue a report to Congress on January 1, 2019, on the establishment and performance of the Breakthrough Devices Program as well as any recommendations to strengthen the program. This report fulfills that requirement and highlights the following accomplishments for the Breakthrough Devices Program:

- FDA developed and published a draft guidance on the Breakthrough Devices Program, which includes FDA's interpretation of the eligibility criteria for inclusion in the program, as specified in section 515B of the FD&C Act and describes procedures for submitting a request for designation as a breakthrough device. After reviewing public comments and making appropriate revisions, FDA issued the final guidance on December 18, 2018.
- As of September 30, 2018, FDA has granted 71 breakthrough device designation requests out of 100 total designation requests received with a final decision. Additionally, we now consider devices granted designation under FDA's precursor program, the Expedited Access Pathway (EAP) Program, to be part of the Breakthrough Devices Program due to the consistency in vision and eligibility criteria between the two programs. There were 56 designation requests received under the EAP Program, and 26 of those requests were granted. Therefore, the total number of devices included as part of the Breakthrough Devices Program is 97.
- As of September 30, 2018, 24 investigational device exemptions (IDEs) have been approved or completed for clinical studies of breakthrough devices.
- As of September 30, 2018, nine breakthrough devices have had a marketing submission approved, cleared, or granted.

Since establishment, the Breakthrough Devices Program has received support from external stakeholders who recognize its potential to enable more timely access to these important medical devices for patients. FDA has recognized that the program may benefit from increased resources and additional options to ensure that it remains strong and able to advance the purpose of the statutory breakthrough device provision.

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I. Purpose

Section 3051 of the 21st Century Cures Act (Public Law 114-255) and section 901 of the Food and Drug Administration's (FDA) Reauthorization Act of 2017 (Public Law 115-52) codified section 515B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), granting FDA authority to establish a program referred to as the Breakthrough Devices Program. The program is intended to apply efficient and flexible approaches to expedite the development and prioritize the review of certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. Section 3051 of the 21st Century Cures Act further required the Secretary of Health and Human Services to issue a report on January 1, 2019, to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on the establishment and performance of the Breakthrough Devices Program as well as any recommendations for program improvement. This report is submitted to fulfill that statutory requirement.

II. Background

A. Innovation Pathway, Priority Review, and Expedited Access Pathway

Congress and FDA have long recognized the need to bring safe and effective medical devices to patients. The Breakthrough Devices Program had several important precursor programs that also aimed to support device innovation and increase patient access to medical devices. Specifically, in 2011, the Center for Devices and Radiological Health (CDRH) established the Innovation Pathway as a mechanism to improve collaboration with medical device innovators and support the overall development and review of medical devices. The Innovation Pathway conducted two pilot programs that concluded in 2014. Participants reported the pilot programs established an environment of trust that stimulated technological enhancements to their device development.

Additionally, consistent with commitments made by FDA as part of the Medical Device User Fee Amendments of 2012 (MDUFA III), FDA established the Priority Review Program and implemented policies and procedures for designating priority review status to certain medical devices that met statutory criteria.¹ As part of these commitments, FDA publicly reported the number of premarket approval applications that were designated as priority review.

Lastly, in April 2015, FDA issued a final guidance document establishing the Expedited Access Pathway (EAP) Program. The EAP Program borrowed some features from the Innovation Pathway and was also based in part on FDA's experience with programs to expedite the development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening conditions in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). However, the EAP Program was a separate and distinct program tailored to medical devices. The goal of the EAP Program was to help patients have more timely access to medical devices

¹ Specifically, FDA issued a guidance entitled "Priority Review of Premarket Submissions for Devices." FDA withdrew this guidance on August 3, 2017.

intended to address unmet medical needs for life-threatening or irreversibly debilitating diseases or conditions by expediting device development, assessment, and review while preserving the statutory standards for FDA marketing authorization.

B. Establishment of the Breakthrough Devices Program

As directed by Congress in section 515B of the FD&C Act, FDA has established the Breakthrough Devices Program. The Breakthrough Devices Program is a voluntary program for certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. This program is intended to help patients have more timely access to these medical devices by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval², clearance of a premarket notification (510(k))³, and marketing authorization via the De Novo classification process⁴, consistent with the Agency's mission to protect and promote public health. Though the Breakthrough Devices Program is consistent in vision to the EAP Program and incorporates priority review, the Breakthrough Devices Program is different from both precursor programs because of certain changes Congress prescribed in section 515B of the FD&C Act. Therefore, the Breakthrough Devices Program has superseded the EAP Program and the Priority Review Program.

C. Principles and Provisions of the Breakthrough Devices Program

As defined in section 515B of the FD&C Act, breakthrough devices are devices:

- (1) that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and*
- (2) (A) that represent breakthrough technologies;*
(B) for which no approved or cleared alternatives exist;
(C) that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or
(D) the availability of which is in the best interest of patients.

Consistent with the activities described in section 515B of the FD&C Act, for the purposes of expediting the development and review of devices designated as a breakthrough device, FDA:

² Federal Food, Drug and Cosmetic Act, Section 515(c)

³ Federal Food, Drug and Cosmetic Act, Section 510(k) and FDA Guidance document entitled "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)] available at: <https://www.fda.gov/downloads/MedicalDevices/.../UCM284443.pdf>

⁴ Federal Food, Drug and Cosmetic Act, Section 513(f)(2) and FDA Guidance document entitled "De Novo Classification Process (Evaluation of Automatic Class III Designation) available at: <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080197.pdf>

- (a) Prioritizes review of regulatory submissions for devices designated as breakthrough (including pre-submissions, investigational device exemption (IDE) applications, and marketing submissions);
- (b) Provides for interactive and timely communication on regulatory submissions (including pre-submissions, IDE applications, and marketing submissions) through review team support and senior management engagement;
- (c) May use timely post-market data collection when scientifically appropriate for devices that require premarket approval;
- (d) May take steps to ensure that the design of clinical trials is as efficient and flexible as practicable, when scientifically appropriate; and
- (e) Expedites the review of manufacturing and quality systems compliance, as applicable.

III. Breakthrough Devices Program Implementation

To implement the Breakthrough Devices Program, FDA has developed a process for reviewing breakthrough device designation requests and designed procedures to expedite the review of breakthrough device regulatory submissions.

A. *Guidance*

One of FDA's first actions in implementing the Breakthrough Devices Program was the development of draft guidance describing the program's policies and procedures. The draft guidance document⁵ was issued on October 25, 2017. The guidance was available for public comment for 60 days. Many of the comments FDA received on the draft guidance document expressed support for the program as well as interest in the mechanisms described therein to facilitate use of timely post-market data collection and efficient clinical trial design for breakthrough devices subject to premarket approval. After consideration of the public comments, FDA issued the final guidance document on December 18, 2018.

The draft guidance document describes key principles and features of the Breakthrough Devices Program and explains procedures for requesting designation as a breakthrough device and the criteria FDA intends to use for evaluating designation requests. The draft guidance also provides examples of what information should be included in such a request to the Agency.

Finally, the draft guidance outlines several mechanisms by which sponsors of breakthrough devices can interact with FDA to expedite the development and review of their devices. One such mechanism described in the draft guidance is the concept of a "sprint discussion." Sprint discussions provide for frequent interactive review on a defined schedule to reach consensus on device development and evaluation proposals related to a specific topic. Through public comments on the draft guidance, external stakeholders communicated support for this concept and expressed that it would improve the success of the program. Other mechanisms for feedback outlined in the draft guidance include collaboration with

⁵ "Breakthrough Devices Program," available at <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM581664.pdf>.

FDA on an optional Data Development Plan, obtaining agreement on clinical protocols, and regular status updates between the sponsor and FDA to help ensure that device development is proceeding and any FDA feedback can be incorporated in a timely manner.

B. Information Management

FDA also developed information technology tools to facilitate the review process of requests for breakthrough device designation and to identify regulatory submissions related to the breakthrough device designation (e.g., a premarket approval application that is submitted for a device that was previously granted breakthrough status). These tools facilitate the statutory requirement for FDA to render a decision on requests for breakthrough device designation within 60 days of receipt. They have also enabled the collection of data about the program that are included in this report and that help FDA operate the program.

C. Data

Data presented in this report documents activity in the Breakthrough Devices Program and reflects submissions for medical devices reviewed by both CDRH and CBER. At the close of fiscal year 2018, FDA had received 100 requests for designation as a breakthrough device, of which 71 were granted, 20 were denied because they did not meet the statutory criteria as defined in section 515B(b) of the FD&C Act, and nine were withdrawn by the requestor, in many cases in response to FDA's questions regarding whether the device met the statutory criteria. These data show that 71 percent of breakthrough device designation requests have been granted.

Due to consistency in vision and the eligibility criteria for the Breakthrough Devices Program and FDA's precursor EAP Program, we have considered those devices granted EAP designation to be part of the Breakthrough Devices Program. Under the precursor EAP program, FDA received 56 requests, of which 26 were granted, 21 were denied, and nine were withdrawn.

Therefore, the total number of devices included in the Breakthrough Devices Program was 97 as of the close of fiscal year 2018.

This information is represented graphically in Figure 1. The data are presented based on designation requests, which were closed as of September 30, 2018. The number of designation requests that have been granted appears in green, requests denied appear in orange, and requests withdrawn appear in gray.

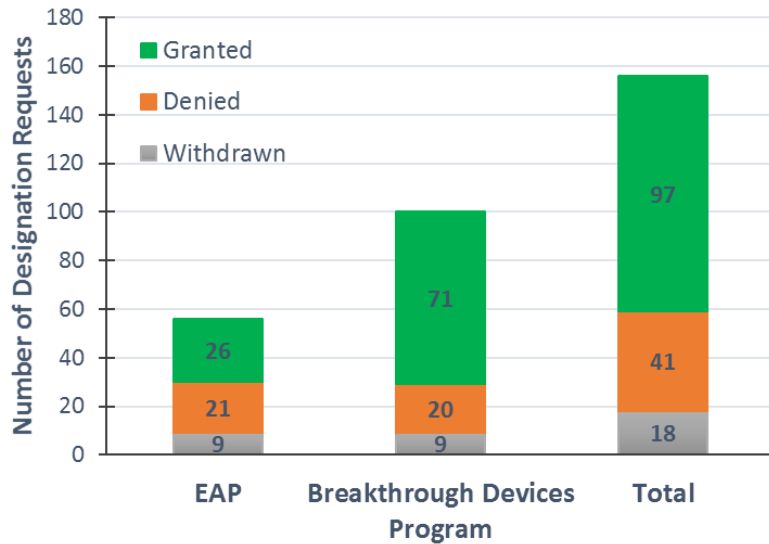


Figure 1. Summary data for breakthrough device designation requests.

FDA has granted breakthrough device designation to devices in multiple clinical specialties. The distribution of granted designation requests by clinical specialty is shown in Figure 2. Of those granted a breakthrough device designation, approximately 30 percent represent in vitro diagnostic technologies, which include microbiology, chemistry and toxicology, molecular genetics and pathology, and hematology and immunology devices. The most common clinical specialties for which breakthrough device designation was granted for a therapeutic device are neurological (18.6%) and cardiovascular (15.6%).

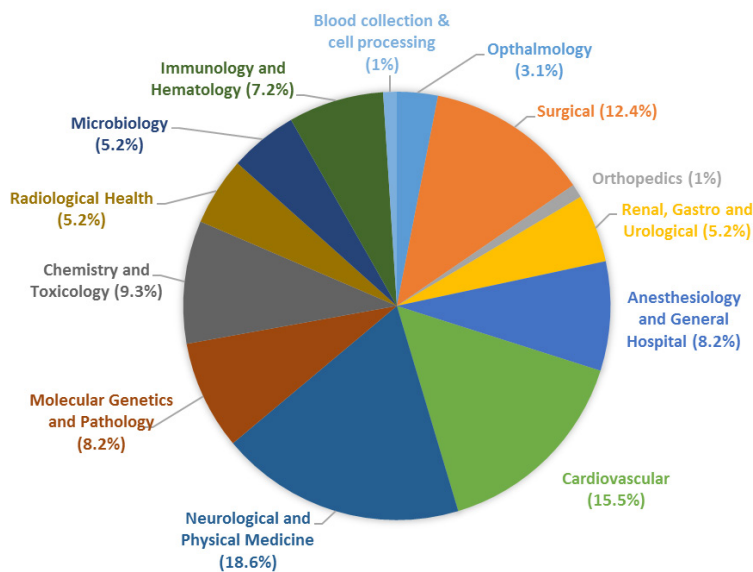


Figure 2. Distribution of granted breakthrough device designation requests across common clinical specialties and medical device areas.

Designation as a breakthrough device precedes marketing authorization of the device and may precede human clinical studies. Several breakthrough devices are being studied clinically under 24 IDEs, which include both early stage feasibility studies and large pivotal trials that are designed to support a marketing application. Additionally, FDA has received 13 marketing submissions for breakthrough devices. Of those 13, eight are premarket approval applications (PMAs or PMA Supplements), three are De Novo classification requests, and two are premarket notifications (510(k)s). Of those 13, FDA has cleared two 510(k)s, granted two De Novo requests, and approved five PMAs.

These data indicate there is strong interest in the Breakthrough Devices Program and support for the program from device manufacturers. In particular, the data on marketing submissions indicate that several sponsors have significantly progressed in their device development and some have even successfully achieved marketing authorization since the establishment of the Breakthrough Devices Program. These trends illustrate FDA's commitment to the success of this program and helping to bring safe and effective devices to patients in a timely manner.

IV. Next Steps and Recommendations for Programmatic Improvements

As awareness of, and confidence in, the Breakthrough Devices Program grows, FDA anticipates receiving and granting more breakthrough device designation requests. Based on early experience, FDA also anticipates that many of these requests and designations may be in the same clinical specialty and for the same indication, significantly impacting particular review teams. The statutorily mandated activities for breakthrough devices are significantly more time- and labor-intensive for FDA staff owing to the increased level of interaction that is the hallmark of the Breakthrough Devices Program. However, the public health benefits realized from investing in breakthrough devices should not come at the expense of other FDA programs. For the Breakthrough Devices Program to continue to be successful, FDA will need to balance its resources for this program while taking into account other review priorities based on statutory deadlines and commitments made as part of negotiations for the Medical Device User Fee Amendments.

The 1976 Medical Device Amendments (Public Law 94-295) to the FD&C Act established a risk-based framework for the regulation of medical devices and the standard of reasonable assurance of safety and effectiveness that must be met for premarket approval and other purposes. Since then, Congress has enacted laws broadening the authority and mission of FDA to also include the promotion of public health⁶ and to make the regulatory paradigms the Agency applies more flexible. This flexibility was manifest in the 21st Century Cures Act. The purpose of the breakthrough devices provisions of the 21st Century Cures Act is to encourage FDA and provide it with sufficient authority “to apply efficient and flexible approaches” to expedite development and prioritize review of breakthrough devices. For this purpose, FDA may take steps to ensure that clinical trial design is as efficient and flexible as practicable (when scientifically appropriate) and facilitate (when scientifically appropriate) expedited and efficient development and PMA review of breakthrough devices through utilization of timely postmarket data collection.

⁶ See section 1003 of the FD&C Act (21 U.S.C. §393)

FDA is considering various approaches to enhancing the goals of the Breakthrough Devices Program and other statutory mandates and authorities. One such approach is leveraging more data collected in the postmarket setting. In the context of the Breakthrough Devices Program, Congress authorized FDA to facilitate, when scientifically appropriate, expedited and efficient development and PMA review through the utilization of timely postmarket data collection. However, the infrastructure for increased reliance on postmarket data collection is still under construction. Entities like the National Evaluation System for health Technology Coordinating Center (NESTcc)⁷ are exploring ways for members of the medical device ecosystem to generate more and higher-quality data by addressing gaps in enterprise data infrastructure and analytic capabilities in a variety of health care settings. Filling these gaps would enhance FDA's and the public's capacity to use real world evidence to evaluate the premarket and postmarket safety and effectiveness of devices, reducing the time and cost of device development and evaluation while providing greater patient safeguards at lower cost. Additional investments in these activities could enable more timely patient access to many devices, including breakthrough devices.

V. Conclusion

The Breakthrough Devices Program is intended to help patients have more timely access to safe and effective medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions and otherwise meet the criteria for breakthrough designation. Early indicators suggest strong external support for the program's vision and implementation. FDA's experience with the program so far demonstrates that collaborating early and often with breakthrough device developers can improve patient access to devices of public health importance.

⁷ <https://nestcc.org/>