

Regulatory Sciences

Expediting drug approval

Speed your time to market with FDA's expedited programs

The faster way to marketing submission and drug approval
for serious conditions and rare diseases

In recent years, the US Food and Drug Administration (FDA) has made great advances in the review of new drugs. The United States is now reported to lead the world in both timeliness and quantity of noteworthy new drug approvals. Case in point: 2015 saw the highest number of novel new drugs approved by the Center for Drug Evaluation and Research (CDER)—45 approvals in all, with 21 (47 percent) of these approved products having orphan designation.

This progress is due, in part, to FDA's ongoing commitment to improve the drug development process and establish robust development programs that are efficient and predictable. The result: products that have a positive benefit-risk profile are effective and available to patients.^{1,3}

This is especially important for patients who have serious and life-threatening diseases or illnesses for which there are few therapeutic options. For these patients, time is of the essence, and the traditional drug development process is far too lengthy. Standard drug development programs involve multiple complex steps, including formulating and manufacturing the drug product, characterizing the new drug, gathering adequate evidence on the product's performance, evaluating safety risks, and confirming the effects observed in early clinical trials.

To minimize the time to get new drugs to market and help seriously ill patients faster, the development process must be compressed and evidence of the drug's effects must be gathered as efficiently as possible.

Cardinal Health Specialty Solutions

FDA approved
a record number
of novel drugs
and new orphan
drugs in 2015.

Fast track designation

Breakthrough therapy designation

Accelerated approval

Priority review designation

Key concepts to determine a drug's program eligibility

- 1 Define and describe a serious condition
- 2 Study existing available therapies
- 3 Determine if product addresses an unmet medical need

Meeting the challenge

FDA established four expedited programs to speed the development and review of new drug and biological products that address unmet medical needs in the treatment of a serious or life-threatening condition.

These programs—fast track designation, breakthrough therapy designation, accelerated approval, and priority review designation—help ensure that therapies for serious conditions are approved and available to patients as soon as they have been proven to provide a clinically meaningful benefit.²

The programs help solve a historical challenge. In the past, industry sponsors were responsible for preparing and presenting to FDA a solid, well-designed strategy and corresponding pathway for the development of their potential drug product, with little input from FDA. Via the breakthrough therapy designation, FDA now supplements, guides, and accelerates sponsor efforts with FDA staff who are experienced in the review process and regulatory health project management.

How the expedited programs work

Over the past few years in the United States, there has been an increasing trend in the number of marketing application filings and novel new drug approvals. In the last two years, there has also been an impressive percentage of products approved that were in one or more expedited designation categories, including breakthrough therapy designation. From 2014 to 2015, FDA's CDER approved 86 novel new drugs, and more than half were in one or more expedited program categories. In addition, of the approved drugs using an expedited program, 92 percent were orphan designated drugs.

These success stories demonstrate that FDA and industry partners are leveraging the expedited pathways to bring innovative products to market faster. They are reducing the time necessary for drug development without compromising the standards for safety and effectiveness.

As a result, patients with serious conditions and rare diseases now have new potential treatment options. These new drugs are serving previously unmet medical needs and significantly aiding in the advancement of patient care and public health.^{1,3}

A look inside the four FDA Expedited Programs

1. Fast track designation

What it does:

Facilitates the development and expedited review of drugs intended to treat a serious condition for an unmet medical need when there is no available therapy

When to use it:

- There is no adequate available therapy for a serious condition or the drug is designated as a qualified infectious disease product
- The potential to address an unmet medical need can be demonstrated by evidence of nonclinical activity, mechanistic rationale, theoretical rationale, pharmacologic data, or clinical data, depending on the stage of development

The features:

Expedites development and review via frequent interactions with the agency review team and rolling review of the marketing application:

- Frequent agency interactions include pre-IND, end-of-phase 1, end-of-phase 2, pre-NDA, or pre-BLA meetings and consultation meetings to discuss clinical study designs, application-enabling data, marketing application structure and content, accelerated approval, and the potential eligibility for priority review of the marketing application.
- Rolling review is a review of portions of the marketing application before the entire application has been submitted, which is granted if FDA determines that the product may be effective based on a preliminary evaluation of the clinical data.²

2. Breakthrough therapy designation

What it does:

Shortens the development and review time when early clinical evidence indicates that the new potential therapy shows a substantial improvement over all available therapies on one or more clinically significant endpoints

When to use it:

- There is potential to address an unmet medical need for a serious condition when an available therapy exists
- There is existence of clinical evidence that the potential therapy demonstrates a substantial improvement over all available therapies on one or more clinically significant endpoints

The features:

- Includes all the features of fast track designation, including frequent interactions with FDA and eligibility for rolling review
- Includes more intensive FDA guidance on an efficient drug development program (beginning as early as phase 1 clinical trials) and an Agency commitment involving FDA management²

FDA has implemented a new procedure, the Preliminary BTDR Advice Request, which can be used to obtain FDA guidance prior to submitting a formal breakthrough therapy designation request.

3. Accelerated approval pathway

What it does:

Accelerates the approval for drugs for serious conditions that fill an unmet medical need based on a surrogate or intermediate clinical endpoint

When to use it:

- The clinical data demonstrates a meaningful advantage over the available therapy to treat a serious condition
- The effect on a surrogate or intermediate clinical endpoint is reasonably likely to predict a clinical benefit when the disease course is long and an extended period is required to measure the drug's intended clinical benefit

The features:

- Allows for earlier approval of a new drug that demonstrates an effect on a surrogate or intermediate endpoint
- A commitment to conduct postmarketing studies to confirm the drug's clinical benefit²

4. Priority review designation

What it does:

Shortens the marketing application's review time for a drug that treats a serious condition and demonstrates the potential to be a significant improvement in the safety or effectiveness in the treatment, diagnosis, or prevention of a disease

When to use it:

There is evidence to demonstrate significant improvement in one of these areas:

- Increased effectiveness in treatment, prevention, or diagnosis of a condition
- Elimination or substantial reduction of a treatment-limiting drug reaction
- Documented enhancement of patient compliance, expected to lead to an improvement in serious outcomes
- Safety and effectiveness in a new subpopulation

The features:

- Allows for a 6-month FDA review clock for a marketing application compared to a 10-month review clock for a standard review of a marketing application²

Accelerating rare disease treatment

More than 25 million Americans suffer from one of 7,000 rare, orphan diseases (defined as a disease that affects less than 200,000 people in the United States). In 1983, the Orphan Drug Act was passed to stimulate the development of products for these patients.

More than 3,500 drugs and biologics have been designated as orphan drugs, with more than 500 approved orphan designated products listed in FDA's

database as of early 2016. Most of these orphan drugs are indicated to treat a serious or life-threatening condition.

In 2014, 17 (41 percent) of 41 drugs approved were orphan-designated drugs, all of which utilized at least one expedited program. Seven (78 percent) of the nine drugs with breakthrough designations were also orphan-designated drugs.

In 2015, the highest number of orphan drugs was approved since passage of the Orphan Drug Act in 1983, marking the best year for rare disease new molecular entity approvals.

In 2015, 21 of the 45 approved drugs were orphan-designated drugs, which surpassed 2014 orphan drug approvals by 6 percent. Also, 18 of the 21 approved orphan drugs received one or more of the FDA expedited program pathways.^{1,3}

Best practices for success

Sponsors face a number of challenges during the marketing application process, such as aligning program components, compressed timelines, and FDA review. Often, the clinical development component is not the rate-limiting step for application submission.

When developing a product with an expedited program, sponsors should be prepared to:

Promote proactive communication with FDA to ensure the development components and submission timing meet expectations for licensure or marketing approval

Pursue a more rapid manufacturing development program to accommodate the accelerated pace of the clinical program

Engage its review and compliance staff to manage review and inspection timing

Gain FDA agreement on the nonclinical program and marketing-application-enabling studies

Communicate early regarding the proposed labeling as well as postmarketing requirements and commitments

Focus on the benefit-risk profile and link to the patient¹

Whether you need assistance with a small part of the regulatory process or a partner to help ensure the approval and success of your product, we have the expertise to help guide your products to market and beyond.

Learn more about Cardinal Health
Regulatory Sciences at:
cardinalhealth.com/regulatorysciences

This white paper was written based on information in

FDA's Expedited Programs for Serious Conditions: An Overview and Leveraging Expedited Programs for Drugs and Biologics for Serious Conditions and Rare Diseases, by Diane M. Beatty, PhD. Dr. Beatty is Managing Director, Regulatory Affairs and Product Development, for the Regulatory Sciences group of Cardinal Health Specialty Solutions and is a subject matter expert regarding FDA's expedited programs and orphan drug development. These articles first appeared in the Regulatory Affairs Professionals Society's online publication Regulatory Focus in March 2015.

- 1 Beatty DM. "Leveraging Expedited Programs Drugs and Biologics for Serious Conditions and Rare Diseases." Regulatory Focus. March 2015. Regulatory Affairs Professionals Society.
- 2 Beatty DM. "FDA's Expedited Programs for Serious Conditions: An Overview." Regulatory Focus. March 2015. Regulatory Affairs Professionals Society.
- 3 Novel Drugs 2015. (2016, January). <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM485053.pdf>

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