VERISTAT

FDA Expedited Pathways

Accelerating the development of therapeutic products intended to treat serious conditions and unmet medical needs has been an increasing interest of the public, legislators, and the scientific community for many years.

Responding to this interest, FDA has issued regulations and guidance documents to establish development programs designed to speed the availability of new therapies to patients with serious conditions, especially when there are no satisfactory alternative therapies.

Below we highlight the benefits of, qualifying criteria for, and timing and procedures for six different expedited programs and designations. Overall, the purpose of these regulatory pathways is to save time and reduce the cost of bringing therapies to market for serious conditions and unmet medical needs.

Expedited pathways to consider during clinical development

Fast Track

BENEFITS

Helps to expedite development and review by providing opportunities for frequent interactions with the FDA review team

Rolling Review

CRITERIA

Product must be intended to treat a "serious condition"

Nonclinical or clinical data must demonstrate the potential to address an "unmet medical need"

TIMING

Submit request (10-20 pages) with IND or after; ideally no later than the pre-BLA or pre-NDA meeting; FDA response in 60 days

Phase I
Phase II
Phase III

Breakthrough Therapy (BT)

BENEFITS

Intensive guidance on efficient drug development

Initial Comprehensive Multidisciplinary BT meeting

Organizational commitment

Intensive guidance on efficient drug development

Rolling Review

CRITERIA

Product must be intended to treat a "serious condition"

Preliminary clinical evidence that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies

TIMING

Can be submitted with IND, but need for clinical evidence precludes this in most cases; ideally submitted prior to pivotal study; FDA response in 60 days

Phase II
Phase III

Qualified Infectious Disease Program (QIPD)

BENEFITS

5-year exclusivity extension

Priority Review (first application)

Fast Track designation (must be specifically requested)

CRITERIA

Must be an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections*

Biologics and devices are not eligible for QIDP

Application should include specific QIDP-qualified indication, rationale for development, and data supporting antibacterial/antifungal activity (in vitro, animal model or human data)

* Includes infections caused by: (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or (2) qualifying pathogens listed in 21 CFR 317.2. Includes: *Clostridium difficile, Enterococcus spp, Helicobacter pylori, Mycobacterium tuberculosis, Neisseria gonorrhoeae, Staphylococcus aureus, Vibrio cholerae,* and many others.

TIMING

Submit prior to submission of marketing application (including pre-IND correspondence); FDA response in 60 days

Pre-Clinical
Phase I
Phase II
Phase III

Regenerative Medicine Advanced Therapy (RMAT)

BENEFITS

All Breakthrough Therapy designation features, including early interactions to discuss any potential surrogate or intermediate endpoints

Statute addresses potential ways to support Accelerated Approval and satisfy post-approval requirements

CRITERIA

Meets the definition of Regenerative Medicine

Preliminary clinical evidence indicates potential to address "unmet medical needs"

Product must be intended to treat a "serious condition"

Unlike Breakthrough designation, RMAT designation does not require evidence to indicate that the drug may offer a substantial improvement over available therapies

TIMING

Can be submitted with IND, but need for clinical evidence precludes this in most cases; ideally no later than EOP2 meeting; FDA response in 60 days

Phase II
Phase III

Expedited pathways to consider at the NDA/BLA stage of development

Priority Review

BENEFITS

Shorter clock for review of marketing application (6 months compared with the 10-month standard review)

CRITERIA

Product must be intended to treat a "serious condition"

Product has been designated as a qualified infectious disease product

Any application or supplement for a drug submitted with a Priority Review voucher

If approved, would provide a significant improvement in safety or effectiveness
OR
Any supplement that proposes a labeling change pursuant to a report on pediatric study under 505A

Request should include nonclinical or clinical data to demonstrate the potential to address "unmet medical need"

TIMING

Submit with original BLA, NDA or efficacy supplement; FDA response in 60 days

Marketing application

Accelerated Approval

BENEFITS

Approval based on an effect on a surrogate endpoint or an intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit

CRITERIA

Product must be intended to treat a "serious condition"

Confirmatory trial is still needed

Generally, provides a meaningful advantage over available therapies
AND
Demonstrates an effect on a surrogate endpoint

TIMING

Not a formal request; should be discussed with the review division during development

Phase I
Phase II
Phase III

VERISTAT EXPERTS CAN HELP AS YOU CONSIDER ANY OF THE FDA EXPEDITED PATHWAYS

FDA

"Which of FDA's different expedited programs do I qualify for? Can I apply for more than one?"

"What are the costs, risks and benefits of each program? Should I apply for one over the other, or more than one?"

"When should I apply?"

"What are some strategic considerations for choosing expedited pathway(s) to pursue for my program?"

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DEFINITIONS

"Serious Condition"

". . . a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible if it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one."

Source: FDA Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. https://www.fda.gov/media/86377/download

"Unmet Medical Need"

1. **Where there is no available therapy**
2. **Where there is available therapy but the investigational agent:**
   - Has an effect on a serious outcome of the condition that is not seen with or is better than available therapy
   - Can be used effectively with other critical agents that cannot be combined with available therapy
   - Provides efficacy comparable to available therapy, while (1) avoiding serious toxicity that occurs with available therapy, (2) avoiding less serious toxicity that is common and causes discontinuation of treatment of a serious condition, or (3) reducing the potential for harmful drug interactions
   - Has a documented benefit that is expected to lead to an improvement in serious outcomes
3. **Where the only available therapy** was approved under the Accelerated Approval program based on a surrogate endpoint or an intermediate clinical endpoint and clinical benefit has not yet been verified

Source: FDA Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. https://www.fda.gov/media/86377/download

Rolling Review

"[Rolling Review] means that a drug company can submit completed sections of its Biologic License Application (BLA) or New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA."

Source: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track

Surrogate Endpoints

". . . a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure, that is not itself a direct measurement of clinical benefit, and (A) is known to predict clinical benefit and could be used to support traditional approval of a drug or biological product; or (B) is reasonably likely to predict clinical benefit and could be used to support the accelerated approval of a drug or biological product in accordance with section 506(c)."

Source: https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure

Regenerative Medicine

". . . a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations. . . . certain human gene therapies and xenogeneic cell products may also meet the definition of a regenerative medicine therapy."

Source: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenerative-medicine-advanced-therapy-designation

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