

FAST TRACK USA REGULATORY APPROVAL FOR DRUGS TO TREAT EMERGING INFECTIOUS DISEASES

PAVITHRA GM, SABA MAANVIZHI*

Department of Pharmaceutics, Sri Ramachandra Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamilnadu, India. Email: sabamaanvizhi@yahoo.co.in

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ABSTRACT

The Food and Drug Administration has established fast track approval to speed the designation of drugs that efficiently treat serious conditions, in particular those that provide improved advantages over available therapy. Fast track designation was initiated to curtail the time period in the new drug approval procedure and to promote the drug discovery and commercialization of drug products for critical and life-threatening illness and expedite the approval of drug products demonstrating advanced efficacy toward the prevailing one. Single Phase II study is reviewed before approving the drug within fast track designation. This review article highlights the consequences, criteria for fast track designation, fast track designation process, and the timeline for fast track approval.

Keywords: Center for Drug Evaluation and Research, Designation, Fast track, Life threatening, Serious Diseases.

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INTRODUCTION

Numerous numbers of unmet medical needs along with limited no of drugs available for treatment of life threatening and rapidly spreading diseases like AIDS, HIV, tuberculosis, cancer, viral infections [1]. The present medicines accessible for treatment are having their assets and liabilities. The long approval process for drugs retards available to new medications that are much almighty required by patients affected by life-threatening diseases and medical conditions [2].

The Food and Drug Administration (FDA) has refined four distinctive programs – one pathway and three designations to expedite approval of promising new drugs intended for unmet medical need [3]. They are fast track, priority review, breakthrough therapy, and accelerated approval. All these processes entail speed authorization [4,5]. The proportion of new drug products obtaining expedited approvals has been at a minimum of 60% for each of the past 5 years. It had been below 60% in the previous five [6].

The FDA usually fast tracks drugs intended to treat life-threatening, rapidly spreading diseases and have fewer or no other treatments. A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the technical and scientific data and proposed labeling. The FDA approves such drugs based on Initial research that specifies the drugs might be effective, instead of long-term studies [7].

Fast track designation was established in 1988. A sponsor can request fast track designation together with the Investigational New Drug (IND) application [8]. The FDA communicates the decision within 60 days to the applicant regarding fast track approval. Whenever the drug product is authorized with the fast track designation process, this empowers investigators to operate together with the FDA to carry out the trial and to submit the related data [9]. Some fast tracked drugs have been major successes, producing proven treatments for maladies such as HIV/AIDS, leukemia, and hepatitis [10].

FAST TRACK DESIGNATION

Fast track designation is defined as an approach aimed to promote the drug development and faster the reviewing of drug products that treat life-threatening illness, and fulfill an unmet medical demand, depend on assuring *in vitro* or *in vivo* data [11,12]. Clinical data are not

a compulsion and the drug may receive designation which will speed up the drug development process and bring the drugs faster into the market [13]. The Request for Fast Track is initiated by the sponsor at all times throughout the development process. Beginning with the request within 60 days the FDA makes a decision [14].

Initial and recurrent conversation among the pharmaceutical industry and the FDA is promoted during the overall new drug development and the review procedures. All the problems and queries are solved rapidly as a result of the frequent conversations, which usually leads to fast drug approval and accessibility by sufferers [15].

All drugs are developed to prevent and treat illness without any concurrent treatment, which is aimed at unmet medical demand. In case, the existing treatments are available, the fast track drug needs to show few benefits above to the available therapy:

- Demonstrating the effect on critical consequences, effectiveness, or enhanced outcome on serious consequences
- Eliminating serious adverse events of existing therapy
- Promote the screening of a serious problem in which initial screening consequence in a better outcome
- Reducing clinical substantial toxicity of an existing treatment is ordinary and induces a stoppage of treatment
- Potential to address emergence or anticipated public health-care need [16,17].

If a drug acquires fast track approval is appropriate for few or altogether consequences

- Recurrent meet with FDA to debate about the new drug development and make sure gathering of relevant data required to aid new drug designation
- Further continual well-written conversation with the FDA around the plan of the present clinical studies and usage of biomarkers
- The ability for priority review and accelerated approval, if a pertinent benchmark is fulfilled
- Rolling review describes a pharmaceutical industry should submit finished sections of its New Drug Application (NDA) for their review by the FDA, instead of waiting till each division of the NDA is finished earlier than the whole application can be reviewed. NDA review generally does not start unless the pharmaceutical industry has submitted the full NDA to the FDA [18-20].

Criteria for fast track designation

Section 506(a)(1) of the Food, Drug, and Cosmetic Act declares that a drug product designated as a fast track is designed toward the therapy on a life-threatening or serious illness and illustrates the feasibility to meet unmet medical demands for the condition.

Serious or life-threatening conditions

The FDA Agency plans to estimate whether a condition is serious and whether a specific drug is meant to treat a serious condition. All circumstances meet the definition of life-threatening conditions as described in 21 CFR 312.81(a) should even be a serious condition. The advantages of fast track designation concern drugs for serious conditions along with drugs for life-threatening conditions, the difference between the two classes of conditions concerning the ability for fast track programs is not required.

Demonstrating the potential to deal with unmet medical needs

The FDA Agency is measured whether the drug carries the potential to deal with unmet medical needs and whether the drug development program is described to assess this potential.

Estimation of whether the drug development plan describes unmet medical needs

An unmet medical need is defined as a medical need particularly not addressed appropriately by an existing therapy.

- No available therapy for the specific condition
- Available therapy for the condition
- Available therapy is approved under the accelerated approval designations.

Demonstration of the drug's potential

The details required to indicate the potential for a new drug product to tackle unmet medical demands will be based on drug product development. Data that being obtainable throughout clinical development shall assist the drug's potential to address unmet medical needs [21].

FAST TRACK DESIGNATION PROCESS

Fast track designation has five steps applicable to the submission and review of fast track (Fig. 1).

Sending a designation submission

- A sponsor might propose a request for fast track designation before obtaining marketing approval of its NDA or Biologics License Application (BLA) [22]
- Before IND Application submission, the potential of fast track designation is discussed in the pre-IND meeting, however, a final

decision on fast track designation would depend on the submission of the IND

- However, advantages related to fast track designation can occur all over the drug development process, starting from the early IND submission to review of a marketing application, requests must usually arise within the sponsor Pre-NDA meet with the FDA Agency, the advantages of fast track approval will no more be appropriate after that time.

Receiving the fast track request

The sponsor should submit a request for fast track in FDA Form 1571, presented as an amendment. The IND or amendment would be provided to the consideration of the suitable division in Center for Biologics Evaluation and Research (CBER) or Center for Drug Evaluation and Research (CDER) and will precisely identify the submission as a "Request for Fast Track Designation." For BLA and NDA, the request should be submitted in FDA Form 356h. Based on the FDAs data, the expedited options have been bringing approval timelines down overtime [23]. The fast track request might be approved or declined (Table 1).

Content of a fast track designation submission

The following details must include in the fast track designation:

- The sponsor proposes the request as an IND amendment, the submission is identified by cover letter as a *REQUEST FOR FAST TRACK DESIGNATION* in block capitals, bold letters
- The sponsor name, contact person name, contact person address, phone number, fax number, and email address, etc., all these details are included in the cover letter
- The IND application number, where appropriate
- If applicable, for biologicals, the trade name and proper name, and for drugs active substance, and trade name
- An intended indication
- A brief overview of details this assists the fast track requisition for these indications consists of the following:
 - a. A reason for seeing the drug product is meant to cure a serious disease
 - b. The product possesses the drug potential to deal with unmet medical demands and evidence of how that drug potential is become assessed within the designed fast track drug development program.

FDA response

Within 60 days of receipt, the FDA must address the fast track designation request. The FDA responds to the request in two forms of letters are designation letter and non-designation letter.

Designation letter

If the FDA evaluates the benchmarks for fast track designation for drug development has been fulfilled, the fast track designation letter will:

- Declare this fast track approval grants concerning the development of the drug product for utilization in the treatment of specific serious or life-threatening conditions
- Identify the sponsor shall design and carry out the studies to meet certain unmet medical demands

Table 1: CDER fast track designation requests received [24]

Year	Total requests received	Granted	Denied	Other
2020	280	187	84	9
2019	255	151	72	32
2018	217	145	63	9
2017	181	115	54	12
2016	188	132	42	14
2015	168	128	35	5
2014	117	89	22	6
2013	97	77	18	2
2012	83	55	24	4

CDER: Center for Drug Evaluation and Research

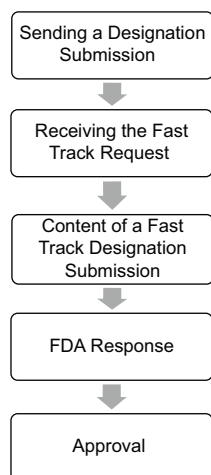


Fig. 1: Fast track designation process

- Warn the applicant to fulfill the requirements to obtain fast track designation.

Non-designation letter

In case, the NDA submission is not satisfied by the FDA agency, they might issue the non- designation letter. The grounds could also be declared as the drug lacked to meet the standards for fast track designation [25].

Continued fast track designation

- The drug in a fast track program might not persist to fulfill the conditions if the drug (1) no more proves a drug potential to meet the unmet medical needs, or (2) is being mannered that could show the drug is fit to treat serious or life-threatening diseases and fulfill unmet medical needs
- It might no longer illustrate the potential to deal with unmet needs, for example, if a new drug was designated under a conventional approval that meets the same necessities
- For drugs in fast track designation programs, the FDA Agency predicts the suitability of drugs taking into account specific drug product development programs within the framework of fast track approval ought to be examined throughout the drug product development program
- In case, the sponsors perceive this the development plan will no more be continued, the sponsor must notify the FDA Agency of this alteration in plans
- The emerging data are no longer available for fast track designation, the FDA Agency prefers to send a note informing the sponsor this designation program is no more classified as a fast track drug approval program [26].

Timeline for Review (days) [27]

- Day 0: The CBER Document Control Centre acquires fast track designation request
- Day 3: Regulatory Project Manager (RPM) conducts a preliminary regulatory review and initiates routing
- Day 3-5: RPM performs review and informs the team
- Day 5-40: Clinical review is completed
- Day 40-50: RPM drafts fast track letter
- Day 50-60: Letter finalized.

CONCLUSION

Based on legal requisites and by rules, guidance documents, and regulations, the FDA initiated a fast track designation program to attain the market rapidly. The fast track designation program assists a sponsor to discuss with FDA during the development of a product [28]. The expedited programs have been used by the CDER for the past two decades. Drug development and review processes had been streamlined in a manner that permits for treatments demonstrating early promise to attain patients faster [29]. While analyzing new molecules, not only must their efficacy be cross-checking with safety issues, however, ethical characteristics should also be taken into consideration earlier than fast track designation is granted [30]. Fast tracks are often exhilarating, however, accelerating too fast can motive a crash [31].

AUTHORS' CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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REFERENCES

- Krulowitz E. Expedited Approvals and Fast Track Designation Explained, The Weinberg Group; 2015. Available from: <https://www.weinberggroup.com/blog/fda-expedited-approvals>. [Last accessed on 2021 May 04].

- Aamir M, Amar B, Tauseef M, Saurabh G. Pharmaceutical regulatory affairs. *Open Access J* 2012;1:218.
- Vengadarga K. Expedited Drug Review Process: Fast, But Flawed; 2016. Available from: https://www.researchgate.net/publication/304613808_expedited_drug_review_process_fast_but_flawed. [Last accessed on 2021 May 04].
- Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review. U. S. Food and Drug Administration; 2018. Available from: <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>. [Last accessed on 2021 Apr 05].
- Carter C. The FDA Drug Approval Process for Serious Medical Conditions: VHL Alliance, VHL Alliance; 2020. Available from: <https://www.vhl.org/fda-drug-approval>. [Last accessed on 2021 Apr 05].
- Burkes C. The PPP Has Run Dry; Now What?-Baton Rouge Business Report, Summary; 2020. Available from: <https://sumairy.com/article/the-ppp-has-run-dry-now-what-baton-rouge-business-report>. [Last accessed on 2021 Apr 05].
- "A New Normal": FDA is Fast-Tracking More Drugs than Ever, But is that Safe? 2019. Available from: <https://www.advisory.com/daily-briefing/2019/07/10/fast-tracked>. [Last accessed on 2021 Apr 05].
- FDA's Expedited Drug Approval Programs, American Cancer Society Cancer Action Network. 2013. Available from: <https://www.fightcancer.org/policy-resources/fdas-expedited-drug-approval-programs>. [Last accessed on 2021 May 04].
- Chary K. Expedited drug review process: Fast, but flawed. *J Pharmacol Pharmacother* 2016;7:57-61.
- Loftus P. Fast-Track Drug Approval, Designed for Emergencies, Is Now Routine, WSJ; 2019. Available from: <https://www.wsj.com/articles/fast-track-drug-approval-designed-for-emergencies-is-now-routine-11562337924>. [Last accessed on 2021 May 04].
- Drug Development and Approval Process, U. S. Food and Drug Administration; 2019. Available from: <https://www.fda.gov/drugs/development-approval-process-drugs>. [Last accessed on 2021 Apr 05].
- Moderna Receives FDA Fast Track Designation for mRNA Vaccine (mRNA-1273) Against Novel Coronavirus; 2020. Available from: <https://www.businesswire.com/news/home/20200512005277/en>.
- Arjun S, Venkatesh M, Balamuralidhara V, Kumar TP. Expedited programs for drug development and approval in USA. *Res J Pharm Technol* 2020;13:1409-14.
- Srivastava G, Winslow A. orphan drugs: Understanding the FDA approval process. *Acad Entrep Med Health Sci* 2019;1:13. Available from: <https://www.repository.upenn.edu/cgi/viewcontent.cgi?article=1037&context=ace>. [Last accessed on 2021 Apr 05].
- Reichert J, Rochon S, Zhang B. A decade of the fast track programme. *Nat Rev Drug Discov* 2008;7:885-6.
- Drug Approval System of the United States of America; 2015. Available from: https://www.nifds.go.kr/brd/m_95/down.do?brd_id=board_mfds_411&seq=21651&data_tp=A&file_seq=2. [Last accessed on 2021 Apr 05].
- An Overview of PRIME, Breakthrough Therapy and Fast Track Procedures, S-Cubed Global; 2020. Available from: <https://www.s-cubed-global.com/articles/regulatory-affairs-an-overview-of-prime-breakthrough-therapy-and-fast-track-procedures>. [Last accessed on 2021 Apr 05].
- Fast Track, U. S. Food and Drug Administration; 2018. Available from: <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track>. [Last accessed on 2021 Apr 05].
- Shoemaker D. Accelerating US Regulatory Approval for Drugs and Biologics that Treat Serious Diseases, White Paper; 2020.
- Terns Pharmaceuticals. Terns Pharmaceuticals Receives Fast Track Designation From the FDA for TERN-101, an FXR Agonist for the Treatment of NASH; 2019.
- U. S. Department of Health and Human Services. Fast Track Drug Development Programs-Designation, Development, and Application Review. U. S. Food and Drug Administration; 2006.
- FDA Expedited Review Programs, Friends of Cancer Research; 2020. Available from: <https://www.friendsofcancerresearch.org/fda-expedited-review-programs>. [Last accessed on 2021 May 04].
- Barham L. How Fast are the FDA Fast Lanes? 2018. Available from: <https://www.pharmexec.com/view/how-fast-are-fda-fast-lanes>. [Last accessed on 2021 May 04].
- CDER Fast Track Designation Requests Received; 2020. Available

- from: <https://www.fda.gov/media/97830/download>. [Last accessed on 2021 Apr 05].
25. Expedited Programs for Serious Conditions-Drugs and Biologics; 2014. Available from: <https://www.fda.gov/files/drugs/published/expedited-programs-for-serious-conditions-drugs-and-biologics.pdf>. [Last accessed on 2021 Apr 05].
 26. Expedited Programs for Serious Conditions-Drugs and Biologics (Draft Guidance); 2013. Available from: <https://www.fda.gov/files/drugs/published/expedited-programs-for-serious-conditions-drugs-and-biologics.pdf>. [Last accessed on 2021 Apr 05].
 27. SOPP 8414: Fast Track Drug Development Programs: Designation and Review Programs; 2001. Available from: <https://www.fda.gov/media/108986/download>. [Last accessed on 2021 April 05].
 28. FDA Fast Track and Priority Review Programs; 2008. Available from: <https://www.everycrsreport.com/reports/rs22814.html>. [Last accessed on 2021 Apr 05].
 29. FDA Expedited Programs for Drug Development and Review, PDG; 2021. Available from: <https://www.pharmdevgroup.com/fda-expedited-programs-explained>. [Last accessed on 2021 Apr 05].
 30. Chary K, Pandian K. Accelerated approval of drugs: Ethics versus efficacy. *Indian J Med Ethics* 2017;2:244-7.
 31. Dowden J. Medicines and Monza: Hazards of the fast track. *Focus Farmacovigilanza* 2016;94:1.