Orphan Drug Development Guidebook

Building Block U203

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	FDA Expedited Program for serious conditions - Fast Track Designation (FDA-FTD)
References	https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf
Description	Process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. FDA recognizes that certain aspects of drug development that are feasible for non-rare diseases may not be feasible for rare diseases and that development challenges are often greater with increasing rarity of the disease. Qualifying criteria (i.e., intended to treat serious condition AND where Non-clinical or Clinical data demonstrate the potential to address the unmet medical need, OR qualified infectious disease product) does not necessarily require that the indication meet United States' definition of rare disease. Fast Track, however, is often applied to drugs developed for rare disease. The designation may be rescinded if it no longer meets the qualifying criteria for Fast Track. A Sponsor may also withdraw the designation.
Category	Regulatory Building Block
Geographical scope	United States of America

Availability	Applicants developing medicines for rare and non-rare diseases.
Scope of use	The purpose is to facilitate and expedite development and review by the FDA of new drugs to treat a serious or life-threatening disease or condition that potentially addresses an unmet medical need for such a disease or condition.
Stakeholders	• IND Sponsor • FDA
Enablers / Requirements	FTD applies to any drug being developed to treat or prevent a serious condition that demonstrates the potential to address unmet medical needs for such a condition. Generally, determination whether a condition is serious is based on whether the drug will have an impact on such factors as survival, day-to-day function, or the likelihood that the condition, if left untreated, will progress from a less severe condition to a more serious one. Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy that may be potentially better than available therapy. When available therapy exists, a new drug must show some advantage over available therapy, such as: • Having an effect on a serious outcome of the condition not influenced by available therapy or in patients unable to tolerate or failed to respond to the available therapy • Having an improved effect on a serious outcome(s) of the condition compared with available therapy • Improving the diagnosis of a serious condition where early diagnosis results in an improved outcome • Having efficacy comparable to available therapy AND (1) avoiding significant toxicity, (2) avoiding less serious toxicity of an available therapy that is common and causes discontinuation of treatment, or (3) reducing harmful drug interactions • Ability to address emerging or anticipated public health need • The only available therapy was approved under Accelerated Approval Program with a clinical benefit not verified in a postmarketing confirmatory trial In general, available therapy is a therapy that is approved or licensed in the United States (U.S.) for the same indication being considered for the investigational drug and is relevant to current U.S. standard of care for the indication.

	The type of information needed to demonstrate the potential of a drug to address an unmet medical need will depend on the stage of drug development at which FTD is requested.
Output	Designation A drug that receives Fast Track designation is eligible for some or all of the following: • More frequent interactions with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval • More frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers • Eligibility for Accelerated Approval and Priority Review, if relevant criteria are met • Rolling Review (RR), which 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, however the RR gives the applicant the possibility to check for dossier/data completeness and potential weakness.
Best time to apply and time window	FTD must be requested by the Sponsor of the IND. The request can be early in development but an IND must be filed with the Agency to apply. Ideally, the request should be submitted with the IND or after and no later than the pre-BLA or pre-NDA meeting. FDA will review the request and make a decision within sixty calendar days of receipt of the request.
Expert tips	– Consider submission with request of initial IND – Can serve as a fallback position if Breakthrough Therapy designation (BTD) request is denied – Expedited Programs Guidance Appendix 1 Section A.3. may serve as a general template for request format – Submit eCTD Module Heading 1.7.1 PROs: • Early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The

	frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients. • Theoretical rationale, mechanistic rationale (based on nonclinical data), or evidence of nonclinical activity, together with the other qualifying criteria, can be used to demonstrate the potential of a new drug to address an unmet medical need • Use of non-clinical data differentiates FTD from BTD and, thus, is a designation that may be obtained earlier in 4development CONs: • BTD offers additional provisions over FTD related to intensive guidance and organizational commitment.