



Tufts Center for the Study of Drug Development

TUFTS UNIVERSITY

Impact REPORT

ANALYSIS AND INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

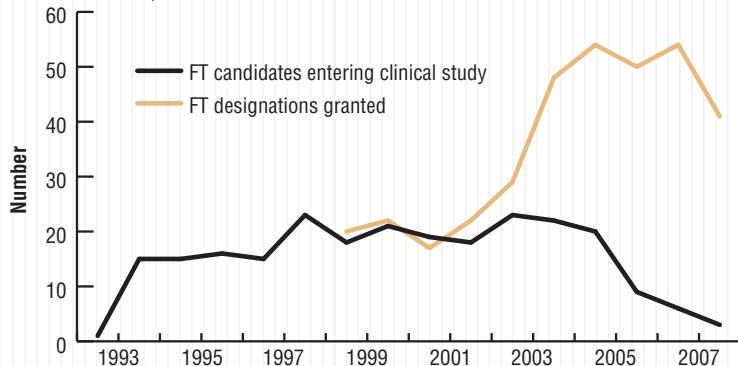
Fast track designations more than doubled during the last five years

Fast track drugs, on average, had shorter total clinical and approval times

- Fast track designations for new drug candidates have grown substantially, from an average of 22 per year during 1998-02 to 49 per year during 2003-07.
- Anticancer candidates received the largest share of fast track designations since the program began.
- Fast track indications are more likely to be terminated during development than non-fast track indications.
- Efficacy was the primary reason for termination of fast track-designated candidates, accounting for 74% of terminations in 1998-02 and 49% in 2003-07.
- Total average clinical and approval time for fast track drugs was 5% faster than for all drugs (73.1 vs. 77.0 months).

Use of fast track designation, introduced in 1998, has increased significantly since 2002

Fast Track Candidate Clinical Entry and Designations Granted, 1993-2007



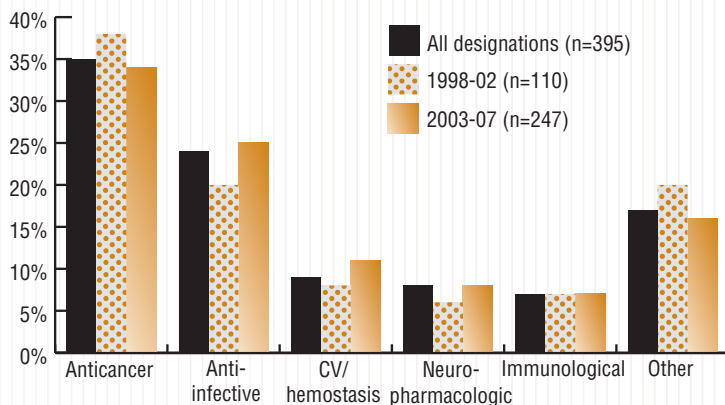
NOTE: Dataset included 344 fast track candidates. 91 candidates with fast track designations entered clinical study prior to 1993; year unknown for 3% of candidates.

Source: Tufts Center for the Study of Drug Development

- During 1993-04, 19 candidates entering clinical study each year, on average, were granted at least one fast track designation.
- During 1998-02, 22 fast track designations, on average, were granted annually; that number more than doubled to 49 during 2003-07.
- Few candidates in early development received fast track designation, suggesting that more of those that entered clinical study in 2005-07 might yet receive fast track designations.
- Most (70%) fast track candidates were small molecule therapeutics, but there were also biologics, vaccines, and a diagnostic.

Anticancer candidates received largest share of fast track designations since program began

Therapeutic Categories of Fast Track Designations



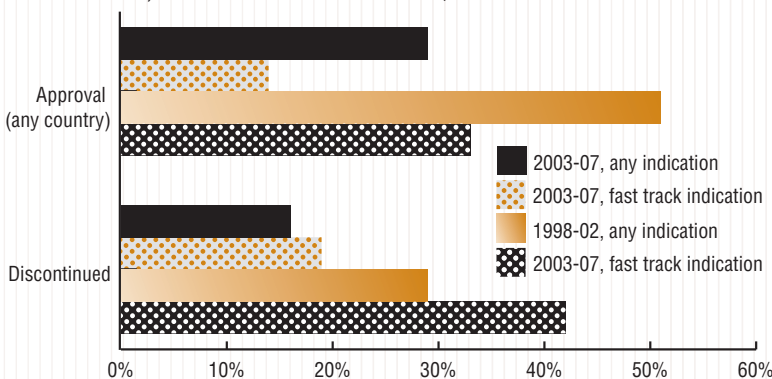
NOTE: 'Other' includes designations for enzyme replacement, gastrointestinal, metabolic disorder, ophthalmic, respiratory, and addiction indications.

Source: Tufts Center for the Study of Drug Development

- To date, only minor variations were observed in the distribution of fast track designations among five therapeutic categories in the program.
- In the anti-infective category, HIV indications comprised approximately half of the fast track designations granted during 1998-02, but only 20% during 2003-07.
- Prophylactic and therapeutic vaccines received 9% of the total number of fast track designations:
 - 5 designations went to anticancer vaccines.
 - 19 designations went to anti-infective vaccines.

Fast track indications are more likely than non-fast track indications to be terminated

Status of Fast Track Candidates, 1998-2007



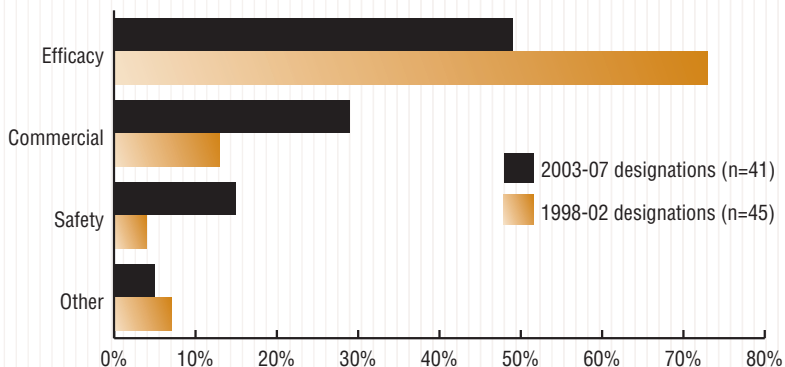
Note: 1998-02 and 2003-07 are periods of fast track designation.

Source: Tufts Center for the Study of Drug Development

- Fast track candidates frequently were studied also for non-fast track designated indications.
- Fast track indications were more frequently terminated and less frequently approved than other indications.
- 21% of candidates of the 1998-02 cohort received designations when they were already in late development, compared to 10% of the 2003-07 cohort.
- The majority of candidates that received fast track designation during 2003-07 are still in clinical study.

Demonstration of efficacy is the biggest hurdle for fast track candidates

Reason for Terminating Fast Track Candidates



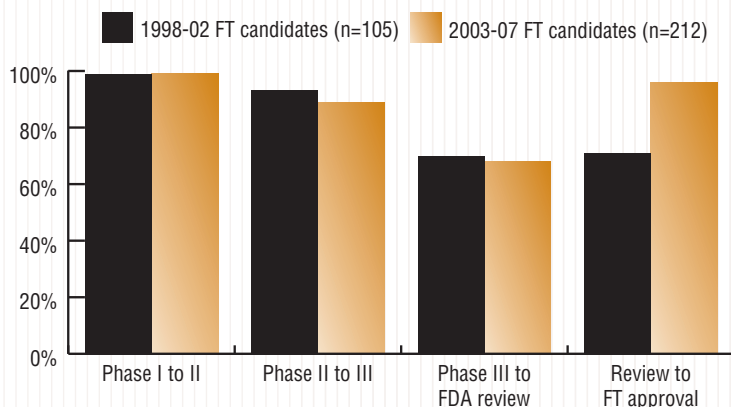
NOTE: 'Other' category includes, for example, inadequate enrollment and formulation issues.

Source: Tufts Center for the Study of Drug Development

- Efficacy was the primary reason for termination of fast track candidates, accounting for 73% of terminations in 1998-02 and 49% in 2003-07.
- Of all fast track candidates terminated to date, 78% and 86% were terminated for efficacy reasons in Phase III or at FDA review, respectively.
- To date, fewer candidates granted fast track designation during 2003-07 have been terminated during FDA review compared to the 1998-02 cohort (2% vs. 29%).
- Approximately half of all terminations in Phase II during 1998-07 were for commercial reasons.

Phase transition probabilities reached a low point at Phase III-to-FDA review transition

Phase Transition Probabilities for Fast Track Candidates, 1998-02 and 2003-07

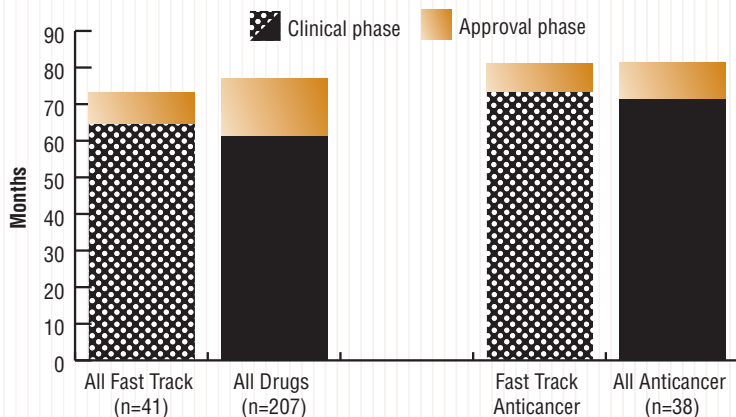


Source: Tufts Center for the Study of Drug Development

- Early development transition probabilities for fast track candidates were relatively high, reflecting the fact that many tend to receive fast track designation after proof-of-concept studies.
- The review-to-approval probability was low for candidates granted designations during 1998-02, but has improved for 2003-07 designated candidates.
- Success rates for candidates granted fast track designation during 2003-07 may ultimately be lower than those in the 1998-02 cohort due to granting of fast track status earlier in development.

Fast track candidates have longer clinical but shorter approval times than drugs in total

Clinical and Approval Phases for Fast Track New Chemical or Biological Entities



NOTE: For products that began clinical tests in 1992 or later and approved during 1998-07

Source: Tufts Center for the Study of Drug Development

- Average FDA approval review time for fast track drugs was considerably shorter than for drugs as a whole – an average of 8.4 months vs. 15.8 months (for products that began clinical testing in 1992 or later and were approved during 1998-07).
- However, average clinical development time for fast track drugs was 6% longer than it was for all drugs (64.7 vs. 61.2 months).
- Despite those differences, on average, total clinical and approval time for fast track drugs took 5% less time than for all drugs (73.1 vs. 77.0 months).
- Fast track cancer drugs had similar total clinical and approval time compared to all cancer drugs (81.0 vs. 81.4 months).

About this study

Findings presented in this report were based on analysis of a Tufts CSDD database of 344 investigational candidates that received at least one FDA fast track designation between January 1998 and June 2008. Data were collected through a survey of pharmaceutical and biotechnology companies and from the public domain. Data on nearly 400 designations, which represent approximately 70% of the fast track designations granted by the FDA, were included.

This analysis was conducted by Janice M. Reichert, Ph.D., Senior Research Fellow at the Tufts Center for the Study of Drug Development.

For other analyses of the fast track program, see *Tufts CSDD Impact Report 2001 Jan/Feb;3(1)*, *Tufts CSDD Impact Report 2003 Nov/Dec;5(6)*, and *Tufts CSDD Impact Report 2006 Mar/Apr;8(2)*.

Definition of terms

Approval phase time — Time from date of submission of an NDA or BLA to date of FDA approval.

BLA — Biologics license application. An application to the FDA for a license to market a biological product.

CBER, CDER — FDA's Center for Biologics Evaluation and Research and Center for Drugs Evaluation and Research.

Clinical phase — Interval from the earliest of either the first investigational new drug (IND) application filing date or the date clinical study was first initiated to the date a marketing application was submitted to the FDA.

NDA — New drug application. An application to the FDA for a license to market a drug product.

Phase transition probability — The likelihood that an investigational candidate that begins a particular development phase will transition to the next development phase.

Success rate — Of those candidates that enter clinical study, the percentage that eventually receive FDA approval.

About the Tufts Center for the Study of Drug Development

The Tufts Center for the Study of Drug Development at Tufts University provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Tufts CSDD conducts a wide range of in-depth analyses on pharmaceutical issues and hosts symposia, workshops, and public forums.

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