On the Edge of Tomorrow: Expedited Regulatory Pathways for Anti-Infective Therapies

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INTRODUCTION

- The FDA has developed a host of expedited review programs and pathways to help increase the speed of drug development for products that possess a favorable clinical profile.
- These pathways include: priority review, fast track designation, accelerated approval, orphan drug status, qualified infectious disease products, and breakthrough therapy designation.

FDA Expedited Drug Development Programs

Program Type	Explanation
Priority Review	Priority review ensures a new drug application will be reviewed within a 6 month window instead of the conventional 10 months.
Fast Track Designation	Fast track designation is available for drugs that are intended to treat serious conditions and show data addressing an unmet need.
Accelerated Approval	Accelerated approval is considered when a drug provides a meaningful advantage over current therapies through a surrogate endpoint that is likely correlated to a clinical benefit; the "conditional" approval is contingent upon verification of the benefit in future confirmatory trials.
Orphan Drug Status	Orphan drug status is available for drugs intended to treat rare diseases where the sponsor receives various incentives including tax credits for clinical trials.
Qualified Infectious Disease Product	Through the GAIN Act that was passed in 2012, drugs in development may be designated as a qualified infectious disease product (QIDP) if they are targeting certain types of infectious diseases. QIDPs are eligible for fast track and priority review status.
Breakthrough Therapy	Breakthrough therapy designation is typically received early in drug development when the IND (investigational new drug) is filed, where the sponsor receives significant guidance on their drug development program from the FDA.

OBJECTIVE

- Assess the use of expedited regulatory pathways in anti-infective drug development.
- Determine if expedited regulatory pathways have been increasingly utilized among the 89 approved anti-infective products approved between 2001-2020.

METHODS

- The FDA Drug Approval Database entitled, "Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals" was analyzed.
- This dataset provides all New Molecular Entities (NMEs) approved from 1985 – 2019, which include both chemical entities approved under an NDA (New Drug Application) and biological agents approved under a BLA (Biologics License Application).
- The analysis focused on anti-infective products approved after 2000 and excluded approvals of new indications or formulations of previously approved drugs, new drug combinations based on existing agents, and non-traditional agents such as vaccines.
- Anti-infective therapies were defined as agents that were used to treat or prevent infectious diseases and include antibiotics, anti-virals and anti-fungals.
- Additionally, the dataset was supplemented with the addition of NMEs approved until June 2020.
- The analysis focused on a comparison of the percentage of approved anti-infective agents that used the aforementioned pathways across 2 decades (2001-2010 & 2011-2020).
- Statistical analyses were completed using the software Prism 8 to conduct Chi-square and Fisher's exact tests for each regulatory pathway.

RESULTS

(1) Comparison of Expedited Regulatory Pathways

Comparison of FDA Expedited Drug Development Programs use between 2001-2010 and 2011-2020

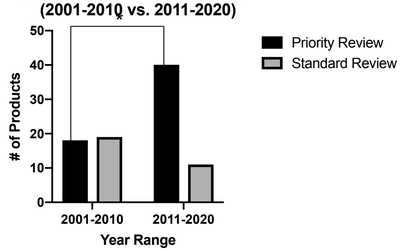
Program Type	% of Products Approved via Program Type (2001-2010)	% of Products Approved via Program Type (2011-2020)	P Value
Priority Review*	49%	78%	0.004
Fast Track Designation*	31%	60%	0.007
Accelerated Approval *	18%	3%	0.03
Orphan Drug Status	5%	19%	0.07
Qualified Infectious Disease Product^	N/A	35%	N/A
Breakthrough Therapy^	N/A	17%	N/A

***P Value less than .05**

^Programs started in 2012

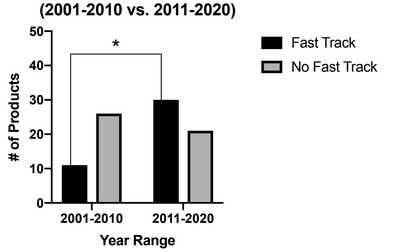
(2) Graphical Analyses of Expedited Regulatory Pathways

Graph 1: Anti-Infective Products with Priority vs. Standard Review Designations (2001-2010 vs. 2011-2020)



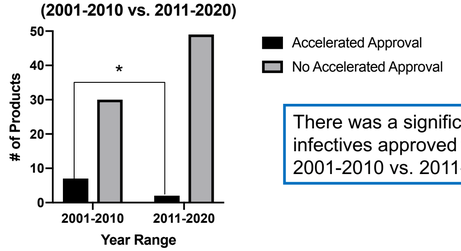
There was a significant difference in the % of anti-infectives approved with **priority review** in 2001-2010 vs. 2011-2020 (49% vs. 78%, p=0.004).

Graph 2: Anti-Infective Products with and without Fast Track Designation (2001-2010 vs. 2011-2020)



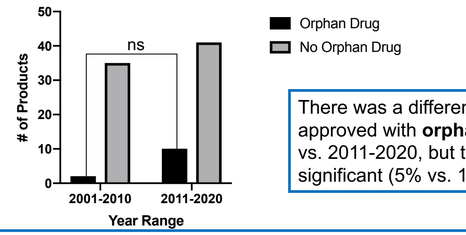
There was a significant difference in the % of anti-infectives approved with **fast track** in 2001-2010 vs. 2011-2020 (31% vs. 60%, p=0.007).

Graph 3: Anti-Infective Products with and without Accelerated Approval (2001-2010 vs. 2011-2020)



There was a significant difference in the % of anti-infectives approved with **accelerated approval** in 2001-2010 vs. 2011-2020 (18% vs. 3%, p=0.03).

Graph 4: Anti-Infective Products with and without Orphan Drug Status (2001-2010 vs. 2011-2020)



There was a difference in the % of anti-infectives approved with **orphan drug status** in 2001-2010 vs. 2011-2020, but the difference was *not* significant (5% vs. 19%, p=0.07).

CONCLUSIONS

- The findings indicate that the use of priority review and fast track designations have increased since 2010 among approved anti-infective products.
- Additionally, there has been increased utilization of the orphan drug designation among approved anti-infectives since 2010, although not in a statistically significant manner.
- There has been considerable use of the QIDP program since its inception, and this program should continue to be explored by academic and industry researchers.
- However, there has been limited use of the breakthrough therapy designation and accelerated approvals for anti-infectives. These two pathways should be increasingly considered by academia, industry, and the FDA to further expedite innovative anti-infective development.

FUTURE DIRECTIONS

- The analysis can be expanded to review all anti-infective products that haven been approved since 2000, including indication expansions, new formulations, and new drug combinations to make more robust conclusions regarding the use of expedited pathways.
- The analysis can also be expanded to consider products that are currently in all phases of clinical development (Phases I,II,III) to determine if there are any associations between the use of expedited regulatory pathways and likelihood of drug approval.

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