

# THERAPEUTIC DRUGS GRANTED BREAKTHROUGH DESIGNATION BY THE US FOOD AND DRUG ADMINISTRATION, 2012–2020

Dhiksha Balaji <sup>1</sup>, G Caleb Alexander MD <sup>2</sup> Thomas J Moore <sup>3</sup>

## Introduction

The US Food and Drug Administration (FDA) administers various programs to expedite the development and review of new drugs that aim to treat serious or life-threatening conditions. In 2012, the Congress established one such program, the “Breakthrough Therapy (BT)” Designation, which requires preliminary clinical evidence that demonstrates substantial improvement in a clinically significant endpoint over available therapy [1]. FDA “Approval” occurs after “Designation,” involving assessment of the safety and efficacy of a new drug and determination that the benefits of the product outweigh known risks. While the goal of the BT Designation is to more promptly bring drugs to market that transform patient care, it also provides for approvals based on more limited clinical trial evidence. We characterized patterns in BT Designations and Approvals by the FDA from 2012 through 2020.

## Methods

The Center for Drug Evaluation and Research (CDER) publicly available data on BT Designation Requests as well as BT Approvals from 2012- 2020 was used for this analysis. Data were collected and analyzed in Microsoft Excel.

## Therapeutic Drugs Approved and Designated Breakthrough Status by the FDA, 2012-2020

Year	Number of Breakthrough Drugs Approved by FDA	Total Requests Received	Granted	Denied	Withdrawn
2012	0	2	1	1	0
2013	3	92	31	52	9
2014	14	96	31	51	14
2015	21	93	32	43	18
2016	20	106	46	48	12
2017	34	111	50	49	12
2018	38	136	59	60	17
2019	26	156	67	68	21
2020	34	125	58	53	14
Grand Total	190	917	375	425	117

## Results

The CDER received 917 BT designation requests from 2012 through 2020. The median of requests received was 106 (interquartile range [IQR], 93-125). Of these requests, 375 (40.9%) were granted, 425 (46.3%) were denied, and 117 (12.8%) were withdrawn. The median of requests granted was 46 (IQR, 31-58), median of requests denied was 51 (IQR, 48-53), and median of requests withdrawn was 14 (IQR, 12-17).

Designation in an early stage of development did not guarantee approval. Of drugs granted the BT designation, a median of 21 (IQR, 14-34) and mean of 38 (standard deviation, 13.5) were approved as of December 31<sup>st</sup>, 2020.

## Discussion

When the BT designation was created, it was expected to only support a few drugs [2]. This analysis shows use of the program has been increasing since 2012. Further analysis should examine the quality of the clinical data required for BT designation and the BT drug performance post-approval to assess the function of the BT designation.

## Sources

- [1] J. J. Darrow, J. Avorn, and A. S. Kesselheim, “New FDA Breakthrough-Drug Category — Implications for Patients,” *N. Engl. J. Med.*, vol. 370, no. 13, 2014, doi: 10.1056/nejmhle1311493.
- [2] A. S. Kesselheim, B. Wang, J. M. Franklin, and J. J. Darrow, “Trends in utilization of FDA expedited drug development and approval programs, 1987-2014: Cohort study,” *BMJ (Online)*, vol. 351. 2015, doi: 10.1136/bmj.h4633.