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Breakthrough Designations: Where's the Value?

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WHERE IS THE VALUE IN BREAKTHROUGH DESIGNATION?

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The true impact of Breakthrough Device designation may not actually be from working more closely with FDA. Experts from Parexel/Health Advances discuss a quantitative analysis and the experiences of several device companies with the Breakthrough process, highlighting benefits beyond a smoother regulatory path.

In 2015, the FDA introduced an expedited pathway for potentially life-saving medical devices to attain approval: the Breakthrough Devices Program. Fundamentally, the program is designed to speed up the regulatory process for devices that improve the treatment or diagnosis of life-threatening conditions, so that these critical devices can reach patients quicker. In practice, this entails: 1) FDA-facilitated "sprint" discussions; 2) a Data Development Plan (DDP); 3) a Clinical Protocol Agreement; and 4) prioritized pre-submission review. However, despite these tangible actions, the regulatory process is not necessarily proceeding any faster. So, where is the value in this designation?

Uncertain Regulatory Advantages

Many companies are excited about getting Breakthrough designation but are then let down when they don't realize any changes. The regulatory benefits of a Breakthrough Device are highly dependent on devices' risk and circumstances. It could be argued that Breakthrough's benefits are meaningful for Class III devices with the innovators having an opportunity to use surrogate endpoints and with pre/postmarket data collection being more balanced. However, for Class I or Class II devices, the benefits with the FDA are meager and at worst the company might actually expand its regulatory burden due to increased consulting requirements with the agency, which tends to be even more conservative for Breakthrough Devices.

Key program principles, like pre/postmarket balance of data collection and efficient and flexible clinical study design, are more applicable to Class III devices reviewed under the premarket approval (PMA) pathway since Class III devices allow for the greatest regulatory control in the postmarket. For example, the FDA may be willing to defer collection of long-term safety data under a postmarket commitment to PMA approval, but a similar mechanism is not available for Class I and Class II devices reviewed through 510(k) or De Novo. In

contrast, premarket review of Class II devices and some Class I devices heavily relies upon regulatory precedent in the form of predicate and reference devices, which basically dictate the regulatory bar the device should meet prior to achieving marketing authorization.

Collaborating with the FDA in defining verification and validation studies for a more-or-less defined pathway may put the sponsor at risk for increasing their regulatory burden (which may have otherwise been avoided if the sponsor took their device through the more traditional pathway) or missing corporate milestones due to the sponsor feeling obligated to address the FDA's recommendations or reach agreement with the FDA on unresolved issues prior to marketing authorization. **AI Medical**, a device company granted Breakthrough designation for its AI-based CADx software for detecting suspicious lesions in the stomach, substantiated the notion that Breakthrough status does not always speed up the review process. "The sprint discussions were not as quick as we expected. We presume that more reviewers need to be involved for Breakthrough Devices and the review process cannot progress as quickly as a result," says Kensuke Yamamoto, AI Medical Regulatory Affairs. However, numerous companies continue to apply for and be granted Breakthrough status, so there must be a benefit beyond regulatory process improvement.

True Benefit of Breakthrough: Funding

Quantitative data analysis performed in Spring 2022 by Health Advances analyst Russ Rapaport for Dartmouth College's economics department found that Breakthrough status improves a device company's chances of attaining funding by 64%. In other words, in a given year, if a company holds Breakthrough status (granted that year or any year prior), it is 64% more likely to achieve funding than if that same company had neither Breakthrough status nor an FDA approval.

Statistically significant at the 5% level, the results suggest that Breakthrough designation has a meaningful impact on device companies' funding. In the same analysis, an FDA approval increases a company's chances of attaining funding by 119%. This reference point validates the analysis: an FDA approval clearly holds more weight than Breakthrough status, and that is evident in the data, but both are impactful. The analysis includes a differences-in-differences regression using a comprehensive data set of all medical device approvals, financing, M&As, and Breakthrough status designations from January 2016 through May 2022.

For **Prapela**, an infant health start-up developing a novel device to treat apnea of prematurity and neonatal abstinence syndrome, Breakthrough status was instrumental in fundraising efforts. According to the company's CEO, John Konsin, "As a start-up, gaining distinction and recognition is important. We attributed a portion of our fundraising success to both Breakthrough Device designations. They were differentiators in both equity and nonequity funding strategies."

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While Konsin minimized the regulatory value of Breakthrough designation, noting that the FDA is often reluctant to give actionable guidance during sprint discussions, Prapela has received over $6.5 million in funding since its first Breakthrough designation was awarded in October 2019. Moreover, in April 2023, Prapela received the NIH Blueprint MedTech grant of $3.5 million over three years to support further development and evaluation of its device.

This particular NIH grant is not the only one that evidently values Breakthrough designation. Several other grants, such as the BRAIN Initiative grant, specifically call out Breakthrough designation in their evaluation criteria. Thus, Breakthrough designation's value stretches across the spectrum of financing mechanisms, encompassing both private and public funding opportunities.

Potential Holy Grail: Medicare Coverage

Another promised but yet to be realized benefit to Breakthrough Device designation is a concrete pathway to

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reimbursement for Medicare patients. As device developers are coming to realize, the process to obtain coding, coverage, and payment from Medicare can take years. In fact, a recent Stanford study of 281 devices from 2016 to 2019 shows a median wait time of 5.7 years between FDA authorization and at least nominal coverage.

To accelerate patient access to Breakthrough technologies, CMS initially proposed a plan known as the Medicare Coverage of Innovative Technology (MCIT). Under CMS' initial premise, Breakthrough devices would have automatically been granted coverage to all Medicare beneficiaries for four years with a National Coverage Determination (NCD). However, after much debate among all the healthcare system's major constituencies, CMS rescinded MCIT in November 2021. The agency then released a proposed alternate pathway called Transitional Coverage for Emerging Technologies (TCET) in June 2023.

Unlike MCIT, TCET does not mandate that Medicare coverage is automatically granted for Breakthrough Devices. Instead, CMS will conduct an early evidence review and allow manufacturers to address evidence gaps with fit-for-purpose studies. While TCET is stingier for device companies, as they will need to provide evidence supporting the value of the device, even the potential for coverage may be where the real value of Breakthrough designation falls for companies of all sizes and product types. Even if TCET suffers the same fate as MCIT, CMS is on record saying it will continue to try to find a clear and consistent pathway to coverage for Breakthrough Devices.

Clarity Is Needed

Although the regulatory impact of Breakthrough Device designation may not be as originally intended by the FDA, the existing funding advantages and potential reimbursement rewards behoove product companies to weigh the pros and cons of Breakthrough status. The benefits of Breakthrough designation for regulatory purposes are most likely to be realized by emerging companies with Class III devices.

On the contrary, Breakthrough designation may actually increase the regulatory burden for well-established, financially stable companies due to the extra consulting requirements with the FDA. The agency's new guidance on the Breakthrough Device Program echoes that many devices have failed to meet their original eligibility requirements and illustrates that the program is still a work in progress. Trumping any regulatory burden of Breakthrough designation, however, lies the potential for funding and accelerated reimbursement coverage through TCET or another future pathway. Overall, companies receiving Breakthrough designation are likely to find benefits and have a leg up on optimizing market access and adoption.

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