Project-Based Regulatory Strategy & Submission Services

BREAKTHROUGH THERAPY DESIGNATION REQUESTS

Not infrequently, regulatory agency review of a submission leads to requests for additional data (technical, nonclinical, or clinical), re-analysis of existing data, or clarification of information. Prominent with expedited programs, these can hold up clearances to conduct clinical studies or marketing approval clearances or approvals.

Sponsors seek breakthrough designation for example for their drug and indication because of the many benefits it offers. For some indications, the rarity of the disease or condition is apparent, and for expedited development, CMC is always the bottleneck. It is an art to identify a strategy that is not transparent in the Guidance to meet the criteria for marketing approval. We prepare and submit designation requests that are scientifically sound and well supported with a proposed strategy.

Assignment of breakthrough Therapy (BT) designation could lead to accelerated clinical programs, which could be two or more years less than a "conventional" development program. Potential accelerated clinical development timelines could lead to insufficient time to complete all "traditional" CMC studies for approval and delivery to the patient within the boundaries of completing the clinical development program for example;

- May have reduced real-time stability for commercial material and need to leverage stability information from development studies
- Likely to have limited manufacturing experience at a commercial scale which presents the opportunity to leverage lifecycle validation principles
- May need to consider launch an initial commercial supply from a clinical manufacturing facility with the clinical fit for purpose formulations then convert overtook commercial formulation of the plant immediately post-approval
- The formulation and process could be ready for transfer but the commercial facilities unavailable or not ready
- Limited data sets from which had direct to derive specification acceptance criteria

Using real-life experiences based on actual CMC development programs, a series of potential scenarios are available which could lead to discussions with the Agency. These experiences highlight from the overall development program the origins of the potential CMC challenges listed. Discussions with the agency should balance the risk of having less traditional CMC data at the time of filing with the potential benefit of speedy delivery of the critical products to patients. Regulatory approaches can be proposed to address the lack of some traditional CMC data at the time of filing by;

- Employing more flexible following processes such as leveraging development and risk assessments in lieu of some commercial-scale experience
- Using post-approval lifecycle management plans
- Including more comparably protocols in NDA submissions
- Employing more interaction opportunities with the agency

MANUFACTURING CONSIDERATIONS FOR BREAKTHROUGH DRUG DEVELOPMENT

DSI can support all critical product and process characterization activities that should be addressed earlier and can help facilitate manufacturing readiness for breakthrough products. To learn more manufacturing considerations for expedited drug development programs, the following approaches could be considered for discussion and agreement with FDA.

DSI Solutions

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