Planning for Data Reporting Processes for Submission: Key Considerations

Parag Shiralkar, MBA, M.S., Director, Biometrics Operations and Strategy

Abstract:

Because of public pressure and advancements in science, regulatory authorities around the world have taken efforts to accelerate drug submission review process. Drug developments pertaining to monoclonal antibodies or biologics experience fierce competition among sponsors to get the drug approved 'first in market'. As a result such submissions are planned very aggressively with overlapping timelines of trial level and pooled data reporting.

Data analysis and reporting functions such as programming and biostatistics usually have limited say in such demanding submissions planning. Often these functions need to stretch extremely thin to meet the regulatory submissions needs efficiently and timely. Advanced planning for such submissions from programming and statistics perspective is extremely crucial. Such planning needs to be based on careful assessment of submission goals and mitigation of any potential risks pertaining to technical, human, logistics, and knowledge resources. This manuscript elaborates on key considerations in such planning by illustrating relevant examples.

Introduction:

Traditionally sponsor companies have been working on drug development under tight timelines dictated by patent life of a drug molecule. With revolutionary steps like electronic submissions, and emergence of CDISC standards which were emerged through public and private collaborations, drug approval process got accelerated a lot. In addition to this, the reforms and research wings developed by leading drug regulatory authorities provisioned a fast track approval of molecules in therapeutic proteins, biologics, and monoclonal antibodies. Since the families of these antibodies and bio-similars are fairly vast, that gave sponsors an avenue to conduct fast paced regulatory submissions. While ethical and legal requirements of sponsors to protect safety of human patients participating in clinical trials still remains a top priority, these changes in industry environment gave sponsors an opportunity to conduct a fast track drug submission. Such fast track drug submission involves aggressive planning of clinical trials, most of which are phase –III. While focusing on efficient and timely completion of all data management and reporting activities pertaining to these large scale trials, sponsors need to simultaneously start evaluating the results based on pooled data. In some cases, the pooled data reporting for submissions involves inclusion of data from phase-II trials as well. Given that schedule of completion of multiple phase-III and phase-II trials span across the period of few years, there is strong possibility that given the sponsor might have utilized multiple clinical research organizations (CROs) to conduct these trials. In other words, data reporting for such fast paced submission requires completion of data reporting for

trials managed by different CROs as well pooling and integrating data managed by different CROs in multiple time span. Despite having all these differences in the trial data, the timeline for submission is usually intact and driven by a broader objective of a sponsor to get the drug out in market sooner.

From sponsor perspective, planning for submission specific data reporting means ensuring reporting of clinical data in a consistent data standards. This involves ensuring that all downstream data operations are appropriately and consistently managed across multiple trials and those operations provide necessary consistency in pooling of data for reporting and analysis of integrated data. As stated earlier, use of different CRO organizations in the time span of few years means there are likely to be different versions of data standards used by sponsors. Even with use of CDISC data standards and models, given its different interpretations by different organizations, ensuring consistency of CDISC based data for regulatory submission becomes a carefully monitored task. While working on data consistency and integrity specific challenges in tight timelines, programming function faces another challenge in terms of meeting statistical reporting requirements. Although there is certainty of statistical reporting by means of well defined statistical analysis plans for trials, for pooled data reporting such analysis plan takes much more time for maturation.

Planning for submission from biostatistics and programming includes detailed assessment of the trials that are getting used for integrated data reporting. In order to ensure clear clinical, safety, efficacy and pharmacological assessment of drug, statisticians should get high level statistical objectives pertaining to these assessments and related reporting requirements. These often include primary, secondary, and exploratory end-points defined through meeting research objectives. Clear and pro-active communication of these aspects and timely actions from different functions can minimize the risk of jeopardizing quality of data reporting.