FDA Focuses On Innovative Trial Designs

The US Food and Drug Administration (FDA) is seeking stakeholder input on the use of complex innovative designs (CIDs) in drug development and regulatory decision-making. The agency intends to launch a CID pilot programme by the end of fiscal year 2018, and publish a draft guidance approximately one year later.

The FDA spoke about its plans relating to CIDs at a public meeting in March. The stated goal of the CID pilot programme is to facilitate the use of complex, Bayesian, and other novel clinical trial designs and to focus on highly innovative trial designs for which analytically derived properties are not feasible and simulations are necessary.

CIDs are defined by the FDA as adaptive designs that are complex due to modifications on multiple factors and/or designs that require simulations to determine operating characteristics. They can also be other designs that incorporate innovative use of external data, innovative criteria for decision-making, or innovative collaborative efforts.

An adaptive design allows for prospectively planned modifications to one or more aspects of clinical trial design based on accumulating data from subjects in the study. Possible adaptations may relate to statistical or scientific aspects of design, patient population, treatment arm selection, endpoint selection, sample size, randomisation ratio, or others.

Those designing clinical trials may opt for adaptations and innovations due to small patient populations, in order to leverage other data sources to provide additional power, or in order to ensure that the trial will be able to answer the relevant questions and provide regulators with information needed for decisions.

The FDA shared its view on the need to provide guidance on CIDs in order for industry to better understand the expectations of the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER), as well as those centres' reasons for accepting innovative designs and for requesting information about submissions. The agency also hopes to ensure consistency of advice the centres give to industry about acceptance of complex trials across therapeutic areas.

The FDA committed to creation of the CID pilot programme in July 2016, with the sixth authorisation of the Prescription Drug User Fee Act (PDUFA VI), part of the FDA Reauthorization Act (FDARA). The pilot programme is designed for highly innovative trial designs that may require simulations to determine operating characteristics. The FDA will select two proposals quarterly for entry into the pilot programme. These proposals must capture sufficient details to facilitate an understanding of the design and analysis. Ultimately, the pilot programme details will be announced via the Federal Register.

In addition to welcoming stakeholder input at the March meeting, the FDA also plans to discuss the CID pilot programme during a session at the Drug Information Association (DIA) Global Annual Meeting in Boston, Mass., at the end of June.

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