FDA-Industry PDUFA VI Reauthorization Meeting – Regulatory Decision Tools Subgroup
October 14, 2015, 12:30pm-2:30pm
FDA White Oak Campus, Silver Spring, MD
Building 51, Room 1211

Purpose

To provide FDA and Industry perspectives on remaining Regulatory Decision Tools enhancements for PDUFA VI.

Participants

FDA		Industry	
Sara Eggers	CDER	Beatrice Biebuyck	BIO (Alexion)
Laura Lee Johnson	CDER	Cartier Esham	BIO
Chris Joneckis	CBER	Jeffrey Francer	PhRMA
Lisa LaVange	CDER	Robert Kowalski	PhRMA (Novartis)
Diane Maloney	CBER	Sandra Milligan	PhRMA (Merck)
Theresa Mullin	CDER	Michelle Rohrer	BIO (Roche Genentech)
Mike Pacanowski	CDER	Mark Taisey	PhRMA (Amgen)
Mary Parks	CDER		
Pujita Vaidya	CDER		

Discussion of Industry Regulatory Decision Tools Enhancement Proposals

In the previous meeting on October 7, Industry representatives had identified three areas for proposed enhancements in PDUFA VI, and discussions focused on benefit-risk and patient-focused drug development. On October 14, Industry discussion focused on innovative trial designs.

1. **Proposal for innovative clinical trial designs, including adaptive study designs and application of Bayesian statistics, to accelerate clinical development.** Industry proposed that FDA establish processes to facilitate appropriate use of innovative clinical trial designs and methods throughout the medical product lifecycle with the goal of making the drug development process more efficient. Industry proposed holding public stakeholder workshops to assess appropriate methodological considerations and various modeling approaches that could be used to develop further guidance for sponsors who choose to utilize such methods to demonstrate safety and effectiveness.

   In response to the industry proposal, FDA stated that innovative clinical trial designs, in contrast to traditional trial designs, are those for which analytic methods may not exist to evaluate the adequacy of a design and strength of evidence provided by the results, and that extensive computer simulations are often needed to determine the operating characteristics of the trial, assess the strength of evidence and determine whether the design is reasonable. This work, for which FDA currently has few dedicated staff, requires adequate time to conduct the simulations and those cannot be done in the shorter time frames proposed by industry. Industry stated that there was currently uncertainty for sponsors related to the use of these designs and greater predictability in interactions with FDA would be desirable.

Discussion of FDA Regulatory Decision Tools Enhancement Proposals

In the previous meeting on October 7, FDA had identified several areas for proposed enhancement of tools in PDUFA VI, including further work on patient-focused drug development, benefit-risk assessment, and enhancement of statistical approaches and data standards. On October 14, FDA continued discussions on enhancement of statistical approaches and data standards.

1. **Proposal for capacity to review complex innovative designs.** FDA proposed increasing its capacity to review innovative trial designs that need computer simulation to determine key operating characteristics, and related development of guidance for sponsors seeking to submit trials involving complex adaptations or other features for which analytically derived properties are not feasible. The increased FDA capacity and guidance would both clarify for sponsors FDA expectations for simulations required to adequately characterize the performance of a complex adaptive or Bayesian trial design and also help FDA in evaluating the adequacy of a sponsor's simulation. As part of this work FDA also proposed convening a public workshop on complex trial designs and their acceptability in regulatory decision-making.

2. **Proposal for improved subgroup analysis.** FDA noted that drug developers and FDA continually face the challenge of differentiating true heterogeneity from random variability during the review and evaluation of patient subgroup findings, at the design, analysis, and reporting stages of drug development, in submitted applications. FDA proposed to compare traditional methods and existing data mining methods and software of subgroup analysis to explore variability in treatment effects. FDA also proposed to convene a public workshop to discuss methods and software for managing heterogeneity of treatments effects.

3. **Proposals for analysis data standards.**
   FDA noted that sponsors need clarity on the new guidance, issued under a FDASIA provision, specifying the format of electronic submissions of standardized study data. Additionally, FDA statisticians have not been able to adequately engage on current therapeutic area data standards due to competing review work and limited resources. To address these issues, FDA proposed recruitment of additional needed applied statisticians for review of analysis data submissions, to develop processes and procedures for efficient receipt of analysis data, and to serve as liaisons to the therapeutic area user guide development groups.

Plan for Future Meetings

Industry and FDA agreed to discuss regulatory decision tools enhancement in greater detail in future meetings focusing on individual proposals at upcoming meetings. Detailed discussion on patient-focused drug development will be on the agenda on October 21.