FDA-Industry PDUFA V Reauthorization Meeting
Premarket Sub-Group
January 6, 2011, 12:00-2:00pm
Teleconference

Purpose

To continue discussion of enhancements related to meeting management, enhanced communication for emerging sponsors, advancing biomarkers and pharmacogenomics, and the pilot program for enhanced review communications.

Participants

FDA		Industry	
John Jenkins	CDER	David Wheadon	PhRMA
Ed Cox	CDER	Sara Radcliffe	BIO
Patrick Frey	CDER	Jay Siegel	Johnson & Johnson
Chris Joneckis	CBER	Kay Holcombe	Genzyme
Dave Roeder	CDER	Bob Meyer	Merck
Matt Sullivan	CDER		

Meeting Management Enhancements

FDA and Industry began the meeting by discussing modifications to existing PDUFA goals related to meeting management proposed by both parties. Industry stated that it would make proposals regarding:

1. Addition of a "Type C2" meeting option where the sponsor could request written responses in lieu of a face-to-face meeting.
2. Meeting packages (i.e., the "backgrounder") for Type A meetings must be submitted with the meeting request.
3. Meetings regarding risk evaluation and mitigation strategies (REMS) requirements outside of a review cycle will generally be classified as Type B meetings.

Additionally, Industry stated that it would make proposals regarding Advisory Committee (AC) Management Goals, including timeframes for FDA to provide briefing materials to sponsors in advance of the AC meeting and goals related to holding AC meetings during the review cycle.

Biomarkers and Pharmacogenomics

Industry requested that FDA provide additional detail regarding resource distribution for this proposal. FDA responded that the additional resources would be needed to review applications submitted throughout the PDUFA V period. FDA stated that the resources necessary to address biomarkers and pharmacogenomics would generally be split equally between the clinical, biostatistics, and clinical pharmacology disciplines. FDA also stated that current staff capacity for reviewing submissions with biomarkers or pharmacogenomic markers and for qualifying biomarkers is being exceeded, and that the number of submissions is expected to increase in PDUFA V.

FDA stated that it would clarify the resource allocations for this proposal at a future meeting.

Pilot Program for Enhanced Review Communications

Industry and FDA discussed the pre-submission meeting as a suggested requirement for participation in the pilot program for new molecular entity new drug applications (NME NDAs) and original biologics license applications (BLAs). FDA stated that meeting with sponsors prior to application submission was an important component of the program to increase communication, and opting-out of the pre-submission meeting may undermine this critical component of the program. Industry stated that an FDA proposal for holding the pre-submission meeting at least 6 months prior to submission would present challenges when considering completion of phase 3 trials that may occur closer to the submission date. FDA noted that the intent is to allow enough time so that issues discussed at the pre-submission meeting could be addressed before submission, but that there would be some flexibility in the timeframe for the meeting.

Industry requested the ability to submit additional data during the 60 day filing period after FDA's receipt of the original submission. Industry stated that these data would be limited in scope, and would have been agreed upon in advance with the review division. FDA stated that it was concerned with allowing the submission of additional information to a planned review process that is based on the contents of the original submission, but that it would discuss and consider this proposal as part of the program.

Industry also requested the ability to discuss what could be considered a solicited amendment to address identified deficiencies during the Mid-Cycle communication, noting that a sponsor may have additional data that could address these issues. Industry stated its opinion that the ability to address application deficiencies may enhance the efficiency of the review process by reducing subsequent review cycles. FDA stated its opinion that discussion of application deficiencies should not be considered a solicitation of an amendment to the application, and that submission of new information in response to an identified deficiency raises the issue of what should be considered a complete application at the time of original submission. FDA did state, however, that it would continue to discuss the issue internally, and both sides agreed to continue discussing the issue.

Industry stated that it would like greater consistency in terms of receiving Discipline Review (DR) letters as part of the background package for the Late-Cycle meeting. Industry stated that receiving timely DR letters and a brief cover memo are critical to holding an effective Late-Cycle meeting for applications heading to an AC meeting as well as those for which an AC meeting is not planned. FDA responded that because this pilot will be carefully monitored, it expected that review divisions would fully comply with Good Review Management Principles and Practices (GRMP) guidelines.

FDA stated that the statement of work for the independent assessment of the pilot program would be the opportunity for Industry, other stakeholders, and the public to comment on the metrics that will be measured during the assessment.

Industry stated its concern that different review divisions classify amendments as "major" or "minor" differently. FDA stated that the definitions of the types of amendments have not changed under PDUFA, and that maintaining flexibility in determining the type of amendment can be beneficial to the review process. FDA and Industry both stated that they would discuss internally and consider proposing new language addressing this issue.

FDA-Industry PDUFA V Reauthorization Meeting
Financial Sub-Group
January 6, 2011, 10:00am-12:00pm
Teleconference

Purpose

To continue discussion of FDA technical proposals, the PDUFA baseline costs, the PDUFA inflation adjuster, and the PDUFA workload adjuster.

Participants

FDA		Industry	
Wade Ackerman	OCC	Andrew Emmett	BIO
Lisa Berry	OC	Jeffrey Francer	PhRMA
Daniel Brounstein	CDER	Sascha Haverfield	PhRMA
Andrew Kish	CDER	Mark Mayer	Lilly
Angela Moy	CBER	Robert Meyer	Merck
Theresa Mullin	CDER		
Donal Parks	CDER		
Frank Claunts	Consultant		

PDUFA Baseline Resources

FDA discussed future cost projections on employee compensation costs for newly-hired review staff over their first few years of tenure at the FDA as a follow-up to the December 13, 2010 PDUFA Financial sub-group meeting. FDA clarified that a large increase of entry-level staff occurred at the beginning of PDUFA IV, including a not-insignificant number of Medical Officers during the 2008 FDA hiring surge. Industry requested that FDA determine the percentage of FDA employees engaged in human drug review that are Medical Officers versus other disciplines.

PDUFA Inflation Adjuster

FDA discussed Industry's proposal to modify the current Inflation Adjuster. FDA began the discussion by pointing out that FDA is a federal public government agency, not a private-sector entity that operates in the private market. As a public health agency, FDA has to abide by different rules, including Government Services Administration's rent rates, Federal Acquisition Regulation, and the Office of Personnel Management regulations and statutes. FDA found that Industry's model is based on the Bureau of Labor Statistic's data on private-sector cost structures, and does not take into account FDA's federally-mandated salary structure, physical and Information Technology security requirements, or GSA rent increases. FDA added that it has access to actual cost data, which is the most accurate basis for calculating cost changes and obviates the need to develop a proxy.

Industry agreed that FDA is subject to different pressures than the private sector. FDA agreed to provide Industry with its Inflation Adjuster presentation and to examine the impact of using two- three- and four-year time periods for development of average annual increases, versus the current method which employs a five-year period.

FDA proposed that the current workload adjuster "complexity factor" also be revisited for the impact of two-three- and four-year time periods.

Technical Proposals Discussion

FDA and Industry further discussed minor changes to language for the technical proposals related to discontinued products and the timeframe for the submission of a sponsor's request for reconsiderations or appeals of denials. FDA agreed to send the technical proposals to Industry for review once the changes were completed.

FDA requested that Industry provide an update on specific cases where the small business waivers proposal would affect Industry's small businesses. Industry requested a minimum of an additional week to continue this analysis. FDA agreed to schedule a teleconference with a smaller group to discuss this issue.

FDA-Industry PDUFA V Reauthorization Meeting
Ad-hoc Sub-Group
January 6, 2:30-4:00pm
Teleconference

Purpose

To discuss the proposal to improve human subject protection in clinical trial oversight and the proposal related to FDA's development of a benefit-risk assessment framework and patient-focused drug development.

Participants

FDA		Industry	
Leslie Ball	CDER	Annetta Beauregard	EMD Serono
Patrick Frey	CDER	Andrew Emmett	BIO
Ann Meeker-O'Connell	CDER	Sascha Haverfield	PhRMA
Theresa Mullin	CDER	Jennifer Stotka	Eli Lilly
Stephanie Shapley	CDER	Mark Taisey	Eisai, Inc.
		Helen Thackray	Glycomimetics

Improving human subject protection in clinical trial oversight

FDA discussed its draft proposal to implement a quality systems approach in clinical trial oversight during PDUFA V. The agency stated that transitioning from the traditional regulatory approach of post-hoc clinical trial inspections to an approach that applies "quality by design" to clinical trial oversight could contribute to improved data quality and human subject protection in clinical trials, particularly given recent increasing trends in trial complexity and the expansion of multiregional clinical trials. By applying risk management principles to identify and manage sources of variation at critical steps in clinical development, sponsors and the agency could focus limited resources on those activities that pose a higher risk to data quality, integrity, and human subject protection.

FDA proposed to develop a plan to implement a quality systems approach in the agency's bioresearch monitoring (BIMO) program during PDUFA V that would be published for public comment. The agency stated that part of this proposal would involve additional staffing to review sponsor-developed quality plans and conduct "real-time" inspections while the trial is still ongoing. FDA also proposed to conduct an evaluation of this approach and develop a strategy to incorporate electronic clinical trial data collection into monitoring activities.

Industry requested that the agency provide additional information on how FDA-sponsor discussions of quality plans would be integrated into the review process. Industry also requested more information on the criteria that would be used in evaluating this program. The agency indicated that it is currently identifying these measures and agreed to add examples of success criteria in a revision of the proposal. Industry also agreed to respond with additional questions related to this proposal for FDA's consideration.

Benefit-Risk

FDA discussed a revision of the proposal to develop an enhanced, structured approach to benefit-risk assessment and communication that would include a series of public workshops throughout PDUFA V

for obtaining patient and other stakeholder perspectives to better establish the clinical context (i.e., severity of the treated condition and the adequacy of the existing treatment armamentarium) for certain therapeutic areas that would be identified through a public process.

FDA explained that its proposal to engage the patient perspective in informing the clinical context for decision-making is a key part of its ongoing work on benefit-risk assessment. FDA noted that having a clearer understanding of patients' views on the adequacy of the existing treatment armamentarium within a given disease area would be very valuable and is currently not consistently available to help inform review decisions. The agency further noted that understanding the clinical context through an analysis of the range of disease severity versus available therapy would not be a static analysis.

Industry requested that FDA specify who would be trained in the responsibility of implementing this benefit-risk framework approach. FDA stated that its intent is to train review and management staff on using the framework for consideration in decision-making throughout the lifecycle of a product. FDA also noted that the agency plans to facilitate implementation of the framework through revisions to Manuals of Policies and Procedures and internal review and decision memo templates. FDA and Industry also discussed potential evaluation criteria that could be used to assess the effect of the framework approach on the regulatory decision-making process. FDA stated that it expects to evaluate the utility of the framework in facilitating decision-making and review team discussions across disciplines, risk management plan decision-making, training of new review staff, and communicating regulatory decisions.