FDA and Industry GDUFA II Implementation Quarterly Meetings – 1Q2018 Meeting
January 10, 2018, 1:30 PM – 3:30 PM
FDA White Oak Campus, Silver Spring, MD
Building 32, Room 1215

Agenda

- Drug Competition Action Plan
- Pre-Abbreviated New Drug Application (ANDA) Program for Complex Products Chapter of the Generic Drug User Fee Amendments (GDUFA) II commitment letter
- Industry analysis of predictive factors and how each factor relates to the length of time to submit a response to a complete response (CR) action in order to inform predictive workload modeling
- Review timelines for non-original applications

Participants

FDA:		Industry:	
Donald Ashley	CDER	Deborah Autor	AAM (Mylan)
Joshua Barton	CDER (capacity planning advisor)	John DiLoreto	BPTF
Amy Bertha	CDER	David Gaugh	AAM
Mary Beth Clarke	CDER	Kiran Krishnan	AAM (Apotex)
Michael Kopcha	CDER	Matthew Moran	EFCG (BioPharmChem)
Robert Lionberger	CDER (pre-ANDA advisor)	Lisa Parks	AAM
Ellen Morrison	ORA	Gil Roth	PBOA
Giuseppe Randazzo	CDER (review advisor)	Scott Tomsky	AAM (Teva)
Edward Sherwood	CDER (review advisor)	Molly Ventrelli	AAM (Fresenius-Kabi)
Maryll Toufanian	CDER (DCAP advisor)		
Kathleen Uhl	CDER		

Drug Competition Action Plan

FDA provided a brief overview of the FDA Commissioner's Drug Competition Action Plan (DCAP). DCAP was established to ensure FDA is maximizing its ability to meet the goals of Hatch-Waxman Amendments to incentivize new drug innovation and facilitation of generic drug access as Congress intended. DCAP aligns with the GDUFA II commitments.

The DCAP deliverables were developed based on the program needs identified by Subject Matter Experts in CDER's Office of Generic Drugs, CDER's Office of Pharmaceutical Quality, CDER's Office of Regulatory Policy and Office of Chief Counsel. DCAP's objectives include streamlining the ANDA review process to increase efficiency, effectiveness and output of approvals, enhancing development and review of complex product ANDAs, and reducing "gaming". As one of the DCAP deliverables FDA held a public meeting in July 2017, "Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access". Industry provided substantive comments to docket which are currently being reviewed by FDA senior staff.

Pre-ANDA Program for Complex Products Chapter

FDA has seen a steady increase in the number of controlled correspondences (controls). Based on first quarter receipts, the annual rate for FY2018 is projected to be approximately 3200 and in

FY2017 FDA received a total of approximately 2670. FDA asked Industry if they anticipate the number of controls to continue to rise. Industry indicted it was hard to predict, as controls are the main mechanism to communicate with the FDA on application specific matters prior to submitting an application. It could be that at some future point, there might be a leveling off, as certain questions with broad applicability only need to be asked once. GDUFA II enhancements to the Inactive Ingredient Database might help in decreasing the number of controls, since information requested in a portion of the controls submitted will be found in the Database. Additionally, Industry requested that FDA consider publishing a Frequently Asked Questions guidance as it might also help in decreasing the number of controls. Industry asked FDA how many requests to clarify ambiguities have been received, since the beginning of GDUFA II. FDA responded that they have only been a few.

FDA continues to publish quarterly batches of Product Specific Guidances (PSG). For non-complex New Molecular Entities FDA is issuing guidances two years before the first legal submission date. Overall, approximately 50% of the PSGs issued are for complex products. A leading reason for revisions to a PSG stems from changes to the reference listed drug. When a PSG is revised, FDA is looking at ways to better highlight the changes. For a complex product, Industry requesting a pre-submission meeting is a pathway for discussion of alternative approaches (that satisfy the requirements of the applicable statues and regulations) other than what is articulated in the PSG.

Regarding pre-ANDA meetings for complex products, FDA has a new electronic portal ("the Portal") for submitting meeting requests. Based on first quarter receipts, the projected number of requests for FY2018 are double the annual rate of requests received in GDUFA I. Industry will need to request a pre-assigned ANDA number prior to submitting a meeting request. This allows FDA to link the development and pre-submission meetings with the ANDA, once the ANDA is submitted. FDA will be granting requests for pre-submission meetings, if a product development meeting was granted after October 2014. A current challenge is how Industry will integrate product development and pre-submission meetings into a product development timeline. As FDA holds more of these meetings and gains experience, FDA may be able to make recommendations around the timing of holding these meetings

Regarding the Industry led Regulatory Science working group, FDA would benefit from obtaining input from the generic Industry on the scientific challenges blocking efficient drug development that could be addressed by FDA research activities. FDA would also benefit from obtaining input on Industry's perspective on prioritizing the various scientific challenges to inform FDA's short-term and longer-term strategic planning, given the Agency's limited resources in this space. FDA and Industry agreed to hold a planning telecon with a small group of people to discuss in more detail Industry's proposals for what topics would be most helpful to the FDA and who the appropriate Industry participants in the working group would be.

Industry analysis of predictive factors and how each factor relates to the length of time to submit a response to a CR action in order to inform predictive workload modeling

As a follow-up to the September 2017 quarterly meeting and in order to help FDA with workload analytics and capacity planning, FDA asked Industry for an analysis. The analysis would include the factors that influence the length of time it takes applicants to submit a response to a CR action and how each factor relates to each other in determining the amount of time it would take to respond. This information would then inform a predictive workload model as part of capacity planning. Capacity planning is a GDUFA II Commitment, as well as a commitment under Prescription Drug User Fee Act (PDUFA) and Biosimilar User Fee Act (BsUFA). While Industry understands the importance of FDA being able to predict and plan its workload, industry's response time to a CR letter is highly variable, subject to change, and is difficult to generalize.

Industry shared general factors impacting response time including, business reasons (e.g., mergers and acquisitions that may result in duplicative applications), legal reasons (e.g., patent litigation), and regulatory reasons (e.g., classification of the Complete Response (CR) letter). More specific factors include bioequivalence issues, need to conduct stability studies, facilities issues, dissolution issues, impurities issues, need to obtain additional drug product for future testing (especially in REMS situations), need to source ingredients or specific testing materials and need to manufacture additional batches.

FDA and Industry discussed possible ways to increase Industry transparency in its intended response timelines for responding to CR actions.

Review timelines for non-original applications

At the September 2017 quarterly meeting, FDA and Industry discussed a typical review timeline for a first-cycle original application submitted under GDUFA II. Industry asked what a typical review time for non-original applications submitted under GDUFA II, such as amendments and prior-approval supplements (PAS), would look like. Specifically, Industry asked if applicants would be receiving Discipline Review letters (DRL) at the mid-point for amendments. FDA explained that the GDUFA II commitment for DRLs applies to original applications; however, FDA plans to continue its practice of sending review communications to the applicant for amendments.

When an amendment or PAS is submitted, FDA will follow the goal dates outlined in the GDUFA II commitment letter. FDA will triage these submissions based on factors such as major versus minor, standard versus priority (major amendments only), whether an inspection is needed (major amendments only – FDA will default to the shortest goal date at the beginning and then change the goal date, if it is determined that an inspection is needed), and whether a pre-submission facility correspondence was submitted.