FDA Talks Generic Drugs: A Look at the Generic Drug Approval Process from the Agency's Perspective

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So you're preparing an abbreviated new drug application submission… what could possibly go wrong? The Food and Drug Administration responds: Let us count the ways… However, much of it can be avoided if one merely knows where to find help, said experts from the FDA's Office of Generic Drugs (OGD) recently at the Generic Drugs Forum 2016. This two-day conference, which AGG attended, was intended to inform small business generic drug companies of the importance of getting ANDA submissions on track right out of the gate, and keeping them on track throughout the entire review process. Knowing what needs to be included in the ANDA submission (and what to keep out), as well as knowing what one can and cannot do during the review process, is critical to the success or failure of the application.

Dr. Kathleen Uhl, Director of the Office of Generic Drugs, opened with a general overview of the functions and structure of the OGD and spoke of the recent success in consistently meeting or exceeding its goals under the Generic Drug User Fee Act (GDUFA). She said that FDA had approved a significant number of "first generic" applications in 2015 and, in the first and second quarters of FY16, OGD issued 348 approvals and 92 tentatively approved applications. December 2015 brought in the highest number ever of approvals and tentative approvals, she said, and since the implementation of GDUFA, FDA has had great success in building a robust, modern generic drug regulatory program that is both sustainable and predicable.

Speakers consistently emphasized a common message: know the processes, know what is required and when, and then do it. No one wants to receive a Refuse-to-Receive (RTR) determination, and that can be avoided, according to FDA officials, by simply following the agency's rules, guidances and procedures.

So where to start? Once a company has submitted the ANDA to OGD, the submission will be assigned a Regulatory Project Manager, who will serve as the point of contact and provide oversight of the application throughout the review divisions. The RPM is very important, because that individual will work to ensure that all reviews of the ANDA are complete while, at the same time, keeping OGD on track to meet its GDUFA goal dates.

Simple, obvious, but incredibly important -- be sure that the application is complete. It may seem self-evident, but the ANDA submission requires basic, yet critical information. FDA officials said that, unfortunately, some applicants have received RTR notifications because their applications contained incomplete or incorrect information. Some common examples include:

- Outdated contact information or incorrect facility addresses. FDA officials said they receive a surprising number of applications containing outdated or incorrect contact information.
- Failure of a foreign firm to designate a U.S. agent or providing poor contact information for that agent.
- Failure to include important scientific data.
- Incorrect Employer Identification Number (EIN) and DUNS numbers. A DUNS number is issued by Dun and Bradstreet and is unique to the physical location of a business.

- Failure to disclose all pertinent facility locations. FDA says that one must disclose the locations of *all* facilities, including all manufacturing, packaging and control sites for drug substance and drug products, even those that are under construction or which have been closed. The company must immediately contact FDA to advise of any changes to the facilities with an amendment and updated Form 356h and cover letter.

- A poorly prepared cover letter. Does the cover letter contain a clear statement of what the submission entails, including, for example, what an amendment is addressing? Missing, unclear, or conflicting information will almost certainly cause delays.

- Other important considerations by FDA include: Don't send FDA information for which it didn't ask. There may be times during the review process that FDA will request additional information, but some respondents include too much, or information that is off-topic and, in doing so, can trigger a response from the agency that will require the submission of a formal amendment, complicating the process and leading to review delay.

- Addressing any patents and exclusivities that may be relevant to the ANDA. An applicant must submit, for example, all required documentation regarding patent certifications, court decisions and orders, adverse decisions, in order for the application to be deemed complete. The firm must update FDA throughout the review process.

- Provide proper labeling content and style (e.g., placement of a logo on the label in such a way that would detract from essential information pertaining to dosage and strength).

- Provide complete or timely responses to data or information requests.

- Provide English translations if originating from a foreign country.

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What's the FDA's bottom line? Think it through and anticipate what FDA wants. An RTR determination letter is something to avoid when submitting an ANDA application, but it does happen. FDA officials said that while these determinations are decreasing, some ANDAs still continue to contain avoidable common pitfalls. Throughout the FDA program, speakers consistently said "help us help you." FDA experts covered many topics in their presentations, but the clear message was that ANDA applications should always be of the highest quality, thoroughly thought-out, conform to FDA requirements, and be complete and adequate for filing and scientific reviews. Applicants should always follow proper procedures when interacting with the agency, and respond on time to requests for additional information or questions from reviewers. The FDA is there to help, they said, and by following FDA's procedures and protocols, a company will maximize the likelihood for success.

If you would like additional information on the meeting or ANDA issues, please contact Mr. Alan Minsk at Alan.Minsk@agg.com. Cathy Fortney attended the FDA meeting and was instrumental in summarizing the meeting contents.

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