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Client Alert

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Recent FDA Warning Letter Enforces Postmarketing Requirements: A Sign of Things to Come?

A recent Food and Drug Administration (FDA) Warning Letter suggests that the agency will not hesitate, when necessary, to exercise its power to enforce postmarketing requirements (PMRs) for approved drug products.[1] The Warning Letter states that the recipient company failed to submit a required study protocol and final study report, pursuant to the company's PMRs, and, therefore, the drug products are misbranded under the Federal Food, Drug, and Cosmetic Act (FDCA).[2] This Client Alert will focus on the FDA's general concerns and its enforcement approach rather than the specific PMRs in the particular case addressed in the Warning Letter. The Warning Letter is significant because it represents that the agency will take enforcement action against a company for failure to comply with PMRs. The industry will have to wait and see whether the Warning Letter represents a new wave of enforcement, but it signals that the FDA will act and companies should stay focused on complying with PMRs.

Background on the Warning Letter

The FDA's current authority to enforce postmarket study requirements was initiated in 2007 under the FDA Amendments Act (known as FDAAA).[3] Prior to FDAAA, the agency required some companies, under limited circumstances, to meet certain mutually agreed upon postmarket commitments. FDAAA added new section 505(o) to the FDCA, which creates more sweeping PMR authority for the agency. Section 505(o)(3) authorizes FDA to require postmarketing studies or clinical trials at the time of approval or after approval if it becomes aware of new safety information.

Citing this relatively new source of regulatory authority in its Warning Letter, FDA explained that the company "did not provide a final protocol submission for a new study that would fulfill the PMRs, as requested ... [and] had not demonstrated good cause for failing to adhere to the agreed upon timeline

1 The Warning Letter is available here: http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm293490.htm. While the Warning Letter is available publicly, we will not disclose here the company that received the correspondence.
2 21 U.S.C. § 352(z).
3 The applicable postmarket study requirements are contained in Section 505(o) of the FDCA (21 U.S.C. § 355(o)). Section 505(o)(3) allows FDA to "require a responsible person for a drug to conduct post-approval study or studies of the drug, or a post-approval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the [agency], including information regarding chemically-related or pharmacologically-related drugs."

for completion." FDA acknowledged that the company submitted information about an independently conducted investigator-initiated study, but the agency had not agreed that this study could be used to satisfy the PMRs. FDA also stated that the data submitted from that study was not sufficient to constitute a final study report, as required by the PMRs. Thus, FDA concluded that the company was more than 20 months late in submitting a final study protocol for a requested three-month study in rats, and more than 8 months late in submitting a final study report that satisfies the originally agreed upon PMR.

The Warning Letter concludes with a reminder that the agency may take additional enforcement action without further notice, including imposing civil monetary penalties up to a maximum of $250,000 per violation. The company now has a very tight timeline to respond to FDA's demand to comply with the PMRs; the Warning Letter mandates a final study protocol within 30 days and states that the agency expects the company to obtain agreement with FDA on an adequate study protocol and to have initiated the study within six months.

Other FDA Action on PMRs

As the first major enforcement action in a relatively new area of FDA regulation, this Warning Letter initially sent a shockwave through the pharmaceutical community. However, in hindsight, perhaps there were some subtle signals that FDA was considering a greater focus on PMR enforcement. In April 2011, FDA issued a guidance document, *Postmarketing Studies and Clinical Trials – Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act*.[4] The guidance document summarizes the new PMR requirements and reporting procedures, and has a section dedicated to enforcement. In that section, FDA emphasizes the importance of compliance with the PMRs and its authority to take action when companies fail to comply:

> [a]n applicant's failure to comply with the timetable, periodic report submissions, and other requirements ... will be considered a violation unless the applicant demonstrates good cause for the noncompliance ... . FDA is authorized to determine what constitutes good cause.

In addition, only a few days after the Warning Letter was issued, the agency added a Notice to Industry on its website, explaining that "FDA intends to vigorously enforce requirements that sponsors conduct postmarket studies and clinical trials."[5] The agency's messaging at this stage certainly suggests that companies should be prepared for future enforcement for non-compliance with PMR obligations. It is also noteworthy that, in January 2011, FDA issued a Warning Letter to a medical device company that failed to comply with postmarket study requirements, thereby making the device misbranded.[6]

4 The guidance document is available here: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM172001.pdf.
5 The Notice to Industry is available here: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm292758.htm.
6 The Warning Letter issued to the medical device company is available here: http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2011/ucm239848.htm.

Conclusion

Companies that have PMRs must recognize that FDA is serious about the agreed-upon timetables for submission of information. Companies that expect a delay should remain in close contact with FDA to show responsiveness and to make the agency aware of any issues that might help establish a good cause argument for deferral of required submissions. Moreover, while it may not be representative of future cases, the current Warning Letter demonstrates that FDA is not likely to accept studies that were not previously agreed upon as satisfying the PMR requirements. Ultimately, the PMR rules under section 505(o) of the FDCA are intended to protect patient safety where FDA has some reason to believe that further study is needed. Where safety concerns are at stake, FDA will enforce its rules.