Say My Name, Say My Name: FDA Posts List of RLD Access Inquiries

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On May 17, 2018, the Food and Drug Administration posted a list of pharmaceutical manufacturers that FDA alleges have blocked potential generic drug applicants from accessing drug samples needed to obtain approval for their products.[1] The list is part of FDA's Drug Competition Action Plan, announced last year, which aims to facilitate "increased competition in the market for prescription drugs through the approval of lower-cost, generic medicines."[2] Like the 1999 Destiny's Child hit, the agency is highlighting what it calls "gaming" of the regulatory system,[3] and rather than merely alluding to companies "actin' kinda shady," FDA is naming names.

Background

To obtain approval for a generic drug, a generic sponsor must demonstrate that its product is bioequivalent to the Reference Listed Drug (RLD), which is often the branded product. To conduct bioequivalence studies, the generic sponsor usually needs to obtain samples of the RLD. However, an RLD sponsor may limit distribution of the product by choice or mandate (e.g., through selling the product only through a central or small group of pharmacies), which can make it more difficult for the generic sponsor to purchase samples.

FDA may impose limitations on distribution of an RLD as part of a Risk Evaluation and Mitigation Strategy (REMS). When FDA implements a REMS, which is intended to help ensure that a drug's benefits outweigh its risks, the program may contain elements to assure safe use (ETASU). FDA is aware that, as a result of these limitations, some RLD sponsors:

1. refuse to sell the product directly to the generic company (or impose terms on the sale that generic companies find burdensome or impossible to comply with), or

2. place limitations on the ability of pharmacies or wholesalers to sell samples to the generic companies for development purposes.[4]

Some RLD sponsors assert that having a REMS with ETASU in place prohibits them from selling RLD samples to prospective generic applicants. In response, prospective generic applicants may request assistance from FDA to facilitate access. First, the agency will review the prospective generic applicant's planned bioequivalence study protocols, evaluating whether they contain safety precautions comparable to the safety precautions imposed by the REMS for the RLD. If so, the prospective generic applicant can request a letter from FDA to the RLD sponsor, informing the RLD sponsor that providing product to the generic applicant will not be considered a violation of the REMS for the RLD. This letter is known as the "Safety Determination Letter." The letter also states that "section 505-1(f)(8) of the Federal Food, Drug, and Cosmetic Act [FD&C Act] prohibits the holder of a new drug application covered by a REMS from using any ETASU to block or delay

1 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm
2 https://blogs.fda.gov/fdavoice/index.php/2017/06/fda-working-to-lift-barriers-to-generic-drug-competition/
3 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm.
4 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm.

approval of an application under section 505(b)(2) or (j) of that Act."[5]

Notably, if a drug is not subject to REMS with ETASU affecting distribution, FDA will not undertake a protocol review in response to an access request (as there are no REMS distribution limitations in place for FDA to evaluate). Instead, the agency may issue a response noting that the product is not subject to a REMS, then encourage the prospective generic applicant to raise the matter with the Federal Trade Commission if the applicant believes there has been anticompetitive conduct.

FDA's RLD Access Inquiries List

Until now, FDA has not maintained a publicly available list of RLD products for which it has received access inquiries. The newly issued RLD Access Inquiries List, which currently contains 52 products, names the RLD sponsor for each product and lists the number of inquiries received by FDA for each product. The list also provides information on whether each product has a REMS with ETASU impacting distribution, and, if so, whether FDA has issued a Safety Determination Letter.

The agency has issued multiple Safety Determination Letters for some products, but RLD sponsors "generally do not inform the Agency whether they have made samples of the RLD available after receiving a Safety Determination Letter."[6] Thus, some companies on the list may have ultimately provided RLD samples. FDA also points out that the agency has not independently investigated or confirmed the access limitations described in the inquiries received from prospective generic applicants. Nevertheless, FDA has decided to publicly say the names of RLD sponsors whose products have generated access inquiries, and FDA will be updating the list on a semiannual basis.

AGG Observations

- The list does not constitute enforcement action by the agency. However, in an accompanying press release, Commissioner Gottlieb stated that FDA would "continue to look at more ways [FDA] can expand upon [this] action and call public attention to situations where the careful balance that Congress sought between product innovation and access may be disrupted." Though FDA may not have a regulatory mechanism to require RLD sponsors to provide samples, the agency is not shying away from implementing public pressure.

- FDA encourages prospective generic applicants to raise these cases with the FTC if they believe anticompetitive conduct has taken place, and FDA will notify the FTC about these inquiries. However, we have not yet seen FTC take public enforcement action against this particular behavior by RLD sponsors. We will continue to monitor whether that changes.

- This list only reflects inquiries from prospective generic applicants (i.e., those who plan to submit ANDAs under 505(j)), but FDA notes that the agency has also received access inquiries from prospective applicants intending to submit new drug applications under section 505(b)(2) of the FD&C Act or biologics license applications under section 351(k) of the Public Health Service Act. For now, FDA is focusing only on ANDA products, but if FDA is tracking access requests related to 505(b)(2) products and biosimilars, the agency could decide to expand the scope of this list.

5 Safety Determination Letter Template available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM602358.pdf.
6 https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm.

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