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Practice Group:

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FDA Interprets 180-Day Exclusivity Forfeiture Provisions

The legal team of Michael H. Hinckle, Gary L. Yingling, and Rebecca L. Dandeker, from the K&L Gates Food, Drugs, Medical Devices and Cosmetics Practice Group, assisted their client Cobrek Pharmaceuticals, Inc. in securing a win to move one step closer to 180 days of marketing exclusivity for a generic drug that will substitute for Hectorol Injection, 2 mcg/mL – a drug used by dialysis patients.

On September 20, 2011, FDA denied a Citizen Petition that had been filed by another generic drug company, Sandoz Inc. Sandoz also wanted to sell a doxercalciferol injection product, but would have been blocked if Cobrek received 180-day exclusivity. Sandoz asked FDA to rule that Cobrek forfeited its exclusivity under the forfeiture provisions that were added to the Federal Food, Drug, and Cosmetic Act (FDC Act) via the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA).

FDA ruled that Cobrek did not forfeit its 180-day exclusivity and, as a result, Sandoz' ANDA will be blocked if Cobrek is awarded exclusivity upon approval. *See* Docket No. FDA-2010-P-0632, FDA Letter to Sandoz Inc., Sept. 20, 2011. This is one of the few times that FDA has interpreted the forfeiture provisions of the MMA.

The facts of the case are unique to drug products that are manufactured as injectable (parenteral), ophthalmic, otic or topical dosage forms. Generic drugs in these dosage forms must use almost the exact formulation as the innovator drug – a policy that FDA calls "Q-and-Q," in that the innovator and generic drugs have "quantitatively and qualitatively" the same formulation of active and inactive ingredients.[1] In this case, the innovator, Genzyme Corporation, initially sold its injectable solution in a glass ampule packaging presentation. Genzyme later changed the Hectoral Injection formulation and sold it in a stoppered amber glass vial. Cobrek was the first to file an ANDA containing a Paragraph IV patent certification for a generic product that would be Q-and-Q to the ampule presentation. Cobrek later mirrored Genzyme's change and amended its ANDA to describe a generic product that would be Q-and-Q to the vial product. Sandoz submitted its ANDA for a generic product that would match Genzyme's older ampule presentation. Sandoz then submitted the Citizen Petition on December 8, 2010, asking FDA to declare that Cobrek had forfeited its 180-day exclusivity because of its change from the ampule to the vial.

First, FDA ruled that an ANDA applicant's resubmission to a Paragraph IV certification is not automatically deemed an "amendment or withdrawal" under the "Amendment of Certification" forfeiture provision. FDC Act § 505(j)(5)(D)(i)(III). Under the law, the first-to-file ANDA applicant will forfeit its 180-day exclusivity if it "amends or withdraws the certification for all of the patents" to which it had submitted a Paragraph IV certification. Sandoz claimed that Cobrek triggered this forfeiture event when it resubmitted a Paragraph IV certification after "voluntarily" reformulating its product from the ampule to the vial presentation. FDA sided with Cobrek, which had argued that a recertification after an ANDA applicant reformulates to respond to a change in a reformulation of an innovator drug did not constitute an amendment or withdrawal under the Amendment of Certification

[1] 21 C.F.R. § 314.94(a)(9).

forfeiture provision. FDA agreed, concluding as follows: "Neither the Act nor FDA's regulations stipulate that a resubmission of patent certifications because of a change in [innovator] formulation mandate the loss of any 180-day exclusivity rights stemming from the original certifications that qualified a first applicant for exclusivity." FDA Letter to Sandoz Inc. at 7. Instead, FDA determined that Cobrek had "merely continuously maintained its paragraph IV certifications to the relevant patents as is statutorily required." *Id*. at 8.

Second, FDA ruled that a change in the innovator drug's packaging presentation is the type of change that is exempt from triggering a forfeiture under the "Failure to Obtain Tentative Approval" forfeiture provision. The law states that if a first-to-file ANDA applicant fails to obtain tentative approval of its ANDA within 30 months after filing it with FDA, it will forfeit its 180-day exclusivity, "unless the failure is caused by a change in or a review of the requirements for approval" imposed after the initial ANDA submission – a Congressional acknowledgement that a change in approval requirements should not negatively affect the first-to-file ANDA applicant. FDC Act § 505(j)(5)(D)(i)(IV). Sandoz had argued that no change occurred in Cobrek's case and the exception provision did not apply. FDA disagreed, ruling instead that the innovator drug's change from an "old" formulation to a "new" formulation "requires an ANDA applicant to respond" and, thus, FDA will consider this to be "a change in or review of" the requirements for approval under the "Failure to Obtain Tentative Approval" forfeiture provision. FDA Letter to Sandoz Inc. at 9. FDA's decision turned on the injectable dosage form requirement (stated above) that a "generic drug is expected to be Q1/Q2 identical to" the innovator. Consequently, a reformulation by the innovator would require either (1) a reformulation of the ANDA product or (2) a request by the ANDA applicant for FDA to (a) determine that the original formulation had not been withdrawn for reasons of safety or effectiveness, and (b) waive the requirement of Q1/Q2 identity. FDA concluded that "either case would constitute a change in the requirements for approval of an ANDA." *Id*.

This FDA ruling means that, when Cobrek's ANDA receives final FDA approval, any other ANDA for a generic doxercalciferol injectable product that is not also a first-to-file applicant will be blocked if Cobrek is awarded 180-day exclusivity. The FDA ruling also gives the generic drug industry some important information about how the agency intends to interpret the FDC Act's 180-day exclusivity forfeiture provisions.

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