For Now, Competitive Generic Therapy Exclusivity Is A Mirage

By **Sinchan Shah, Jaimin Shah and Stephen Auten** (February 12, 2019)

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Exorbitantly high prices are not just a problem for patented drugs. Even off-patent drugs are subject to high prices when there is inadequate generic competition due to market size or regulatory barriers. For example, the toxoplasmosis drug Daraprim, which has a small market (approximately, $10 million in 2015-16). Turing Pharmaceuticals acquired the product and immediately raised the price from $13.50 to $750 a pill.[1] The tuberculosis drug cycloserine is another example, where the price for 30 pills was raised from $500 to $10,800.[2]

Congress noticed the problem, creating in response a new form of market exclusivity, known as competitive generic therapy exclusivity, to spur generic competition for such competition-deprived drugs. At first, the generic drug industry responded favorably by initiating development of such drugs. But, the statute as written has an unintended loophole, which frustrates the purpose of the statute. Congress needs to address that ambiguity, and remove the uncertainty prevalent in the industry at the moment.

Competitive Generic Therapies Generally

Congress attempted to address the aforementioned problem via the Food and Drug Reauthorization Act of 2017. Under this new statutory regime, the U.S. Food and Drug Administration may designate a drug as a "competitive generic therapy" if there is "inadequate generic competition" with respect to a drug.[3] There is inadequate generic competition when the market has only one option available, either the brand-name drug or, if withdrawn, a corresponding generic.[4]

The first company to obtain FDA approval of a competitive generic therapy — and thus to benefit consumers by increasing competition for that drug — would be entitled to 180 days of exclusivity for its drug, with the exclusivity period running from the date of first commercial marketing.[5] And to ensure that this new form of exclusivity would not unduly delay approval and marketing of later-approved generic versions of the drug, Congress provided that the exclusivity would be forfeited if the exclusivity holder failed to launch the drug within 75 days of FDA approval.[6]

Reps. Kurt Schrader, D-Ore., and Gus Bilirakis, R-Fla., introduced the CGT provisions as an amendment to the bill that became FDARA. Rep. Schrader explained the purpose of the amendment in his opening remarks in a subcommittee vote hearing:

> The amendment [] creates an incentive for this select set of particular generic drugs to come to market by guaranteeing them the same [six] months of exclusivity that the vast majority of first generic drugs receive. Under current law, generic drugs challenging a patented drug, they get this treatment. This would extend that treatment for new generic drugs competing with off-patent brand drugs where there is no competition.[7]

Likewise, Rep. Bilirakis stated that the amendment was designed to "create[] an exclusivity incentive for drug companies to develop a generic drug where there are no generic drugs available. This will help encourage competition and drive down costs."[8]

Soon after the enactment of FDARA, the generic drug industry started responding favorably. The concept of competitive generic therapy exclusivity made business sense for generic companies.

The Business Case for CGT Exclusivity

Though the cost of generic drug development is ordinarily not high, generic drug companies tend to stay away from drugs with a small market size for many reasons. First, generic drugs are typically offered at anywhere between 50 percent and 99 percent of the brand price, trimming the profit margin. For a brand drug with sales of $50-100 million a year, the return on investment for generic development is low. Assuming that at least three to five other generic companies will likely compete in the same market, the incentive shrinks even more.

Second, brand companies often have exclusive tie-ups with the sole supplier of the active ingredient for such drugs, forcing generic companies to develop the active ingredient themselves. That injects more delay in generic drug development, which is also a deterrent. Third, even if an abbreviated new drug application is developed and filed, there could be delays in regulatory approval, such as due to lack of specific guidance from the FDA on bioequivalence or other characterization studies. All of this dissuades generic companies from investing resources in developing drugs with small market sizes and regulatory uncertainties.

Enter CGT exclusivity. The uncertainty and risks explained above may be offset by the economic incentive inherent in the six months of market exclusivity. Take, for example, Genus Lifesciences Inc.'s potassium chloride oral solution (10 percent and 20 percent) to treat hypokalemia. Apotex Corp., one of the leading generic drug companies in the world, was granted CGT exclusivity for PCOS — the first CGT exclusivity granted ever.[9] But, as explained below, a statutory loophole caused the FDA to approve another PCOS product despite Apotex's CGT exclusivity.

The Statutory Loophole Hurting the Business Case for CGT

A key question faced by generic companies is: When does CGT exclusivity vest? Does it vest when the ANDA is filed, when the ANDA is approved, or when the ANDA product is launched? Consider the plain language of the statutory provision that appears to vest CGT exclusivity upon commercial marketing, thereby permitting approval of additional ANDAs until the exclusivity-bearing product is launched:

> (v) 180-day exclusivity period for competitive generic therapies
>
> (I) Effectiveness of application. – Subject to subparagraph(D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.[10]

The FDA reads the above provision to mean that CGT exclusivity vests upon the commercial

marketing of such product.[11] That is, in the FDA's view, if a CGT product is approved but not yet commercialized, approval of other ANDAs is allowed under the statute. But approval of another ANDA — despite an ANDA product's eligibility for CGT exclusivity that has not been forfeited — is tantamount to a forfeiture of the CGT exclusivity. But can exclusivity be forfeited before it has even vested? After all, one cannot forfeit something one never had.

If the FDA's reading is correct and CGT exclusivity vests on "the date of the first commercial marketing," does the exact time of day of the first commercial marketing matter? In other words, can the FDA approve another ANDA just minutes or hours before the commercial marketing of the CGT product commences on the same day?

These are not theoretical concerns. About four months ago, the FDA approved another ANDA for PCOS merely 43 minutes before Apotex commenced commercial marketing of its own CGT-designated ANDA product.[12] That Apotex held the CGT exclusivity for PCOS, and that Apotex rushed to launch within 21 days of approval (instead of waiting 75 days), made no difference.

Uncertainty as to the above statutory questions thus hurts the business case for CGT. The time period between the approval of a CGT-designated ANDA and the commercial marketing of the CGT product is an "anxiety zone" for the CGT ANDA holder: The FDA could approve another ANDA or ANDAs for the same product during that time period. That diminishes the economic value of the CGT exclusivity, rendering it a mere mirage at the moment.

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[1] See Andrew Pollack, The New York Times, Drug Goes From $13.50 a Tablet to $750, Overnight (Sep. 20, 2015), available at https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html.

[2] Id.

[3] See 21 U.S.C. § 356h(b).

[4] Id. § 356h(e).

[5] Id. §355(j)(5)(B)(v)(I).

[6] See 21 U.S.C. § 355(j)(5)(D)(iv).

[7] Preliminary Transcript of Subcommittee Vote on H.R. 1222, H.R. 2410, and H.R.2430, FDA Reauthorization Act of 2017, 115th Cong. 78–79 (May 18, 2017) ("FDA Reauthorization

Act Transcript"), available
at: https://docs.house.gov/meetings/IF/IF14/20170518/106022/HMKP-115-IF14-Transcript-20170518.pdf (statement of Rep. Schrader).

[8] Id. at 80.

[9] U.S. Food & Drug Administration, FDA approves first generic drug under new pathway aimed at enhancing market competition for sole source drugs(Aug. 8, 2018), available at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm616167.htm.

[10] 21 U.S.C. § 355(j)(5)(B)(v) (emphasis added).

[11] U.S. Food & Drug Administration, Denial-Request to rescind approval of ANDA 209786 (Oct. 2, 2018), available
at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM623290.pdf. Recall that, by contrast, the traditional 180-day exclusivity for a first company to file a Paragraph-IV ANDA vests upon the act of filing the ANDA, not commercial marketing of the ANDA product.

[12] Id.