Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
"The Future of Medicine: Legislation to Encourage Innovation and Improve Oversight"
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The Honorable Earl L. "Buddy" Carter (R-GA)

1. Dr. Vereshchagina, would you explain how H.R. 7032, the "Increasing Transparency in Generic Drug Applications Act," could limit patient access to new therapies by forcing companies to divulge highly valuable trade secrets?

Representative Carter, thank you for your question for the record regarding H.R. 7032, the "Increasing Transparency in Generic Drug Applications Act." I appreciated the invitation to testify before the United States House of Representatives Committee on Energy and Commerce, Subcommittee on Health, and welcome the opportunity to provide additional thoughts on this bill.

H.R. 7032 (the bill) would authorize FDA to disclose to generic drug applicants highly valuable proprietary information (including trade secrets and confidential commercial information) about the inactive ingredients in the reference listed drug (RLD). Specifically, the bill would authorize FDA to disclose information on the precise type and amount of inactive ingredients in a drug. Information about a drug product's formulation, including the precise quantities of inactive ingredients in a pharmaceutical product, typically constitutes a trade secret if it is not disclosed to the public.[1]

[1] *See, e.g.*, *Enteris Biopharma, Inc. v. Clinical Pharmacology of Miami, Inc.*, 2015 WL 12085848, at *8 (S.D. Fla. Mar. 20, 2015) (denying a motion to dismiss a trade secret claim where the alleged trade secret included, among other things, a "proprietary excipient formulation for enteric coating of HPMC capsules . . ."); *Appleton v. FDA*, 451 F. Supp. 2d 129, 141 (D.D.C. 2006) (upholding, in a suit brought under the Freedom of Information Act (FOIA), FDA's withholding of information about "drug chemical composition" as trade secrets); *In re Gabapentin Patent Litig.*, 312 F. Supp. 2d 653, 660 (D.N.J. 2004) (affirming a magistrate judge's decision to require redaction of summary judgment papers because they contained an ANDA sponsor's trade secrets, based on a declaration stating that "[t]he composition statements . . . provide a recipe for making the products. Purepac would suffer serious commercial injury if the information became known to others."); *Citizens Comm'n on Human Rights v. FDA*, 1993 WL 1610471 (C.D. Cal. May 10, 1993), at *7 (upholding, in a FOIA suit, FDA's withholding of information because "an NDA by definition contains trade secret information because it contains significant information about how a pioneer drug product is formulated [and] chemically composed . . ."); *Myers v. Williams*, 819 F. Supp. 919, 921 (D. Or. 1993) (granting a preliminary injunction against the plaintiff's disclosure of the Halcion formula because "Upjohn has made a strong showing that the Composition Statement falls within the definition of a trade secret[.]").

The Bill Undermines the Long-standing Hatch-Waxman Amendments and Incentives for Innovative Drug Development

The broad disclosure of proprietary information that the bill would authorize would fundamentally alter the careful balance that Congress created in the Hatch-Waxman Amendments between encouraging innovation and facilitating access to generic drugs. Hatch-Waxman contemplates that a generic sponsor may avoid resource-intensive clinical trials by relying on FDA's approval of the innovator's drug without having access to the underlying data—not that FDA would disclose the innovator's proprietary information, such as confidential inactive ingredient information, to the generic sponsor as well.

By removing protections for innovators' proprietary formulation information, the bill would undermine incentives for development of novel pharmaceutical formulations that benefit patients. Drug product development is a time- and resource-intensive part of research and development. Disclosure of formulation information to generic sponsors would harm innovators by allowing competitors to potentially take advantage of innovators' formulations. Potential competitor uses include uses other than developing the generic drug at issue, such as to design around intellectual property or develop their own future formulations. The disclosure that the bill would authorize therefore would undermine innovator's investments in formulation research and development and erode protections on proprietary information.

The Bill is Unnecessary

In addition to limiting patient access to new therapies by forcing companies to divulge highly valuable trade secrets, the legislation is unnecessary. Indeed, the bill would allow disclosure of quantitative and qualitative inactive ingredient information even when FDA has not required or recommended that the inactive ingredients in a generic drug product be quantitatively and qualitatively the same in those as the RLD. H.R. 7032 would authorize FDA to share with generic drug applicants proprietary information about the inactive ingredients in the RLD, with the apparent goal of enabling generic applicants to more easily obtain approval. But the Federal Food, Drug and Cosmetic Act (FDCA) does not contemplate that this information will be shared with the generic sponsor or be needed for generic approval.

There is no general requirement under the FDCA that a generic drug product have the same inactive ingredients in the same concentrations as in the RLD.[2] Instead, the concept of qualitative and quantitative sameness of inactive ingredients ("Q1/Q2") at issue in the bill arises in two non-statutory contexts. First, under FDA's non-binding guidance for some products, inactive ingredient sameness may help an ANDA applicant to show its generic drug is bioequivalent to the RLD through a less costly or less time-consuming method. Second, FDA regulations (not the statute) impose Q1/Q2 sameness requirements for establishing bioequivalence and for approval of certain generic dosage forms, subject to exceptions.

More specifically, generic applicants must show the proposed generic drug is bioequivalent to the RLD to support approval.[3] Bioequivalence means that the drugs' rate and extent of

[2] *See* FDCA § 505(j)(2)(A).
[3] *Id*. § 505(j)(2)(A)(iv).

absorption in the body do not differ significantly.[4] For many drugs, bioequivalence can be shown by testing the drug's blood levels in simple clinical studies (in vivo studies) in healthy volunteers. For locally acting drugs, however, blood tests might be insufficient to show bioequivalence. The FDCA authorizes FDA to "establish alternative, scientifically valid methods" to show bioequivalence.[5]

In non-binding guidance for certain products, FDA offers ANDA applicants the choice of performing either in vivo or in vitro testing to satisfy the requirement to show bioequivalence, but may condition use of the in vitro option on a showing that the proposed generic product has the same inactive ingredients as those in the RLD in concentrations that are within five percent of the concentrations in the RLD. FDA describes this type of qualitative and quantitative sameness of inactive ingredients as "Q1/Q2."

Additionally, FDA's regulations require Q1/Q2 sameness in two circumstances. First, FDA considers bioequivalence to be self-evident without the need for additional data if a generic injectable, ophthalmic, or otic solution is Q1/Q2 to the RLD.[6] This approach has been described as a "solution biowaiver." Second, FDA requires that generic injectable, ophthalmic, otic, or topical products be Q1/Q2 to the RLD to use the ANDA pathway, subject to exceptions.[7]

Accordingly, any Q1/Q2 requirement or recommendation is a creation of FDA and not of Congress. FDA has ample authority to approve ANDAs without any Q1/Q2 requirement, and to recommend and accept bioequivalence methods that are not based on a showing of Q1/Q2 sameness. Therefore, the disclosure of proprietary information that the bill would authorize is not necessary to enable ANDA applicants to comply with any statutory requirement.

Moreover, the bill would not restrict the disclosure of proprietary inactive ingredient information to the limited circumstances where FDA has required or recommended Q1/Q2 sameness. Rather, the bill would broadly authorize disclosure of such proprietary information about the RLD, even where such information is unnecessary to satisfy any FDA requirement or recommendation—or to the apparent intent of facilitating generic approvals.[8]

The Bill Raises Constitutional Issues

Disclosure of proprietary information as required by the bill also would raise constitutional issues under the Takings Clause of the Fifth Amendment to the U.S. Constitution.[9] This constitutional concern arises because the bill would interfere with sponsors' property rights, including their reasonable investment-backed expectation—rooted in the statutes and regulations

[4] *See id*. § 505(j)(8)(B).
[5] *Id*. § 505(j)(8)(C).
[6] 21 C.F.R. § 320.22(b)(1).
[7] 21 C.F.R. § 314.94(a)(9)(iii)-(v).
[8] In this way, the bill would go well beyond FDA's current practice of reviewing a proposed generic formulation for Q1/Q2 sameness to the RLD, which is limited to situations where FDA recommends or requires Q1/Q2 sameness in a regulation or guidance. FDA, Guidance for Industry, *Controlled Correspondence Related to Generic Drug Development*, at 12 (Dec. 2020) ("Consistent with the Agency's past and current practices, FDA does not intend to review proposed formulations that are neither required by regulation nor recommended in guidance to be Q1/Q2 to the RLD.").
[9] U.S. CONST. amend. V.

cited above governing disclosure[10]—that FDA will not disclose an RLD sponsor's proprietary inactive ingredient information. The bill therefore would effect a prohibited "taking" in the absence of just compensation, potentially subjecting the government to significant liability.[11]

[10] *See supra* note 4.

[11] *See Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1020 (1984); *see also Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978) (establishing test for regulatory takings); *Lucas v. S.C. Coastal Council*, 505 U.S. 1003, 1019 (1992) (establishing test for takings based on deprivation of all economically viable use of affected property).