UNITED STATES
FOOD AND DRUG ADMINISTRATION

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Considerations in Demonstrating Interchangeability with a Reference Product: Update; Draft Guidance for Industry	Docket No. FDA-2017-D-0154

COMMENT OF THE UNITED STATES
FEDERAL TRADE COMMISSION

FTC Comment
August 20, 2024

I. Introduction

The Federal Trade Commission ("FTC" or

scrutinizing brand drug companies' potentially improper listing of patents in the FDA's Orange Book, which can delay and deter entry of low-cost generic and biosimilar competitors.[21] Further, the FTC has supported rulemaking efforts of the U.S. Patent Office to curtail brand drug firms' patent thicket strategies, which increase patent barriers to generic and biosimilar entry by misusing terminal disclaimers.[22]

In July 2024, the FTC's Interim Staff Report on Pharmacy Benefit Managers ("Interim Staff Report") identified conduct by other market participants that can inhibit robust competition in generic and biologic marketplaces. In response to orders issued by the FTC to study the business practices of Pharmacy Benefit Managers,[23] the largest PBMs provided documents and information concerning their influence on the drugs prescribed to patients, the pharmacies patients can use, and how much patients ultimately pay at the pharmacy counter. Staff's initial review of agreements between brand drug companies and PBMs showed rebate structures that may impede competition and patient access to affordable medicines such as generics and biosimilars.[24] Additionally, the Interim Staff Report discussed how vertical integration of PBMs with pharmaceutical manufacturers may distort PBMs incentives. For example, CVS Caremark made formulary changes for Humira and its biosimilars that resulted in a sharp increase in prescriptions for Hyrimoz, a biosimilar from CVS's own private label, even though Hyrimoz was

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Permanent Injunction and Equitable Monetary Relief and Dismissal, FTC v. Reckitt Benckiser Group PLC, No. 1:19-cv-00028 (W.D. Va. filed Jul. 11, 2019), ECF No. 2, https://www.ftc.gov/system/files/documents/cases/reckitt_joint_motion_for_stipulated_order_7-11-19.pdf

[21] Press Release, Fed. Trade Comm'n, FTC Challenges More Than 100 Patents as Improperly Listed in the FDA's Orange Book (Nov. 7, 2023), https://www.ftc.gov/news-events/news/press-releases/2023/11/ftc-challenges-more-100-patents-improperly-listed-fdas-orange-book; Press Release, Fed. Trade Comm'n, FTC Expands Patent Listing Challenges, Targeting More Than 300 Junk Listings for Diabetes, Weight Loss, Asthma and COPD Drugs (Apr. 30, 2024), https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma; see also Press Release, Fed. Trade Comm'n, FTC Issues Policy Statement on Brand Pharmaceutical Manufacturers' Improper Listing of Patents in the Food and Drug Administration's 'Orange Book' (Sep. 14, 2023), https://www.ftc.gov/newsevents/news/press-releases/2023/09/ftc-issues-policy-statement-brandpharmaceutical-manufacturers-improper-listing-patents-food-drug ("The FDA appreciates and supports the FTC's efforts to examine whether brand drug companies are impeding generic drug competition by improperly listing patents in the Orange Book,' said FDA Commissioner Robert M. Califf, M.D.").

[22] Fed. Trade Comm'n, Comment of the U.S. Fed. Trade Comm'n on the United States Patent and Trademark Office's Proposed Rulemaking on Terminal Disclaimer Practice to Obviate Nonstatutory Double Patenting (July 9, 2024), https://www.ftc.gov/system/files/ftc_gov/pdf/FTC-Comment-on-USPTO-Terminal-Disclaimer-NPRM-7-9-2024.pdf

[23] Press Release, Fed. Trade Comm'n, FTC Launches Inquiry Into Prescription Drug Middlemen Industry (June 7, 2022), https://www.ftc.gov/news-events/news/press-releases/2022/06/ftc-launches-inquiry-prescription-drug-middlemen-industry

[24] Fed. Trade Comm'n, Interim Staff Report, Pharmacy Benef

not the lowest price product.[25] Hyrimoz's share of prescriptions jumped from five percent to 35 to 45 percent of adalumimab products within a month.[26]

In addition to these efforts, the FTC has also been working together with the FDA to help advance competition for biologics, including biosimilars and interchangeable biosimilars. On February 3, 2020, the FTC and the FDA issued a joint statement regarding collaborative efforts to advance competition in the biologic marketplace.[27] Among other things, this statement addressed the agencies' shared concerns about the misleading statements and their impact on competition and public health.[28] As the Joint Statement explained, "false or misleading comparisons of reference products and biosimilars may constitute unfair or deceptive practices that undermine confidence in biosimilars."[29] Following this statement, the FDA and the FTC held a public workshop, entitled "FDA/FTC Workshop on a Competitive Marketplace for Biosimilars,"[30] and later issued a joint report summarizing the workshop.[31] The workshop "highlighted serious concerns about false or misleading communications regarding reference, biosimilar, and interchangeable products, and the potential for such communications to negatively affect public health, patient access, and competition."[32] The joint report concluded that "false or misleading comparisons of reference products and biosimilars may constitute unfair or deceptive practices that undermine confidence in biosimilars."[33]

The FTC is committed to ensuring that healthcare professionals and patients receive truthful and non-misleading information about biosimilar and interchangeable biosimilar products. The FTC's law-enforcement efforts against deceptive advertising deter the dissemination of misleading information, including claims about healthcare products and services, and enable consumers to make well-informed decisions.[34]

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[25] FTC Interim Staff Report at 27-28.

[26] FTC Interim Staff Report at 28.

[27] Fed. Trade Comm'n, Joint Statement of the U.S. Food & Drug Admin. and Fed. Trade Comm'n Regarding a Collaboration to Advance Competition in the Biologic Marketplace [hereinafter "Joint Statement"] (Feb. 3, 2020), https://www.ftc.gov/legal-library/browse/joint-fda-ftc-statement-regarding-collaboration-advance-competition-biologic-marketplace.

[28] Joint Statement at 3.

[29] Id.

[30] FDA, Public Workshop: FDA/FTC Workshop on a Competitive Marketplace for Biosimilars (March 9, 2020), https://www.fda.gov/drugs/news-events-human-drugs/public-workshop-fdaftc-workshop-competitive-marketplace-biosimilars-03092020

[31] FDA & Fed Trade Comm'n, Summary Report, supra, at note 11.

[32] Id. at 24.

[33] Id.

[34] See, e.g., In re POM Wonderful, LLC, 155 F.T.C. 1 (2013), aff'd in part, POM Wonderful LLC v. FTC, 777 F.3d 478 (D.C. Cir. 2015) (deceptive treatment, prevention, and risk claims for heart disease, prostate cancer, erectile dysfunction, and other diseases); In re Daniel Chapter One, 148 F.T.C. 832 (2009) (deceptive cancer prevention,

III. The Draft Guidance Supports Increased Competition in Biologic Marketplaces

In order for a biosimilar to be designated by the FDA as interchangeable, the applicant must show that its product "can be expected to produce the same clinical result as the reference product in any given patient," and that "for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch."[35] As noted earlier, when the FDA designates a biosimilar product as "interchangeable," pharmacists can substitute that product for a biologic without prescriber intervention, consistent with state law. This system of pharmacy-level drug substitution for generic and biosimilar drugs supports increased access to treatments and price competition.

Under existing guidance, the FDA recommends that biosimilar applicants provide clinical switching studies to demonstrate that the biosimilar can be interchangeable with the reference biologic.[36] In clinical switching studies, patients are treated with an alternating regimen of the reference product and the biosimilar, and then those patients are compared to patients who did not receive alternating treatment regimens.[37] Clinical switching studies can be time-consuming and expensive, and in the Draft Guidance the FDA has concluded that they are no longer recommended for applications seeking an interchangeable designation.[38]

Relying on clinical switching studies to establish interchangeability has likely contributed to marketplace confusion about biosimilars. The FDA itself has recognized that the distinction between biosimilars and interchangeable biosimilars creates confusion for patients and providers

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loss claims); FTC v. Direct Mktg. Concepts, Inc., 569 F. Supp. 2d 285 (D. Mass. 2008), 624 F.3d 1 (1st Cir. 2010) (deceptive prevention, treatment, and cure claims for cancer, Parkinson's disease, heart disease, diabetes, and autoimmune diseases such as multiple sclerosis and lupus); FTC v. QT, Inc., 448 F. Supp. 2d 908 (N.D. Ill. 2006), aff'd, 512 F.3d 858 (7th Cir.) (deceptive pain relief claims); In re Novartis Corp., 127 F.T.C. 580, 1999 WL 33913005 (May 13, 1999), aff'd, Novartis Corp. v. FTC, 223 F.3d 783 (D.C. Cir. 2000) (deceptive back pain remedy claims).

[35] Public Health Service Act ("PHS Act") §§ 351(k)(4)(A)(ii) and (k)(4)(B).

[36] Draft Guidance at 3, *supra* note 9 ("In the Interchangeability Guidance, the Agency recommended that applications or supplements seeking a determination of interchangeability include data from a switching study or studies to help provide the added assurance with respect to any immunogenicity risk associated with switching or alternating between the reference product and the proposed interchangeable biosimilar."). Switching studies are sometimes referred to as immunogenicity studies.

[37] See FDA, FDA Review and Approval, "Are there additional data requirements for interchangeable biosimilar products?", https://www.fda.gov/drugs/biosimilars/review-and-approval.

[38] Draft Guidance at 4 (explaining that over the last several years the agency has gained further experience and confidence using current analytical technologies to evaluate the potential clinical differences between proposed biosimilar products and their reference products and to help characterize the structure of the products and predict their functional effect); see also Lauren Biscaldi, Hurdles in Access: Costly Switch Studies Block Wider Biosimilar Use, Drug Topics (May 2, 2024), https://www.drugtopics.com/view/hurdles-in-access-costly-switch-studies-block-wider-biosimilar-use.

biosimilar products approved by the FDA as of July 1, 2024, there are 43 that are not designated as interchangeable.[47] There is no guidance for how an already-approved biosimilar may request an interchangeable designation under the simplified process. Applying the draft guidance to all biosimilars, including already-approved products that treat conditions affecting large patient populations, such as insulins and Humira biosimilars, would support increased access to biosimilars and facilitate patient choice among safe and effective treatments.

Further, to ensure Americans receive the benefits of the increased access to interchangeable biosimilars that FDA's revised guidance would support, agencies must continue to be attentive to the risk that anticompetitive practices, if left unchecked, could foreclose or forestall such access. For example, the Commission's Interim Staff Report on Pharmacy Benefit Managers exposed that some brand pharmaceutical companies and PBMs are entering contracts that categorically prohibit insurance from reimbursing pharmacists who fill a prescription with a