Statement of the Federal Trade Commission
to the Department of Health and Human Services
Regarding the HHS Blueprint to Lower Drug Prices and
Reduce Out-of-Pocket Costs

July 16, 2018

The Federal Trade Commission ("Commission" or "FTC")[1] submits the following comments in response to the Department of Health and Human Services' ("HHS") call for public comments on the *Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs* ("Blueprint").[2] According to the Blueprint, HHS seeks to "increase competition and end the gaming of regulatory processes that may keep drug prices artificially inflated or hinder generic, branded, or biosimilar competition."[3]

Competition brings substantial benefits to consumers through lower prices, greater access to higher quality goods and services, and increased innovation. As one of the two federal agencies charged with enforcing the nation's antitrust laws, the FTC supports efforts to promote and preserve competition by reducing abuses of regulatory processes and, where necessary, clarifying regulations that may unduly limit competition.

Health care competition has long been a Commission priority because of its critical importance to consumers and the economy. In particular, for many years, the Commission has engaged in enforcement, study, and advocacy to promote competition in drug markets. Drawing on this significant experience, the Commission focuses this statement on two areas identified in the Blueprint: (1) combatting abuse of Risk Evaluation and Mitigation Strategies ("REMS");[4]

[1] The FTC approved this statement by a vote of 5-0.

[2] *HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs*, 83 Fed. Reg. 22,692 (May 16, 2018), https://www.gpo.gov/fdsys/pkg/FR-2018-05-16/pdf/2018-10435.pdf [hereinafter "Blueprint"].

[3] Blueprint, *supra* note 2, at 22,692.

[4] *See id*., at 22,695-96. As the Blueprint explains:

and (2) spurring biologics competition. Both areas are a high priority for the Commission because they significantly affect U.S. health care expenditures. Any reduction in competition in these areas can cause substantial consumer harm, and any additional competitive pressure on prices can lead to significant consumer benefit. In addition, as our statement explains, a tension between regulation and competition underlies each of these areas.[5]

I. FTC Interest and Experience in Pharmaceutical[6] Markets

The FTC is an independent administrative agency charged by Congress with protecting consumers by enforcing competition and consumer protection laws.[7] The FTC is primarily responsible for federal antitrust enforcement in the pharmaceutical industry.[8] It has devoted significant resources to examining the health care industry by sponsoring workshops and studies on topics such as generic drug entry prior to patent expiration, the impact of authorized generic drugs, and the proper role of competition in addressing challenges in health care markets.[9] Most recently, in 2017, the FTC collaborated with the Food and Drug Administration ("FDA") on two

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> Certain prescription drugs are subject to limitations on distribution. Some of these distribution limitations are imposed by the manufacturer, while others may be imposed in connection with an FDA-mandated [REMS]. Some manufacturers may be gaming these distribution limitations to prevent generic developers from accessing their drugs to conduct the tests that are legally required for a generic drug to be brought to market, thereby limiting opportunities for competition that could place downward pressure on drug prices.

Id. This statement focuses on REMS containing restricted distribution systems mandated by the FDA.

[5] *See e.g.*, FED. TRADE COMM'N & U.S. DEP'T OF JUSTICE, IMPROVING HEALTH CARE: A DOSE OF COMPETITION (2004) [hereinafter FTC/DOJ Health Care Report], https://www.ftc.gov/sites/default/files/documents/reports/-improving-health-care-dose-competition-report-federal-trade-commission-and-department-justice/040723healthcarerpt.pdf.

[6] The term "pharmaceuticals" used throughout this comment includes both drug and biologics. Further, the term "branded manufacturer" includes both branded drug and reference biologic manufacturer.

[7] 15 U.S.C. §§ 41-58.

[8] *See* FED. TRADE COMM'N, OVERVIEW OF FTC ANTITRUST ACTIONS IN PHARMACEUTICAL PRODUCTS AND DISTRIBUTION (2017), https://www.ftc.gov/system/files/attachments/competitionpolicyguidance-/overview_pharma_april_2017.pdf.

[9] *See, e.g.*, FED. TRADE COMM'N, AUTHORIZED GENERIC DRUGS: SHORT-TERM EFFECTS AND LONG-TERM IMPACT (2011), https://www.ftc.gov/sites/default/files/documents/reports/authorized-generic-drugs-short-term-effects-and-long-term-impact-report-federal-trade-commission/authorized-generic-drugs-short-term-effects-and-long-term-impact-report-federal-trade-commission.pdf; FTC/DOJ Health Care Report, *supra* note 5; FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY (2002), https://www.ftc.gov/sites/-default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf; Fed. Trade Comm'n & U.S. Dep't of Justice Workshop Series, *Examining Health Care Competition* (Mar. 20-21, 2014 & Feb. 24-25, 2015), https://www.ftc.gov/news-events/events-calendar/2014/03/examining-health-care-competition, https://www.ftc.gov/news-events/events-calendar/2015/02/examining-health-care-competition.

public events: one examining regulatory barriers in pharmaceutical markets;[10] and the other on the role of intermediaries in the distribution of pharmaceuticals.[11] Over its many decades of experience evaluating health care competition, the FTC has gained a deep understanding of the market dynamics that contribute to robust pharmaceutical competition.

Of particular relevance to this comment are the Commission's two *amicus curiae* briefs and recent Congressional testimony detailing the FTC's concern that branded pharmaceutical manufacturers may misuse certain REMS to thwart generic competition,[12] and policy and advocacy work regarding competition in biologic product markets.[13]

II. Branded Pharmaceutical Manufacturers' Misuse of REMS May Impede Competition

For pharmaceuticals with certain potential safety risks, the FDA may require a REMS. REMS are strategies intended to manage the known or potential safety risks associated with the use or distribution of certain pharmaceutical products. In some cases, implementation of a REMS

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[10] Food & Drug Admin., Public Meeting, *The Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access* (July 18, 2017), https://www.gpo.gov/fdsys/pkg/FR-2017-06-22/pdf/2017-12641.pdf.

[11] Fed. Trade Comm'n, Public Workshop, *Understanding Competition in Prescription Drug Markets: Entry and Supply Chain Dynamics* (Nov. 8, 2017), https://www.ftc.gov/news-events/events-calendar/2017/11/understanding-competition-prescription-drug-markets-entry-supply. As explained by former Acting Chairman Ohlhausen during her opening remarks at this event, "[c]ompetition is key to containing prescription drug costs. . . . In light of concerns about rising drug prices, it's critical we identify barriers that may prevent drugs from entering the market, even after applicable patent protections have expired." *Id.*

[12] *See* Fed. Trade Comm'n Brief as *Amicus Curiae*, *Mylan Pharm., Inc. v. Celgene Corp.*, No. 2:14-CV-2094 (D.N.J. June 17, 2014), https://www.ftc.gov/policy/advocacy/amicus-briefs/2014/06/mylan-pharmaceuticals-inc-v-celgene-corporation; Fed. Trade Comm'n Brief as *Amicus Curiae*, *Actelion Pharm. Ltd. v. Apotex Inc.*, No. 1:12-cv-05743 (D.N.J. Mar. 11, 2013), http://www.ftc.gov/sites/default/files/documents/amicus_briefs/actelion-pharmaceuticals-ltd.et-al.v.apotex-inc./130311actelionamicusbrief.pdf; *Antitrust Concerns and the FDA Approval Process Hearing Before the H. Jud. Comm., Subcomm. on Reg. Reform, Commercial and Antitrust Law*, 115th Cong. (2017) [hereinafter 2017 FTC Congressional Testimony], https://docs.house.gov/meetings/JU/JU05/-20170727/106333/HHRG-115-JU05-Wstate-MeierM-20170727.pdf.

[13] The FTC held several workshops from 2008 to 2015, issued a report on biologics in 2009, and submitted a public comment to the FDA in 2015. *See* Fed. Trade Comm'n, Public Workshop, *Follow-On Biologic Drugs: Framework for Competition and Continued Innovation* (Nov. 21, 2008), https://www.ftc.gov/news-events/events-calendar/2008/11/emerging-health-care-competition-consumer-issues-competition; FED. TRADE COMM'N, EMERGING HEALTHCARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION (2009) [hereinafter FTC FOB REPORT], https://www.ftc.gov/sites/default/files/documents/reports/emerging-health-care-issues-follow-biologic-drug-competition-federal-trade-commission-report/p083901biologicsreport.pdf; Fed. Trade Comm'n, Public Workshop, *Follow-On Biologics Workshop: Impact of Recent Legislative and Regulatory Naming Proposals on Competition*, 78 Fed. Reg. 68,840 (Nov. 15, 2013), https://www.ftc.gov/sites/default/files/documents/federal_register_notices/2013/11/131115biologicsfrn.pdf; Fed. Trade Comm'n, *Staff Comment to FDA on Draft Guidance for Industry on the Nonproprietary Naming of Biological Products* (Oct. 27, 2015) [hereinafter 2015 FTC Naming Comment], https://www.ftc.gov/system/files/documents/advocacy_documents/ftc-staff-comment-submitted-food-drug-administration-response-fdas-request-comments-its-guidance/151028fdabiosimilar.pdf.

may involve restricting distribution of a pharmaceutical to ensure that its benefits outweigh its risks. But when branded manufacturers misuse REMS to thwart entry by would-be generic competitors, they threaten to upset the careful balance between competition and innovation that Congress established in the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act ("BPCIA"). REMS abuse can occur in two ways.

- *First*, for products subject to REMS with restricted distribution systems, branded manufacturers sometimes invoke REMS requirements improperly to justify their refusal to make samples of their products available to firms seeking to obtain FDA approval of generic or biosimilar products.[14]

- *Second*, if a competing firm applies for FDA approval of a generic, biosimilar, or interchangeable product, the branded manufacturer may improperly deny that competitor access to a single, shared REMS system, which leaves the FDA unable to approve the competitor's application and labeling.[15]

Using either strategy, a branded manufacturer could exploit a REMS system to delay – or block indefinitely – an entrant poised to become its closest competition.

Below, we provide additional detail about the competitive problems posed by each of these strategies. Given the potential limitations of antitrust enforcement to address these problems, we also outline and reiterate our support for carefully considered regulatory and legislative efforts to address REMS abuses.

A. Denial of Reference Product Samples

The Hatch-Waxman Act and the BPCIA establish abbreviated routes to market for firms able to demonstrate to the FDA that their products are equivalent to a branded pharmaceutical or biologic product.[16] These abbreviated regulatory pathways rely on branded manufacturers making samples of their product available for purchase on the open market by firms wishing to develop and obtain FDA approval for lower-cost alternatives. But when the branded product is subject to a restricted distribution REMS, samples typically are not available for purchase through customary pharmaceutical distribution channels, because of strict limitations on how those products can be sold.[17] In these instances, a branded manufacturer may prevent a firm that needs to conduct bioequivalence testing from obtaining samples. As HHS stated in the Blueprint:

[14] We note that branded pharmaceutical manufacturers sometimes restrict distribution of their products voluntarily – without an FDA requirement that they do so – and that those voluntary restrictions on distribution may have the same anticompetitive effect as misuse of FDA-required REMS.

[15] *See* 2017 FTC Congressional Testimony, *supra* note 12.

[16] For a description of the time and costs differences to obtain FDA approval of a generic drug compared to a branded drug, as well as between a biosimilar and reference biologic, *see* FTC FOB REPORT, *supra* note 13, at Chapter 1 and Appendix A.

[17] *See* Blueprint, *supra* note 2, at 22,696.

> In some instances for products that are subject to REMS that impact distribution, manufacturers continue to restrict access to generic developers even after the FDA issues a letter stating that it has favorably evaluated the developers' proposed safety protections for testing and would not consider the provision of drug samples to this developer for generic development to violate the applicable REMS.[18]

By improperly blocking the product developer from obtaining samples, the branded manufacturer can potentially delay or indefinitely block generic or biosimilar competition to its product, thereby reducing the competition that Congress specifically sought to facilitate via the Hatch-Waxman Act and the BPCIA.[19]

The FTC continues to monitor legal and regulatory developments in this area. For example, the FTC has investigated allegations that restrictions on the distribution of certain branded drug products are preventing generic firms from offering competing generic versions of those products.[20] In 2017 Congressional testimony and 2013 and 2014 *amicus curiae* briefs, the FTC explained that, under certain circumstances, a branded firm's refusal to sell product samples to a potential competitor may violate the antitrust laws.[21] To date, the Commission has not filed any law enforcement action challenging conduct in this area.

The FDA, similarly, has taken a number of steps to provide additional transparency and guidance in this area, including:

- recent release of a list identifying all drug products for which prospective generic competitors have reported an inability to obtain branded product samples, as well as the brand manufacturer and the number of such reports;[22]

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[18] *See* Blueprint, *supra* note 2, at 22,696-97.

[19] A more complete description of the Hatch-Waxman Act's balancing of innovation and competition is contained in the Commission's recent *amicus curiae* briefs on the REMS issue. *See* Fed. Trade Comm'n Brief as *Amicus Curiae*, *Mylan*, *supra* note 12; Fed. Trade Comm'n Brief as *Amicus Curiae*, *Actelion*, *supra* note 12.

[20] *See* 2017 FTC Congressional Testimony, *supra* note 12. The Commission's *amicus* briefs in the *Mylan* and *Actelion* cases explained that the Hatch-Waxman regulatory framework cannot function as Congress intended if generic firms are unable to obtain samples of branded products. Even if the generic firms prevail in their antitrust actions against the branded firms, and subsequent appeals therefrom, these litigations take many years and can create substantial delays in obtaining the needed samples and a corresponding delay in generic approval. Accordingly, even a successful antitrust challenge to REMS abuse is unlikely to provide immediate redress. *See* Fed. Trade Comm'n Brief as *Amicus Curiae*, *Mylan*, *supra* note 12; Fed. Trade Comm'n Brief as *Amicus Curiae*, *Actelion Pharm.*, *supra* note 12.

[21] *See* 2017 FTC Congressional Testimony, *supra* note 12; Fed. Trade Comm'n Brief as *Amicus Curiae*, *Mylan*, *supra* note 12; Fed. Trade Comm'n Brief as *Amicus Curiae*, *Actelion Pharm.*, *supra* note 12.

[22] *See* FOOD & DRUG ADMIN., *Reference Listed Drug (RLD) Access Inquiries*, https://www.fda.gov/Drugs-/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm.

- 2014 publication of draft guidance detailing how generic firms seeking to enter with generic versions of drugs covered by restricted distribution REMS may obtain letters validating that their safety protocols are comparable to the branded firm's safety protocols;[23] and

- continuing public statements highlighting the potential problems arising from branded firm's misuse of restricted distribution systems.[24]

The FTC commends the FDA on these efforts, and supports the FDA's efforts to highlight misuse of REMS with restricted distribution systems.[25]

B. Denial of Access to the Single, Shared System

Even if a would-be competitor obtains samples of a branded product, subject to a restricted distribution system or not, the branded manufacturer still can delay or deter market entry by denying access to its REMS system, commonly referred to as a shared system REMS. A shared system REMS encompasses multiple prescription drug products and is developed and implemented jointly by two or more firms. Branded and generic drug manufacturers must – as a condition of FDA approval – use a single, shared system REMS, unless the FDA waives that requirement.[26] In practice, however, the FDA has rarely granted such a waiver. This can create a strong strategic incentive for the branded firm to refuse to cooperate with the generic entrant in order to delay generic entry.[27]

The FDA has recognized this concern. In a statement announcing the FDA's two recent draft guidance documents on shared system REMS, Commissioner Gottlieb highlighted the risk that the shared system REMS requirements could "become a tool that drug companies can use to delay or block competition from generic products or hinder their ability to enter the market."[28]

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[23] FOOD & DRUG ADMIN., *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD: Guidance for Industry* (2014), https://www.fda.gov/-downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425662.pdf.

[24] *See e.g.*, Scott Gottlieb, M.D., Comm'r, Food & Drug Admin., *Understanding Competition in Prescription Drug Markets: Entry and Supply Chain Dynamics* (Nov. 8, 2017), https://www.fda.gov/NewsEvents/Speeches/ucm584195.htm.

[25] *See Antitrust Concerns and the FDA Approval Process, Hearing Before the H. Jud. Comm., Subcomm. on Reg. Reform, Commercial and Antitrust Law*, 115th Cong. (July 27, 2017) (statement of Scott Gottlieb, Comm'r, Food & Drug Admin.), https://docs.house.gov/meetings/JU/JU05/20170727/106333/HHRG-115-JU05-Wstate-GottliebS-20170727.pdf; 2017 FTC Congressional Testimony, *supra* note 12.

[26] 21 U.S.C. § 355-1(i).

[27] *See* 2017 FTC Congressional Testimony, *supra* note 12.

[28] Food & Drug Admin., *Statement from FDA Comm'r Gottlieb, New Policies to Reduce the Ability of Brand Drug Makers to Use REMS Programs as a Way to Block Timely Generic Drug Entry, Helping Promote Competition and Access* (May 31, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609365.htm.

As Commissioner Gottlieb explained, "the generic drug maker has to negotiate with the brand firm to enter into shared REMS programs before the generic drug can be approved. We know that these negotiations between a brand and generic company – to reach agreement on shared system REMS – can extend for long periods of time. This can delay market entry of a generic drug."[29] The FDA's two draft guidance documents are intended to help generic firms navigate the shared REMS issue. They describe "general principles and recommendations" for developing shared REMS systems and "when and how the FDA will consider waiving" the shared REMS requirement.[30]

The FTC supports the FDA's efforts to clarify the circumstances under which it will grant waivers of the shared REMS requirement. Clarity on the shared REMS issue is particularly important because, as explained in the FTC's recent Congressional testimony, at least one court has held that the existence of the waiver option bars an antitrust claim centered on a branded manufacturer's refusal to grant its competitor access to its REMS.[31] Under current law, it seems unlikely that the prospect of antitrust liability alone will create the proper incentives for branded and generic firms to reach agreement on a shared REMS program.

C. Regulatory and Legislative Action to Address REMS Misuse

As explained in sections II.A and II.B above, the FTC supports the FDA's efforts to bring clarity and transparency to the REMS issues. The FTC stands ready to work with the FDA on these and other issues of importance to competition and consumers.

In addition, the FTC has supported well-crafted legislation aimed at correcting the misuses of REMS related to obtaining branded product samples and accessing shared REMS systems. A legislative solution to these issues could avoid the uncertainty of litigation and, unlike a lengthy antitrust case, provide an immediate solution to this challenging problem. Legislation also could provide a clearer path for competing firms to establish separate FDA-approved REMS programs.[32]

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[29] *Id*.

[30] *Id*.; FOOD & DRUG ADMIN., *Development of a Shared System REMS: Guidance for Industry* (June 2018), https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM609045.pdf; FOOD & DRUG ADMIN., *Waivers of the Single, Shared System REMS Requirement: Guidance for Industry* (June 2018), https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/-UCM609048.pdf.

[31] *See* 2017 FTC Congressional Testimony, *supra* note 12. The case was *In re Suboxone Antitrust Litigation*, 64 F. Supp. 3d 665, 685-688 (E.D. Pa. 2014).

[32] *See* 2017 FTC Congressional Testimony, *supra* note 12.

III. Regulatory Uncertainty May Create Undue Barriers to Biosimilar Development, Approval, Education, and Access

Biologics have become a mainstay of modern medicine, comprising a third of all new medicines approved by the FDA annually.[33] Biologics are used to treat a variety of serious medical conditions for which patients have no other therapeutic alternative, including rare genetic disorders, autoimmune diseases, and cancer.[34] But biologics are, on average, 22 times more expensive than traditional medications.[35] Some biologic drugs cost more than $200,000 per year. Biologics' prices also are increasing about 10 to 15 percent each year.[36] Consequently, biologics comprise the fastest growing and one of the most expensive segments of prescription medicine spending.[37] The federal government spends more than $5 billion each year on biologic therapies through the Medicare and Medicaid programs.[38]

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[33] Food & Drug Admin., *Statement from FDA Comm'r Scott Gottlieb, M.D., Capturing the Benefits of Competition for Patients* (Mar. 7, 2018), https://www.fda.gov/NewsEvents/Speeches/ucm599833.htm.

[34] *Id.* ("Taken together, biologics now account for about 40% of all U.S. drug spending -- and 70% of spending growth.").

[35] *See* SCOTT MORTON, L.T BOLLER, *Enabling Competition in Pharmaceutical Markets*, Brookings, Hutchins Center Paper #30, at 6 (May 2017), https://www.brookings.edu/wp-content/uploads/2017/05/wp30_scottmorton_-competitioninpharma1.pdf (*citing* Statement of Ed Weisbart, M.D., Chief Med. Officer, Express Scripts, *Hearing Before the Subcomm. on Health of the Comm. on Energy and Commerce*, 125, 128 (May 2, 2007), https://www.gpo.gov/fdsys/pkg/CHRG-110hhrg40500/pdf/CHRG-110hhrg40500.pdf) ("The average cost per day of a biopharmaceutical is $45 compared with $2 per day for a traditional medicine."), https://www.brookings.edu/wp-content/uploads/2017/05/wp30_scottmorton_competitioninpharma1.pdf; *see also* Express Scripts 2017 Drug Trend Report, http://lab.express-scripts.com/lab/drug-trend-report/2017-dtr; *Medicines use and spending in the U.S.*, IQVIA INSTITUTE (May 4, 2017), https://www.iqvia.com/institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2016.

[36] MORTON & BOLLER, *supra* note 35; Gottlieb, *supra* note 33.

[37] *See* DEP'T HEALTH & HUM. SERVS, OFFICE OF THE ASS'T SEC'Y PLANNING AND EVAL., *Observations on Trends in Prescription Drug Spending* (Mar. 8, 2016), https://aspe.hhs.gov/sites/default/files/pdf/187586/Drugspending.pdf; MEDPAC, *Medicare Part B drug payment policy issues*, Table 2-1 (June 2017) (9 of the 10 top spending Part B drugs are biologics), http://medpac.gov/docs/default-source/reports/jun17_ch2.pdf?sfvrsn=0; ALLAN COUKELL, CHUCK SHIH, *What's Driving Increased Pharmaceutical Spending?*, PEW (May 26, 2016), http://www.pewtrusts.org/en/research-and-analysis/analysis/2016/05/26/whats-driving-increased-pharmaceutical-spending; PEW, A Look at Drug Spending in the U.S., http://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2018/02/a-look-at-drug-spending-in-the-us.; IQVIA, Medicine Use And Spending in the United States (2017), https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us-a-review-of-2017-and-outlook-to-2022.pdf; THE BIOSIMILARS COUNCIL, *The Next Frontier for Improved Access to Medicines: Biosimilars and Interchangeable Biologic Products* 14 (2015), http://www.biosimilars-council.org/pdf/GPhA-biosimilars-handbook.pdf (annual U.S. spending on biologic drug therapies in the United States exceeding $100 billion). Several biologics covered by Medicare cost more than $50,000 per beneficiary per year. U.S. Gov't Accountability Office, *Report to the Ranking Member, Comm. on the Budget, House of Representatives*, 19 Tbl. 4 (Oct. 2015), http://www.gao.gov/assets/680/673304.pdf; *see also* Judith A. Johnson, CONG. RESEARCH SERV., *Biologics and Biosimilars: Background and Key Issues* 2 (Sept. 7, 2016), https://fas.org/sgp/crs/misc/R44620.pdf.

[38] GAO, *supra* note 37; *see also* JOHNSON, *supra* note 37.

Considering the high and growing costs of biologics, patients would benefit from increased competition between biologics and biosimilars. Congress has indicated its willingness to foster biosimilar competition, once top-selling biologics lose their patent exclusivity.[39] But certain FDA regulatory processes may erect undue barriers to biosimilar and interchangeable development, approval, education, and access. To date, no FDA-approved biosimilar has obtained an interchangeable designation.

The FTC has experience studying the market for biologic drugs. In 2009, the FTC issued a report that expressed concerns about the market factors likely to limit biologic competition, including: (1) lack of state-level automatic substitution laws for biosimilar products; (2) potential chilling effects if products do not share the same nonproprietary chemical names; and (3) market acceptance of biosimilar drugs.[40] In 2015, FTC staff submitted a comment to the FDA on its draft guidance on nonproprietary naming of biologics. In that comment, the FTC expressed concerns that the guidance recommendation for a four-letter "distinguishing suffix that is devoid of meaning,"[41] appended to the active ingredient root name, may hinder consumer acceptance and biosimilar price competition.[42]

This section discusses the limited biosimilar competition that has occurred to date and suggests that the FDA consider certain steps to improve biosimilar and interchangeable competition. Specifically, we recommend the FDA: (1) continue to create a pathway for expedited approval of interchangeable biologics; (2) reconsider the current naming guidance for biologics in light of the Blueprint; and (3) improve the Purple Book.

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[39] *See* Rep. Anna Eshoo letter to the FDA (Apr. 20, 2012); *Eshoo Statement on First FDA Approval of Biosimilar Medicine* (statement of Rep. Eshoo, Member, Senior Member, House Comm. Energy & Commerce) (Mar. 6, 2015), https://eshoo.house.gov/issues/health-care/eshoo-statement-on-first-fda-approval-of-biosimilar-medicine/; Senate Comm. on Health, Educ., Labor & Pensions, Press Release, *Lawmakers Praise Committee Passage of Biologics Legislation*, 110th Cong. (June 27, 2007), https://www.help.senate.gov/ranking/newsroom/press/lawmakers-praise-committee-passage-of-biologics-legislation.

[40] FTC FOB REPORT, *supra* note 13. Prior to issuing this report, the FTC held a public workshop to examine these issues. *See* FED. TRADE COMM'N, *Public Workshop, Follow-On Biologic Drugs: Framework for Competition and Continued Innovation* (Nov. 21, 2008), https://www.ftc.gov/news-events/events-calendar/2008/11/emerging-health-care-competition-consumer-issues-competition.

[41] FOOD & DRUG ADMIN., *Guidance for Industry: Nonproprietary Naming of Biological Products*, at 8 (Jan. 2017) ("A distinguishing suffix that is devoid of meaning and composed of four lowercase letters will be attached with a hyphen to the core name of each originator biological product, related biological product, or biosimilar product."), https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf.

[42] *See* 2015 FTC Naming Comment, *supra* note 13. Prior to submitting this comment, the FTC held a public workshop in 2014 to examine how regulatory proposals regarding state substitution laws and biologic naming systems may help or hinder biologic competition. *See* FED. TRADE COMM'N, *Public Workshop: Follow-On Biologics Workshop: Impact of Recent Legislative and Regulatory Naming Proposals on Competition* (Feb. 4, 2014), https://www.ftc.gov/news-events/events-calendar/2014/02/follow-biologics-workshop-impact-recent-legislative-regulatory.

A. Limited Biosimilar Competition to Date

Congress passed the BPCIA in 2009 to foster competition between and among biologics, biosimilars, and interchangeable biosimilars, as well as to support continued innovation of new biologic products.[43] The BPCIA was modeled on the decades-long success of the Hatch-Waxman Act in facilitating competition by lower-cost generic products in small-molecule pharmaceutical markets. The BPCIA mandated an abbreviated regulatory approval process for biosimilars and interchangeables and required the FDA to promulgate guidance implementing the statute.[44] The FDA issued three final industry guidances for biosimilar approval in 2015.[45] Since that time, the FDA has approved eleven biosimilars in the United States.[46] Only three of them are commercially available.[47]

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[43] *See Lawmakers Praise Committee Passage of Biologics Legislation*, *supra* note 39; statement of Rep. Eshoo, *supra* note 39 ("Seven years ago, I authored legislation with Senator Edward Kennedy to create a pathway for the approval of generic versions of biologics, known as 'biosimilars.'").

[44] Under the BPCIA, the FDA is authorized to approve biosimilar versions of the reference biologics if it finds that "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." 42 U.S.C. § 262 (i)(2). To meet the higher standard of "interchangeability," an applicant must demonstrate that the biosimilar can be expected to produce the same clinical result as the reference product in any given patient and, if the biologic is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biological and the reference product is not greater than the risk of using the reference product without such alternation or switch. 42 U.S.C § 262 (i)(3). Interchangeable biosimilars may be substituted for the reference product by a pharmacist without the intervention of the prescribing healthcare provider. 42 U.S.C. § 262(i)(3). While biosimilars are not automatically substitutable at the pharmacy, interchangeable biosimilars are capable of automatic substitution if such substitution is permitted under the relevant state's pharmacy law. *See also* FOOD & DRUG ADMIN., *Guidance for Industry on Biosimilars: Q&A's Regarding Implementation of the BPCIA of 2009: Background*, https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/-ucm259806.htm.

[45] FOOD & DRUG ADMIN., *Biosimilars*, http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/-Guidances/ucm290967.htm.

[46] Sue Sutter, *US FDA's Biosimilars Program: Five Years in, Complete Response Letters Still Outnumber Approvals*, PINK SHEETS (May 29, 2018), https://pink.pharmaintelligence.informa.com/PS123179/US-FDAs-Biosimilars-Program-Five-Years-In-Complete-Response-Letters-Still-Outnumber-Approvals. As of June 13, 2018, FDA had approved 11 biosimilars. *See* FDA, *Biosimilar Product Information*, https://www.fda.gov/biosimilarlist.-htm.

[47] Avalere, *Use of Step Through Policies for Competitive Biologics Among Commercial US Insurers* (May 2018), http://avalere-health-production.s3.amazonaws.com/uploads/pdfs/1525698973_Use_of_Step_Through_-Policies_for_Competitive_Biologics_Among_Commercial_US_Insurers.pdf. As of January 2018, 60 biosimilars were enrolled in the FDA's Biosimilar Development Program, targeting 27 different reference biologics products. Of the 11 biosimilars FDA-approved for marketing in the United States, only three are currently marketed. No interchangeables have been approved yet. Gottlieb, *supra* note 33 ("Despite our efforts, however, of the nine products we've approved for marketing in the U.S., only three are currently marketed. Delays may be attributed, in part, to ongoing litigation.").

When Congress passed the BPCIA nine years ago, the Congressional Budget Office estimated that the statute would reduce total U.S. expenditures on biologics by $25 billion over a ten-year period, with $5.9 billion of those savings accruing to the federal government.[48] But the market for biosimilars and interchangeables has evolved more slowly than predicted, and those savings have yet to fully materialize. Recent analysis estimates the actual savings from biosimilar competition to be $240 million over a nine-year period – a fraction of the originally anticipated savings.[49] Several factors, discussed below, may have contributed to limited market penetration of biosimilars, including FDA regulatory choices that have imposed barriers relating to interchangeability and naming.[50]

Although market penetration of biosimilars has been limited, the three biosimilars launched in the United States have generated estimated discounts ranging from 15 to 45 percent off reference biologic prices.[51] In Europe, biosimilar laws were passed several years before the BPCIA, and the European Medicines Agency ("EMA") (the FDA equivalent agency in Europe) has approved 43 biosimilars.[52] While there are several reasons that European market dynamics are different from those in the United States,[53] biosimilar competitors in the EU have reportedly

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[48] CONGRESSIONAL BUDGET OFFICE, *Cost Estimate: S. 1695 Biologics Price Competition and Innovation Act of 2007*, (2008), https://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/94xx/doc9496/s1695.pdf.

[49] *See* Avalere, *supra* note 47. Biosimilars could generate $54 billion in savings over 10 years, according to some estimates. *See* Andrew Mulcahy *et al.*, *Biosimilar Cost Savings in the United States*, RAND (Oct. 23, 2017), https://www.rand.org/pubs/perspectives/PE264.html; *Delivering on the Potential of Biosimilar Medicines. The Role of Functioning Competitive Markets. IMS Institute for Healthcare Informatics*, IQVIA (Mar. 2016), https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/delivering-on-the-potential-of-biosimilar-medicines.pdf.

[50] Richard Frank, *Friction in the Path to Use of Biosimilar Drugs*, NEJM (Mar. 2018), https://www.nejm.org/doi/full/10.1056/NEJMp1714908?query=featured_home.

[51] *See* Ben Hirschler & Michael Shields, *Novartis launches first U.S. 'biosimilar' drug at 15 percent discount*, REUTERS (Sept. 3, 2015), https://www.reuters.com/article/us-novartis-drug/novartis-launches-first-u-s-biosimilar-drug-at-15-percent-discount-idUSKCN0R30C220150903 ("the 15 percent discount is the same price gap when Zarxio was launched in Europe in 2009, although the discount in Europe has since widened to an average or around 20 to 30 percent."); *see also* Mulcahy, *supra* note 49; Kesselheim, *et al*, *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 (8) JAMA 858–71 (Aug. 23–30, 2016) (economic studies showing that pre-rebate price reductions for biosimilars are as great as 30-45 percent below the reference biologics list price).

[52] *See* European Medicines Agency, European Public Assessment Reports (EPAR) on Biosimilars, http://www.ema.europa.eu/ema/index.jsp?curl=pages%2Fmedicines%2Flanding%2Fepar_search.jsp&mid=WC0b01ac058001d124&searchTab=searchByAuthType&alreadyLoaded=true&isNewQuery=true&status=Authorised&keyword=Enter+keywords&searchType=name&taxonomyPath=&treeNumber=&searchGenericType=biosimilars&genericsKeywordSearch=Submit (visited Jun. 25, 2018); Ian Schofield, *EU Biosimilar Action: New Competitors for Remicade/Herceptin, Four More Products Await CHMP OK*, PINK SHEET (May 30, 2018), https://pink.pharmaintelligence.informa.com/PS123181/EU-Biosimilar-Action-New-Competitors-For-RemicadeHerceptin-Four-More-Products-Await-CHMP-OK.

[53] *See* Fiona Scott Morton *et al.*, *The Impact of the Entry of Biosimilars: Evidence form Europe*, HARVARD BUS. SCH. TECH & OPER. MGMT, at 43 (Working Paper No. 16-141) (Apr. 2018) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2812938 (in European countries after biosimilar entry "[q]uantities and dollar amounts of biosimilars that are purchased trend upward across almost all countries over time. . . . Prevailing market prices fall over time at an average rate of about 3.5 percentage points per year following biosimilar entry, and this decline is

generated price concessions of up to 75 percent off reference biologic prices due, in part, to greater biosimilar approvals and interchangeability.[54]

B. FDA Approval of Interchangeable Biologics Will Improve Biosimilar Competition

In January 2017, the FDA issued draft guidance for the approval of interchangeable biosimilars.[55] The agency has announced that it will issue its final guidance by May 2019.[56] The FTC encourages the FDA to issue final regulations on interchangeable biosimilars as quickly as possible, to encourage investment in interchangeable biosimilars by enhancing regulatory predictability. Experience with generic drugs teaches that automatic substitution is crucial for successful generic drug entry, market acceptance, and consumer savings. Interchangeable biosimilars are most likely to be eligible for automatic substitution at pharmacies. Automatic substitution likely will increase market acceptance and market penetration of biosimilars, resulting in more substantial consumer savings. Without an interchangeable designation, however, a biosimilar product must be specifically prescribed by a health care provider and

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even steeper in Epoetin and Filgrastim markets."); Henry Grabowski, *Biosimilar Competition: Lessons from Europe and Prospects for the US*, OHE (Oct. 2014), https://www.ohe.org/publications/biosimilar-competition-lessons-europe-and-prospects-us#.

[54] *See e.g.*, Ronny Gal, *Biosimilars:Adoption update in EU and US*, BERNSTEIN GLOBAL SPECIALTY PHARMA & US BIOTECH (Apr. 2018); Eric Palmer, *Deep Discounts Allow Remicade Biosimilar to grab 50% of Norway's Market*, FiercePharma (Apr. 22, 2015), https://www.fiercepharma.com/m-a/deep-discounts-allow-remicade-biosimilar-to-grab-50-of-norway-s-market ,(reporting 70 percent discount); Makkiko Kitamura, *Bullied in Norway, Merck Sees Sales of Blockbuster Dive*, BLOOMBERG BUSINESS (Apr. 22, 2015), https://www.bloomberg.com/news/articles/2015-04-22/merck-gets-bullied-in-norway-with-remicade-price-war ,("[W]hen Norway called for bids for this year, it widened its discount from 39 percent a year earlier to 69 percent of the original drug's $10,600-a-year tab. Hospira lost out by offering a price cut of only 51 percent, according to Madsen [Medical Director, Norwegian Medicines Agency]"); Grabowski, *supra* note 53; Morton, *supra* note 53; Pawal Kawalec *et. al.*, *Pricing and Reimbursement of Biosimilars in Central and Eastern European Countries*, FRONT PHARMACOL. (June 8, 2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5463127/.

[55] FOOD & DRUG ADMIN., *Considerations in Demonstrating Interchangeability with a Reference Product: Guidance for Industry* (Jan. 2017), https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation-/Guidances/UCM537135.pdf.

[56] FDA Commissioner Gottlieb announced an intention to publish a biosimilars action plan to enhance regulatory predictability for biosimilar development, encourage market acceptance, and foster competition. Additionally, the action plan would update the agency's January 2017 draft guidance on interchangeability, including allowing for easier extrapolation across indications. *See* Cathy Kelly, *US FDA Biosimilar Guidance Update Will Relax Interchangeability Standards*, PINK SHEET (Apr. 21, 2018), https://pink.pharmaintelligence.informa.com-/PS122952/US-FDA-Biosimilar-Guidance-Update-Will-Relax-Interchangeability-Standards ("one major issue that has arisen is the draft's strong recommendation that biosimilar developers only use US reference products to demonstrate interchangeability . . . an agency official recently indicated FDA may be open to use of non-US reference products in some cases."). Recently, the FDA has also withdrawn its guidance on biosimilar analytical studies. *See* Ed Silverman, *Frustrated at the Pace of Biosimilar Development, FDA Yanks a Draft Guidance*, RAPS (June 21, 2018), https://www.statnews.com/pharmalot/2018/06/21/fda-withdraws-biosimilars-guidance/; *see also* Michael Mezher, *FDA Withdraws Guidance on Biosimilar Analytical Studies*, RAPS (June 21, 2018), https://www.raps.org/news-and-articles/news-articles/2018/6/fda-withdraws-guidance-on-biosimilar-analytical-st.

cannot be automatically substituted for a reference biologic at the pharmacy level.[57] Thus, the lack of FDA guidance on interchangeable biosimilars likely hinders automatic substitution, along with the associated market acceptance and consumer cost savings.

FDA guidance is crucial to clinical trial development for interchangeable biosimilars. In the absence of final FDA guidance, companies face significant uncertainty regarding how to construct and conduct the pivotal clinical trials that would prove interchangeability.[58] Indeed, no FDA-approved biosimilar has yet obtained an interchangeable designation, suggesting that the absence of guidance may be contributing to delays in the investment, application, approval, and entry of interchangeable biologics that otherwise would likely provide the greatest price competition in these markets. FDA Commissioner Gottlieb has recognized that "greater scientific and regulatory clarity for sponsors, and greater efficiencies in the review of biosimilar and interchangeable applications," would increase competition and benefit American consumers.[59]

As an additional barrier to interchangeability, current draft FDA guidance strongly recommends that companies complete switching studies using only samples of reference biologics sourced in the United States.[60] But, similar to REMS tactics discussed above, U.S. manufacturers of reference biologics may not be making enough samples available – even at full price.[61] And, even though the FDA has allowed biosimilar developers to conduct switching studies using internationally sourced samples of reference biologics as long as they analytically bridge each batch and lot to the U.S. reference,[62] these bridging studies are expensive and time-consuming.

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[57] *See* FOOD & DRUG ADMIN., *Purple Book: Lists of Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations* (page last updated Jul. 2, 2018), https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm.

[58] Derrick Gregory, *Industry May Like FDA's Biosimilar Guidance Withdrawal, But Not the New Information Vacuum*, PINK SHEETS (June 22, 2018), https://pink.pharmaintelligence.informa.com/PS123350/Industry-May-Like-FDAs-Biosimilar-Guidance-Withdrawal-But-Not-The-New-Information-Vacuum.

[59] Gottlieb, *supra* note 33.

[60] FOOD & DRUG ADMIN., *Considerations in Demonstrating Interchangeability with a Reference Product: Guidance for Industry*, at 16 (Jan. 2017), https://www.fda.gov/downloads/Drugs/GuidanceCompliance-RegulatoryInformation/Guidances/UCM537135.pdf.

[61] According to media reports, one of the main reasons for the withdrawal of the guidance had to do with industry complaints regarding the FDA requirement for a minimum of ten lots of US-sourced reference product to be sampled in order "to establish meaningful similarity acceptance criteria." Industry participants raised concerns about the potential for lot-to-lot variability and the statistical methods for evaluating analytical similarity proposed in the guidance especially where access to reference product lots is limited. "'The goal is for future draft guidance to address potential challenges faced by biosimilar sponsors in designing studies that are intended to demonstrate that a proposed biosimilar product is highly similar to a reference product, including consideration of appropriate methods to analyze analytical data to account for potential lot-to-lot variability of the reference product,' according to the FDA." Mezher, *supra* note 56.

[62] *See* Cathy Kelly, *Interchangeability Standards*, *supra* note 56; *see also* Credit Suisse, *Global Pharmaceuticals*, at 56 (May 25, 2018). This is similar to the denial of reference product samples for certain REMS products described above in Section II. The FTC believes that the FDA's final guidance on interchangeable biosimilars should address

Recently, FDA Commissioner Scott Gottlieb acknowledged that reference biologic manufacturers are "gaming the system to try to block competition," and suggested that the FDA may be considering ways to make interchangeable designations easier and less expensive to obtain.[63] Some scientists have demonstrated that one source of a branded biologic could serve as the global reference for all biosimilars, when the U.S.-sourced and ex-U.S. sourced reference products were approved based on the same clinical studies. This approach would eliminate the need for the analytical bridging studies.[64]

Commissioner Gottlieb also recently announced withdrawal of draft biosimilar guidance in order to ensure the final guidance takes into consideration the most current and relevant science.[65] He stated that he was concerned about the slow development of biosimilar competition and that FDA policies should encourage growth. The FTC agrees. Specifically, Commissioner Gottlieb stated:

> FDA can do more to support the development of biosimilars, as well as promote the market acceptance of these products . . . . As the cost to develop a single biosimilar product can reach hundreds of millions of dollars, it's important that we advance policies that help make the development of biosimilar products more efficient, and patient and provider acceptance more certain.[66]

The FTC encourages the FDA to consider incorporating into its final interchangeable and biosimilar guidances ways to reduce barriers to entry and to expedite the approval of biosimilars and interchangeables.

C. To Improve Competition, the FDA Should Reconsider the Final Naming Guidance for Biologics

In 2015, FTC staff responded to the FDA's request for comment on its draft guidance addressing nonproprietary names for biologics.[67] In the draft guidance, the FDA had proposed

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this concern, to ensure that sufficient quantities of reference biologic samples are available to biosimilar developers in a timely manner.

[63] Sarah Jane Tribble, Liz Starab, *FDA Head Vows to Tackle High Drug Prices And Drugmakers 'Gaming the System*, Kaiser Health News, (Feb. 15, 2018), https://khn.org/news/fda-head-vows-to-tackle-high-drug-prices-and-drugmakers-gaming-the-system/.

[64] *See* Christopher Webster & Gillian Woollett, *A 'Global Reference' Comparator for Biosimilar Development*, 31(4) BIODRUGS 279-86 (2017), https://link.springer.com/content/pdf/10.1007%2Fs40259-017-0227-4.pdf.

[65] Derrick Gregory, *Industry May Like FDA's Biosimilar Guidance Withdrawal, But Not the New Information Vacuum*, PINK SHEETS (June 22, 2018), https://pink.pharmaintelligence.informa.com/PS123350/Industry-May-Like-FDAs-Biosimilar-Guidance-Withdrawal-But-Not-The-New-Information-Vacuum.

[66] *See* Gregory, *supra* note 65.

[67] 2015 FTC Naming Comment, *supra* note 13.

adding a new, random suffix to the nonproprietary name of each biological product.[68] The purpose of the FDA's naming convention was to improve pharmacovigilance and minimize possible inadvertent substitution of biological products that the FDA had not determined to be interchangeable.[69]

Building on the FTC's extensive experience in evaluating health care competition and studying competitive issues affecting biologics, the 2015 FTC staff comment suggested that the FDA's naming convention, which departed from FDA tradition, could cause physicians to believe mistakenly that the products have clinically meaningful differences. Such confusion arising from the naming convention may dissuade physicians from prescribing the biosimilar and consequently diminish competition in biologic drug markets.[70] The comment also noted ways in which the naming proposal may create unnecessary costs and conflicts with efforts toward global naming harmonization.[71] Finally, the comment suggested an alternative approach for achieving the FDA's goal of: (1) avoiding inadvertent substitution; and (2) improving the reporting to the FDA adverse events involving biologics.[72]

In 2017, the FDA adopted final guidance consistent with its 2015 draft guidance. In particular, the FDA's final *Nonproprietary Naming of Biological Products: Guidance for Industry* ("Naming Guidance") assigned a "distinguishing suffix that is devoid of meaning."[73] Because the FTC continues to believe that the FDA naming convention for biologic drugs may reduce price competition in biologic drug markets and may create unnecessary costs, the Commission renews the points raised in the earlier FTC staff comment. In particular, in response to the Blueprint's request for comment on means to improve competition in biopharmaceutical markets and to reduce out-of-pocket spending for patients,[74] the FTC recommends that the FDA reconsider the Naming Guidance in light of the HHS Blueprint goals.

First, the FDA's Naming Guidance may hinder biosimilar competition. As FTC staff noted in 2015, the FDA's decision to assign different suffixes to the drug substance names of biosimilars and their reference biologics could result in physicians incorrectly believing that biosimilars' drug substances differ in clinically meaningful ways from their reference biologics' drug substances. That is especially the case since differences in drug substance names have

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[68] FOOD & DRUG ADMIN., *Notice of Nonproprietary Naming of Biological Products: Draft Guidance for Industry; Availability*, 80 Fed. Reg. 52,296 (Aug. 28, 2015), https://federalregister.gov/a/2015-21383.

[69] *Id*.

[70] 2015 FTC Naming Comment, *supra* note 13.

[71] *Id*.

[72] *Id*.

[73] FOOD & DRUG ADMIN., *Nonproprietary Naming of Biological Products, Guidance for Industry*, at 8 (2017), https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf.

[74] *See, e.g.*, Blueprint, *supra* note 2, at 22,692.

traditionally connoted meaningful differences in drug substances.[75] As former HHS Assistant Secretary for Planning and Evaluation and current Harvard University economist Richard Frank noted recently:

> One concern is that such naming creates the impression that the clinical effects of a biosimilar may differ meaningfully from the reference product. Perceived differences between competing products weaken price competition, and the existing evidence suggests that such perceptions are having this effect in the biosimilar market."[76]

That concern is supported by standard economic theory, which holds that perceived differences between products may diminish price competition. When products are (or are perceived to be) differentiated, they compete along more dimensions than just price. The corollary is that closer economic substitutes typically drive more intense price competition, and, accordingly, lower prices.[77] Biosimilars are required to be highly similar to, and have no clinically meaningful differences in safety and efficacy from, their reference biologic – meaning they should be competing vigorously with reference biologics on price. But this price competition between reference biologics and biosimilars may be less vigorous if physicians incorrectly believe that there are clinically meaningful differences between biosimilars and their reference biologics based on different suffixes attached to the same, shared root name. These naming conventions thus may diminish biosimilar price competition, which, in turn, could lead to higher prices.

For this reason, in 2014, the American Medical Association ("AMA") recommended further research: "Any change in current nomenclature rules or standards should be informed by a better, and more complete, understanding of how such changes, including requiring a unique identifier for biologic INNs [International Nonproprietary Names], would influence prescriber attitudes and patient access, and affect post marketing surveillance."[78] As the AMA noted, actions that act as barriers to clinical uptake are counterproductive.[79]

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[75] The Biologics Price Competition and Innovation Act ("BPCIA") requires a "biosimilar" to be "highly similar to the reference product notwithstanding minor differences in clinically inactive components," with "no clinically meaningful differences between the biologic product and the [FDA-licensed biological] reference product in terms of safety, purity, and potency of the product." 42 U.S.C. § 262(i)(2).

[76] Frank, *supra* note 50 ("One concern is that such naming creates the impression that the clinical effects of a biosimilar may differ meaningfully from the reference product.").

[77] *See* DENNIS W. CARLTON & JEFFREY M. PERLOFF, MODERN INDUSTRIAL ORGANIZATION 225 (4th ed. 1994) ("the greater the perceived difference between two firms' products, the more each firm can charge.").

[78] *See* Pub. Comment from Am. Med. Ass'n to the Fed. Trade Comm'n at 3 (Feb. 28, 2014), https://www.ftc.gov/system/files/documents/public_comments/2014/02/00023-88679.pdf; N. AM. CTR. FOR CONTINUING MED. EDUC., *CME Survey on Biosimilars* 4 (May 24, 2013), http://www.naccme.com/2013-biosimilars-cme-survey-results-full-report; *see, e.g.*, Kevin McCaffrey, *Most Docs Are in the Dark About Biosimilars: Survey*, MED. MARKETING & MEDIA (Aug. 13, 2015), http://www.mmm-online.com/-dataanalytics/most-docs-are-in-the-dark-about-biosimilarssurvey/article/432650/ (researchers polled 120 prescribing specialists regarding knowledge gap on biosimilars: most specialists wanted educational information about safety and efficacy to better understand biosimilars).

Second, as FTC staff noted in 2015, experience with biosimilars in Europe suggests that biosimilars with distinct nonproprietary names are less commercially successful than biosimilars with the same nonproprietary name as the reference biologic.[80] Biosimilar manufacturers presented evidence at the 2014 FTC workshop that, in Europe, the market penetration of biosimilars with a different active ingredient name than the reference biologic trails the market penetration of biosimilars with the same active ingredient name as the reference biologic.[81]

Third, FTC staff continue to believe that reliance on trade names would address the FDA's pharmacovigilance concerns and address the FDA's concerns with unintended switching of products not determined by the FDA to be interchangeable. Likewise, as discussed below, using the Purple Book in the same manner as the Orange Book, together with physician/prescriber consent to substitution, provides an existing mechanism to prevent inadvertent substitution.

Finally, while not raised in the 2015 comment, with respect to interchangeable biologics, the FDA could implement a biologics naming system for interchangeables similar to the one used for generic equivalents. Such a system would require unique brand names for all biologics, while preserving the same active ingredient name across all therapeutically substitutable products in the same biologic category.[82]

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[79] *Id; see also* Frank, *supra* note 50.

[80] *Delivering on the Potential of Biosimilar Medicines: The Role of Functioning Competitive Markets*, IMS INSTITUTE, at 24, https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf ("In October 2015, PharmaPhorum surveyed doctors in France, Spain and the UK and found that: fewer than 25 per cent of them report prescribing biosimilars and, while almost half have reported that they expect they will prescribe them in the future, biosimilars are expected to account for only 17 per cent of their prescriptions over the next three years . . . .The main reason that biosimilars are not prescribed is that many physicians continue to express concern over the efficacy and safety of these agents.").

[81] *See* Sumant Ramachandra, Senior V.P. , Hospira, *Presentation at FTC Follow-On Biologics Workshop: Lessons for the United States: Biosimilar Market Development Worldwide* at 8 (Feb. 4, 2014), https://www.ftc.gov/system/files/documents/public_events/FollowOn%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Competition/ramachandra.pdf.

[82] Europe has used this type of naming system (brand names, same active ingredient, no suffix, NDC codes) since 2006. This system was recently adopted by Australia. This system has worked well to increase biosimilar competition that benefits consumers. *Naming of Biosimilars*, GENERIC PHARM. ASS'N, http://www.gphaonline.org/gpha-media/gpharesources/1naming-biosimilars (last visited June 11, 2018) ("the [nonproprietary names] assigned to biosimilars and already used in Europe, Japan, and other highly regulated markets match that of their reference."); *see* Sreedhar Sagi, Hillel Cohen, & Gillian Woollett, *Pharmacovigilance of Biologics in a Multisource Environment*, 23(12) J. MANAG. CARE SPEC. PHARM. 1249-5 (2017), https://www.jmcp.org/doi/10.18553/jmcp.2017.23.12.1249, (European safety surveillance systems work using brand name and NDC codes and no need for suffix); EPAR, *Biosimilars*, *supra* note 52; Biosimilar Council, *IGBA Congratulates the Australian Government for Maintaining Their Biologics Naming Convention and for Strengthening Pharmacovigilance*, https://biosimilarscouncil.org/igba-congratulates-the-australian-government-for-maintaining-their-biologics-naming-convention-and-for-strengthening-pharmacovigilance/ (the Australian Government decision is to maintain the existing naming convention for biological medicines: "that is to continue using the Australian biological name (without a suffix) and to strengthen the adverse event reporting including mandatory trade name, as well as the non-

Consequently, the FTC recommends that HHS and the FDA revisit the FDA Naming Guidance in light of the Blueprint, and consider alternative approaches that achieve the FDA's objectives without hindering competition.

D. Improving the Purple Book Will Benefit Biosimilar Competition

The Commission supports the FDA's efforts to improve the Purple Book,[83] which lists biological products, including any biosimilar and interchangeable biological products licensed by the FDA. As the FDA notes, the Purple Book publishes information about biological products that is useful to prescribers, pharmacists, patients, and other stakeholders.[84] This information includes any biological product licensed by the FDA, the date licensed, and whether the FDA evaluated the biological product for reference product exclusivity.[85] Timely and detailed information about reference product exclusivity promotes biosimilar competition because it allows potential competitors to more fully understand the regulatory landscape.

The FDA has emphasized that it does not intend the Purple Book to be equivalent to the Orange Book, as the legal regimes governing licensure of biologics and approval of drugs are different. Despite such differences, the Purple Book could be more useful if it included a search functionality similar to that of the FDA's Orange Book.[86] For example, a user can search the FDA's Orange Book website by active ingredient name, proprietary name, dosage form, route of administration and other features.[87] By contrast, the Purple Book is in a static PDF format and does not contain the same information.[88] Analogous information in the Orange Book that is currently not included but should be included in the Purple Book would include applicant name, date application filed, active ingredient name (not product proper name), patents if any, applicant holder (if different than applicant), and or application number. These changes would make it

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proprietary name, a mandatory field when reporting an adverse event to the Australian Therapeutic Goods Administration").

[83] Blueprint, *supra* note 2, at 22,696.

[84] *Id*.

[85] *See* FOOD & DRUG ADMIN., *Purple Book: Lists of Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm (last updated Jul. 2, 2018).

[86] *Id*. ("How could the Purple Book be more useful to health care professionals, patients, manufacturers, and other stakeholders.").

[87] FOOD & DRUG ADMIN., *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, https://www.accessdata.fda.gov/scripts/cder/ob/.

[88] *See, e.g.*, FOOD & DRUG ADMIN., *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, https://www.fda.gov/drugs/development-approvalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm.

easier for health care professionals, patients, manufacturers, academics, attorneys, and other stakeholders to evaluate relevant information, which would, in turn, allow parties to understand better the competitive landscape for biosimilar drugs.

The FDA also could reorganize information presented in the Purple Book to increase its utility.[89] As described above, the FTC has expressed concern with the FDA's Naming Guidance because the "meaningless suffix" may lead to physician confusion, and negatively affect prescriber attitudes, patient access, and post-marketing surveillance. The FDA could ameliorate these concerns by emphasizing the root name of biologic products and reducing the prominence of the FDA-designated suffixes. For example, the FDA could place a biologic product's active ingredient name and its FDA-designated suffix in separate columns in the Purple Book. This editorial change would make it clearer to physicians when a biosimilar shares an active ingredient name with the reference product, reducing any physician confusion.

IV. Conclusion

The Commission appreciates this opportunity to provide its views on the Blueprint. As explained above, we support HHS and the FDA's efforts to examine ways to increase competition in health care markets and to address abuses of government processes that facilitate maintenance of market power after patent expiry. The Commission and its staff look forward to continuing to work with HHS and the FDA on these and other issues related to competition and consumer welfare.

[89] Blueprint, *supra* note 2, at 22,696 ("What additional information could be added to increase the utility of the Purple Book?").