

Federal Communications Commission

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FEDERAL RESERVE SYSTEM

Formations of, Acquisitions by, and Mergers of Bank Holding Companies

The companies listed in this notice have applied to the Board for approval, pursuant to the Bank Holding Company Act of 1956 (12 U.S.C. 1841 *et seq.*) (BHC Act), Regulation Y (12 CFR Part 225), and all other applicable statutes and regulations to become a bank holding company and/or to acquire the assets or the ownership of, control of, or the power to vote shares of a bank or bank holding company and all of the banks and nonbanking companies owned by the bank holding company, including the companies listed below.

The applications listed below, as well as other related filings required by the Board, are available for immediate inspection at the Federal Reserve Bank indicated. The applications will also be available for inspection at the offices of the Board of Governors. Interested persons may express their views in writing on the standards enumerated in the BHC Act (12 U.S.C. 1842(c)). If the proposal also involves the acquisition of a nonbanking company, the review also includes whether the acquisition of the nonbanking company complies with the standards in section 4 of the BHC Act (12 U.S.C. 1843). Unless otherwise noted, nonbanking activities will be conducted throughout the United States.

Unless otherwise noted, comments regarding each of these applications must be received at the Reserve Bank indicated or the offices of the Board of Governors not later than December 12, 2013.

A. Federal Reserve Bank of Richmond (Adam M. Drimer, Assistant Vice President), 701 East Byrd Street, Richmond, Virginia 23261-4528:

1. *CapGen Capital Group III LLC and CapGen Capital Group III LP*, both in New York, New York; to acquire additional voting shares, for a total of 25 percent of, the voting shares of Seacoast Banking Corporation of Florida, and thereby indirectly acquire additional voting shares of Seacoast National Bank, both in Stuart, Florida.

Board of Governors of the Federal Reserve System, November 12, 2013.

Michael J. Lewandowski,

Associate Secretary of the Board.

[FR Doc. 2013-27373 Filed 11-14-13; 8:45 am]

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FEDERAL TRADE COMMISSION

Public Workshop: Follow-On Biologics: Impact of Recent Legislative and Regulatory Naming Proposals on Competition

AGENCY: Federal Trade Commission.

ACTION: Notice of workshop and request for comments.

SUMMARY: The Federal Trade Commission (“FTC” or “Commission”) announces it will hold a workshop to explore competition issues involving biologic medicines and follow-on biologics. The workshop will focus on the potential impact of state regulations and naming conventions on such competition, including how regulations may be structured to facilitate competition while still protecting patient health and safety. The experience of developing follow-on competition from small-molecule generic drugs will be considered and, as relevant, compared. Topics will include the circumstances under which potential entrants would be willing to invest in the development of follow-on biologics in order to use the abbreviated regulatory approval pathway created by federal legislation. The workshop will also survey the experience of other countries with regulatory systems that enable follow-on biologic competition. This Notice poses a series of questions about which the FTC seeks public comment. The FTC will take these comments into account in its examination of these topics.

DATES: The workshop will be held on December 10, 2013, in the FTC headquarters at 600 Pennsylvania Avenue NW., Washington, DC. The FTC workshop is free and open to the public and will also be webcast. Prior to the workshop, the Commission will publish an agenda and further information on its Web site. Comments in response to this notice must be received on or before March 1, 2014.

ADDRESSES: Interested parties may file a comment online or on paper, by following the instructions in the Request for Comment part of the **SUPPLEMENTARY INFORMATION** section below. Write “Workshop on Follow-On Biologics: Project No. P131208” on your comment, and file your comment online at <https://ftcpubcommentworks.com/>

ftc/biologicsworkshop, by following the instructions on the web-based form. If you prefer to file your comment on paper, mail or deliver your comment to the following address: Federal Trade Commission, Office of the Secretary, Room H-113 (Annex X), 600 Pennsylvania Avenue NW., Washington, DC 20580.

FOR FURTHER INFORMATION CONTACT: Elizabeth Jex, Attorney Advisor, Office of Policy Planning, Federal Trade Commission, 600 Pennsylvania Avenue NW., Washington, DC 20580; (202) 326-3273; biosimilars@ftc.gov.

SUPPLEMENTARY INFORMATION: The Federal Trade Commission vigorously promotes competition in the health care industry through enforcement, study, and advocacy. Competition in health care markets benefits consumers by helping to control costs and prices, improve quality of care, promote innovative products, services, and delivery models, and expand access to health care goods and services. As addressed below, this proposed workshop is consistent with these FTC priorities.

I. Background: Follow-On Competition in Pharmaceutical Markets

In particular, the Commission has sought to protect competition among pharmaceutical products, including generic drugs providing price competition against brand-name drugs. Until relatively recently, the potential for follow-on competition was limited to products involving traditional “small-molecule” generic drugs. Producers of these drugs obtain approval from the Food & Drug Administration (“FDA”) pursuant to an abbreviated regulatory pathway established by the Hatch-Waxman Act.¹

Biologic medicines have now become among the most important pharmaceutical products in the United States. Biologics comprise the fastest growing sector within pharmaceuticals, and target such difficult to treat diseases as cancer, diabetes, and multiple sclerosis.² “Biologics” include, for

¹ See The Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.* (2011), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, Public Law 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 21 & 35 U.S.C.) (known as Hatch-Waxman), and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, § 1112, 117 Stat. 2066, 2461-63 (codified at 21 U.S.C. 355).

² *Health Policy Brief: Biosimilars*, Health Affairs 1 (Oct. 10, 2013), http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_100.pdf (“[Biologics] account for a substantial and increasing share of the pharmaceutical market and a growing share of health care costs”).

example, vaccines, antitoxins, blood products, proteins, and monoclonal antibodies.³ Although their characteristics vary widely, “biologics are typically larger and more structurally complex than traditional drugs (also known as ‘small-molecule’ drugs).”⁴ Thus, “[they] are substantially more expensive to develop, manufacture, and monitor [than small-molecule drugs].”⁵ Biologics generally are very expensive; the cost of one year of treatment can range from \$50,000 to \$250,000, and access to therapeutic biologics is often restricted because of cost.⁶ Currently, biologics account for approximately 25 percent of the \$320 billion spent annually in the United States for pharmaceutical treatments.⁷

The FDA approves biologics under the Public Health Service Act (“PHSA”).⁸ To encourage competition

in the market for biologic, in 2010 Congress passed the Biologics Price Competition and Innovation Act (“BPCIA”),⁹ which amended the PHSA to establish an abbreviated regulatory pathway for FDA approval of follow-on biologics. The provisions of the BPCIA differ in some respects from those of the Hatch-Waxman Act. Still, some brief background information on the development of generic drug competition is helpful to understand how follow-on biologic competition may develop.

A. Competition From Generic Drugs

To facilitate follow-on competition to brand-name small-molecule drugs, in 1984 Congress passed the Hatch-Waxman Act.¹⁰ This Act created an abbreviated regulatory pathway through which safe and effective generic drugs could obtain approval from the FDA to enter a market without replicating all of the costly testing required for a brand-name drug.¹¹ To be approved under Hatch-Waxman, the applicant must show that its generic drug product is “bioequivalent” to (basically, as safe and effective as) the branded drug product.¹² A bioequivalence showing is much less expensive than the clinical testing required to establish the safety

set forth under 42 U.S.C. 262(a); whereas follow-on biologics are approved pursuant to the requirements set forth under 42 U.S.C. 262(k).

⁹ See Biologics Price Competition and Innovation Act of 2009, Title VII, Subtitle A, §§ 7001–7003 of the Patient Protection and Affordable Care Act, Public Law 111–148, 124 Stat. 119, 804–21 (2010).

¹⁰ See note 1 *supra*.

¹¹ “Hatch-Waxman does not require generic applicants to duplicate the clinical testing of drugs already proven safe and effective. Duplication of safety and efficacy information is costly, an inefficient use of scarce resources, and, as the FDA has explained, raises ethical concerns associated with unnecessary human testing.” Fed. Trade Comm’n, Emerging Healthcare Issues: Follow-On Biologic Drug Competition *exec. summ.* at ii (2009), <http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf> [hereinafter FTC FOB Report].

¹² The applicant also must meet other requirements. “To gain FDA approval, a generic drug must: (1) Contain the same active ingredients as the innovator drug (inactive ingredients may vary); (2) be identical in strength, dosage form, and route of administration; (3) have the same use indications; (4) be bioequivalent; (5) meet the same batch requirements for identity, strength, purity, and quality; and (6) be manufactured under the same strict standards of FDA’s good manufacturing practice regulations required for innovator products.” See *What are Generic Drugs?*, U.S. Food & Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm144456.htm> (last updated May 12, 2009); see also Bureau of Consumer Prot’y, Fed. Trade Comm’n, Drug Product Selection (1979) [hereinafter Drug Product Selection].

and efficacy of a new branded drug product.

Because the generic drug is “bioequivalent” to the branded drug, it can be safely substituted for the branded drug and is expected to be as safe and effective as the branded drug. To take full advantage of generic competition, many states have laws that allow pharmacists automatically to substitute a generic for a branded drug, unless a doctor has indicated otherwise.¹³ Moreover, because an FDA-approved generic drug has the identical active substance and is “biologically equivalent” to its “brand-name” counterpart, the generic drug is given the same active ingredient name as the branded drug product.¹⁴

Since 1984, the FDA has “approved more than 8,000 generic drugs, which has resulted in hundreds of billions of dollars in cost savings to consumers.”¹⁵ Overall, generic drug competition has substantially reduced many prescription drug prices and total prescription drug expenditures, and increased access to therapeutic drugs for more Americans.¹⁶

B. Competition From Follow-On Biologics

No abbreviated approval process for follow-on biologics (“FOBs”) existed until 2010.¹⁷ The BPCIA created an abbreviated licensure pathway for two types of follow-on biologics: Biosimilars and interchangeable biological

¹³ See FTC FOB Report, *supra* note 11, *exec. summ.* at i.

¹⁴ Generic drugs are required to have the same active ingredient, strength, dosage form, and route of administration as the brand name product. Generic drugs do not need to contain the same inactive ingredients as the brand name product. 21 U.S.C. 355(j)(2)(A)(ii), (iv); *Facts About Generic Drugs*, U.S. Food & Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm> (last updated Sept. 19, 2012).

¹⁵ See *Fact Sheet: New “Biosimilars” User Fees Will Enhance Americans’ Access to Alternatives to Biologic Drugs*, U.S. Food & Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/SignificantAmendmentsToTheFDCA/FDASIA/ucm311121.htm> (last updated on July 16, 2012).

¹⁶ See FTC FOB Report, *supra* note 11, *exec. summ.* at i; See generally Jennifer S. Haas, et al., *Potential Savings From Substituting Generic Drugs for Brand-Name Drugs: Medical Expenditure Panel Survey, 1997–2000*, 142 ANNALS INTERNAL MED. 891 (2005); Wendy H. Schacht & John R. Thomas, Cong. Research Serv., RL33901, Follow-On Biologics: Intellectual Property and Innovation Issues 4, 18 (2008).

¹⁷ The Hatch-Waxman Act applies only to drugs regulated under the Federal Drug & Cosmetics Act; these drugs are generally chemically synthesized, small-molecule products, not biologics. FTC FOB Report, *supra* note 11, at 3–4, app. B–1.

³ *Id.*

⁴ *Id.*

⁵ *Id.*

⁶ See *id.*; see also IMS Institute for Healthcare Informatics, IMS Health, The Use of Medicines in the United States: Review of 2011 (2012), http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_Medicines_in_US_Report_2011.pdf [hereinafter IMS, Use of Medicines]; IMS Institute for Healthcare Informatics, IMS Health, Generic Drug Savings in the U.S.: Savings \$1 Trillion Over 10 Years 2 (4th ed. 2012), <http://www.gphaonline.org/media/cms/IMSStudyAug2012WEB.pdf> (Study commissioned by GPhA) (“Current biologic medicine costs are staggering, putting these lifesaving treatments out of reach for many patients. Even after insurance coverage, co-pays can be thousands of dollars each year. A Congressional Research Service (CRS) study completed in 2010 showed that the cost of biologics is often prohibitively high, both for patients and the government. The report found that average annual costs for the rheumatoid arthritis treatment Enbrel® was \$26,000, Herceptin® for breast cancer averaged \$37,000, Humira® for Crohn’s disease was more than \$51,000 per year, and the annual cost for Cerezyme® to treat Gaucher’s disease was \$200,000.”); Andrew Pollack, *Biotech Firms, Billions at Risk, Lobby States to Limit Generics*, N.Y. Times (Jan. 28, 2013), http://www.nytimes.com/2013/01/29/business/battle-in-states-on-generic-copies-of-biotech-drugs.html?_r=0.

⁷ See IMS, Use of Medicines, *supra* note 6, at 27; Staff of Comm. on Health Policy, Fla. S., 2013 Session, Bill Analysis and Fiscal Impact Statement, CS/SB 732, at 3, (2013), <http://www.flsenate.gov/Session/Bill/2013/0732/Analyses/FckEw94up4AYkLzGQBz3ErRA=PL=pg=%7C14/Public/Bills/0700-0799/0732/Analysis/2013s0732.hp.PDF>; see also Cong. Budget Office, Congressional Budget Office Cost Estimate: S. 1695 Biologics Price Competition and Innovation Act of 2007, at 5 (2008), <http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/94xx/doc9496/s1695.pdf> [hereinafter CBO Report] (“In recent years, total spending on biologics has grown rapidly, with nominal spending growth averaging roughly between 15 percent and 20 percent annually; spending amounted to about \$40 billion in 2006. . . . We estimate that by 2018 about \$70 billion in national spending on biologics could face competition by FOBs. . . .”).

⁸ 42 U.S.C. § 262. Generally, the reference biologic is approved by the FDA with a full Biologics License Application pursuant to the requirements

products.¹⁸ Under the BPCIA, a “biosimilar” product is “highly similar to the reference product notwithstanding minor differences in clinically inactive components,” and “there are no clinically meaningful differences between the biological product and the [FDA-licensed biological] reference product in terms of safety, purity, and potency of the product.”¹⁹ The BPCIA requirements for an “interchangeable” biologic product are more stringent. An interchangeable biologic product is expected to produce the same clinical result as the FDA-licensed biological reference product in any given patient. Furthermore, for a product administered more than once, the safety and reduced efficacy risks of switching from the reference drug to an interchangeable drug, or alternating between the reference drug and an interchangeable drug, cannot be greater than the risks posed by use of the reference product without alternating or switching.²⁰

BPCIA provides that interchangeable biologics “may be substituted for the reference biologic without the intervention of the health care provider who prescribed the reference product.”²¹ It does not address substitution of non-interchangeable biosimilars. The FDA is authorized to issue regulations that define the requirements for applicants claiming “interchangeability” or “biosimilar” status, but the agency has not finalized guidelines on these issues.²²

In 2009, the Commission issued a report, *Emerging Healthcare Issues: Follow-On Biologic Drug Competition* (“FTC FOB Report”),²³ which discussed the results of its November 21, 2008 workshop to examine “whether the price of biologics might be reduced by competition if there were a statutory process to encourage [FOBs] to enter and compete with pioneer biologics once a pioneer drug’s patents have expired.”²⁴ In its report, the Commission noted that the scientific differences between biologic and small-molecule drug products would complicate efforts to devise an approval process for FOBs.²⁵ Biologics are often three-dimensional folded proteins, derived from living matter or manufactured within living cells using recombinant DNA biotechnologies.²⁶ They are generally more complex and immunogenic, and more complex to manufacture, than traditional small-molecule drugs.²⁷

Indeed, “[s]mall changes in the manufacturing process can lead to variations in the final product, which can in turn affect safety and clinical effectiveness. Even biologics produced in the same manufacturing facility will have some variation between lots.”²⁸ As of 2011, FDA experts concluded that, “for the foreseeable future,” at least some clinical trials would likely be required in order to assure the therapeutic equivalence of FOBs.²⁹ Thus, compared to the relatively inexpensive and simple abbreviated approval pathway for generic drugs, the abbreviated pathway for biosimilars and

interchangeables will likely be expensive and time consuming.³⁰

Accordingly, the Commission’s report predicted that FOB competitors would offer less price competition to reference biologics than the price competition generated by generic drugs to branded drugs.³¹ Nonetheless, the Commission pointed out, given the enormous costs of biologics, even modest FOB discounts could lead to significant consumer savings.³² As the Congressional Budget Office (“CBO”) has estimated,³³ increased FOB competition leading to lower biologics prices could save consumers millions of dollars each year.

II. Workshop Topics

“Biologics are among the biggest-selling medicines today. In 2010, nine out of the top 20 selling drugs in the U.S. were biologics.”³⁴ Currently, fourteen biosimilars are believed to be in clinical development in the United States, but to date, no FOBs have been approved by the FDA under the abbreviated pathway offered by the BPCIA.³⁵

As was the case with small-molecule generic drugs, the future of FOB competition may be influenced by state laws that regulate the substitution of biosimilars or interchangeable biologic products for reference biologic products. The ability of FOBs to compete against reference biologic products will also depend on whether they are allowed to have the same nonproprietary names. The workshop will also examine the evolution of FOB competition in the United States so far, including possible

¹⁸ 42 U.S.C. 262(k) (2011).

¹⁹ § 262(i)(2).

²⁰ § 262(i)(3).

²¹ *Id.*

²² On February 9, 2013, the FDA issued three draft guidance documents regarding Scientific Considerations, Quality Considerations, and Q&As, and solicited public comments for the draft guidance documents; the public comment period has now closed. No final guidance documents have yet been issued. The Draft Guidance included: (1) “Scientific Considerations in Demonstrating Biosimilarity to a Reference Product;” (2) “Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product;” and (3) “Guidance for Industry on Biosimilars: Q & As Regarding Implementation of the BPCI Act of 2009.” See *Questions and Answers: Issuance of Three Draft Guidance Documents on Biosimilar Product Development*, U.S. Food & Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm291186.htm> (last updated Feb. 9, 2012); see also *Fact Sheet: Issuance of Draft Guidances on Biosimilar Products*, U.S. Food & Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm291197.htm> (last updated Feb. 9, 2012).

²³ See Press Release, Fed. Trade Comm’n, FTC Releases Report on “Follow-on Biologic Drug Competition”: Providing FDA With Authority to Approve Follow-on Biologics Would be an Efficient Way to Bring Them to Market, Lowering Consumers’ Health Care Costs (June 10, 2009), <http://www.ftc.gov/opa/2009/06/biologics.shtm>.

²⁴ FTC FOB Report, *supra* note 11, exec. summ. at i.

²⁵ *Id.* exec. summ. at ii.

²⁶ *Id.* at 8–9.

²⁷ A biologic drug is “immunogenic” if it stimulates an immune response in the patient; this can raise safety and efficacy concerns. See Letter from Frank M. Torti, Principal Deputy Comm’r & Chief Scientist, U.S. Food & Drug Admin., to Frank Pallone, Jr., Chairman, H. Subcomm. on Health 1 (Sept. 18, 2008), available at http://step.berkeley.edu/journal_Club/paper2_110309.pdf.

²⁸ Health Policy Brief: *Biosimilars*, *supra* note 2, at 1.

²⁹ See Steven Kozlowski, Janet Woodcock, Karen Midthun & Rachel Behrman Sherman, *Developing the Nation’s Biosimilar Program*, 365 *New Eng. J. Med.* 385, 386 (2011), available at <http://www.nejm.org/doi/pdf/10.1056/NEJMp1107285> (“additional animal and clinical studies will generally be needed for protein biosimilars for the foreseeable future, the scope and extent of such studies may be reduced further if more extensive fingerprint-like characterization is used.”).

³⁰ FTC FOB Report, *supra* note 11, at 12; accord Mandy Jackson, *Pharma Recovering from Patent Cliff Before Next Hit in 2015*, *Scrip Intelligence*, July 5, 2013; Henry Grabowski et al., *Implementation of the Biosimilar Pathway: Economic and Policy Issues*, 41 *Seton Hall L. Rev.* 511 (2011); Editorial, *Building a wall against Biosimilars*, 31 *Nature Biotech.* 264 (2013), available at <http://www.nature.com/nbt/journal/v31/n4/pdf/nbt.2550.pdf>.

³¹ The workshop proposed in this notice will consider whether new facts require revisions to the Commission’s prior predictions.

³² FTC FOB Report, *supra* note 11, exec. summ. at v; CBO Report, *supra* note 7, at 5.

³³ The CBO predicted that the BCPIA, if enacted, would “reduce total expenditures on biologics in the United States by \$0.2 billion over the 2009–2013 period and by about \$25 billion over the 2009–2018 period.” CBO Report, *supra* note 7, at 1.

³⁴ Thomas M. Burton & Jonathan D. Rockoff, *FDA Sets Path for Biotech Drug Copies*, *Wall St. J.*, Feb. 10, 2012, available at <http://online.wsj.com/news/articles/SB1000142405297020464260457213143424515820>.

³⁵ Steven Kozlowski, Director, Office of Biotechnology Products, U.S. Food & Drug Admin., Remarks at 11th EGA International Symposium on Biosimilar Medicines: U.S. FDA Perspectives on Biosimilar Development and Approval (April 26, 2013). Whether any applications have been filed with the FDA is not public.

updates to information included in the FTC's 2009 FOB Report, and the experience with FOB competition to date in Europe, Australia, and New Zealand.

A. How State Substitution Laws May Affect the Development of FOB Competition

Whether a follow-on pharmaceutical product is as safe and effective as the brand-name product is a critical issue for doctors and patients considering whether to switch from a brand-name to a follow-on pharmaceutical product. States struggled with this issue as generic drug competition evolved during the 1970s. At first, many state laws prevented the substitution of generic for branded drugs. As states began to consider whether and, if so, how to modify these laws, the FTC also examined whether state anti-substitution laws then in effect struck the appropriate balance between legitimate public health concerns and free market competition.³⁶

The FTC Staff's report, *Drug Product Selection*, concluded that the FDA approval process would result in the approval of safe and effective generic drugs that would be therapeutically equivalent to the reference branded drugs; therefore, the use of such drugs would not create undue public health risks.³⁷ Moreover, the FTC Staff concluded, if pharmacists were free to dispense generic drugs without unnecessary regulatory hurdles, generic drugs would generate price competition that would benefit consumers.³⁸

Many state legislatures reached the same conclusion and legislated a variety of methods to encourage generic drug substitution. In response, and to support state efforts, the FDA created the so-called "Orange Book" to simplify the substitution of generic drugs in the states.³⁹ According to the FDA, "it became apparent that FDA could not serve the needs of each state on an

individual basis[, and t]he Agency also recognized that providing a single list based on common criteria would be preferable to evaluating drug products on the basis of differing definitions and criteria in various state laws."⁴⁰

The Orange Book now "provide[s] a list of all prescription drug products that are approved by FDA for safety and effectiveness, along with therapeutic equivalence determinations for multisource prescription products."⁴¹ The list of FDA-approved drugs has increased by thousands, and in the United States, the FDA's Orange Book provides critical information about drug safety, drug effectiveness, and therapeutic equivalence determinations for multisource prescription drug products.⁴² The availability of this resource has been critical to enabling generic drug competition that has saved consumers billions of dollars through lower prices.

Similar issues affect the adoption of FOBs. Physicians and patients may be reluctant to switch to an FOB product because of the risk that the patient will react differently to the new drug. In its 2009 FOB Report, the FTC predicted that "lingering or institutionalized uncertainty about interchangeability and safety differences between pioneer and FOB products" would likely hamper FOB market penetration.⁴³

Recently, some state legislatures have considered, and some have passed, laws that could affect the substitution of FOBs for biologics and thus would have implications for the development of meaningful competition from FOBs.⁴⁴ Some commentators have raised concerns that differing regulatory barriers among

the states may raise costs, and lessen incentives, to develop FOBs, thereby deterring FOB competition. One commentator has questioned whether policymakers realize how "constraints currently being constructed by some state legislatures" reduce the economic rewards of introducing an FOB as compared with a generic drug.⁴⁵ Questions arise about the costs of complying with all of the provisions in a variety of state laws; whether such provisions are necessary to protect consumers; whether alternative, less burdensome provisions might be sufficient; and whether such proposals and laws are consistent with the standards and definitions established pursuant to the BCPIA.⁴⁶ The workshop will consider these and related questions, as listed below.

Questions Regarding State FOB Legislative Proposals and Laws

1. How would new state substitution laws passed in 2013, or similar proposals pending in other states, affect competition expected to develop between biosimilar or interchangeable biologics and reference biologics? In the context of state substitution laws, what is the likely competitive impact of a biologic product being designated "interchangeable?"

2. What are the compliance costs associated with new state law requirements? How are those costs likely to affect competition from biosimilar and interchangeable biologics?

3. What are the rationales behind new state proposals and laws for regulating FOB substitution? Which provisions are most important? Are some provisions redundant or otherwise unnecessary?

4. Could an FDA publication concerning biologics and FOBs, comparable to the Orange Book, provide an authoritative listing of FOBs that are biosimilar to or interchangeable with reference biologics? Would such a publication facilitate substitution? Would such a publication need to be limited to interchangeable FOBs, or should it include both biosimilar and interchangeable FOBs?

5. Does the potential for many different state laws regulating FOBs affect the prospects for the development of FOBs? Does the answer differ

⁴⁰ *Id.*

⁴¹ *Id.*

⁴² *Id.*

⁴³ FTC FOB Report, *supra* note 11, at 16.

⁴⁴ As of October 2013, five states have enacted substitution laws that apply expressly to FOBs: Florida, North Dakota, Oregon, Utah, and Virginia. H.B. 365, 2013 H.R., Reg. Sess. (Fla. 2013); S.B. 2190, 63rd Leg. Assemb., Reg. Sess. (N.D. 2013); S.B. 460, 2013 Senate, Reg. Sess. (Or. 2013); S.B. 78, 60th Senate, Reg. Sess. (Utah 2013); H.B. 1422, 2013 Gen. Assemb., Reg. Sess. (Va. 2013). In one state, the legislature passed the bill, but the Governor vetoed it. S.B. 598, 2013–2014 Senate, Reg. Sess. (Cal. 2013); see Andrew Pollack, *Gov. Brown of California Vetoes Biotech Drug Bill*, N.Y. Times, October 13, 2013, at B3, available at <http://www.nytimes.com/2013/10/13/us/governor-vetoes-bill-to-limit-use-of-generic-drugs-in-california.html>. In ten states, such efforts apparently failed: Arkansas, Arizona, Colorado, Delaware, Illinois, Indiana, Maryland, Mississippi, Texas, and Washington. Legislation was pending or is pending in two states: Massachusetts and Pennsylvania. We believe that bills died but went to study in two states: Arkansas and Indiana. See Laura Olson, *Assembly Approves Bill on 'Biosimilar' Medicines*, Bloomberg Businessweek (Aug. 27, 2013), <http://www.businessweek.com/ap/2013-08-27/assembly-approves-bill-on-biosimilar-medicines>.

⁴⁵ See Editorial, *supra* note 30, at 264 ("The question for policymakers is whether they realize how meager the economic advantages are likely to be of introducing a biosimilar onto the market compared with a generic small molecule, especially under the constraints currently being constructed by some state legislatures.").

⁴⁶ There may be a federal preemption issue raised by some state restrictions on FOB substitution by pharmacists.

³⁶ See *Drug Product Selection*, *supra* note 12, at 1.

³⁷ See *id.* at 1.

³⁸ In sum, the FTC Staff Report concluded that (1) "ant substitution laws impose substantial unwarranted costs on consumers by unduly restricting price competition in the multisource prescription drug market;" and (2) repeal of ant substitution laws would "produce significant consumer benefits without compromising the quality of health care." *Id.* To remedy the situation and facilitate pharmacists' use of therapeutically equivalent, but less expensive generic drugs, the FTC Staff recommended that the states adopt a Model Drug Product Selection Act. See *Id.* at 1.

³⁹ See FDA Approved Drug Products with Therapeutic Equivalence Evaluations preface at iv (33rd ed. 2013), <http://www.fda.gov/downloads/drugs/developmentapprovalprocess/ucm071436.pdf>.

between biosimilar versus interchangeable biologic products?

6. Would it be helpful to develop a model state substitution biosimilar law? If so, what provisions should the law include? Should state laws coordinate their guidance with provisions in the BPCIA and guidance from FDA?

B. How Naming Conventions May Affect FOB Competition

As the FTC noted in its FOB report, an FOB's name can influence physician and patient acceptance of the product as a substitute for the branded biologic.⁴⁷ "[Institutionalized uncertainty about interchangeability and safety differences between pioneer and FOB products] may be heightened if the FOB product does not share the same name as the pioneer biologic product."⁴⁸

Branded drugs usually have two names: a brand name, sometimes called a proprietary or trade name; and an active ingredient name, which is a nonproprietary name. A biologic also usually has two names: the brand name and the nonproprietary name, which reflects certain scientific characteristics of the product, such as chemical structure and pharmacological properties. In the United States, the FDA has the authority to determine the nonproprietary name for a biological product.⁴⁹ Non-governmental organizations like the United States Pharmacopeial Convention and the United States Adopted Name Council also have a role in developing nonproprietary names for biological products in the U.S.⁵⁰

A lack of consensus exists regarding the nomenclature to use for FOBs. At

issue is whether biosimilar and interchangeable FOBs should have the same nonproprietary name as the reference biologic. The resolution of this issue has implications for both competition and consumer safety. Differences in the nonproprietary name between a biologic and FOB could affect pharmacy substitution of the FOB for the reference biologic and might cause consumer confusion in the market. On the other hand, some have argued that the absence of adequate "track and trace" systems for biologics requires different FOB and biologic nonproprietary names in order to gather and differentiate adverse events caused by the use of branded biologic or FOB products.⁵¹ This workshop will explore the implications of various nonproprietary naming conventions in FOBs for the development of FOBs, FOB competition, and consumer protection.

Questions Related to the Naming of FOBs

1. What has been learned from the experience under Hatch-Waxman about the incentives necessary to encourage physicians and patients to switch

⁴⁷ See e.g., Amgen Inc., *Biologics and Biosimilars 20–23* (2012), http://www.amgen.com/pdfs/misc/Biologics_and_Biosimilars_Overview.pdf (section titled "Pharmacovigilance and traceability"); Erika Leitzan, Laura Sim & Emily Alexander, *Biosimilar Naming: How Do Adverse Event Reporting Data Support the Need for Distinct Nonproprietary Names for Biosimilars*, 3 FDLI's Food and Drug Policy Forum, Mar. 27, 2013. The FDA monitors drug, biologics, and device safety through its postmarketing surveillance system. 21 CFR §§ 314.80, 314.98, 803.1, 803.30, 803.40, 803.50 (2013). See generally *FDA Adverse Event Reporting System (FAERS)* (formerly *AERS*), U.S. Food and Drug Admin., U.S. Dept. of Health & Human Servs., <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm> (last updated Sept. 10, 2012). This is a database of voluntary reporting by healthcare professionals and consumers of adverse events associated with FDA-approved products. The terms pharmacovigilance and track and trace systems are industry-wide terms generally referring to the various FDA and private mechanisms, such as a product's National Drug Code, and manufacturers quality control and quality assurance programs, that can be utilized during public health crisis, such as the heparin contamination, to resolve the critical public health issues as quickly as possible. However, these pharmacovigilance systems are not without weaknesses and difficulties. See e.g., U.S. Gov't Accountability Office, *Food and Drug Administration: Response to Heparin Contamination Helped Protect Public Health Controls That Were Needed for Working With External Entities Were Needed for Working With External Entities Were Recently Added* (2010), <http://www.gao.gov/assets/320/311879.pdf>. FDA informed the GAO that under the FDA's adverse event reporting system, it does not necessarily receive a report for every adverse event that occurs. Manufacturers are required to submit adverse event reports to FDA if known; however, health providers and consumers are not required to do so but submit adverse event reports on a voluntary basis. *Id.* at 36 n.65.

between branded and lower cost, therapeutically substitutable products? Do naming and name changes affect switching? If so, how?

2. How do the European Medicines Agency ("EMA") and other regulatory authorities comparable to the FDA handle the names of FOBs?

3. A prefix or suffix, such as "ado" or "TBO", has been attached to the nonproprietary names of several biological products licensed under a stand-alone biologic license application. How does the use of such prefixes or suffixes affect the inclusion of that product in third-party publications, compendia references, and health information systems, such as electronic health records and prescription processing systems?

4. How does the use of certain identifiers, such as National Drug Codes, brand names, or nonproprietary names, work with existing adverse event reporting, track and trace, or other pharmacovigilance systems?

5. With respect to prescription drugs, does the use of nonproprietary names globally contribute to or detract from competition and consumer protection? Do any studies exist to show increased or decreased consumer benefits or harms, due to changes in names or naming conventions?

C. How FOB Competition Has Evolved in Other Countries With Comparable Prescription Drug Regulation Regimes, and How FOB Competition Is Evolving in the United States

Some countries or intergovernmental organizations, such as the European Union ("EU"), have drug regulatory approval schemes similar to those in the United States, and have already approved biosimilars. In the EU, for example, the EMA already has an established regulatory pathway for biosimilars, and since 2006 has approved fifteen biosimilars for marketing in the EU.⁵² Unlike the FDA FOB abbreviated approval process, the EMA approval process does not contemplate interchangeable biologics; the EMA approves only biosimilars. Several other countries, including Australia, Canada, and Japan, have adopted similar regulatory approaches

⁴⁸ FTC FOB Report, *supra* note 11, at 16–17 & n.55; see also Stanton J. Lovenworth, *The New Biosimilar Era: The Basics, The Landscape, and the Future*, 6 Life Sci. L. & Industry Rep. 972 (2012), available at http://www.omm.com/files/upload/The%20New%20Biosimilar%20Era_The%20Basics,%20the%20Landscape,%20and%20the%20Future.pdf ("A drug's name significantly influences the degree to which it is embraced and prescribed by health care professionals, which in turn affects the drug's financial viability. If a biosimilar's name matches its reference product's name, physicians likely will feel comfortable substituting it, and pharmacy systems are more likely to integrate the biosimilar.")

⁴⁹ See 21 U.S.C. 358, which provides in relevant part: "The Secretary [of HHS] may designate an official name for any drug or device if he determines that such action is necessary or desirable in the interest of usefulness and simplicity." See also 42 U.S.C. 262(a)(1)(B)(i).

⁵⁰ Outside the United States, the World Health Organization ("WHO") administers the international naming convention known as the International Nonproprietary Naming ("INN") system. See *International Nonproprietary Names, World Health Org.*, <http://www.who.int/medicines/services/inn/en/index.html> (last visited Oct. 31, 2013).

⁵² See European Comm'n, *What you Need to Know about Biosimilar Medicinal Products* 9 n.11 (2013), http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf; Lovenworth, *supra* note 47; Press Release, Hospira Inc., *Hospira's Inflectra (infliximab) the first biosimilar antibody to be approved in Europe* (Sept. 10, 2013), <http://phx.corporate-ir.net/phoenix.zhtml?c=175550&p=irol-news-Article&ID=1853480>.

to the approval of biosimilars.⁵³ Reports indicate that biosimilars have offered price competition in various EU markets, resulting in ten to forty percent price discounts from branded biologics pricing.⁵⁴

At the workshop, the FTC will explore the status of the development of biosimilars in the United States. Further, the FTC will examine other countries' experiences with the regulation and marketing of biosimilars.⁵⁵ The Commission will explore how biosimilar competition has developed and the extent of biosimilar price competition, along with related questions listed below.

Questions Related to Biosimilar Competition in the United States and in Other Countries

1. What, if any, predictions made in the FTC's 2009 FOB Report should be revised in light of more recent data available on approved biological products or biosimilar development programs?

2. What has been the competitive effect of the market entry of biosimilar competitors in countries with drug regulatory approval standards comparable to those of the U.S. FDA, such as the EU, Australia, or New Zealand? After such entry, have reference biologic manufacturers lowered their prices, offered discounts, engaged in enhanced marketing activities, or increased innovation or next-generation developments?

3. Are there empirical models that could predict the nature of U.S. biosimilar or interchangeable biologics

competition based on existing biologic product competition in Europe, Australia, New Zealand, or other countries? Are there empirical models that could predict the nature of U.S. biosimilar or interchangeable biologics competition based on existing competition in specialty drug markets? What factors increase or detract from robust competition between reference biologic and biosimilars or interchangeable biologics in other countries?

4. Based on the experiences in other countries, does competition from biologics influence investments in research and development for new biologics, improvements to existing biologics, and the timing and rollout of new and/or improved biologics? Does the market experience with generic drugs provide insights into these issues?

5. What data or empirical evidence exist in Europe or other countries regarding immunogenicity or other serious adverse events, if any, caused by substitution or switching between biosimilar and reference biologics?

III. Request for Comment

You can file a comment online or on paper. For the Commission to consider your comment, we must receive it on or before March 1, 2014. Write "Workshop on Follow-On Biologics: Project No. P131208" on your comment. Your comment—including your name and your state—will be placed on the public record of this proceeding, including, to the extent practicable, on the public Commission Web site, at <http://www.ftc.gov/os/publiccomments.shtm>. As a matter of discretion, the Commission tries to remove individuals' home contact information from comments before placing them on the Commission Web site.

Because your comment will be made public, you are solely responsible for making sure that your comment does not include any sensitive personal information, like anyone's Social Security number, date of birth, driver's license number or other state identification number or foreign country equivalent, passport number, financial account number, or credit or debit card number. You are also solely responsible for making sure that your comment does not include any sensitive health information, like medical records or other individually identifiable health information. In addition, do not include any "[t]rade secret or any commercial or financial information which is obtained from any person and which is privileged or confidential," as provided in Section 6(f) of the FTC Act, 15 U.S.C. 46(f), and FTC Rule 4.10(a)(2), 16 CFR 4.10(a)(2).

In particular, do not include competitively sensitive information such as costs, sales statistics, inventories, formulas, patterns, devices, manufacturing processes, or customer names.

If you want the Commission to give your comment confidential treatment, you must file it in paper form, with a request for confidential treatment, and you have to follow the procedure explained in FTC Rule 4.9(c), 16 CFR 4.9(c).⁵⁶ Your comment will be kept confidential only if the FTC General Counsel grants your request in accordance with the law and the public interest. Postal mail addressed to the Commission is subject to delay due to heightened security screening. As a result, we encourage you to submit your comments online. To make sure that the Commission considers your online comment, you must file it at <https://ftcpublic.commentworks.com/ftc/biologicsworkshop>, by following the instructions on the web-based form. If this Notice appears at <http://www.regulations.gov/#!home>, you also may file a comment through that Web site.

If you file your comment on paper, write "Workshop on Follow-On Biologics: Project No. P131208" on your comment and on the envelope, and mail or deliver it to the following address: Federal Trade Commission, Office of the Secretary, Room H-113 (Annex X), 600 Pennsylvania Avenue NW., Washington, DC 20580. If possible, submit your paper comment to the Commission by courier or overnight service.

Visit the Commission Web site at <http://www.ftc.gov> to read this Notice and the news release describing it. The FTC Act and other laws that the Commission administers permit the collection of public comments to consider and use in this proceeding as appropriate. The Commission will consider all timely and responsive public comments that it receives on or before March 1, 2014. You can find more information, including routine uses permitted by the Privacy Act, in the Commission's privacy policy, at <http://www.ftc.gov/ftc/privacy.htm>.

By direction of the Commission.

Donald S. Clark,

Secretary.

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⁵³ Biosimilars also exist in other countries. See e.g., Pharmaceutical Product Development, Developing Biosimilars Across Emerging Markets: Clinical and Regulatory Considerations (2013), <http://www.healthtrustpg.com/biosimilars/pdf/ppd.pdf>.

⁵⁴ See European Comm'n, *supra* note 53, at 16. See also *Health Policy Brief: Biosimilars*, *supra* note 2, at 2 (average price discount on EU biosimilars is "about 25 percent," and overall EU savings by 2020 "are projected to total \$16-43 billion," although level of biosimilar penetration varies substantially among EU countries, depending on "differences in payment systems and policies, laws related to drug substitution, and the overall size of the generics market within each country").

⁵⁵ See European Comm'n, *supra* note 53, at 9-10 ("The EU is the first region in the world to have set up a legal framework and a regulatory pathway for 'similar biological medicinal products', more commonly called 'biosimilars'. The EU regulatory framework inspired many countries around the world, e.g., Australia, Canada, Japan, Turkey, Singapore, South Africa, Taiwan, USA etc. as well as the World Health Organisation (WHO).") The concept of a "similar biological medicinal product" was adopted in EU pharmaceutical legislation in 2004 and came into effect in 2005. The first biosimilar medicine was approved by the European Commission in 2006.") The FTC will focus on countries with regulatory approval schemes comparable to those of the FDA.

⁵⁶ In particular, the written request for confidential treatment that accompanies the comment must include the factual and legal basis for the request, and must identify the specific portions of the comment to be withheld from the public record. See FTC Rule 4.9(c), 16 CFR 4.9(c).