



Notifications and Names: FTC Workshop Explores Effect of State Legislation and Naming Conventions on Follow-On Biologic Competition

By *Valentina Rucker and Roisin Comerford*¹
Wilson Sonsini Goodrich & Rosati



Introduction

Biologic medicines represent some of the most significant—both clinically and financially—pharmaceutical products in the United States today. Biologics have had remarkable success in the treatment of patients with many common diseases and disorders such as cancer, diabetes, multiple sclerosis, arthritis, and anemia. However, biologics remain one of the most expensive categories of medicines on the market. According to the Federal Trade Commission (“FTC”), the cost of one year of treatment of a biologic medicine can range from \$50,000 to \$250,000.²

Biologics’ active drug substances are cultivated from living organisms by means of recombinant DNA or controlled gene expression methods. Biologics include a wide range of products such as vaccines, blood and blood components,

allergens, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins.³

Biologics are “typically larger and more structurally complex molecules” than the traditional small molecule drugs.⁴ Therefore, production of biologics requires more difficult and expensive manufacturing processes and techniques to ensure consistency.⁵

A biologic can either be introduced by an innovator company or by a follow-on competitor. The follow-on biologic is a subsequent version of the reference biologic. Follow-on biologics further divide into biosimilars and interchangeable biologics. Biosimilars are follow-on biologics that may not be completely identical, but which are so “highly similar” to the previously approved reference biologic that “notwithstanding minor differences in clinically inactive components,”⁶ the same clinical outcome can be expected. Interchangeable biologics are follow-on

¹ Valentina Rucker and Roisin Comerford are a senior associate and an associate, respectively, in the Washington, D.C., office of Wilson Sonsini Goodrich & Rosati. The views and opinions expressed by the authors are theirs alone, and do not necessarily reflect the views and opinions of Wilson Sonsini Goodrich & Rosati.

² Federal Trade Commission, Notice of Workshop and Request for Comments, Public Workshop: Follow-On Biologics: Impact of Recent Legislative and Regulatory Naming Proposals on Competition, 78 Fed. Reg. 68,840 (November 15, 2013), available at http://www.ftc.gov/sites/default/files/documents/federal_register_notices/2013/11/131115biologicsfrn.pdf.

³ U.S. Food and Drug Administration, Vaccines, Blood and Biologics, <http://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Consumers/default.htm> (last visited Feb. 27, 2014).

⁴ Health Policy Brief, Biosimilars, Health Affairs, 1 (Oct. 10, 2013), http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_100.pdf.

⁵ *Id.*

⁶ 42 U.S.C. § 262(i)(2) (2011).



biologics that produce the same clinical result as the FDA-licensed biological reference product in any given patient. Additionally, to be approved as interchangeable, a biologic needs to show that if administered more than once, the safety and reduced efficacy risks of switching from the reference biologic to an interchangeable biologic, or alternating between the reference biologic and an interchangeable biologic, cannot be greater than the risks posed by use of the reference product without alternating or switching.⁷

In addition to the structural differences outlined above, biologics, unlike traditional small molecule drugs, are not regulated under the Food Drug and Cosmetic Act,⁸ and Hatch-Waxman Act of 1984,⁹ and are therefore not subject to the Hatch-Waxman's accelerated FDA approval processes. Biologics are also not covered by state laws that allow pharmacists to automatically substitute therapeutically-equivalent small molecule generics for reference brand name drugs.

To address this void, Congress passed the Biologics Price Competition and Innovation Act¹⁰ ("BPCIA"), which introduced an abbreviated approval pathway for follow-on biologics. The provisions of the BPCIA were patterned, in some respects, after the Hatch-Waxman Act and allow an applicant—who is seeking FDA approval of a follow-on biologic product—to rely on certain existing scientific knowledge about the safety and effectiveness of the approved reference biologic in their application for approval.¹¹

In several other respects, however, the BPCIA is different from the Hatch-Waxman Act. First, assessments of biosimilarity differ under the BPCIA to account for the difference in analytical processes available for biologic medicines. Second, the BPCIA includes a 12-year exclusivity period for the innovator product, instead of a 5-year period provided by Hatch-Waxman.¹² Notwithstanding these differences, the purpose of the BPCIA was largely the same: promoting competition in the market and thereby reducing the cost of these expensive medicines for consumers.

In practice, the BPCIA has had limited effect on competition from follow-on biologics. In fact, since the introduction of the BPCIA, no follow-on biologic has received FDA approval via the abbreviated pathway, although several applications are currently pending review by the FDA,¹³ and several issues have arisen. Firstly, despite the fact that no follow-on biologics have been approved, several states have proposed or enacted legislation that imposes certain restrictions on the substitution of follow-on biologics for the reference product. Secondly, debate has grown over the naming conventions that should be adopted for follow-on biologics. To explore and address these issues, the FTC held a day-long workshop on February 4, 2014 to discuss the impact on competition of these recent legislative and regulatory naming proposals.¹⁴

⁷ § 262(k)(4).

⁸ 21 U.S.C. ch. 9 § 301 et seq.

⁹ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended 21 U.S.C. §355 (1994)).

¹⁰ 42 U.S.C. § 262 (2011).

¹¹ *Id.*

¹² § 262(k)(7).

¹³ 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); see also Food and Drug Administration, Information for Consumers (Biosimilars), available at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241718.htm> (last updated November 3, 2011).

¹⁴ Federal Trade Commission, *supra* note 2.



Chairwoman Ramirez's Opening Remarks

Andrew Gavil, Director of Policy Planning at the FTC, opened the workshop by welcoming attendees.¹⁵ Then, FTC Chairwoman Edith Ramirez offered further welcoming remarks and stressed the significance of biologic medicines for difficult to treat diseases such as cancer, diabetes, and multiple sclerosis. Chairwoman Ramirez also highlighted the high cost of these therapeutics, noting that these costs may prevent some patients from accessing potentially life-saving therapies. Further, she noted that introducing competition into the biologics marketplace represents one of the most promising ways to reduce prices and expand access. While recognizing the need for more robust competition, Chairwoman Ramirez noted the impact of the regulatory landscape on competition for biologics. Specifically, she stressed that the “the ultimate goal . . . is to develop policies that protect patient health and safety, but to do so without unnecessarily chilling competition and deterring investment in follow-on biologics.”

After introducing the general objectives, the Chairwoman summarized the issues to be discussed during the workshop. She pointed out that these issues are not novel. In the 1970s, when generic drugs and the Hatch-Waxman Act were first contemplated, there were similar issues. Because of perceived safety concerns, many states prohibited pharmacists from substituting generic drugs for their branded counterparts. To address these state laws, the FTC studied competitive effects of these “anti-substitution” laws. A staff report issued in 1979¹⁶ concluded that the FDA’s review process

would result in the approval of safe and effective generic drugs and that, if pharmacists were free to dispense generic drugs without unnecessary regulatory hurdles, this would stimulate beneficial price competition for consumers. Subsequently, on the FTC’s recommendation, state legislatures adopted laws allowing for automatic substitution.

Chairwoman Ramirez closed with the following guiding principle for the workshop’s discussions: while follow-on biologics are more complex, the basic concept of competition still applies and the ultimate goal remains the same—to develop policies that protect patient health and safety without chilling competition or deterring investment in follow-on biologic medicines.

The Rising Cost of Biologic Medicines

A fundamental tenet of the discussions at the FTC workshop was the prediction that follow-on biologic competition promises cost savings and increased patient access. There was little debate as to the need for biologic competition, and many speakers highlighted the high cost of, and growing dependence on, biologic medicines.

For example, consumer organization AARP put forward evidence of the rising cost of biologic medicine consumption, a point echoed by payor representatives.¹⁷ According to AARP representative Leigh Purvis, on average biologics are 22 times more expensive than traditional drugs, with the average annual cost of a branded biologic estimated at \$34,500.¹⁸ Even for patients who are insured, lifesaving biologics may be cost prohibitive, because many

¹⁵ Elizabeth A. Jex, an Attorney Advisor in the FTC’s Office of Policy Planning, and Susan DiSanti, an attorney in the Western Regional Office of the FTC, also offered remarks and helped moderate the workshop throughout the day.

¹⁶ FED. TRADE COMM’N, STAFF REPORT TO THE FEDERAL TRADE COMMISSION, DRUG PRODUCT SELECTION (1979).

¹⁷ Steve Miller, M.D., *Customer Perspective on Biosimilars*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 2 (Feb. 4, 2014).

¹⁸ Leigh Purvis, M.P.A., *Consumer Perspective on Biosimilars*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 3 (Feb. 4, 2014) (citing E.A. Blackstone and J.P. Fuhr, Jr., “Innovation and Competition: Will Biosimilars Succeed?” *Biotechnology Healthcare*, Spring 2012).



medical plans, including Medicare, include cost-sharing structures.¹⁹ Ms. Purvis described the present costs of biologics as “not sustainable” and urged regulators to implement systems that will make these medicines accessible and affordable, arguing that medical advances are meaningless if no patient can afford to use them.²⁰

Some panelists forecasted that more than 50 percent of the U.S. prescription drug budget will be spent on biologics by 2018,²¹ and the list of diseases that biologics can be used to treat is expanding.²² Meanwhile, Harry Travis, Vice President and General Manager of Aetna Specialty and Home Delivery Pharmacy, revealed that even today close to 50 percent of Aetna’s entire drug spend is spent on specialty medicines, mainly biologics. Notably this 50 percent of spend represents only 1 percent of patient prescriptions.²³ Mr. Travis asserted that as spending on biologics continues to increase, it diverts funds away from other drugs and health care costs.

Industry participants and patients alike have high hopes for follow-on biologics to offset these ever expanding costs. Dr. Kesselheim highlighted the successes of generic competition in small molecule drugs in reducing costs and increasing access.²⁴ Steven Miller, M.D., M.B.A., Senior Vice President & Chief Medical

Officer of Express Scripts referenced a study carried out by Express Scripts which showed the potential savings from the use of follow-on biologics would be at least \$250 billion by 2024.²⁵ Dr. Miller emphasized the importance of broad stakeholder cooperation in ensuring the success of the follow-on biologic pathway and resulting competition, in order to reduce these costs.²⁶

State Substitution Laws

The first issue on the workshop agenda was the introduction of state legislation that encumbers automatic substitution. The proponents of such laws argue that, since biologics are more complex, automatic substitution afforded to small molecule drugs is inappropriate. The opponents of such laws argue that the current framework already addresses these concerns and anti-substitution state laws are premature.

The Basics of State Notification Legislation

To start, Jessica Mazer, J.D., Assistant Vice President for State Affairs of the Pharmaceutical Care Management Association, identified the main state substitution law proposals.²⁷ To date, states’ proposed or adopted bills impose the following types of requirements on pharmacists and prescribers when substituting biologics: (1) a requirement that a pharmacist notifies a patient and/or her prescriber upon dispensing an interchangeable biologic within a specified time period; (2) a requirement to record any such substitution; and (3) a requirement that the

¹⁹ *Id.* at 7-12.

²⁰ *Id.* at 20.

²¹ *Id.* at 3.

²² *Id.* at 4.

²³ Harry Travis, B.S. Pharm., M.B.A., *Private Payor Perspective on Growth of Specialty Medicines and Naming*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 2 (Feb. 4, 2014).

²⁴ Aaron Kesselheim, M.D., J.D., M.P.H., *Lessons for Follow-On Biologics from Small Molecule Drugs*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 8 (Feb. 4, 2014). Dr. Kesselheim noted that 84 percent of prescriptions in 2012 were filled with generic drugs, saving the health care system up to \$1 trillion dollars in the last 10 years.

²⁵ Miller, *supra* note 17, at 6.

²⁶ *Id.* at 13.

²⁷ All panelists prepared helpful presentations that can be accessed via the FTC website. See FTC Events Calendar, Follow-On Biologics Workshop: Impact of Recent Legislative and Regulatory Naming Proposals on Competition, <http://www.ftc.gov/news-events/events-calendar/2014/02/follow-biologics-workshop-impact-recent-legislative-regulatory>. Additionally, the FTC posted video recordings of the workshop and will post and official transcript, once available. See *id.*



state's board of pharmacy maintain a list of interchangeable biologics. Notably, these requirements apply to interchangeable follow-on biologics, medicines that must meet a higher standard than biosimilars to secure the FDA approval.

To date, five states have enacted such legislation—Florida, North Dakota, Oregon, Utah, and Virginia.²⁸ The state with the most extensive additional requirements is North Dakota.²⁹ North Dakota's legislation, signed into law March 29, 2013, requires that the pharmacist notify the prescribing practitioner orally, in writing, or via electronic transmission within 24 hours of the substitution, and notify the patient who maintains a right to refuse the substitution.³⁰ The pharmacy and the prescribing practitioner must also retain a written record of the substitution for at least five years.³¹ Less extensive, but still substantial, requirements have been adopted in Oregon, Utah, and Virginia. Legislation enacted in Oregon³² and Utah³³ requires a pharmacist to notify the prescriber of any substitution within three days.³⁴ Notably, however, both Oregon's and Utah's laws include a sunset provision relating to this clause, meaning the requirement will likely expire before any relevant follow-on biologic becomes available.³⁵ Virginia too has enacted legislation that requires prescriber notification, with a corresponding sunset provision, though that law affords the pharmacy

five days to notify the prescriber.³⁶

Additionally, all three of these “middle of the road” laws contain pharmacy record keeping requirements, though only Virginia requires the prescriber to maintain a record for at least two years.³⁷ Finally, the legislation with the fewest requirements has been enacted in Florida. There is no prescriber notification provision,³⁸ but the law still requires patient notification and retention of a record by the pharmacist for at least two years.³⁹

In California, a bill was passed, but subsequently vetoed by the governor. The California bill required pharmacists to notify both the patient and the physician of any substitution.⁴⁰ Governor Brown vetoed this bill, stating that “[t]he FDA, which has jurisdiction for approving all drugs, has not yet determined what standards will be required for biosimilars to meet the higher threshold for ‘interchangeability,’ [and that therefore] to require physician notification at this point strikes [me] as premature.”⁴¹

As of February 2014, nine states are due to consider follow-on biologics legislation in 2014.⁴² Among them is Massachusetts,⁴³ whose bill contains a slightly novel provision, under which physician notification will not be required until full interoperability of an electronic health

²⁸ Jessica S. Mazer, J.D., *Introduction to State Biosimilar Substitution Laws*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 6 (Feb. 4, 2014).

²⁹ N.D. CENT. CODE § 19-02.1-14.3 (2013).

³⁰ Mazer, *supra* note 28.

³¹ *Id.*

³² OR. REV. STAT. § 689.522

³³ UTAH CODE ANN. § 58-17b-605.5

³⁴ Mazer, *supra* note 28, at 7.

³⁵ *Id.*

³⁶ VA. CODE ANN. § 54.1-3408.04 (2013); Mazer, *supra* note 28, at 7.

³⁷ VA. CODE ANN. § 54.1-3408.04 (2013).

³⁸ FL. STAT. ANN. § 465.0252, § 465.019; Mazer, *supra* note 28, at 8.

³⁹ Mazer, *supra* note 28, at 8.

⁴⁰ S.B. 598; Mazer, *supra* note 28, at 9.

⁴¹ Mazer, *supra* note 28, at 9.

⁴² *Id.* at 11. Remarks made during the FTC workshop indicate that in addition to the states identified in Ms. Mazer's presentation, Vermont will also consider follow-on biologics legislation in 2014.

⁴³ H.B. 3734.



record system.⁴⁴ While the proposed bill does require prescriber notification within a reasonable time following a substitution, entry of the substitution into a patient's electronic health record would constitute notification.⁴⁵

Arguments in Support of State Legislation

During the workshop, various stakeholders participated in the debate as to whether legislation requiring additional steps for biologic substitution is necessary. The proponents argued generally that since biosimilars are very complex and are only similar, rather than identical, automatic substitution afforded to small molecule drugs is inappropriate. They argued that the patient should be notified (and given a choice to refuse such substitution) of the potential risks of taking a medicine that is only similar to what the doctor has prescribed. Notably, while these arguments apply to biosimilars generally, the legislation that has been enacted in the five aforementioned states applies to biologics that have been designated as interchangeable by the FDA, which requires a showing of complete therapeutic equivalence.

Additionally, they argued that the prescriber notification would allow for an accurate and unambiguous medical record, which is necessary to ensure patient safety and proper adverse event reporting. For example, Geoffrey Eich, M.B.A., Executive Director for Regulatory Affairs at Amgen, summarized patient risks that may result from an incomplete medical record.⁴⁶ According to Mr. Eich, because biologics persist within the body for a much longer period of time than most chemical drugs, an overlap of exposure to circulating

biologics from different sources is likely.⁴⁷

Latent immune responses, leading to changes in the efficiency or tolerance of a biologic medicine, make attribution to a specific product more challenging, increasing the importance of a complete and accurate medical record, Mr. Eich argued.⁴⁸

Finally, another reason for notification is to ensure effective post-market surveillance, i.e., to promote pharmacovigilance. All biologics are sensitive to unintended occurrences during manufacture and handling—therefore post-market surveillance, facilitated by keeping a record of all substitutions, is an important safeguard to ensure patient safety.⁴⁹ In fact, pharmacovigilance was discussed at length during the workshop (mostly in connection with the naming conventions) and is addressed later in the article.

Arguments Against State Legislation

On the other hand, the opponents of such state laws argue that the current framework already addresses these concerns or, alternatively, that such laws are premature. During the workshop, various stakeholders, including representatives from academia, industry analysts, consumer organizations, dispensers, payors and biosimilar developers argued that the FDA approval process of follow-on biologics is sufficient to ensure that approved follow-on biologics are safe and appropriate for substitution and that the practicalities of medical record keeping render physician notification requirements onerous and unnecessary.

To start the discussion, a consultant at ThinkFDA, LLC, Emily Shacter, Ph.D., presented an overview of the FDA's approach for follow-on biologic approval in order to

⁴⁴ Mazer, *supra* note 28, at 10.

⁴⁵ *Id.*

⁴⁶ Geoffrey S. Eich M.B.A., *Establishment of a Vibrant U.S. Biosimilars Approval Pathway*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 4 (Feb. 4, 2014).

⁴⁷ *Id.*

⁴⁸ *Id.*

⁴⁹ *Id.*



dispute that the complexity of the large molecule makes substitution inherently dangerous. Ms. Shacter explained that the FDA would need to subject follow-on biologics to the most rigorous testing and analysis to ensure approval is granted only where appropriate and focused on the highly advanced nature of analytics used in the industry. Ms. Shacter predicted that only those biosimilars that are “virtually interchangeable” with the innovator biologic would be approved by the FDA.⁵⁰ She argued that modern scientific tools can adequately detect variances or potential issues in follow-on biologic structure, and that these tools could be used to sufficiently prove biosimilarity to the FDA.

Second, Jessica Mazer of the Pharmaceutical Care Management Association suggested that given the trust placed in the FDA for approval of small molecule generics, any distrust of the agency in the follow-on biologic realm is misplaced.⁵¹ Once the FDA has approved a follow-on biologic as safe and either interchangeable or highly similar to the reference biologic, such that no clinically meaningful effects would present in the patient, such determination by the FDA should be sufficient. As such, according to Ms. Mazer, state legislation proposing notification or record keeping requirements is not necessary to ensure patient safety.

This view was echoed by both Krystalyn Weaver, Pharm. D., Director of Policy and State Relations at the National Alliance of State Pharmacy Associations and Leigh Purvis, M.P.A. Senior Strategy Policy Advisor with the AARP.⁵² Biosimilar developers too relied on this point, including Bruce Leicher, J.D., Senior

Vice President & General Counsel at Momenta Pharmaceuticals, who also referenced the rigorous standards of the FDA.⁵³

Finally, Marissa Schlaifer, M.S., R.Ph., Head of Policy at CVS Caremark identified several practical problems with the enacted and proposed notification requirements. Requiring notification and consent for follow-on biologics, according to Ms. Schlaifer, would create unnecessary communication between a pharmacy and a physician’s office. Information exchange between pharmacy and physician is crucial for tasks like readjusting a dose or questioning a treatment because of allergy, and imposing a notification requirement in the case of follow-on biologic substitution has a potential of introducing unnecessary noise into, and therefore disrupt, this critical communication pathway. Ms. Schlaifer also referenced the wealth of information that is recorded and maintained by a pharmacy, information that ensures a patient receives the correct medicine at the appropriate time, and therefore argued that a medical provider’s record may not in fact reflect an entirely comprehensive and accurate patient health record.

Naming Conventions

After the break, representatives from various camps debated naming conventions for biosimilars. When Congress passed BPCIA, it did not include specific statutory language regarding the naming of approved follow-on products, leaving the decision up to the FDA. Some stakeholders wanted to see biosimilars given nonproprietary names that are completely unique, or at least have a unique suffix or prefix, in order to ensure patient safety and exact adverse event tracking. Others advocated that follow-on biologics should have the same

⁵⁰ Emily Shacter Ph.D., *The Rigorous FDA Review Process for Biosimilars and Interchangeables*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 9 (Feb. 4, 2014).

⁵¹ Mazer, *supra* note 28, at 12.

⁵² Purvis, *supra* note 18, at 15.

⁵³ Bruce A. Leicher J.D., *Anti-Competitive Deterrents to Investment and Innovation in Biosimilars and Interchangeable Biologics*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 13 (Feb. 4, 2014).



nonproprietary names as their reference biologics.

The Basics of Medicine Naming Conventions

Generally, a medicine can carry several names—usually, a proprietary brand name, selected by the innovator company, and a nonproprietary active ingredient name.⁵⁴ As it relates to the small molecule drugs, a generic is named using the same nonproprietary name as the reference drug. As it relates to a biologic, however, there was a significant debate whether follow-on biologics should bear the same nonproprietary name as the reference biologic. Angela Long, M.S., a Sr. Vice President, Global Alliances and Organizational Affairs and Secretariat, Council of Experts for USP, opened this segment with an overview of the various naming conventions. In the United States,⁵⁵ each marketed medicine is assigned a unique nonproprietary name by the United States Adopted Names (USAN) Council. The USAN Council works in conjunction with the World Health Organization International Nonproprietary Name (INN) Expert Committee to standardize drug nomenclature, but USAN is independent of INN. USAN is co-sponsored by the American Medical Association, the United States Pharmacopeial Convention (USP),⁵⁶ and the American Pharmacists Association. USP's drug standards are in turn enforced by the FDA. USP's role in naming applies to both drug substances and drug products. When the FDA

approves a small molecule drug for marketing, two things may happen with respect to the nonproprietary name. First, if the applicable USP monograph already exists, monograph's "official title" can be used as a nonproprietary name. Alternatively, if the FDA approves a drug and there is no applicable USP monogram, the FDA provides an "interim established name" that serves as a nonproprietary name until USP creates a monograph.⁵⁷ This naming process could hold true with respect to biologics and, according to Ms. Long, USP should be allowed to use its already established naming procedures to assign nonproprietary names to follow-on biologics. This way, if a follow-on biologic were to meet the requirements of an existing USP monograph, it could use the monograph's "official title" as its nonproprietary name. While this may be a logical extension of the current small molecule naming paradigm, opponents argued this approach should not apply to biologics because glycosylation⁵⁸ makes proof of sameness very difficult. Glycosylation (i.e., how a protein folds) is a type of modification in a biologic molecule that is hard to see, but which may affect the molecule's activity, immunogenicity, and, in some cases, its pharmacokinetics. Innovator companies have long argued that because process conditions affect glycosylation, it is impossible to create a protein with the same glycosylation patterns in two different processes, and therefore there could never be an identical version of a biologic.

⁵⁴ The FDA has authority to determine nonproprietary names. 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).

⁵⁵ There are no universal global rules governing the classification of new substances.

⁵⁶ USP is a scientific nonprofit organization that sets standards for the identity, strength, quality, and purity of medicines. See U.S. Pharmacopeial Convention, About USP, <http://www.usp.org/about-usp>.

⁵⁷ Angela G. Long, M.S., Tina S. Morris, *Introduction to Drug Naming*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 8 (Feb. 4, 2014).

⁵⁸ PTMs are chemical transformations that occur after a protein's translation from RNA and include numerous changes, some well-known and others quite obscure. The best-known PTM is glycosylation, the addition of sugar residues to amino acids bearing amino or hydroxyl groups. See Glycosylation main approval issue with biosimilars posted 01/09/2009, <http://www.gabionline.net/Conferences/Glycosylation-main-approval-issue-with-biosimilars>.



Glycosylation is certainly an intricate concept, but panelists argued that the new generation analytical technology could make proof of sameness possible. For example, Tina Morris, Ph.D., Vice President, Biologics and Biotechnology, USP-NF in the Global Science and Standards Division at USP, stated that “[t]he analysis of complex glycosylation patterns and the level of heterogeneity made visible is directly linked to the resolving power of the applied analytical technology.”⁵⁹ Thus, as the analytical technology improves, “generic” biologics may well be a reality.

Further, Ms. Morris argued that while sameness is an important determination for the purpose of finding bioequivalency, molecules do not need to be identical to be assigned the same nonproprietary USP name. In fact, a USP monograph under the same title may describe multiple articles in commerce.⁶⁰ Therefore, according to Ms. Morris, if the definition of sameness is the main concern as it relates to the identification test for an existing USP monograph, the proper answer is for the FDA to prescribe additional standards for how to determine said sameness and not to completely overhaul the process and require unique nonproprietary names for biologics.

Arguments in Support of Unique Nonproprietary Names for Biosimilars

After the overview of general naming conventions, representatives from Amgen, Pfizer and AbbVie took turns arguing that the small molecule naming paradigm is not applicable to biologics and that allowing biosimilars to have the same nonproprietary name will create confusion. Additionally, panelists argued that biosimilars should be uniquely identified to protect patient safety and to promote accurate adverse event reporting.

First, panelists argued that non-unique nonproprietary names would introduce confusion. Gustavo Grampp, Ph.D., Director of R&D Policy at Amgen, noted that since biologics are made from living cells, biosimilars are not in fact structurally identical to the originator biologic or other biosimilars,⁶¹ thus using the same nonproprietary name is scientifically inappropriate.⁶²

Emily Alexander, J.D., Director of U.S. Regulatory Affairs in the Biologics Strategic Development group at AbbVie, agreed and cited survey statistics where 76 percent of physicians said that having an identical nonproprietary name implies that two products have identical structures, which in her opinion would not be accurate (and would create confusion) as it relates to biosimilars.⁶³

Second, panelists argued that non-unique nonproprietary names would hinder pharmacovigilance. Pharmacovigilance is a process of identifying and assessing adverse events and possible side effects associated with a product. To function properly, this process requires the ability to link specific adverse events or event trends to the responsible product. The shared concern voiced by several panelists was as follows: if doctors and patients report adverse effects using only the non-unique nonproprietary name, it may be impossible to properly attribute product flaws to the correct manufacturer. This concern is especially strong for jurisdictions (e.g., China) that prohibit doctors from prescribing by brand name, but at the same time report adverse effects of its

⁶¹ Gino Grampp, Ph.D., *A Science-Based Naming Policy for Biologics: FTC Public Meeting on Biosimilar Policy*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 4-5 (Feb. 4, 2014).

⁶² *Id.* at 11.

⁶³ Emily A. Alexander, J.D., *Reference Biologic Perspectives On Naming*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 9 (Feb. 4, 2014).

⁵⁹ Long, *supra* note 57, at 20.

⁶⁰ *Id.* at 17.



citizens to the FDA (presumptively using nonproprietary names only).

For example, to support her argument that unique nonproprietary names are desirable for effective pharmacovigilance, Helen Hartman, Ph.D., Director, Worldwide Regulatory Strategy at Pfizer, presented results of a study conducted by Pfizer. The study was designed to evaluate the frequency with which a specific manufacturer was reported as part of an adverse event report.⁶⁴ Pfizer found that in instances where multiple drugs had the same nonproprietary names (i.e., a small molecule case study), in 14 percent of reports the manufacturer could not be identified; however, where proprietary names were the only identifiers available (i.e., a biologics case study), only in less than 1 percent of reports the manufacturer could not be identified.⁶⁵

Thus, Dr. Hartman concluded that unique names (proprietary and nonproprietary) are preferred for proper attribution. Specifically, Dr. Hartman concluded, based on the study's results, that "[i]n the absence of a requirement that *all* biosimilars and follow-on biologics adopt unique trade names, ... identification of manufacturers in [adverse event] reporting will be hindered if the products share the same [nonproprietary] name" (emphasis in original).⁶⁶ Ms. Alexander suggested a milder approach: a biosimilar should have both a distinct brand name and a *related but distinguishable* nonproprietary name. According to Ms. Alexander, under this approach, a "related 'core' non-proprietary name [would] help assess adverse events across a class of products but [a] distinguishing prefix or suffix [would] allow for

differentiation."⁶⁷ This approach is similarly taken by Australia and Japan.⁶⁸

Arguments Against Unique Nonproprietary Names for Biosimilars

In contrast, the opponents of unique names argued that such nomenclature may increase market confusion and does not necessarily promote pharmacovigilance. Multiple groups were represented, including the FTC, biosimilar applicants, patient-advocacy groups, and pharmacy representatives.

First, panelists argued that unique nonproprietary names may actually abet, rather than resolve, patient confusion. Bruce Leicher from Momenta Pharmaceuticals, noted that to be approved by the FDA as a biosimilar a follow-on biologic must show to have no clinically meaningful differences from the reference product.⁶⁹ Thus, there is no defensible basis for different nonproprietary names.⁷⁰ Mark McCamish, M.D., Ph.D., Global Head of Biopharmaceutical Development for Sandoz International, further disputed the "similar but not identical" claims of the earlier panelists stating that "'non-identity' is a normal principle in biotechnology,"⁷¹ and that no two batches of any biologic are identical. Thus, so long as differences between a biosimilar and its reference biologic do not affect safety or effectiveness, a certain degree of natural variability should be acceptable. Panelists used other countries' examples to show that different nonproprietary names will actually lead to

⁶⁴ Helen B. Hartman, Ph.D., *Looking Into the Future Biosimilar Landscape: A Case Study*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 7 (Feb. 4, 2014).

⁶⁴ *Id.*

⁶⁵ *Id.*

⁶⁶ *Id.* at 9.

⁶⁷ Alexander, *supra* note 63, at 10.

⁶⁸ *Id.*

⁶⁹ Interchangeable biologics must also be demonstrated to be capable of being substitutable at the pharmacy without the need for intervention of a physician.

⁷⁰ Leicher, *supra* note 53, at 21.

⁷¹ Mark McCamish, M.D., Ph.D., *Effect of Naming on Competition and Innovation*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 6 (Feb. 4, 2014).



confusion and discrimination of biosimilars, affecting access and affordability.⁷²

Second, opponents of the unique nonproprietary names for biosimilars argued that pharmacovigilance does not justify unique naming conventions.⁷³ Sumant Ramachandra, M.D., Ph.D., M.B.A., Senior Vice President and Chief Scientific Officer at biosimilar developer Hospira, reviewed post-approval market surveillance and concluded that biosimilars do not need a unique nonproprietary name for effective post-market identification because the brand name is already used in nearly all cases and can serve as a differentiator.⁷⁴ Responding to suggestions of a unique suffix or prefix to distinguish a biosimilar's name in order to allow for easier adverse event tracking and other post-market safety purposes, Alan Lotvin, M.D., Executive Vice President of Specialty Pharmacy for CVS Caremark, noted that "[s]uch proposals confuse the role of the nonproprietary name, which describes the active ingredient, with the brand name which describes the product."⁷⁵ Finally, according to Mr. Leicher, safety reporting is not dependent on nonproprietary names, and any concerns regarding inadequacy of the reporting relate to all medicines and not biologics in particular.⁷⁶ Similarly, Neal Hannan, Attorney Advisor in the FTC's Office of Policy Planning, agreed with Mr. Leicher by suggesting that product names may not be the best way to capture adverse event information at all. In fact, he pointed out inherent flaws in the

way information is currently collected.

Therefore, to the extent adverse event reporting system falls short of collecting the necessary information, the appropriate response is to fix the collection methodology rather than institute unique nonproprietary names for biosimilars.⁷⁷

The Effects of Follow-On Biologics on Competition

Panelists argued state laws inhibiting automatic substitution and preventing follow-on biologics from using the same nonproprietary name as the reference biologic will stifle competition. With respect to state substitution laws, some went as far as describing state substitution laws as "anti-competitive deterrents to investment and innovation." For example, Mr. Leicher alleged that there has been "a long established campaign against biosimilar innovation and competition" in which state substitution legislation is the next tactic. Some, like Krystalyn Weaver from the National Alliance of State Pharmacy Association and Bruce Lott, Vice President of State Government Relations at Mylan Pharmaceuticals, took a more tempered approach, merely opining on the impact of such laws on biologic competition based on their experience with small molecule generics. Ms. Weaver used the example of Tennessee state legislation meant to regulate certain epilepsy drugs, to demonstrate how inhibiting automatic substitution may impact a generic. In Tennessee, certain epilepsy drugs were carved out and given specific substitution requirements, including physician notification. This resulted in a 29 percent increase in brand usage, increasing costs to the state and to patients. Separately, Dr. Kesselheim noted that 80 percent of prescribing physicians still use the brand name to refer to both an actual brand drug and any available generics. Therefore, panelists argued that the success of follow-on biologic

⁷² *Id.* at 15.

⁷³ Leicher, *supra* note 53, at 26.

⁷⁴ Sumant Ramachandra, M.D., Ph.D., M.B.A., *Lessons for the United States: Biosimilar Market Development Worldwide*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 7 (Feb. 4, 2014).

⁷⁵ Alan M. Lotvin, M.D., *Customer Perspective on Biosimilars and Interchangeable Biologics: Naming and State Legislative Issues*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 6 (Feb. 4, 2014).

⁷⁶ Leicher, *supra* note 53, at 24.

⁷⁷ Neal Hannan, J.D., *Intro to Naming Discussion*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 5 (Feb. 4, 2014).



competition is dependent on automatic substitution at the dispensary level, as has been the case with small molecule generics. With respect to the unique nonproprietary names, panelists argued that these too could have a negative impact on competition. Specifically, according to some, unique nonproprietary names will have the potential to create unnecessary confusion resulting in lessening of competition among healthcare providers and patients by perpetrating the notion that an interchangeable biosimilar is “different.”⁷⁸ Also, some panelists argued that using unique nonproprietary names for biosimilars may create a future barrier for when products are ultimately designated by the FDA as interchangeable. In such cases, panelists argued, the different nonproprietary name would be used to suggest that the active ingredient in the two medicines is different, even though the FDA would have determined otherwise. As Alan Lotvin from CVS Caremark put it, such “naming issue[s] threaten to thwart [the] promise of biosimilars.”⁷⁹ Harry Travis from Aetna Specialty and Home Delivery Pharmacy, echoed Dr. Lotvin’s concerns.

In addition to the immediate topics of the workshop, panelists voiced concerns over some additional “roadblocks” that may discourage pharmaceutical developers from pursuing follow-on biologics. For example, Aaron Gal, Ph.D., Senior Analyst at Sanford C. Bernstein Research LLC, listed the following, among others, as potential roadblocks: (1) new intellectual property issues that have not yet been ‘cleaned’ by decades of litigation (unlike small molecule drugs); (2) high rebates from originator manufacturers that make switching to follow-on biologics inefficient for payors; and (3) “first dose” phenomena.⁸⁰ Another obstacle

to follow-on biologic entry identified during the workshop was the high cost of biosimilar development itself, detailed by Dr. Ramachandra, from Hospira. According to Dr. Ramachandra, biosimilars are more costly to develop than small molecule generics and require manufacturers to take considerable risk, and legislators must ensure that the marketplace is designed to reward such investment.⁸¹ Dr. Ramachandra advocated for successful biosimilar market formation in the US, which he said, will require a combination of many factors including naming conventions, a stable regulatory environment, payor policies to advance patient access and education.⁸²

Effect on Biologic Competition in non-U.S. Jurisdictions

Mr. Gal used follow-on biologic adoption rates in various European countries to illustrate that the success of the biosimilar pathway is critically dependent on the regulatory environment.⁸³ He used Germany as an example to demonstrate how a properly modulated regulatory infrastructure could increase follow-on biologics adoption. There, the government has encouraged adoption with quota requirements, independent prescribers have drug budgets so are more disposed to use follow-on biologics as a cost saving measure, and most follow-on biologics originate locally so physicians and patients garner a more favorable view of follow-on biologic quality.⁸⁴

⁷⁸ Lotvin, *supra* note 75, at 7.

⁷⁹ *Id.* at 6.

⁸⁰ Aaron Gal, Ph.D., *Biosimilars: Commercial Perspective*, FTC FOLLOW-ON BIOLOGICS WORKSHOP, 8,

9 (Feb. 4, 2014). “First dose” is a concept that when patients are given their first dose of a drug at a hospital or clinic, where the reference drug is cheaper, they may then find it difficult to switch to a follow-on biologic or generic drug if regulations restrict switching.

⁸¹ Ramachandra, *supra* note 74, at 3.

⁸² *Id.* at 17.

⁸³ Gal, *supra* note 80, at 8-9.

⁸⁴ *Id.*



with follow-on biologics capturing approximately 75 percent of the market.⁸⁵ Dr. Ramachandra too looked at follow-on biologic market development worldwide and reported that trust in follow-on biologics continues to increase in Europe, as do the associated cost savings for patients and payors.⁸⁶ Dr. Ramachandra repeated Mr. Gal's point that regional and national policies will drive the rate of adoption of follow-on biologics after approval, as they have done in Europe.⁸⁷ Dr. Ramachandra demonstrated a measurable increase in patient access and cost savings in Europe since the introduction of follow-on biologics.⁸⁸

Conclusion

While many questions remain and no clear winners have emerged, all panelists agreed on one thing—the FTC should be commended for providing a forum for various stakeholders to voice their opinions. As Chairwoman Edith Ramirez made clear in her opening remarks, the FTC continues to be dedicated to finding the right balance between the need for competition in the growing field of biologics and the need for protecting patient safety, promoting effective pharmacovigilance, and addressing other concerns raised by the panelists. In addition to the concerns stated by the panelists during the workshop, the FTC also invited public comments (which were due to the FTC by March 1, 2014 according to the original workshop announcement) to make sure all voices were heard.

After a similar follow-on biologics debate in November 2008, which explored the introduction of an approval process for follow-on biologics, the FTC issued a report that

recommended introduction of a legislative process for an abbreviated FDA approval pathway for follow-on biologics. Subsequently, Congress passed the BPCIA, which created an abbreviated regulatory pathway for FDA approval of follow-on biologics. While the FTC has not committed to a formal report following this workshop, it would be helpful if the FTC issued a comprehensive report with its official stance on the proposed state legislations and naming conventions.

⁸⁵ *Id.* at 8.

⁸⁶ Ramachandra, *supra* note 74, at 9.

⁸⁷ *Id.* at 11.

⁸⁸ *Id.* at 12-13.