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7272 Wisconsin Avenue  
Bethesda, Maryland 20814  
301-657-3000  
Fax: 301-664-8877  
www.ashp.org

February 27, 2014  
Federal Trade Commission  
Office of the Secretary  
Room H-113 (Annex X)  
600 Pennsylvania Avenue NW  
Washington, DC 20580

Re: Workshop on Follow-On Biologics: Project No. P131208

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit comments to the Federal Trade Commission (FTC) on the topic of biosimilars as requested in the Federal Register on November 13, 2013.<sup>1</sup> The FTC held a public workshop on February 4, 2014 to discuss the potential impact of state regulations and naming conventions on the competitiveness of biosimilars.

ASHP is the national professional organization whose 40,000 members include pharmacists, pharmacy technicians, and pharmacy students who provide patient care services in acute and ambulatory care settings, including hospitals, health systems, and clinics. For more than 70 years, the Society has been on the forefront of efforts to improve medication use and enhance patient safety.

Biosimilars have been moving from concept to reality following the establishment of a pathway for approval of these products via passage of the Biologics Price Competition and Innovation Act (BPCIA) and subsequent issuance of guidance from the Food and Drug Administration (FDA). While biosimilars are expected to result in significantly less cost savings than that achieved with traditional generic drugs, overall savings to patients, payers, and health systems will still be substantial given the high cost and utilization of these products.

ASHP policy has been to support a legislative and regulatory pathway for biosimilars in the U.S. and encourage the development of safe and effective biosimilar medications in order to make such medications more affordable and accessible to patients.<sup>2</sup>

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<sup>1</sup> Federal Register, Vol. 78, No. 221, Pages 68840 – 68845.

<sup>2</sup> ASHP Policy 1218

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The FDA approval process provides some insight on how biosimilars will be regulated and adopted, including establishing a two-step process, first establishing biosimilarity followed by a determination of interchangeability. According to this process, a product that has achieved biosimilarity would mirror the innovator product in terms of mechanism of action and immunogenicity. However, a product deemed biosimilar could still differ in terms of inactive ingredients, purification processes, and other areas that are proprietary. Therefore, a product that achieves only biosimilarity will not be considered a therapeutic equivalent and will not be eligible for direct substitution without prescriber notification and approval. Once a product achieves the second phase, interchangeability, it should be substitutable in a manner similar to small molecule generic drugs approved under the Hatch-Waxman Act (i.e., a “dispense as written” or “do not substitute” option would be available). ASHP has fully supported the process outlined by the FDA and are eagerly awaiting draft guidance in 2014 on how the Agency will approach the determination of interchangeability.

### **Adoption of Biosimilars by Health Systems**

Of importance to ASHP members are the approaches interdisciplinary pharmacy and therapeutics (P&T) committees will use to determine how these products will be used within the health system. For all drugs being considered for formulary inclusion, the P&T committee will use an evidence-based process to evaluate factors that include the drug’s safety and effectiveness profile. Further, P&T committees determine strategies and guidelines for ensuring appropriate use of the medication within the health-system. These strategies may include, but are not limited to, determining appropriate patient populations, monitoring parameters, and protocols for therapeutic interchange, when appropriate.<sup>3</sup>

ASHP believes the drugs approved at the first level of biosimilarity could be substituted via the formulary process if reviewed by the P&T committee and deemed eligible for therapeutic interchange. Considerations for this process would include evaluating what is meant when a drug is deemed to have no clinically significant differences (by definition of the BPCIA) and developing processes for interchange, if warranted. Pharmacodynamic studies in actual patients should be used in this evaluation whenever available. While the FDA intends to recommend these studies, they may not be required. Application of evidence to unique populations (e.g., pediatric patients) that are not usually included in clinical studies will be especially challenging. Whether FDA approval for one indication could be extended to use for unlabeled (“off-label”) indications is another area that P&T committees must consider. Regardless of what decisions are made at the health system level, patient outcomes and safety will be the primary consideration, with cost benefits relegated to secondary status.<sup>4</sup>

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<sup>3</sup> For further discussion of the recommended processes and techniques for formulary system management, please see *ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System*; <http://www.ashp.org/doclibrary/bestpractices/formgdptcommformsyst.pdf>

<sup>4</sup> For an in-depth discussion of the scientific and regulatory challenges facing health systems in the rapidly evolving biosimilar market, please see Lucio S; Stevenson J, Hoffman J. Biosimilars: Implications for Health-System Pharmacists. *Am. J Health-Syst Pharm.* 2013; 70: 2004 – 17.

## **Naming Conventions and Biosimilars**

There are two distinct opposing positions on naming biosimilars – identical names or unique names. Pros and cons of these approaches were presented at the FTC workshop and are described in multiple public statements, comment letters, and citizen petitions from organizations such as (1) the Generic Pharmaceutical Association, (2) the Pharmaceutical Research and Manufacturers of America and the Biotechnology Industry Organization, (3) the National Council for Prescription Drug Programs (NCPDP), and (4) the American Pharmacists Association, the National Association of Chain Drug Stores, and the National Community Pharmacists Association.

Using unique names has been proposed because of patient safety concerns. However, much of this concern is based on conjecture about potential patient harm, although past concerns that certain products might result in different patient outcomes simply have not been realized (e.g., converting animal to human based insulins).

ASHP, through its participation in NCPDP's Work Group 2, helped develop the Work Group's August 20, 2012 letter to Commissioner Hamburg on biosimilar naming. As stated in that letter:

Applying unique names to each biosimilar, despite their having common active ingredients, would undoubtedly invite confusion. Compounding the issue is the time pressure under which medical decisions are often made which makes simple product identification critical to patient safety. Furthermore, unique International Nonproprietary Names (INN) may lead to medication errors, such as therapeutic duplication, due to unlike names. INNs must continue being the same to associate like products for health and safety edits in pharmacy practice systems. Additionally, unique INNs would complicate the collection of product safety data across the industry. Lastly, unique INNs would make US product names different than those in the rest of the world and such a policy would be contrary to the World Health Organization (WHO) naming system.

Grouping products by active ingredient that is conceptually equivalent provides a uniform, predictable, and effective way for healthcare professionals to identify drugs. For small molecule products, this grouping method has worked well for decades and this practice does not implicitly denote substitutability nor does this categorization inherently communicate bioequivalence or interchangeability. In addition, the current US standard nomenclature for naming clinical drug concepts, the National Library of Medicine's RxNorm, uses common root names among other things to normalize group products that conceptually are equivalent. This terminology is critical in supporting semantic interoperability among drug terminologies and pharmacy knowledge base systems, allowing computer systems to communicate drug-related information efficiently and unambiguously.

ASHP recommends that it is essential that biosimilars be given the same root name following standards for nonproprietary names established by the United States Adopted Name Council (USANC) and approved by the INN Expert Panel. However, the Society acknowledges that the higher complexity of biosimilars warrants increased pharmacovigilance, especially in cases of adverse events and quality issues. In some cases, existing systems will support that pharmacovigilance, in others there will continue to be gaps in information that need to be closed.

For the purposes of identifying a product, the National Drug Code (NDC) has been proposed as a method to track specific drug products that patients are prescribed. However, the NDC identifier may not currently be used to track a product in all settings and other challenges such as the reuse of NDC numbers by manufacturers may make this approach currently difficult. Therefore, we do not oppose the addition of suffixes (e.g., alpha, beta) to the INN name if experts believe this approach is needed to facilitate pharmacovigilance. Use of prefixes is not recommended because it could introduce confusion and add unnecessary complexity to programming of information systems. In addition, substantial public health concerns already have arisen with Kadcyra<sup>®</sup> as a result of this poor naming practice using prefixes.<sup>5</sup> Given the different systems and process standards used in inpatient and outpatient settings, best efforts must be made to ensure that solutions work for all practice settings.

### **State Regulation of Biosimilars**

Although the FDA has not yet approved any medications as biosimilars, as of late 2013, the Agency had received about 60 requests for initial meetings to discuss development of 13 different reference products. At the state level, legislation has been proposed, and in some cases enacted, requiring patient and/or prescriber notification that a biosimilar medication has been interchanged.

Five states have passed legislation requiring notification and record keeping for biosimilars, although some states have a sunset clause on the physician notification provision which is likely to expire before any biosimilars are approved in the US.<sup>6</sup>

It should be noted that at present, there is no system for ensuring that the notification is documented in the patient record or elsewhere, rendering it a meaningless barrier to use.

Such legislation has failed to pass in 10 states in 2013, although four of these states have reintroduced or indicated introduction of biosimilar legislation in 2014.<sup>7</sup> California passed a

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<sup>5</sup> Food and Drug Administration. Kadcyra (ado-trastuzumab emtansine): Drug Safety Communication - Potential Medication Errors Resulting from Name Confusion. May 6, 2013.

<sup>6</sup> Florida, North Dakota, Oregon, Utah, and Virginia have passed legislation with a physician notification requirement. Oregon, Utah, and Virginia have laws with the sunset provision.

<sup>7</sup> The states where biosimilar legislation did not pass are Arizona, Arkansas, Colorado, Delaware, Illinois, Indiana, Maryland, Mississippi, Texas, and Washington.

biosimilar law in 2013, but it was vetoed by Governor Brown on the grounds that, in the absence of FDA criteria for interchangeability, such legislation would be premature at the state level. Five other states have some pending legislation. In sum, 21 states have engaged in some legislative effort on biosimilar substitution since passage of the BCPIA.

After careful consideration, ASHP has revised its biosimilar policy to include the following provision:

*To oppose the implementation of any state laws regarding biosimilar interchangeability prior to finalization of FDA guidance;*

This policy has been approved by the ASHP Board of Directors and will be sent to the House of Delegates in June of 2014.<sup>8</sup>

The Society appreciates the opportunity to provide ASHP's perspective on biosimilars. Please contact me if you have any questions or wish to discuss our comments further. I can be reached by telephone at 301-664-8806, or by e-mail at [ctopoleski@ashp.org](mailto:ctopoleski@ashp.org).

Sincerely,



Christopher J. Topoleski  
Director, Federal Regulatory Affairs

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<sup>8</sup> For the full ASHP policy on biosimilars, please see ASHP policy 1218.