



June 3, 2016

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2016-D-0643; Labeling for Biosimilar Products; Draft Guidance for Industry; Availability; 81 Fed. Reg. 19194 (April 4, 2016); Comments of the Generic Pharmaceutical Association and the Biosimilars Council

The Generic Pharmaceutical Association (GPhA) and the Biosimilars Council acknowledge and appreciate the Food and Drug Administration's (FDA) interests and expertise in biosimilars labeling. We thank you for the opportunity to share our comments to the Draft Guidance for Industry on Labeling for Biosimilar Products ("Draft Guidance") (Docket No. FDA-2016-D-0643). As discussed in more detail below, GPhA and the Biosimilars Council support most aspects of the Draft Guidance, including FDA's recommendation that biosimilar labeling should be modeled on the labeling for the reference product ("RP") and, in most cases, should focus on the clinical studies for the RP rather than the studies and analyses supporting biosimilarity. GPhA and the Biosimilars Council, however, continue to have concerns that the proposed biosimilarity statement could be confusing to patients and physicians.¹

GPhA represents the manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical chemicals, and suppliers of other goods and services to the generic pharmaceutical industry. Generics represent greater than 88% of all prescriptions dispensed in the U.S., but only 28% of expenditures on prescription drugs. GPhA is the sole association representing America's generic pharmaceutical sector in the U.S. The GPhA Biosimilars Council, a Division of GPhA, works to ensure a positive regulatory, reimbursement, political and policy environment for biosimilar products, and will educate the public and patients about the safety and effectiveness of biosimilars. Areas of focus will include education, access, the nascent regulatory environment, reimbursement and legal affairs. Member organizations include any company or stakeholder organization working to develop biosimilar products with the intent to compete in the U.S. market. While this response letter represents the views of the association, some members of GPhA may have differing positions and may provide those positions under separate submissions.

¹ GPhA previously submitted comments to a Citizen Petition submitted by AbbVie, Inc. (AbbVie) raising similar issues regarding the labeling of biosimilars. Because those comments are directly relevant to the issues raised by the Draft Guidance, we are re-submitting those comments to the above-referenced dockets and incorporating them herein by reference. See GPhA Comments to AbbVie, Inc., Citizen Petition (Docket No. FDA-2015-P-2000).



The Biosimilars Council and GPhA also call on the FDA to finalize the biosimilar naming policy. Drugs must be properly identified by healthcare professionals if they are to prescribe the right product, and if patients are to know what they have been prescribed. A global system was established through various regulatory bodies, including the WHO, to make sure drugs with the same active ingredient/drug substance have a standard “nonproprietary” name. Existing WHO INN nomenclature rules are science-based and should remain.

GPhA and the Biosimilars Council Support Most Aspects of the Draft Guidance

As an initial matter, GPhA and the Biosimilars Council applaud FDA for taking steps in the Draft Guidance to ensure that biosimilar labeling reflects the scientific information necessary for health care providers to use a product safely and effectively, consistent with FDA regulations. *See* 21 C.F.R. § 201.56(a)(1). GPhA and the Biosimilars Council thus support FDA’s recommendation that biosimilar labeling should focus on information on the clinical studies for the RP rather than the studies and analyses supporting biosimilarity. In most cases, the scientific information necessary to facilitate an understanding of how to use a biosimilar safely and effectively will be the clinical studies conducted to establish the safety and effectiveness of the RP, not the analytical, animal and clinical studies conducted to establish biosimilarity. These latter studies are intended simply to confirm biosimilarity – and thereby allow the biosimilar to rely upon the existing safety and effectiveness data for the RP – not to independently establish the safety and effectiveness of the biosimilar itself. As such, these data generally would not be relevant to the safe and effective use of the biosimilar and thus would not be required in biosimilar labeling under FDA’s existing labeling regulations.

Likewise, GPhA and the Biosimilars Council support the recommendation in the Draft Guidance that biosimilar labeling generally should be modeled on the labeling for the RP, much like generic drug labeling in the small-molecule drug context. The Biologics Price Competition and Innovation Act (“BPCIA”) does not prohibit, either expressly or by implication, the approval of biosimilar labeling that is “the same” as, or similar to, the RP’s labeling and, in fact, grants FDA broad discretion with regard to biosimilar labeling. Given the statutory requirement that a biosimilar must be “highly similar” to a RP – with no clinically meaningful differences in terms of safety, purity, or potency – biosimilar labeling will, of necessity, closely track the labeling for the RP. Consequently, FDA’s “modeling” approach is appropriate.

GPhA and the Biosimilars Council also support FDA’s position that biosimilar labeling may differ from the RP labeling in some cases. For example, different labeling may be necessary to reflect allowable differences between products, such as carved-out indications or differences in administration and preparation. It also may be appropriate when new or different data are important to the safe and effective use of the biosimilar (although this situation may not be common) or requested for inclusion by the sponsor, in which case the information should be incorporated into the labels of both the biosimilar and its corresponding RP.



Finally, GPhA and the Biosimilars Council support inclusion of the proposed immunogenicity disclaimer in biosimilar labeling. This disclaimer provides helpful context regarding the safety of biosimilars and underscores the fact that they have no clinically relevant differences from the RP.

GPhA and the Biosimilars Council Remain Concerned That the Proposed Biosimilarity Statement May Be Confusing

Although GPhA and the Biosimilars Council support most aspects of the Draft Guidance, we remain concerned that the proposed biosimilarity statement not only is unnecessary but also may be confusing to patients and healthcare providers.

As an initial matter, the proposed biosimilarity statement is unnecessary to the safe and effective use of biosimilars and thus can be omitted in full compliance with FDA’s labeling regulations. In other words, it does not provide any information that physicians or patients need in order to use the product in a safe and effective manner. This becomes obvious upon reviewing FDA’s labeling regulations, which do not identify any appropriate section of the labeling in which to place a biosimilarity statement. Although FDA attempts to “shoe horn” this information into the “Highlights” section of labeling, it certainly does not merit placement there because it unquestionably is not one of the most important pieces of information about a biosimilar product. Nor does it not fit anywhere else in the labeling of a biosimilar product.

For this reason, FDA has never required a product’s approval pathway or therapeutic equivalence code to be disclosed on prescription labeling. Generic drug products approved via section 505(j) of the Federal Food, Drug, and Cosmetic Act, for example, are not required to be labeled as “Generics” nor are drugs approved via section 505(b)(2) required to identify their reference product or the extent to which they relied upon FDA’s prior findings of safety or effectiveness for the listed drug. Such information simply is immaterial to prescribing decisions.² Although Congress has authorized multiple approval pathways for drugs and biological products, all products that satisfy the relevant approval standards are considered to be safe and effective.

More significantly, the biosimilarity statement may suggest to patients and healthcare professionals that biosimilars have clinically meaningful differences from their RPs in terms of safety, purity, or potency when, in fact, they do not. This, in turn, could impede the uptake and use of biosimilar products and impair effective competition. We appreciate that FDA attempted to mitigate the potential confusion by including an explanatory footnote providing the precise meaning of the term “biosimilar” and the fact that biosimilars have no clinically meaningful differences from the RP. However, as FDA has recognized in the context of promotional

² Moreover, while such information may be useful to pharmacists making substitution decision, it is immaterial to prescribing decisions made by healthcare providers. Pharmacists, however, can use the Purple Book to identify biosimilars and interchangeable biological products much like they use the Orange Book today without the need to search for detailed information in the labeling.



labeling, a footnote is poorly suited to overcoming the potential confusion created by language presented more prominently in the body of a document.³ Because FDA's proposal thus may inadvertently subvert the goals of the BPCIA to increase competition and patient access to safe, effective and affordable biosimilars, FDA should reconsider requiring a biosimilarity statement on biosimilar labeling.

We thank you for your consideration of these comments and look forward to a continued effort of working together with FDA and other stakeholders to improve the lives of consumers by providing timely access to affordable pharmaceutical and biological products.

Sincerely,

A handwritten signature in black ink, appearing to read "D.R. Gaugh".

David R. Gaugh, R.Ph.
Senior Vice President for Sciences and Regulatory Affairs

³ See, e.g., Letter from Office of Prescription Drug Promotion Regarding Abilify (aripiprazole) Tablets Pharmacology Aid, p. 3 (April 17, 2015) ("We acknowledge that the bolded headline claims on pages one through three and six include a footnote more accurately describing what is known about the mechanism of action for Abilify. However, this footnote does not mitigate the misleading nature of the claims and presentations described above.").



Current GPhA Membership List

Regular Members

3M Drug Delivery Systems
Actavis Inc.
Alvogen Inc.
Amneal Pharmaceuticals LLC
ANI Pharmaceuticals
Apotex Corporation
Aurobindo Pharma USA Inc.
BD Rx, Inc.
Cipla
Dr. Reddy's Laboratories, Inc.
Fresenius Kabi USA LLC
G & W Laboratories, Inc.
Glenmark Generics Inc., USA
Heritage Pharmaceuticals Inc.
Impax Laboratories, Inc.
Kremers-Urban Pharmaceuticals Inc.
Lupin Pharmaceuticals Inc.
Mallinckrodt Pharmaceuticals
Momenta Pharmaceuticals Inc.
Mylan N.V.
Natco Pharma Limited
Novel Laboratories-Gavis Pharma
Par Pharmaceutical Companies, Inc.
Perrigo PLC
Sagent Pharmaceuticals, Inc.
Sandoz Inc.
Strides Pharma Inc.
Sun Pharmaceutical Industries, Inc.
Teva Pharmaceuticals USA
Therapeutic Proteins International, LLC
West-Ward Pharmaceuticals
Wockhardt USA Inc.
Zydus Pharmaceuticals USA

Associate Members

A.J. Renner & Associates
Aceto Corporation
ACIC
Amerisource Bergen Corp.
Baker, Donelson, Bearman, Caldwell & Berkowitz, P.C.
BioRasi LLC
Capsugel
Cardinal Health
Caremark Rx Inc.
ChemWerth Inc.
Clarkston Consulting
Colorcon
Deloitte Consulting Services LLP
Econdisc Contracting Solutions, LLC
(formerly Express Scripts)
Gedeon Richter USA
Greenblum & Bernstein
GYMA Laboratories
Haynes and Boone, LLP
Husch Blackwell LLP
InnoPharma Inc.
Interchem Corporation
Johnson Matthey Pharmaceutical Materials
Knobbe Martens Olson & Bear LLP
Lachman Consultant Services Inc.
McKesson Corporation
Midas Pharmaceuticals Inc.
Natoli Engineering Co. Inc.
New Chemic, Inc.
Novum Pharmaceutical Research Services
Polsinelli Shughart
Putney Inc.
Ren-Pharm International Ltd.
Rising Pharmaceuticals Inc.
Soverign Pharmaceuticals LLC
Spear Pharmaceuticals
Symbio LLC
TWi Pharmaceuticals USA
Vinchem Inc.
Walgreen Company



Current Biosimilar Council Membership List

Accord Healthcare, Inc.
Amneal Biosciences
Apotex Corporation
Biocon Ltd.
Dr. Reddy's Laboratories, Inc.
Momenta Pharmaceuticals Inc.
Mylan N.V.
Pfenex Inc.
Sandoz Inc.
Sun Pharmaceutical Industries, Inc.
Teva Pharmaceuticals USA
Therapeutic Proteins International, LLC
Zydus Pharmaceuticals USA