American Autoimmune Related Diseases Association, Inc.

www.aarda.org

August 2, 2016

By Electronic Submission to www.regulations.gov

The Honorable Robert M. Califf, M.D.
Commissioner
Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA–2016–D–0643 — Notice; Labeling for Biosimilar Products; Draft Guidance for Industry; Availability

Dear Commissioner Califf:

The American Autoimmune Related Diseases Association (AARDA) and the additional undersigned organizations appreciate the opportunity to comment on the Labeling for Biosimilar Products; Draft Guidance for Industry (Draft Guidance) published by the Food and Drug Administration (FDA) in the *Federal Register* on April 4, 2016.[1] We also appreciate the comment extension published on June 6, 2016.[2] AARDA is the only national nonprofit organization dedicated to raising awareness and addressing the problem of autoimmunity, which affects more than 50 million Americans and is the second-leading cause of chronic disease in the United States.

AARDA is also the founder and facilitator of the National Coalition of Autoimmune Patient Groups (NCAPG), a coalition of more than 40 patient advocate organizations representing numerous autoimmune diseases. The mission of the NCAPG is to consolidate the voice of autoimmune disease patients and to promote increased education, awareness, and research into all aspects of autoimmune diseases through a collaborative approach.

Individuals with autoimmune diseases face significant health challenges, often requiring lengthy evaluation and referral processes involving many specialists as well as therapeutic trial-and-error in order to diagnose, treat, and manage their symptoms. We have witnessed firsthand the impact that biologics have made in improving and extending the lives of autoimmune patients with diseases such as rheumatoid arthritis, lupus, Crohn's, multiple sclerosis, Sjögren's syndrome, relapsing polychondritis, and others. We are excited about the potential benefits and possibility for additional therapeutic options that biosimilars can bring to patients. On behalf of these individuals and their families, and in light of AARDA's deep commitment to ensuring adequate access to appropriate care for patients with autoimmune diseases, we offer the following comments to the Draft Guidance. Our comments focus on the importance of clear and transparent information on biosimilars labeling to ensure that prescribers and patients can make knowledgeable and safe medication decisions, particularly for patients with complex and chronic conditions.

[1] 81 Fed. Reg. 19,194 (April 4, 2016).
[2] 81 Fed. Reg. 36,313 (June 6, 2016).

I. We Support the Requirement for a Biosimilar Statement on Biosimilar Product Labeling.

We share FDA's important goals to ensure the safety and effectiveness, as well as the accessibility, of medicines approved for use by U.S. patients. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) has created hope for patients with autoimmune diseases with respect to encouraging the development and availability of additional therapies for a number of diseases that, currently, have very limited treatment options. Biosimilars hold great promise to expand the therapeutic options for patients across the country and to encourage competition, which, in turn, may also lead to lower costs for many drugs. But, in order to realize this promise—and to ensure continued patient safety as new products are developed and brought to market—biosimilars must be responsibly regulated, including clear and transparent labeling that provides pertinent information for safe prescribing. Transparent labeling is essential to ensuring that prescribers and patients are equipped with sufficient and accurate information about the product being prescribed and have access to information that will help identify the product that will work best for the particular person's condition.

Accordingly, we strongly agree with the recommendation in the Draft Guidance for a biosimilar's product labeling to clearly state that the product is biosimilar to the reference product and to provide the BPCIA's definition of "biosimilar" as part of this biosimilarity statement. We further believe that this biosimilarity statement should be a requirement, not merely a recommendation. Such a statement is necessary to ensure clarity among providers as they assess and determine whether a particular product is appropriate for a given patient. Because "biosimilar" is not "identical," we fear that the failure to expressly identify a biosimilar product as a biosimilar would cause significant safety risks for patients.

We note, as well, that we are perplexed as to why certain stakeholders appear to claim that providing a biosimilarity statement would be "confusing" to providers or to patients. We fail to see how noting the true fact that a product is biosimilar to its reference product could be anything but helpful and appropriately transparent to anyone reviewing the label, particularly where the statement itself—as provided in the Draft Guidance—includes a notation with the meaning of the term "biosimilar" and the basis for a product's approval as a "biosimilar" biological product. We believe it would be incomplete at best—and likely misleading or otherwise harmful—to fail to identify the fact that a product is a biosimilar. The relative newness of "biosimilarity" as a concept in U.S. medicine is no reason to withhold such information from healthcare professionals and consumers; to the contrary, it is critical context for prescribing decisions.

We also appreciate FDA's statements that the labeling must include "appropriate product-specific modifications," such as "a clinical study of a proposed biosimilar product … when necessary to inform safe and effective use by a health care practitioner."[3] We echo FDA's concern for patient safety and support the language that would require deviations from the reference product's labeling where there may be safety or effectiveness distinctions. We further encourage FDA to provide additional guidance (in the final guidance or otherwise) that would explain and provide examples of the circumstances under which product-specific labeling modifications would be needed for safety and effectiveness purposes. We also urge FDA to seek input from stakeholders—including physicians and patient advocates—in developing such guidance.

II. We Encourage the Inclusion of Additional Information on Biosimilars Product Labeling.

In addition to our support for the biosimilarity statement and definition in all labeling for biosimilar biological products, we believe that FDA should also consider certain limited additions to the draft labeling guidance. We summarize these recommended additions below.

[3] FDA, Labeling for Biosimilar Products; Draft Guidance for Industry, p. 3.

First, we believe that the data upon which FDA has relied in making a biosimilarity determination is important to provide or at least summarize in the labeling of a biosimilar product. Biological products are complex, as are the conditions of the patients who are treated with them. Not all patients will respond to the same biological product in the same way, even those who may be diagnosed with the same condition. Our members who rely on biologics know all too well that different treatments—even if "similar"—can cause varied reactions for different patients, particularly those with complex diseases. What works for one patient with a complex condition often will not work for another patient with the same disease.[4] Accordingly, it is important for patients and their healthcare providers to have access to the basis upon which a product is found to be biosimilar to its reference product. This information is not confusing to trained healthcare professionals or to patients. And, even if it may difficult in some cases for a patient to interpret such information, we note that no patient will have access to these products without them being prescribed by a trained healthcare professional who is working with the patient and available to discuss any questions the patient may have. Thus, this information should be provided in the biosimilar product labeling.[5]

In addition, for similar reasons, we urge FDA to require that the labeling for a biosimilar product include the following: (1) a statement as to whether the product is interchangeable with the reference product, as well as the definition of "interchangeability"; (2) an explicit statement of any indication(s) approved for the biosimilar (because, as the Draft Guidance notes, a biosimilar could be approved for different indications than the reference product); and (3) any adverse event data specific to the biosimilar.

These additional components of biosimilar product labeling are necessary to ensure patient safety. Indeed, "similar" products, by definition, are not *identical*, and any dissimilarity can result in significant differences for patients in terms of efficacy and safety. Given the complex, chronic, and often life-threatening nature of autoimmune disorders, cancers, primary immune deficiencies, and a number of other rare diseases, as well as how they interact with other conditions that a patient might have or other medications that a patient may need, the inclusion of whether a biosimilar product is also "interchangeable" with the reference product (as well as a notation of the definition for the term "interchangeable" under the BPCIA), as well as the specific indications and adverse event data for the biosimilar, are essential to include. Patients and prescribers must be able to understand readily which product is being prescribed and to track cleanly patients' reactions and responses to that particular therapy. The information that we describe here is critical in understanding how a product, even if *biosimilar* may differ from its reference product.

---

[4] *See, e.g.*, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), "Handout on Health: Systemic Lupus Erythematosus," http://www.niams.nih.gov/HEALTH_INFO/LUPUS/DEFAULT.ASP#Lupus_6 (May 2013) (noting that "lupus is different in different people and is characterized by autoimmunity in various systems of the body," and that "[m]any symptoms can come and go overtime," such that a treatment plan must be based on the patient's specific symptoms and characteristics, and "tailored to the individual's needs"); NIAMS, "Handout on Health: Rheumatoid Arthritis," http://www.niams.nih.gov/health_info/Rheumatic_Disease/default.asp#ra_10 (April 2013) (describing various treatments for rheumatoid arthritis and how they may vary from person to person); Am. College of Rheumatology, "Sjögren's Syndrome," http://www.rheumatology.org/Practice/Clinical/Patients/Diseases_And_Conditions/Sj%C3%B6gren_s_Syndrome/ (noting that "[s]ymptoms vary in type and intensity" and describing several types of treatments that may work in "some" patients but not others, depending on the patient's specific characteristics and symptoms).

[5] We do not disagree with the Draft Guidance's statements that the safety and effectiveness data in the labeling for a biosimilar product may be that of the reference product, in light of the fact that biosimilar products are required to show "biosimilarity" to a reference product before being approved and, thus, typically rely on certain reference product safety and effectiveness data. *See* Draft Guidance at 3. However, we think the is all the more reason to require the biosimilar product's labeling to include at least a summary of the data demonstrating the product's biosimilarity to the reference product—because the biosimilar product's safety and effectiveness will not have been independently established but will have been found by FDA to be "biosimilar" to the reference product. The basis for that biosimilarity determination is, therefore, highly relevant to prescribers and their patients.

III. We Continue to Support Distinguishable Names for All Biologics, Including Biosimilars with Meaningful Suffixes.

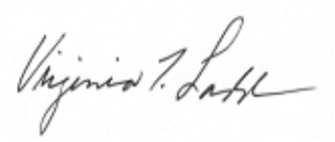
Because product naming is referenced and discussed in the Draft Guidance, AARDA also would like to take this opportunity to express our continued support for FDA's policy requiring distinguishable names for all biological products, including biosimilars. This policy strikes an appropriate and important balance in helping facilitate a pathway for additional biological product treatment options while preserving patient safety and transparent tracking of which specific medicines are being used, how they are being used, and the resulting outcomes for patients. Distinguishable naming enables clear communication between the physician, pharmacist, and patient. Shared names would create unacceptable risks of confusion, which could lead to inappropriate substitutions due to a lack of clear communications or potential ambiguities as to which product is being prescribed. The result would be detrimental to patients, including patients with autoimmune diseases, who have very specific and individualized immune responses to medications (among other things); indeed, FDA has recognized the "clinical consequences" that can result for patients, including those with autoimmunity and other serious conditions, who receive a different product from that which is prescribed.[6]

We also continue to believe that the four-letter suffixes used for purposes of biological product naming should *not* be meaningless. We fear that a suffixes "devoid of meaning" would be difficult to remember and could cause confusion among providers or lead to inadvertent errors or other negative outcomes. Accordingly, we urge FDA to designate a meaningful suffix that can be applied consistently to all products, such as a naming format in which the suffix attached to the core name would be derived from the name of the product's listed license holder. We believe that a uniform, intuitive suffix that is applied consistently to all products by a single manufacturer would be more user-friendly for providers, less prone to confusion, and, therefore, in the best interest of patients. Given the importance of distinguishing between specific products and the significant harms that can result when switching (inadvertent or otherwise) occurs, we believe that meaningful suffixes should be used—along with clear and transparent labeling, as discussed in Sections I and II of this letter, above—to help promote patient safety and positive outcomes.

* * *

Thank you again for your consideration of our comments, and we look forward to continuing to work with you on these important issues.

Sincerely,



Virginia T. Ladd
President/Executive Director, American Autoimmune Related Diseases Association

On behalf of
American Autoimmune Related Diseases Association
[additional organizations listed on next page]

[6] *See, e.g.*, FDA, Proposed Rule, Designation of Official Names and Proper Names for Certain Biological Products, 80 Fed. Reg. 52,224, 52,226 (Aug. 28, 2015) ("Inadvertent switching between biological products that have not been shown to be interchangeable may affect immune response. For example, in some instances, immune responses to therapeutic proteins may pose safety and efficacy issues . . . [and] immune responses can lead to significant clinical consequences . . . ."); *see also id.* ("If originator biological products, related biological products, and biosimilar products share the same proper name, a patient could receive a product different from what was intended to be prescribed, leading to medication errors.").

American Behcet's Disease Association
International Foundation for Autoimmune Arthritis
International Pemphigus and Pemphigoid Foundation
National Alopecia Areata Foundation
Relapsing Polychondritis Awareness & Support Foundation
Scleroderma Foundation
The Myositis Association
U.S. Pain Foundation
GBS|CIDP Foundation International
Interstitial Cystitis Association

22100 Gratiot Avenue East Detroit, MI 48021-2227 Phone (586) 776-3900 Fax (586) 776-3903 E-mail: aarda@aarda.org