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Stephen Ostroff, M.D.
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Comment on Food and Drug Administration Draft Guidance "Nonproprietary Naming of Biological Products: Guidance for Industry"

Submitted electronically via www.regulations.gov

October 26, 2015

Acting Commissioner Ostroff:

As the Coalition of State Rheumatology Organizations (CSRO), part of our mission is to advocate for access to the highest quality medical care for Rheumatic disease patients with autoimmune inflammatory and degenerative diseases. As patient and physician advocates, we have been deeply involved in the debate surrounding implementation of the Biologics Price Competition and Innovation ACT (BPCIA) and wish to provide you with our input on the Food and Drug Administration's (FDA) "Nonproprietary Naming of Biological Products: Guidance for Industry" ("draft guidance").

The draft guidance proposes that a biosimilar will share a Unique Nonproprietary Name (INN) with its reference product, but that each of the two products will have a unique, distinguishable suffix consisting of four, lowercase letters. The suffix would be proposed by the manufacturer and subject to FDA review and approval. The suffix would be unique to each individual product, or to each manufacturer. In the guidance, FDA request public input on whether an interchangeable biosimilar should share a suffix with its reference product. CSRO has long advocated distinguishable nonproprietary names for all biosimilars and, as such, we support the agency's proposed approach. We urge FDA to ensure that the suffix is unique to each manufacturer, and to extend this policy to interchangeable biosimilars as well, for the reasons outlined below.

The FDA's motivations for requiring biological products to bear a four-letter suffix are instructive. First, as the agency states in the draft guidance, "the goal of this naming convention is to help minimize inadvertent substitution. Inadvertent substitution may lead to unintended alternating or switching of biological products that have not been determined by FDA to be interchangeable." As frequent prescribers of these complex products, we appreciate that sentiment. It is also why we support a distinct suffix for biosimilars that meet the higher threshold of interchangeability.

Since the standards for interchangeability have yet to be announced by FDA, CSRO cannot determine at this time whether we believe they are stringent enough. However, assuming that FDA announces sufficiently robust standards for interchangeability, we still believe that the ultimate prescribing decision should rest with the treating physician. An FDA finding of interchangeability does not eliminate the risk of inadvertent substitution. Even if an interchangeable biosimilar is available, a physician may still wish to prescribe the brand product for reasons related to the particular patient's history and past responses to treatment changes. Thus, to minimize inadvertent substitution, we support requiring a distinguishable suffix for interchangeable biosimilars as well.

Second, the agency notes that "NDC numbers are not routinely recorded in billing and patient records in many clinical settings in which biological products are dispensed and administered. Similarly, in many passive pharmacovigilance systems, proprietary names and NDC numbers are often not included in adverse event reports. As a result, the use of distinct proprietary names or NDC numbers is insufficient to address concerns regarding pharmacovigilance." We agree wholeheartedly with this statement but, again, do not believe this concern is adequately addressed by a finding of interchangeability. Even if two products are deemed interchangeable, one can still cause an adverse reaction, while the other might not. In addition, since some adverse events only appear in the post-marketing period, it is extremely important to identify which product is actually responsible for the adverse event report to the FDA, as the product will be in the hands of patients at that point. Enabling quick and accurate tracking of the "culprit" product to the source can ensure quick action by FDA and the manufacturer.

In addition, quick identification can also leave the "innocent" product on the market as an option for patients. If an adverse event is reported without a distinct name, there could be a misattribution of that event to the reference product *and* to all other biosimilars produced by other manufacturers. The reference product manufacturer will be forced to respond and potentially perform additional trials and/or make changes in its product labeling, even though only one single biosimilar may have caused the adverse event.

This concern is not ungrounded. The FDA's existing Adverse Event Reporting System (FAERS) teaches us that release of a generic small molecule product is frequently followed by an increase in adverse drug event reporting for the drug under the generic name. This increase in reported adverse events occurring after the introduction of generic small medications occurs even as the sales of the innovator small molecule medication decline. This makes it clear that the introduction of generic medications (even in the simple molecule domain) is associated with more adverse drug events and, while these are likely due to the generics and not the reference product, they are often attributed to all of the products across the board.[1] With respect to biological agents,

[1] See, e.g., "Biosimilar Naming: How Do Adverse Event Reporting Data Support the Need for Distinct Nonproprietary Names for Biosimilars?" by Erika Lietzan, Laura Sim, and Emily Alexander, The Food and Drug Law Institute's *Food and Drug Policy Forum*, Vol. 3, Issue 6 (March 27, 2013).

these occurrences will be compounded since they are so much more complex and affected by more variables in development, cell line use, packaging, storage, delivery systems and even bottle stoppers, as well as routes of administration.

Because of these concerns, we urge FDA to consider recognizable suffixes, so that a manufacturer can use the same suffix across its portfolio of products. This will help the agency and prescribers quickly identify the source of an adverse event. In addition, it may increase prescribing confidence and assist with the uptake of biosimilars.

In closing, we reiterate our support for requiring all biosimilars to bear a unique, four-letter suffix, and we urge the agency to extend that policy to interchangeable biosimilars as well. Please do not hesitate to contact us, should you require additional information.

Sincerely,

Michael Schweitz, M.D.
Federal Advocacy Chair
Coalition of State Rheumatology Organizations