



December 22, 2010

Leslie Kux, Acting Assistant Commissioner
Office of Policy
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Ms. Kux,

I would like to provide comments on behalf of the American College of Rheumatology (ACR) for **Docket No. FDA-2010-N-0477, Approval Pathway for Biosimilar and Interchangeable Biological Products**. The ACR seeks to advance rheumatology through programs of education, research, advocacy and practice support that foster excellence in the care of people with arthritis and rheumatic and musculoskeletal diseases. In accordance with the mission of the organization, the College often provides comments and feedback in areas related to its mission of advancing rheumatology.

Biological response modifiers or biologics have had an important impact in many areas of medicine, and in particular in rheumatology. The ACR recognizes that the high cost of these agents is a growing concern, particularly as more products become available and their use for the treatment of immune-mediated inflammatory diseases continues to expand. Biosimilars have been viewed as a potential cost-saving alternative to traditional therapies. Currently a biosimilar product is defined as one that is 'highly similar' to the reference product, with no clinically meaningful differences in terms of safety, purity and potency. A biosimilar product may be deemed interchangeable if it meets the higher standard that it produces the same clinical result as the reference product with no increased risk or diminished efficacy from alternating or switching between the test product and the reference product.

The ACR strongly believes that safe and effective treatments should be available to patients at the lowest possible cost. However, the organization also believes that decisions about biosimilarity and interchangeability must be driven by sound science that takes into account several observations and guiding principles, including:

1. The size, complexity, and heterogeneity of biologics (and thus biosimilars) necessitate a greater degree of scrutiny in their analytical evaluation than what is typically required for small molecule generics.
2. Subtle differences in the production of biologics can dramatically affect their functional properties in ways that are not readily predictable. For example, production of the same biologic in different cell lines may result in products with different post-translational modifications with functional consequences.
3. Distinct biologics that target the same molecule are not identical in terms of efficacy and toxicity in clinical use.
4. A biosimilar proven effective for one indication may not necessarily be effective for a second indication for which the reference compound has been shown to be effective.



5. Different biologics may require different degrees of testing to establish safety and efficacy. It may be necessary to consider each biologic separately.
6. Long-term post-marketing registry-based data collection is necessary to monitor for less common but nevertheless important adverse events.
7. Post-marketing surveillance studies are needed in children as well as adults, as toxicities and long-term sequelae may be different. The Best Pharmaceuticals for Children Act (BPCA), which reauthorizes the pediatric studies provision of FDA Modernization and Accountability Act to improve safety and efficacy of pharmaceuticals for children, should apply to biosimilars.
8. The decision to substitute an interchangeable product should not be made without the prescribing health care provider's knowledge.
9. Biosimilars should have distinct names allowing them to be distinguished from their reference products.

In light of these considerations, the ACR position is that safety and efficacy of most biosimilars used in patients with rheumatic diseases will need to be established in human subjects in comparison to another established agent in the same class. While cost savings are highly desirable, the approval process for biosimilars - so-called generic biologics - needs to place safety and efficacy, supported by scientifically sound evidence, as the highest priorities.

Thank you for your consideration.

Sincerely,

David G. Borenstein, MD
President

Cc: Sandra J. Benton, FDA Center for Drug Evaluation and Research
Robert A. Colbert, MD, PhD, Chair, ACR Committee on Research
Mary J. Wheatley, ACR Sr. Director, Research & Training