May 19, 2017

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

Submitted via Regulations.gov

Re: Draft Guidance Considerations in Demonstrating Interchangeability With a Reference Product (FDA 2017-01042)

Dear Ladies and Gentlemen:

The American College of Rheumatology (ACR) represents over 9,500 rheumatologists and health professionals. Rheumatologists provide ongoing care for over 50 million Americans with complex chronic and acute conditions that require specialized expertise. We commend the Food and Drug Administration’s draft guidance on demonstrating interchangeability, titled “Considerations in Demonstrating Interchangeability with a Reference Product”, for striking an appropriate balance between ensuring safety and efficacy of drugs while also bringing biosimilar products to the marketplace as efficiently as possible.

Early and appropriate treatment by rheumatologists slows disease progression, improves patient outcomes, and reduces the need for costly downstream procedures and complicated care made more expensive by advanced disease states. A growing body of evidence shows that by slowing disease progression biologic treatments including biosimilars may reduce costly disease-related complications, including adverse outcomes related to cardiovascular disease, metabolic syndrome, and expensive procedures such as joint replacement.

Biologics and biosimilars serve as lifelines for patients with rheumatic diseases. These innovative treatments are often necessary when other disease-modifying anti-rheumatic drugs (DMARDs) are either ineffective or not tolerated by a patient. Most notably, biologic and biosimilar treatments tend to work rapidly and may achieve control of the disease more quickly than DMARDs – a critical factor when facing a brief window of opportunity for maximum therapeutic effect. The development of biosimilar interchangeability standards is vital to lowering prices, but must also ensure that patients receive drugs consistent with their health care provider’s treatment plan.

I. Switching Studies Must Be Required
We strongly support the FDA’s proposal to require manufacturers to use robust switching studies to determine whether alternating between a biosimilar and its reference product impacts the safety or efficacy of the drug. Exposing patients in the experimental arm to each drug twice (A, B, A, B), a protocol that requires three switches, is a reasonable attempt to simulate what our patients are likely to experience with changing formularies in a multi-payer, multi-state, and ever-changing market. The requirement for multiple-switch studies to demonstrate the safety of interchangeability is particularly vital in light of the fact that providers will often not know their patient’s medication has been switched.

The ACR strongly supports clinical trial development to focus on markers of immunogenicity, such as trough drug levels, induction of antidrug antibodies and loss of clinical efficacy, as well as adverse effects due to switching between drugs. These data should be made available in the interchangeable drug’s label via text or hyperlink. Data collection should continue through robust post-marketing surveillance. The ACR suggests that FDA allow ready access to pharmacovigilance data for investigators to analyze, and that the FDA promote and disseminate information about the program and the available data. The FDA should also consider requiring manufacturers to submit updated and standardized pharmacovigilance data as a prerequisite to certain post-market labeling changes.

II. Extrapolation Should Be Rigorously Studied and Fully Utilized

Extrapolation of indications is crucial for the biosimilar pathway to reduce drug prices. The ACR does not support automatic extrapolation, but does support extrapolation after carefully identifying a minimum slate of diseases and outcomes to be studied, depending on factors including mechanism of action and predicted immunogenicity.

If an interchangeable drug does not garner FDA approval for all indications of the originator drug, it is possible that the drug could be inappropriately substituted for a patient being treated for a disease for which the drug is not approved. Therefore, care must be taken in the final guidance, and throughout the approval process, to promote and ensure that a drug pursuing interchangeability has successfully demonstrated extrapolation for all indications for which the originator is approved. Guidance should also address future FDA-approved indications for the originator.

III. Clear Labeling and Dispensing Guidance is Needed

The ACR has previously asked for the following:

- Statements in each biosimilar FDA label indicating whether the drug is interchangeable (in addition to whether a drug is biosimilar)
- Inclusion of clinical data for biosimilars in FDA labels, via text or hyperlink
Specific guidance for pharmacists to prevent inadvertent substitution of a non-interchangeable biosimilar as a stand-alone document and as a prominent message inside the “Purple Book” list

We are further concerned about non-medical switching, also known as forced switching, whereby payers force patients from one biopharmaceutical to another using formulary changes. This already occurs in the absence of interchangeable status and will no doubt accelerate with the advent of biosimilars. Individual treatment decisions should be made by physicians and patients who are informed about an individual patient’s unique condition, comorbidities and circumstances. Such decisions should be made in the best interests of the patient and should not be determined solely by population-based cost considerations. We encourage the FDA to consider the issue of non-medical switching as future guidance is developed.

IV. Clear Guidance is Needed for Interchangeability Naming Conventions

We support the FDA’s stated plans to use distinguishing suffixes to help minimize “inadvertent substitution,” particularly for biosimilars that have not been determined to be interchangeable. We believe that the Agency’s final guidance titled “Nonproprietary Naming of Biological Products” was an important first step toward ensuring that biosimilars reach our patients as safely, transparently, and efficiently as possible. We have long advocated for explicit guidance about distinct names and suffixes for biosimilars in order to prevent inadvertent or inappropriate substitution, to increase prescriber confidence and uptake of use of biosimilars, and to ensure pharmacovigilance. Furthermore, the ACR proposes that the FDA no longer suggest the use of suffixes devoid of meaning, and instead suggest the use of meaningful suffixes. Meaningful suffixes will be more memorable, less subject to accidental substitution and could thereby improve clinical care and pharmacovigilance.

We note that the Agency’s guidance does not outline the naming conventions that will be applied to products found to be interchangeable. Interchangeability presents naming convention concerns that go beyond those necessary for biological products. The ACR supports the use of the International Nonproprietary Name (INN) with distinct, meaningful suffixes for biosimilars determined to be interchangeable to a reference product. Distinguishable names for biosimilars deemed interchangeable will reduce any confusion among health care providers and ensure that manufacturers can better report any adverse events. Permitting the use of proprietary names for interchangeable biologic products is likely to cause many stakeholders to falsely believe that there are clinically meaningful differences between interchangeable products—a belief which would be contrary to the purpose of the designation. Such confusion could stymie the adoption of biosimilars.

V. The FDA Serves a Vital Role in Protecting Patients’ Access to Services
The ACR supports rigorous trials to ensure safety and efficacy of biosimilars and robust review by experts through the approval process. We believe that giving the FDA the resources it needs to issue guidances and to review and approve biosimilars is an important step to ensure that patients have choice not only on which drug is best for them but also at competitive prices. Biopharmaceuticals remain expensive not only because they are complex, but also because competition is limited and the markets are opaque.

We are encouraged by the FDA’s work thus far regarding biosimilars and we believe that passage of The Biosimilar User Fee Act II (BsUFA II) is a critical step to ensure the FDA has the resources it needs to continue. Additionally, the ACR supports addition of specific budget authority for FDA to support biosimilars for the purpose of enhancing industry guidance and drug approvals. Finally, the FDA should use its authority granted by the 21st Century Cures act (section 3072) to use innovative hiring methods to quickly onboard people with the expertise needed to accomplish its mission in the area of biosimilars. We believe that supporting the emerging marketplace at this time will enhance cost savings and subsequent access to treatments.

VI. The ACR is Eager to Work with the FDA to Develop Interchangeability Standards

The ACR shares the FDA’s goal of ensuring that more affordable treatments reach patients as quickly as possible. We applaud the FDA’s measured and thoughtful approach to addressing provider confidence concerns while also prioritizing the safety of our patients. We look forward to being a resource for you and working with you to address these and other matters. Please contact Adam Cooper, Senior Director of Government Affairs, at acooper@rheumatology.org or (404) 633-3777, if you have questions or if we can be of assistance.

Sincerely,

Sharad Lakhanpal, MBBS, MD
President, American College of Rheumatology