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August 20, 2024

Robert M. Califf, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Submitted electronically at www.regulations.gov

RE: Considerations in Demonstrating Interchangeability with a Reference Product, Draft Guidance, Docket No. FDA-2017-D-0154

Dear Dr. Califf,

The Coalition of State Rheumatology Organizations (CSRO) is comprised of nearly every active state rheumatology society in the nation, representing over 40 states, with a mission of advocating for excellence in the field of rheumatology, ensuring access to the highest quality of care for the management of rheumatologic and musculoskeletal disease. Our coalition serves the practicing rheumatologist.

CSRO appreciates and acknowledges the FDA's evolving confidence in the safety and efficacy of biosimilars, as reflected in the updated guidance. Allowing for more flexibility in demonstrating interchangeability, particularly by permitting the use of comparative analytical and clinical data without requiring additional switching studies, should improve patient access to lower-cost alternative therapies. However, ***CSRO remains concerned about the broader and long term implications of the FDA's updated guidance regarding the interchangeability designation.***

While the FDA does not have direct authority over payer practices, the standards it sets have far-reaching implications. When the FDA deems a biosimilar as interchangeable, it allows pharmacists to substitute them for the reference product at the pharmacy without consulting the prescribing doctor. This is similar to pharmacy substitution of generic drugs for brand-name drugs. Except at this point in time the "interchangeable" biosimilars can only be substituted for the reference product not other biosimilars.

We appreciate that emerging science and data has convinced the FDA that switching studies may not be needed if the other analytical and clinical data supports the interchangeable designation. It is important that the FDA continues to have unique standards for this designation at this time and not allow all biosimilars to be deemed interchangeable without additional evaluation. That would exacerbate existing challenges posed by payer practices in the form of non-medical switching, step-therapy, prior authorization, and

other utilization management tactics. Unique standards for granting interchangeability status, though sometimes ignored by payers, provide a necessary safeguard that helps guide clinical decision-making and protects patients from the potentially harmful effects of inappropriate drug switching.

Further, when patients are switched to a new therapy (different name, different packaging) without prior notice to their physicians, it increases the risk of the nocebo effect—a phenomenon where patients experience negative side effects simply because they believe the medication has been changed and noone told them about it. This can lead to decreased efficacy and increased side effects, further complicating treatment. The FDA has prioritized physician involvement in other areas, such as the regulation of laboratory-developed tests (LDTs), recognizing the importance of the physician's role in ensuring appropriate patient care. A similar emphasis on physician involvement is necessary when it comes to the substitution of complex biologic therapies.

While we support the FDA's efforts to enhance the biosimilar market, it is essential that the agency retains oversight and maintains rigorous standards for biosimilar interchangeability. ***The FDA must ensure that the interchangeability designation continues to signify a high level of confidence in a biosimilar's ability to be switched numerous times with the reference product without compromising safety or efficacy.***

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Thank you for your consideration of our comments. Please do not hesitate to contact us at info@csro.info should you require additional information.

Sincerely,

Gary R. Feldman, MD, FACR
President

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Vice President, Advocacy & Government Affairs