January 5, 2024

Re: *CMS-4205-P;* Action: *Proposed Rule (Oppose)*
Submitted electronically at: https://www.regulations.gov/document/CMS-2023-0187-0001

Dear Sir or Madam,

Thank you for the opportunity to provide comments on CMS' Proposed Rule (CMS-4205-P), specifically *Section 8. Additional Changes to an Approved Formulary—Substituting Biosimilar Biological Products* outlined in the *Summary of the Major Provisions,* which permits Medicare Part D plan sponsors to substitute reference biologics with biosimilars that have not been deemed interchangeable by FDA.

Founded in 2010, the Alliance for Safe Biologic Medicines (ASBM) is a diverse group of stakeholders including physicians, pharmacists, patients, researchers, and manufacturers of both biologics and biosimilars; working together to advance patient-centered health policy. We believe biosimilar medicines are a valuable tool for helping control costs. However, these cost savings should be realized in a manner that does not compromise patient safety or treatment stability.

Based on this principle, ASBM offers the following comments regarding CMS' proposal to permit the substitution of non-interchangeable biosimilars in place of biologic medicines:

A. Substitution of biosimilars by someone other than the prescribing physician is a controversial practice that is banned in many countries. US state laws nationwide permit pharmacy-level substitution of only "interchangeable" biosimilars.

Automatic substitution of biosimilars is highly controversial among physicians and is banned in many countries, including most of Europe. Proposing to change this standard in the U.S. not only undermines FDA regulatory guidance and the intent of the legislation passed by Congress and the entirety of our state legislatures, but also betrays the assurances given to patients, physicians, and other organizations who have supported the protections offered by biosimilar substitution laws nationwide.

FDA requires that interchangeable biosimilars meet a higher regulatory standard for approval. It is the ASBM's view that biosimilars and interchangeable biosimilars are two separate classes of medicines. The statutory requirements to achieve the designation of interchangeability are appropriately designed to necessitate a higher burden of proof, with a greater focus on the individual patient.

To meet these standards, a robust clinical program is required to demonstrate, with near certainty, that the biosimilar product will produce the same clinical result as the reference product in any given patient, AND in the case of a biological product administered more than once to a patient, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biosimilar product and the reference product is not greater than the risk of using the reference product without such alteration or switch.

CMS' proposal to permit the automatic substitution of non-interchangeable biosimilars for their reference medicine weakens FDA's current interchangeability standard and will have harmful effects nationwide. Beginning in 2013, all 50 states and Puerto Rico enacted legislation that allows for pharmacy-level, automatic substitution *only* for biosimilars given interchangeable status based on additional data provided to the FDA that demonstrates safe switching. *Importantly*, this legislation provided that all other biosimilars (i.e., those without an interchangeable status) would not be substituted at the pharmacy level without physician involvement or approval.

State legislatures were able to gain support for permitting biosimilar substitution from medical societies and patient advocacy organizations nationwide, due to these assurances.

In addition to risking patient safety, the permission to automatically substitute non-interchangeable biosimilars for their reference medicines would penalize biosimilar manufacturers that have prioritized seeking extra safety data for their products to gain an interchangeability status, while rewarding those who have not carried out these additional studies.

The proposed policy change would discourage clinical studies and scientific evaluation of biosimilars, depriving patients and prescribers of information they value. Both doctors and patients have expressed that the data gathered to demonstrate interchangeability increases their confidence in and comfort with biosimilars and in biosimilar substitution. Under CMS's proposed policy, such data would not be generated in the future. Not finding differences (e.g. in safety or efficacy following switching of products) because you failed to look for them must not be equated with the absence of differences. The proposed policy inappropriately conflates these two categories of biosimilars, obfuscating their differences and performing a disservice to patients.

B. Treatment plans are not "one-size fits all."

While all FDA-approved biosimilars are safe and effective, the FDA's concept of interchangeability ensures that switching decisions also account for the unique treatment needs of individual patients. Treatment plans are not one-size-fits-all: chronic illnesses such as arthritis, Crohn's disease, psoriasis, and various forms of cancer often require treatment plans tailored over years of trial and error with different products before a patient's disease or

condition is stabilized. Any change to a patient's medication, including the automatic substitution of a biosimilar for the originator biologic without physician involvement, can pose a significant risk to patient stability.

C. The interchangeable designation has been shown to dramatically boost physician confidence in biosimilar medicines.

The FDA's interchangeability standard, with its extra data requirements, has proven successful in promoting physician and patient confidence in these medicines. A 2021 survey of US physicians representing 12 therapeutic areas revealed that 57% of them would be more likely to prescribe an interchangeable biosimilar, and 59% reported that an interchangeable designation makes them more comfortable with a pharmacy-level substitution of that biosimilar in place of the prescribed originator medicine.[i] Only a third of physicians surveyed indicated that an interchangeable designation would not affect their prescribing behaviors.

Similarly, in another survey of US physicians who prescribe biologics, participants were asked how important it is that the product label clearly indicates that a biosimilar is or is not interchangeable; approximately 80% of physicians rated the importance of knowing the interchangeability status of a biosimilar either a 4 or 5 on a 5-point scale.[ii] Likewise, a survey of over 400 pharmacists indicated that almost 90% of those polled rated the importance of clearly labeling the interchangeability status of a biosimilar as a 4 or 5 on a 5-point scale.[iii]
These surveys of practicing health care professionals clearly indicate that a statement of interchangeability is important to them and impacts their prescribing practices.

The interchangeable designation has not only boosted physician and patient confidence, but it has also done so without becoming a barrier to biosimilar uptake and savings. In the US, filgrastim, trastuzumab, and bevacizumab biosimilars have an uptake rate of 80%. Rituximab biosimilars stand at 60% and infliximab, pegfilgrastim, and erythropoietin-stimulating agent biosimilars have 40% market share. This has translated to $21 billion in savings in the past 6 years alone.[iv]

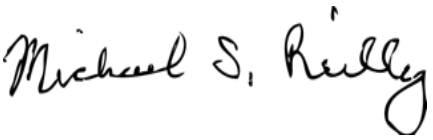
D. The proposed policy represents an inappropriate reversal of recent CMS assurances that automatic substitution would be limited to interchangeable biosimilars.

The dramatic change in policy proposed by CMS comes less than a year after a CMS Rule[v] permitting Part D plan sponsors to substitute interchangeable biosimilars explicitly reassured the public it would not permit substitution of non-interchangeable biosimilars because they "have not met the requirements to support a demonstration of interchangeability."

Nothing has changed regarding non-interchangeable biosimilars since last year's CMS Rule. Non-interchangeable biosimilars still haven't met the FDA data requirements for interchangeability and still shouldn't be substituted by a third party without physician approval.

In summary, *Section 8. Additional Changes to an Approved Formulary—Substituting Biosimilar Biological Products* of the Proposed Rule stands in stark contrast to the opinions of the medical community, the wishes of patients, a decade of substitution policymaking across 50 states, the substitution policies of most advanced nations, and CMS' own recent assurances. We respectfully urge CMS to reconsider and withdraw this rule.

Sincerely,



Michael S. Reilly, Esq.
Executive Director, Alliance for Safe Biologic Medicines

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[i] http://gabi-journal.net/us-prescribers-attitudes-and-perceptions-about-biosimilars.html
[ii] US-February-2015-Labeling-Report.pdf (wpengine.com)
[iii] 2015-US-Pharmacists-Report-OCT4.pdf (wpengine.com)
[iv] 2022 Biosimilar Trends Report | Amgen Biosimilars
[v] https://www.ropesgray.com/en/insights/alerts/2023/01/the-centers-for-medicare-medicaid-services-proposes-changes-to-the-medicare-advantage-and-medicare