September 21, 2018

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-N-2689 – “Facilitating Competition and Innovation in the Biological Products Marketplace; Public Hearing; Request for Comments”

Delivered electronically through http://www.regulations.gov

To the Food and Drug Administration:

The Ohio Public Employees Retirement System (OPERS) appreciates the opportunity to submit comments to the Food and Drug Administration (FDA or Agency) regarding its public hearing on “Facilitating Competition and Innovation in the Biological Products Marketplace,” which was held on September 4, 2018.

OPERS is the largest public retirement system in Ohio, with more than one million active, inactive and retired members. Of this number, OPERS provides health care coverage for more than 200,000 Medicare and pre-Medicare plan participants. Like many health care payors, OPERS is faced with increasing health care costs and inflation, particularly in the area of prescription drugs, as well as the pressures of maintaining a health care plan that is both sustainable and meaningful for our members. As such, cost containment within the broader health care system is extremely important to us.

For too long, payors and patients have shouldered the burden of increasing prescription drug costs through plan design and cost-shifting to consumers. However, we are quickly approaching a time when these types of solutions will no longer be sufficient to maintain meaningful and affordable health care coverage for our members. A combination of market-driven solutions and government intervention is needed to address high prescription drug costs and ensure that consumers can access the medications they need.

OPERS recently submitted comments¹ to the Department of Health and Human Services (HHS) wherein we recommended the Administration for its renewed focus on prescription drug pricing and urged the Department to adopt policies that foster competition within the prescription drug marketplace and improve transparency throughout the drug distribution system. We expressed

concern that anti-competitive behavior by drug manufacturers and the current lack of transparency in drug pricing had created an uneven playing field for consumers and payors.

As we noted in our previous comments, drug pricing will only become more important in the coming years as more innovative and high-cost biologic therapies come on the market. We urge the FDA to take advantage of the public’s current awareness and outrage over brand and specialty drug costs, to encourage true competition within the biologic and specialty drug marketplace.

OPERS has chosen to provide its members with access to health care coverage since 1959, not because we are required to, but because we believe that access to meaningful health care coverage is an essential component of retirement security. Out of control health care inflation, particularly in the area of specialty drugs, threatens our ability to provide affordable coverage and puts our members at risk at a time in their lives when they are least prepared to adapt.

**Supporting Market Competition By Addressing Attempts to Game FDA Requirements or Otherwise Delay Market Entry of Competing Biological Products**

In 2017, OPERS’ total pre-Medicare prescription drug cost was $142 million, $65.2 million of which was spent on specialty/biological drugs. In comparing our 2017 per member-per month prescription drug experience to 2016, OPERS experienced an increase of 13.6 percent in our overall prescription plan costs, whereas specialty prescription costs increased by 21.3 percent. While only 4.4 percent of current OPERS retiree health plan participants utilized specialty/biological drugs, these medications accounted for 45.9 percent of the System’s overall drug spend and represented the fastest growing segment of our annual drug cost. Without biosimilar and interchangeable drugs to drive price competition, specialty drug costs are projected to grow 14 to 17 percent per year through 2021.²

Biosimilar and interchangeable drug competition is an integral part of OPERS’ long-term strategy to manage the growth of its health care expenditures and increase patient access to safe, effective and affordable biological medications. These innovative and life-changing drugs have the potential to revolutionize medical care, but only if consumers and payors can afford them.

Like many payors, we are counting on biosimilar competition to decrease prices within the specialty drug market. However, creating a truly competitive marketplace will require that biosimilar and interchangeable products are treated as similarly as possible to their reference products and allowed to compete on an equal footing. The methods by which biosimilar and interchangeable products are named, labeled and approved all factor in to the prescriber’s and public’s perception of these market alternatives, and should be reviewed and revised as appropriate to ensure they are not creating barriers to biosimilar adoption.

True competition also means addressing the anti-competitive efforts used by some manufacturers to discourage the development and marketability of biosimilar and interchangeable products. These include tactics like product hopping, pay-for-delay agreements, shadow pricing, patent litigation, and

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most recently, exclusionary long-term contracting\(^3\), which have tilted the playing field against generic and biosimilar manufacturers, resulting in reduced access and higher drug prices for payors and patients.

In one well-known example, some manufacturers misuse the fact that one of their products is subject to a Risk Evaluation and Mitigation Strategies (REMS) plan as an excuse for denying samples of the product to generic or biosimilar manufacturers who are seeking to develop market alternatives. Other manufacturers have created patent thickets in an effort to prevent previously approved biosimilar products from being marketed to consumers and unfairly extend market exclusivity for their products. In the aggregate, these tactics forestall market competition and in so doing, cost consumers and other payors billions\(^4\) in lost savings.

We are encouraged that the FDA is working with the Federal Trade Commission (FTC or Commission) to investigate anti-competitive behaviors and point out actionable fact patterns. From our perspective, the FTC’s willing participation in this process is long overdue and welcomed. We are hopeful that, by combining efforts, the FDA and FTC will be able to successfully address current incentives to delay market entry of biosimilar and interchangeable products.

In our recent letter to HHS, we asked the Department to consider offering its support for pending legislative initiatives such as the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act, and/or the Fair Access to Safe and Timely (FAST) Generics Act. Both of these proposals would address the current misuses of the REMS program by establishing a private cause of action for generic or biosimilar manufacturers that are unjustly denied samples of a reference product. In the same way, we urge the FDA to consider participating in the on-going legislative debate over the anti-competitive behaviors used by drug manufacturers to delay biosimilar competition. We believe the Agency’s insights and experience with these matters would be helpful as policymakers work to build consensus on legislative solutions.

Finally, in response to recent comments\(^5\) made by FDA Commissioner Dr. Scott Gottlieb regarding the role of health plans and others in supporting the developing biosimilar market, OPERS has taken steps to address the market barriers that delay or obstruct biosimilar adoption. In 2017, OPERS worked with Express Scripts to create a separate co-payment level for biosimilar products and generic specialty drugs. Although very few of these products are currently available, we believed there was value in proactively adopting a plan design that rewards members for using non-brand biologic and specialty drugs. In so doing, OPERS is incentivizing its members to choose non-brand biologic and specialty drugs with lower out-of-pocket costs. In essence, we will be sharing our savings with our members.

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Increase Health Care Provider, Patient, and Payor Understanding of Biological Products, Including Biosimilar and Interchangeable Products

OPERS agrees that physician and patient knowledge of and confidence in biosimilar and interchangeable products is critical to increased market adoption of these products. A central theme of OPERS’ education to its members and providers is the notion that non-brand biologics should be treated as similarly as possible to their reference products.

OPERS has previously engaged with the FDA on issues of biosimilar naming, labeling and interchangeability, and has consistently held the position that unnecessary disparities in the treatment of brand and non-brand biologics can cause confusion among providers and consumers. For example, OPERS has previously commented that interchangeable products should have the same non-proprietary name, or at least the same four-letter suffix, as their reference products. We have taken this position because we are concerned that the FDA’s decision to “treat two products that have been shown to produce the same clinical result in any given patient” differently could confuse patients and providers, thereby providing reference brand manufacturers with an advantage in the marketplace. Further, we have respectfully disagreed that the unique, four-letter suffix is necessary to ensure patient safety and avoid inadvertent substitutions. As we have noted in the past, medications may also be uniquely identified by their proprietary name or, barring that, by their national drug code number.

We understand that the FDA has gone to great lengths to ensure the safety and efficacy of biosimilar and interchangeable products, but we urge the Agency to consider the ramifications of its final guidance in the areas of biosimilar and interchangeable product naming. In treating brand and non-brand biologic products differently, we are concerned that the FDA’s guidance will create additional confusion among providers and consumers regarding the biosimilarity of non-brand biologic products. Perception is key, and biosimilar and interchangeable products are already at a disadvantage because, unlike their generic drug forebears, they cannot be “identical” to their reference products – even though they may produce an identical result.

In order for biosimilar and interchangeable products to succeed in the marketplace, prescribers, pharmacists and consumers must accept them as they currently do with generic drugs. To the extent the FDA has acted to differentiate the names and labels of biosimilar and interchangeable products, there is a greater need to educate consumers and providers on why they should accept non-brand biologics instead of their neatly advertised and relentlessly promoted reference products.

Improving the Interchangeability of Biosimilars

Like many payors, OPERS was supportive of the Biologics Price Competition and Innovation Act’s (BPCIA) abbreviated approval pathway for biosimilar and interchangeable products, and hoped that the BPCIA

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would usher in a new era of drug price competition. We share the Agency's frustration that, almost a decade later, the biosimilar market is not yet firmly established.

Previously, OPERS provided comment on many aspects of the BPCIA, including the determination and designation of interchangeability. When the FDA published its proposed guidance on interchangeability, “Consideration In Demonstrating Interchangeability with a Reference Product,” in January 2017, OPERS commended the Agency for (1) supporting the extrapolation of interchangeability for additional indications for which the reference product is licensed, and (2) not requiring numerous additional clinical studies to demonstrate interchangeability. However, we also urged the FDA to reconsider several parts of its proposed guidance in order to better incentivize manufacturers to develop interchangeable products.

Our concern remains that the FDA’s proposed guidance places overly burdensome requirements on developers of interchangeable products. Of the 12 biosimilars approved by the FDA to date, not one has been designated as being therapeutically interchangeable. While we understand and support the FDA’s focus on patient safety, we believe the proposed interchangeability guidance is overly conservative and should be revised to encourage development of interchangeable products. As it stands, we lack confidence that even if a developer were to seek interchangeable status for one of its biosimilar products, the resulting interchangeable product would be any cheaper than its reference product because of the additional requirements with which they must comply. The current lack of clarity, certainty and incentive are factors in our members not having access to more biologic drugs, and should be addressed.

We continue to believe that changes described below will improve the interchangeability of biosimilar products with minimal impact to either drug safety or efficacy. As the FDA finalizes its guidance on interchangeability, we ask that the following items be considered.

a. **Data and information to support a demonstration of interchangeability**

While OPERS understands the reasons why the FDA has required a higher data burden of proof for interchangeability compared to biosimilarity alone, we believe that this could be largely accomplished by increasing reliance on innovation in the use of non-clinical analytical techniques to characterize all structural and functional differences between the interchangeable product and reference product. As these non-clinical analytical techniques continue to advance, they should begin replacing the need for clinical studies to reduce residual uncertainty regarding interchangeability, just as they do today for biosimilarity and comparability in support of manufacturing changes.

We are concerned that if the FDA requires a broad approach to clinical studies necessary to demonstrate interchangeability, it will increase manufacturers' costs and potentially, development time, which could either reduce the incentive to develop more affordable Interchangeable products or increase the cost of the interchangeable products. In either case, consumer access to more affordable biological drugs will be reduced. After all, an interchangeable product will be a biosimilar product on which additional studies have been completed, not a newer or better product. This is all the more evident as the FDA is encouraging sponsors to apply for a biosimilar license first, and only then pursue
interchangeability as the second regulatory hurdle. As products themselves are the same, there is little need for additional clinical studies.

b. Considerations for the design and analysis of a switching study or studies to support a demonstration of interchangeability

While we appreciate that switching studies are likely the most expeditious way to meet the requirements in Section 351(k)(4)(B) of the Public Health Service Act to demonstrate interchangeability, we are concerned about the proposed FDA requirements of conducting a switching study or studies on patients only and requiring at least two separate periods for the two products in the switching arm.

These study requirements can be burdensome in terms of the length of time required for review and substantial patient study size. We believe they will delay patient access to interchangeable products, as well as provide an opportunity for manufacturers to increase costs, which would then be passed onto consumers and other payors. And, in the end, the interchangeable product demonstrated will be the same product that was already approved as biosimilar.

It is important that the FDA’s approval process for interchangeable products strikes an appropriate balance between bringing safe and effective interchangeable products to the market and maximizing patients’ access to these more affordable biologics.

c. Recommendations regarding the use of a United States-licensed reference product in a switching study or studies

OPERS is concerned that the FDA’s recommendation that sponsors use a United States-licensed reference product in a switching study or studies could delay patient access to interchangeable products and increase manufacturer costs that ultimately will be passed to consumers and other payors.

As noted above, sponsors currently have difficulty accessing some United States-licensed reference products due to anti-competitive behaviors such as misusing the FDA’s REMS requirements to deny product samples. This lack of access to reference products would be extremely harmful to sponsors that need reference product samples to conduct bioequivalence testing in order to gain an FDA interchangeability designation.

Additionally, sponsors will likely incur significant additional costs if mandated to use United States-licensed reference products. These reference products are twice as expensive as obtaining the same biological product from the European Union and account for between 25 and 30 percent of switching study costs.7

Lastly, the requirement of using a United States-licensed reference product does not make sense from a scientific perspective, especially for those sponsors who have previously used bridging studies with the same product approved elsewhere to establish the initial biosimilar approval for their product.²

d. Considerations for developing presentations, container closure systems and delivery device constituent parts for proposed interchangeable products

OPERS is also concerned that the FDA’s proposed requirement that sponsors developing a product for licensure as an interchangeable biologic should be limited to seeking licensure for the same presentation rather than the focus remaining on the same clinical outcome for the patient. We are concerned this will delay patient access to interchangeable products as reference product manufacturers use intellectual property blocks on their devices. Additionally, this requirement limits presentation improvements that could be provided by interchangeable products.

e. Considerations in regulating post-approval manufacturing changes of interchangeable products

OPERS believes comparability requirements should be the same for all approved biological products. If the FDA appears to impose a higher standard for interchangeable products for post-approval manufacturing changes, we are concerned this will create uncertainty in the process. For example, if both the interchangeable product and its reference product are undergoing manufacturing changes concurrently, it will be unclear who has to match whom.

OPERS opposes unnecessary disparities in the treatment of reference, biosimilar and interchangeable products, as these can confuse prescribers and consumers, discourage market acceptance of biosimilar and interchangeable products, and ultimately, reduce confidence in the safety and efficacy of non-brand biologics that will most likely undergo many post-approval manufacturing changes.

The FDA has more than two decades of experience using comparability in support of manufacturing changes, and we have every confidence that the Agency will apply that knowledge equally and appropriately to biosimilar and interchangeable products in the future.

f. Conditions of use that are licensed for a reference product after an interchangeable product is licensed

OPERS supports extrapolation of indications as a key concept behind the abbreviated biologics pathway established under section 351(k) of the Public Health Service Act. If a new condition of use is licensed for the reference product after an interchangeable product is licensed, once any exclusivities or other intellectual property for the new condition expire, the interchangeable biologic sponsor should be able to seek licensure for the new condition of use, as long as the sponsor provides sufficient scientific justification for extrapolating data to support determination of interchangeability for the new condition. This would require the same scientific reasoning as any extrapolation already applied to the biosimilar and/or interchangeable product and would not necessarily involve the expectation of any further clinical studies.

² For example, Sandoz utilized an EU-approved comparator in their switching study to support FDA approval for their biosimilar Erelzi™ (etanercept).
Conclusion

We appreciate the FDA's efforts to identify and address the behaviors and abuses that preserve unsustainable prescription drug prices. We are hopeful that the FDA will carefully consider the remarks it receives from patients who struggle to pay high prescription drug costs, and payors that must continually alter their health plan design in order to provide their members with meaningful health care coverage. For too long, these groups have been asked to shoulder the burden of health care cost increases. We eagerly await the Agency's actions to ease this growing burden.

Ensuring that biosimilar and interchangeable products have a real chance to take hold and flourish in the marketplace is a necessary first step. Equally important is drug price transparency, which we believe will result in lower list prices, as well as lower costs for plan sponsors and consumers. There is also an on-going need to educate providers and patients regarding the safety, efficacy and value of non-brand biologic medicines. With these actions, the FDA can lay the groundwork for a competitive and vibrant marketplace where consumers can afford to access the life-changing biologic and specialty medications they need.

Finally, anti-competitive behaviors, from product shopping to exclusionary contracting, are harming our members in the form of higher drug prices and reduced access. We ask that the FDA continue to expose these practices and to take whatever steps are necessary to promote the growth and vitality of the biosimilar marketplace.

If you have questions or would like additional information regarding OPERS' comments, please contact Tonya Brown, Director of Member Operations, at 614-224-6204.

Sincerely,

Karen E. Carraher
Executive Director