PREMIER TRANSFORMING HEALTHCARE TOGETHER®

September 21, 2018

The Honorable Scott Gottlieb, M.D.
Commissioner, Food and Drug Administration
Attention: Dockets Management Staff (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: FDA-2018-N-2689, Facilitating Competition and Innovation in the Biological Products Marketplace

Submitted electronically at https://www.regulations.gov/

Dear Commissioner Gottlieb:

The Premier healthcare alliance appreciates the opportunity to submit comments on the Food and Drug Administration (FDA) request for comments titled "Facilitating Competition and Innovation in the Biological Products Marketplace," which was published in the July 25, 2018 *Federal Register*. The request for comments outlines the FDA's approach to enhancing competition and innovation in the biological products marketplace, including by facilitating greater availability of biosimilar and interchangeable products.

Premier strongly supports the creation of a competitive biosimilars marketplace and applauds the FDA for recognizing the value of biosimilars and its important role in minimizing the time and cost to develop biosimilars and in promoting effective competition. Premier further applauds the FDA for releasing the *Biosimilars Action Plan* (BAP) to outline the agency's approach to striking the appropriate balance between innovation, access and competition for biosimilars. Premier offers the following comments on elements of the BAP that it believes can be enhanced to further promote a robust biosimilars marketplace and encourage broader adoption of biosimilars by providers and patients.

Premier is a leading healthcare improvement company, uniting an alliance of more than 4,000 U.S. hospitals and health systems and approximately 165,000 other providers and organizations to transform healthcare. With integrated data and analytics, collaboratives, supply chain solutions, consulting and other services, Premier enables better care and outcomes at a lower cost. A 2006 Malcolm Baldrige National Quality Award recipient, Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with members to co-develop long-term innovations

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that reinvent and improve the way care is delivered to patients nationwide. A key component of our alliance is our Integrated Pharmacy Program, which combines essential clinical data with purchasing power to deliver reduced costs, improved quality and safety, and increased knowledge-sharing with other healthcare professionals.

Premier is a Leader in Promoting a Competitive Biosimilars Marketplace

Premier views the accessibility of biosimilars as a key element in decreasing the cost of healthcare through the creation of a more competitive drug marketplace in the U.S. and has been a leader in promoting a competitive biosimilars marketplace through our supply chain, clinical support, education, advocacy and thought leadership efforts. Premier currently has all marketed biosimilars on contract and employs a dedicated biosimilars team that works with biosimilar manufacturers through a product's lifecycle, from pre- to post-launch, to ensure continued access to biosimilars. Clinically, Premier develops value analysis toolkits, provides product-specific information, including clinical and financial considerations, and supports its members with reimbursement considerations for biosimilars within the Medicare and 340B programs. Regarding education, Premier maintains a dedicated website on biosimilars for health system pharmacy members that provides factual and un-biased information on biologics and biosimilars. In addition, Premier has developed several continuing education programs and outreach efforts for healthcare providers and health system stakeholders to educate and promote the adoption of biosimilars. From an advocacy perspective, Premier has been actively engaged in ongoing efforts with Congress, the FDA, the Centers for Medicare & Medicaid Services (CMS) and other stakeholders to ensure the pathway to market for biosimilars prioritizes patient access and safety and encourages development of these cost-saving medicines. Finally, Premier has authored several peer-reviewed journal articles, white papers and blog posts discussing the current biosimilars landscape and encouraging adoption and serves on the advisory board for *The Center for Biosimilars*.

Improving the Efficiency of the Biosimilar and Interchangeable Product Development and Approval Process

To improve the efficiency of biosimilar and interchangeable product development and approval as an overarching principle, the FDA should permit a designation of biosimilarity parallel to granting an interchangeability designation if the applicant seeks both. The FDA has previously advised that applicants should seek designation of biosimilarity first and then subsequently seek interchangeability designation, a bifurcated process that creates procedural inefficiencies and potentially delays the introduction of interchangeable biosimilars to the marketplace. Therefore, **Premier recommends the FDA create a parallel review process to permit applicants to seek a simultaneous designation of biosimilarity and interchangeability to create procedural efficiencies and improve access to interchangeable biosimilars**.

To incentivize biosimilar manufacturers to enter the marketplace and create predictability in the regulatory process, **Premier urges the FDA to consider an accelerated approval pathway for biosimilars, similar to accelerated pathways available for brand and generic medications**. For example, the Competitive Generics Therapy (CGT) pathway was created to expedite the development and review of a generic drug for products that lack competition. The CGT pathway allows for expedited review of Abbreviated New Drug Applications (ANDA) and provides for a 180-day exclusivity period for the first approved applicant. To prevent gaming of the CGT pathway, there is a special forfeiture rule that requires applicants to commercially market the product within 75 days of the approval date of the ANDA or forfeit its exclusivity. A similar pathway for biosimilars could encourage manufacturers to enter the marketplace due to the expedited review and exclusivity while fostering competition due to the forfeiture rules. Furthermore, an accelerated approval pathway for biosimilars will also help address the issue of carve outs where an indication for a biosimilar may need to be added or removed after initial FDA-approval due to patent or exclusivity issues protecting one or more of the FDA-approved indications for a reference biologic product. An accelerated pathway will allow the FDA to efficiently approve these additional indications once the reference biological's protection lapses and further the establishment of a competitive biosimilars marketplace.

In addition, biosimilar licensure is currently based on comparison between a reference biologic product and a biosimilar. However, there is increasing interest in understanding how one biosimilar compares to another biosimilar for the same reference biologic product, especially in regards to switching and automatic substitution. Furthermore, understanding the ability to interchange one biosimilar for another biosimilar is important if the reference biologic is no longer marketed or if there is a drug shortage for one of the biosimilars. Therefore, **Premier urges the FDA to release clear policies and guidance that facilitate and promote biosimilar to biosimilar interchangeability.**

Some additional opportunities for the FDA to improve the efficiency of biosimilar and interchangeable product development include: prioritizing inspection of facilities for biosimilar applicants; developing product-specific guidance for biologics as the FDA currently does for brand small-molecular products to encourage generic drug development and increase patient access to generic and complex drugs; completing hiring of staff allocated under the Biosimilar User Fee Amendments of 2017 (BsUFA II); and expediting review for biosimilars manufactured at the same facility and on the same line as an already internationally approved biosimilar.

Maximizing Scientific and Regulatory Clarity for the Biosimilar Product Development Community

To maximize scientific and regulatory clarity for biosimilar manufacturers, Premier supports the FDA's intent to improve regulatory predictability for manufacturers, harmonize international regulation of biosimilars and the acceptance of non-U.S. comparator products, and implement the use of real-world evidence in supporting regulatory decision-making.

Regarding harmonization and the acceptance of non-U.S. comparator products, one area to note, however, is that the FDA's draft interchangeability guidance released in January 2017 states that use of a U.S.-licensed reference product is strongly recommended and discourages the use of a non-U.S. comparator to demonstrate interchangeability.[1] Therefore, **Premier urges the FDA to revise this requirement when issuing final interchangeability guidance to permit the use of non-U.S. comparators when seeking interchangeability designation.**

Premier appreciates the FDA's recognition of the importance of gathering real-world evidence (RWE) to monitor for ongoing safety and efficacy of both biologics and biosimilars. RWE is integral to understanding the long-term safety of switching a patient from a reference biologic product to a biosimilar, switching a patient from one biosimilar to another biosimilar and understanding any safety or efficacy implications associated with maintaining a patient on a reference biologic as variations in lots may occur. RWE is also valuable in conducting comparative effectiveness research to determine which products have the best outcomes for subsets of patients and can potentially be used in the regulatory-decision making process. Finally, RWE is important for assessing the cost-effectiveness of a product and understanding the total cost of care for specific disease states often treated with biologics and biosimilars. Gaining insight into safety, efficacy, patient outcomes and cost-effectiveness of both biologicals and biosimilars are all integral elements to assuaging concerns from providers, patients, payers and others regarding the introduction of biosimilars in the marketplace and encouraging their adoption.

The Premier Healthcare Database (PHD) is one of the most comprehensive electronic healthcare databases containing robust data on more than 108 million inpatient admissions and 765 million outpatient encounters for over 208 million unique patients. The PHD has been leveraged by hospitals, health systems, academia, pharmaceutical manufacturers, the Centers for Disease Control and Prevention (CDC), CMS, the National Institutes of Health (NIH) and others to use real-world data to conduct evidence-based and population-based analyses of drugs, devices, other

[1] Considerations in Demonstrating Interchangeability With a Reference Product Guidance for Industry – Draft Guidance issued January 2017. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537135.pdf

treatments, disease states, epidemiology, resource utilization, healthcare economics and clinical outcomes. **Premier welcomes the opportunity to discuss how the Premier Healthcare Database and its dedicated staff of skilled professionals trained in medicine, pharmacy, epidemiology, public health, economics and statistics can partner with the FDA to support the development of RWE for biologics and biosimilars.**

Delivering Effective Communications to Improve Understanding of Biosimilars Among Patients, Clinicians and Payers

To improve the understanding of biosimilars, Premier agrees that it is critical to educate healthcare professionals and other stakeholders. Premier applauds the FDA on their efforts thus far with the *Biosimilar Education and Outreach Campaign* and their commitment to creating additional innovative educational materials to explain biosimilars and interchangeability. Some specific areas where Premier believes additional educational materials would be beneficial to strengthen provider confidence in prescribing biosimilars include:

- Enhanced education around interchangeability to convey that in the U.S. interchangeability is a regulatory term that essentially signifies the ability to perform pharmacist-level substitution and does not represent a higher standard or higher quality product. **Premier believes it is imperative for the FDA to dispel misnomers that interchangeability designation is superior to biosimilarity designation and convey that all biosimilars approved by the FDA are safe and effective.**
- Education around extrapolation to convey that extrapolation is supported by scientific data, does not represent an inferior product, and is safe and effective. Specifically, education should articulate that extrapolation is not automatic and is considered only after biosimilarity to the reference biologic product has been established by a comprehensive comparability program, including safety, efficacy and immunogenicity in a key indication that is suitable to detect potentially clinically relevant differences, and there is sufficient scientific justification for extrapolation. **Premier believes education on extrapolation is critical to increase provider confidence in prescribing a biosimilar for all FDA-approved indications.**
- Education that highlights data regarding the safety and efficacy of biosimilars in the European Union. While biosimilars are relatively new to the U.S. market, they have been available in Europe for many years and there is robust European data demonstrating their long-term safety and efficacy. **Premier believes the FDA has a significant opportunity to highlight data from the European experience to enhance provider confidence in prescribing biosimilars as well as patient acceptance in utilizing biosimilars.**

Furthermore, Premier encourages the FDA to ensure all educational materials intended for patients account for varying health literacy rates throughout the country and align with the Agency for Healthcare Research and Quality (AHRQ) Health Literacy Universal Precautions.[2]

As the FDA looks to develop these innovative educational materials, **Premier encourages the FDA to work with private partners who have already created these types of materials to adapt existing, factual and un-biased educational materials to help speed the availability of these educational materials**.

Supporting Market Competition by Reducing Gaming of FDA Requirements or Other Attempts to Unfairly Delay Competition

To support market competition, Premier agrees that it is necessary to reduce the gaming of FDA requirements or other attempts to unfairly delay competition. Premier offers several specific recommendations to help improve market competition.

First, some manufacturers restrict access to samples for biosimilar manufacturers by citing compliance with limited distribution or REMS requirements. This practice inhibits the ability of biosimilar manufacturers to demonstrate bioequivalence and thereby delays the availability of biosimilars in the marketplace. The FDA has acted in this area by highlighting manufacturers they are aware of who are abusing REMS requirements to deny samples by listing these manufacturers on the FDA website and commenting publicly that *"…a path to securing samples of brand drugs for the purpose of generic drug development should always be available. Even in the case of limited distribution programs such as those required by certain REMS, there should be a path forward for generic drug development*."[3] More, however, needs to be done to prevent these practices from occurring and to give the FDA the authority to take action against manufacturers who restrict access to samples. Therefore, **Premier recommends the FDA work with Congress to ensure access to product samples needed for bioequivalence testing for biosimilar development.[4]**

[2] Agency for Healthcare Research and Quality Healthy (AHRQ) Health Literacy Universal Precaution Toolkit, 2nd Edition. Last updated. May 2017. Available at: https://www.ahrq.gov/professionals/quality-patient-safety/qualityresources/tools/literacy-toolkit/index.html

[3] Statement from FDA Commissioner Scott Gottlieb, M.D., on new agency efforts to shine light on situations where drug makers may be pursuing gaming tactics to delay generic competition. May 17, 2018. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm607930.htm

[4] Congress is currently considering a bipartisan, bicameral bill [S.974/H.R.2212 - Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2018] that would ensure access to product samples needed for bioequivalence testing for biosimilar development. The Senate Judiciary Committee reported favorably on the bill on June 21, 2018.

Second, there has been an increase in patent disputes and settlements between biologic and biosimilar manufacturers delaying the availability of biosimilars in the marketplace beyond market exclusivity granted under the Biologics Price Competition and Innovation Act (BPCIA). Currently, this process is not transparent as biologic manufacturers do not have to report patent settlements to the Federal Trade Commission (FTC) in the same manner that brand manufacturers must. This process is considered a deterrent for brand manufacturers to enter into a patent settlement. **Premier recommends the FDA work with Congress and the FTC to require biologic and biosimilar manufacturers to report patent settlements to the FTC.**[5] Premier also recommends the FDA engage in ongoing dialogue with the FTC to identify additional opportunities to thwart anti-competitive practices inhibiting the introduction of biosimilars in the marketplace.

Third, there have been recent concerns with claims made by reference biologic manufacturers regarding material differences between biologics and biosimilars, and implying that an interchangeability designation is superior to a biosimilarity designation. These claims are contributing to confusion amongst providers and patients, thereby inhibiting the uptake of biosimilars. The FDA has a duty to protect the public health by ensuring that prescription drug information is truthful, balanced and accurately communicated. Therefore, **Premier urges the FDA to issue guidance outlining expectations for permissible, truthful and non-misleading communications about biosimilars.**

Fourth, concerns have been raised about the potential abuse of the Orphan Drug Act by manufacturers that initially apply for a single indication that qualifies for orphan drug status but then apply for broader non-orphan indications once the product is approved by the FDA. This practice delays the introduction of generic and biosimilar alternatives to the marketplace, as the product is protected under extended exclusivity given its orphan drug status. To combat this practice, **Premier urges the FDA to work with Congress to consider changes to the Orphan Drug Act to ensure it is meeting its original intent of fostering the development of innovative drugs for rare conditions and not unintentionally delaying competition for biosimilars.** While awaiting legislative change, in the interim, the FDA can request additional information of manufacturers seeking orphan drug status, such as disclosing additional indications the manufacturer intends to seek FDA approval for. Requiring disclosure of this information may deter some manufacturers from abusing the Orphan Drug Act.

Finally, in recent years, manufacturers have begun to file for multiple patents for their products that cover not only the active ingredient but also cover manufacturing, delivery systems and other

[5] Congress is currently considering bills that would require biologic and biosimilar manufacturers to report patent settlements to the FTC. The Senate advanced S.2554 - The Patient Right to Know Drug Prices Act on September 17, 2018. The House Energy & Commerce Subcommittee on Health is considering H.R. 6478 – The Biosimilars Competition Act of 2018.

elements. This extends exclusivity for the product beyond the patent for the active ingredient alone, thereby delaying introduction of alternatives to the marketplace. In addition, manufacturers will sometimes make minor changes to their product, such as an extended release formulation or once a day vs. twice a day dosing, and seek additional patent protection to extend exclusivity for their product. To help combat these practices that delay the introduction of alternatives to the marketplace, **Premier urges the FDA to work with the United States Patent and Trademark Office (USPTO) to ensure that patents are appropriately awarded for truly innovative and new discoveries.**

Additional Areas Not Included in the Biosimilars Action Plan

Lastly, one additional area not included in the *Biosimilars Action Plan* that Premier would like to raise is the naming convention for biosimilars. The current naming convention finalized by the FDA in January 2017 adds complexity to the healthcare system. This could lead to errors in prescribing medications and poses a risk to patient safety, hampers clinical decision-making and the ability to identify lower cost therapeutic alternatives, and causes unnecessary confusion among patients and providers – all issues that do not lend themselves to increasing the adoption of biosimilars. **Premier urges the FDA to rescind the current naming guidance and reissue guidance that uses the same international non-proprietary name (INN) for biosimilars as the reference biologic product.**

Conclusion

In closing, the Premier healthcare alliance appreciates the opportunity to submit comments on FDA-2018-N-2689. Premier looks forward to working with the FDA and other stakeholders to encourage a robust biosimilars marketplace by striking the appropriate balance between innovation, access and competition for biosimilars.

If you have any questions regarding our comments or need more information, please contact Soumi Saha, Senior Director of Advocacy, at soumi_saha@premierinc.com or 202-879-8005.

Sincerely,

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