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Submitted via the Federal eRulemaking Portal: http://www.regulations.gov

Commissioner Scott Gottlieb, M.D.
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2017-D-0154 Comments on "Considerations in Demonstrating Interchangeability with a Reference Product"

Dear Dr. Gottlieb:

Vizient, Inc., respectfully submits our comments to The Food and Drug Administration's (FDA or the Agency) regarding the notice "Considerations on Demonstration Interchangeability with a Reference Product" as published on March 9, 2017 in the Federal Register (82 FR 13819).

Vizient, Inc., is the largest member-driven health care performance improvement company in the country. Vizient provides innovative data-driven solutions, expertise and collaborative opportunities that lead to improved patient outcomes and lower costs. Vizient serves a diverse membership and customer base including academic medical centers, pediatric facilities, community hospitals, integrated health delivery networks and non-acute health care providers. Vizient is headquartered in Irving, TX with locations in Chicago, Washington, D.C., and other cities across the country. Vizient welcomes this opportunity to share our view with FDA on this important topic.

Background

At Vizient, our purpose is to ensure our members deliver exceptional, cost-effective care. Vizient is member-driven and member-minded, working tirelessly to amplify every organization's impact by optimizing every interaction along the continuum of care.

Vizient appreciates The Food and Drug Administration's ongoing development and implementation of the provisions of the *Biologics Price Competition and Innovation Act of 2009* (BPCI Act). We are committed to minimizing health care costs and mitigating increasing drug expenditures to preserve access to care. Vizient supports the introduction and adoption of biosimilars as safe and effective alternatives to originator biologics, and continues to provide education to physicians and other providers to minimize barriers to product acceptance.

We appreciate FDA's thoughtful approach, commitment to increased awareness of biologic manufacturing and regulatory principles, and application of scientifically based decision-making in the introduction of biosimilar medications. We applaud the Agency's efforts in continuing to define key aspects of biosimilar approvals through stakeholder engagement, evaluating the BPCI Act statute, and planning the necessary steps toward implementation.

Recommendations

Considerations for Developing Presentations for Proposed Interchangeable Products

We commend FDA for the attention to detail regarding the assessment of presentations for a proposed interchangeable biologic in comparison to its originator reference counterpart. Unlike biologic molecular ingredients, which can be assessed with a great deal of specificity, the manner in which a health care provider, care giver, or patient interacts with a delivery device can be subject to many difficult to measure variables. Such differences could create unnecessary hurdles to biosimilar acceptance and use. Vizient has confronted a related

issue given the absence of dosage forms for certain biosimilars as compared to the originator counterpart (e.g., lack of vial presentation for filgrastim-sndz and effect on pediatric patients). Therefore, we strongly support FDA's proactive approach to prevent issues related to product formulation.

Product-Dependent Factors That May Impact the Data Needed to Support a Demonstration of Interchangeability

Over the last six years, Vizient has provided a wide breadth of educational experiences, over 200 presentations, web conferences, and written commentary, to both its members and external audiences to facilitate an improved understanding of the biosimilar paradigm. A critical concept Vizient has stressed to physicians, pharmacists, and other clinicians, is the fact that while biosimilars are a novel product category, the relationship between manufacturing changes and biologic product variability is not a new consideration. Originator reference products demonstrate variation during normal production. Furthermore, manufacturing modifications up to and including the use of different expression system cell lines occur throughout the life cycle of the originator brand.

The Agency's notice includes the statement: "current analytical methodologies may not detect or characterize all relevant structural and functional differences between the reference product and the proposed interchangeable product." We respectfully request clarification and additional detail from FDA regarding these "differences" that are undetectable through current analytical capabilities. Variations between an originator biologic pre- and post-manufacturing change are primarily assessed using analytical techniques. Vizient is concerned that FDA is setting an inappropriately higher standard for interchangeable biologics without scientific justification. The Agency currently uses analytical techniques to evaluate differences in an originator biologic pre- and post-change (essentially an interchangeable relationship). Therefore, when comparing a biosimilar or interchangeable biologic to the reference product, using analytical data and techniques is an appropriate approach. If variations were to exist, it is important to describe those with clarity for providers and patients. Failure to provide additional insight contributes to a narrative that biosimilars carry a higher degree of risk and that analytical characterization is somehow insufficient in evaluation of structure and functional activity.

Use of a U.S.-Licensed Reference Product in a Switching Study or Studies

As evidenced by the products approved to date, biosimilar development greatly benefits from the efficiencies derived through the use of analytical data as the foundation for approval, extrapolation of information to support licensing for multiple indications, and the capacity to establish a scientifically justified bridge between U.S. and non-U.S. labeled originator reference product. These considerations help minimize the need for conducting redundant clinical trials in the determination of biosimilarity. Therefore, we encourage FDA to reconsider its stated approach in excluding the use of non-U.S. licensed originator reference product in interchangeability studies. Analytical capabilities provide the capacity to determine the structural and functional comparability of various biologics, including the degree of similarity between U.S. and non-U.S. labeled originator reference products. Restricting interchangeability trials to U.S. licensed originator biologics only would contribute to increased development expense, and thus would limit the degree of savings offered through biosimilar competition. This exclusion is contradictory to the BPCI Act's original intent.

Additional Responses

FDA invited comments on two topics, the ongoing comparability assessments of interchangeable biologics and the impact of new indication approval for originator reference products. In both situations, Vizient would encourage FDA to apply the same standard to biosimilars and interchangeable biologics that exists for originator reference drugs. FDA should maintain consistent standards throughout life cycles of originator reference products, biosimilars, and interchangeable biologics. While we do not believe that any additional assessments are necessary, we urge the Agency to educate and inform health care providers by disclosing manufacturing changes.

Similarly, we recommend that biosimilars and interchangeable biologics receive comparable licensing when originator reference agents obtain additional indications, provided no orphan exclusivity considerations exist. As originator reference drugs are labeled for all uses that have accrued throughout their marketing, interchangeable and biosimilars should similarly be licensed for all applicable uses of the originator.

We commend and support FDA in its implementation of the *Biologics Price Competition and Innovation Act* and the biosimilar approval process. Biologic competition is a critical step in controlling the trajectory of drug costs –

and ultimately lowering prices for patients. Vizient will continue to support the education of physicians, pharmacists, and other providers through its evidenced based resources (e.g. infliximab-dyyb white paper), its budget projection tools (e.g. the twice annual Vizient Drug Price Forecast report), web conferences and other communication vehicles. In addition, Vizient continues to implement sourcing strategies to support members in their efforts to lower costs through biosimilar adoption.

Conclusion

Vizient appreciates the FDA extending the comment period on the notice in order to allow interested persons additional time to submit comments. We welcome FDA's discussion and its emphasis on stakeholder involvement, which provides a significant opportunity for the health care industry to inform the next phases of the process.

Vizient membership includes a wide variety of hospitals ranging from independent, community-based hospitals to large, integrated health care systems that serve acute and non-acute care needs. Additionally, many are specialized, including academic medical centers and pediatric facilities. Individually, our members are integral partners in their local communities, and many are ranked among the nation's top health care providers.

In closing, on behalf of Vizient, Inc., I would like to thank FDA for providing us this opportunity to comment on this notice. Please feel free to contact me at (202) 354-2600 or Chelsea Arnone, Director of Regulatory Affairs and Government Relations (chelsea.arnone@vizientinc.com), if you have any questions or if Vizient can provide any assistance as you consider these issues.

Respectfully submitted,

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Vizient, Inc.