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THREE WAYS THE FDA CAN FACILITATE CLAIMS OF INTERCHANGEABILITY

In the US, an interchangeability designation by the Food & Drug Administration (FDA) is perceived as the holy grail in biosimilars development by some, and yet regarded as irrelevant by others. Why the difference? Perceptions that an interchangeable biologic is a "better" biosimilar persist and physicians are being encouraged to wait for them. But as a legal matter, the designation is only relevant for substitution by pharmacists (subject to state law); thus, it is not applicable to physician-administered drugs, which represent the vast majority of biologics.

How to demonstrate interchangeability is a subject of much debate by stakeholders. FDA's draft guidance on interchangeability issued in January 2017 is cautious and demanding; meeting FDA's guidance is an expensive proposition that would make it difficult for biosimilar manufacturers to make a return on their investment. Recognizing this potential barrier, the White House Council of Economic Advisors, in a recent report outlining policy solutions to address drug prices, encourage FDA to finalize their interchangeability draft guidance in a way that is "relatively easy and inexpensive to adhere to."

The FDA has substantial experience with approving originator biologics, as well as nine biosimilars to six reference products, and monitoring them for consistency throughout their product life cycle. The agency can apply the same standards for all medicines and retain patient and provider confidence in the safety and efficacy of all the products that they approve. This also allows the agency to remain scientifically sound while reconsidering the requirements for interchangeable biologics that will not compromise outcomes for patients.

In as little as a few weeks, FDA is expected to release a Biosimilar Innovation Plan to "promote the development and adoption of safe, high quality biosimilar drugs." At a meeting last fall, FDA Commissioner Scott Gottlieb remarked that creating a robust biosimilar market will demand innovative, "potentially disruptive" solutions, a challenge that could be previewing the agency's own ambitious plan.

There are three ways the FDA can facilitate applications and approvals for interchangeable biosimilars:

1. **Making reference products more readily available for conducting any necessary switching studies.** According to FDA's draft guidance on interchangeability, switching studies must be done with a US-sourced reference. But reference product sponsors are reluctant to make that reference available in the quantities necessary for those switching studies. FDA can take actions similar to those it has taken in the small molecule drug space, in which it has publicly rebuked branded drug manufacturers and pharmaceutical

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supply chain intermediaries that restrict access to samples of their drugs to generic drug manufacturers.

2. **Applying appropriate scientific reasoning and clear international guidance to choice of reference product for biosimilar development.** To support an interchangeability claim in the US, FDA suggests comparisons of an approved biosimilar to the US-sourced version of the reference product. These "bridging" studies can be very expensive to pursue. FDA can recognize when the reference product is the same even when it is sourced outside the US. This way a single version of a reference biologic could act as a 'global reference' for all biosimilar development. Such an approach would support the World Health Organization's proposed program to prequalify biosimilars as comparable to their reference products in quality, safety, and efficacy with the goal of expanding worldwide access to these increasingly essential medicines.

3. **Encouraging efficient development and approval of all biologics, not just biosimilars.** FDA can support scientifically-meaningful studies that reduce the need for sponsors to generate data that drains resources yet is not actionable for regulatory decision making. So called "feel good" or confirmatory studies should be questioned as they can delay access and add to costs. FDA can encourage state-of-the-art methods, such as minimizing unnecessary animal and human testing by using functional assays instead. FDA can also apply its global leadership, experience, and expertise with comparability to inform their decisions on biosimilarity and interchangeability. They can also learn from the experience with biosimilars from Europe, and from the decisions of other stringent regulators.

The science is the best it has ever been. 2018 looks to be the year when FDA will begin to update its regulatory requirements to better leverage that science and their own scientific expertise and experience for the development of more treatment options, including originator biologics, biosimilars, and interchangeable biologics. This will enable greater access and affordability for patients through competition, a goal that Commissioner Scott Gottlieb has articulated for the agency.

To receive more expert insights on interchangeability and biosimilars, connect with us.

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