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FDA Eases Way For Gold-Standard Biosimilars

By **Jeff Overley**

Law360 (May 10, 2019, 9:13 PM EDT) -- The U.S. Food and Drug Administration on Friday cemented its criteria for approving cream-of-the-crop biosimilars that pharmacies can automatically substitute in place of pricier biologics, simplifying standards it previously proposed and handing a badly needed win to the struggling biosimilars industry.

In final guidance, the FDA outlined its key considerations for deeming a biosimilar "interchangeable" with an innovator biologic. That's the gold standard to which all biosimilars aspire so they can be substituted at the pharmacy counter without a doctor's permission, just like traditional generic drugs.

"With this final guidance, I think we are closer to seeing the first interchangeable product out there," Christopher J. Betti, a Morgan Lewis & Bockius LLP partner, told Law360. "Biosimilars have been waiting for this particular clarity before moving down a path to show interchangeability."

The wait has been long. It's been more than nine years since the Affordable Care Act birthed a biosimilar approval pathway to usher in competition for biotech drugs with annual price tags that sometimes hit six figures.

The FDA has approved almost 20 biosimilars, but because of daunting patent protections, fewer than half of those are on the market. Even biosimilars that are available have struggled to gain traction, with some biosimilar makers saying anti-competitive maneuvers have thwarted their sales.

None of the approved biosimilars have won the coveted interchangeability designation, and it's not clear that any have even sought it, perhaps because the FDA's criteria are demanding and were not set in stone until Friday.

But Friday's guidance, which was generally well received by biosimilar advocates, could shake things up. The Association for Accessible Medicines, which is the top lobbying group for biosimilar makers, said that the FDA's guidance "streamlined" approval requirements and created more "flexibility" for the design of required studies.

In the most conspicuous change, the final guidance only ran 23 pages, down from 30 in the draft version that the FDA released in 2017. The deleted pages related mostly to containers and delivery devices that accompany biologic products, which are usually injectable.

"The removal ... was probably done to simplify the final guidance," Hogan Lovells partner David M. Fox said Friday. "It may be that by removing these sections ... the agency is preserving its ability to give biosimilars more flexibility regarding the look and feel of their products."

In another area, the FDA maintained a requirement for "switching studies" that require patients to alternate between biosimilars and their innovator counterparts to ensure equivalence. But it also made clear that switches can compare biosimilars to versions of biologics that were approved outside the U.S. That's helpful because non-U.S. biologics tend to be readily available and much less expensive to acquire.

"FDA believes that when supported by adequate data and information, it may be reasonable to use a non-U.S.-licensed comparator in a switching study," the guidance said.

In addition, the final guidance contained new language suggesting that biosimilar makers may sometimes be able to skip switching studies altogether.

"If a sponsor of a proposed interchangeable product believes that data from a switching study is not necessary, FDA expects the sponsor to provide a justification for not needing such data as a part of the demonstration of interchangeability," the final guidance said.

Stacie Ropka, a partner at Axinn Veltrop & Harkrider LLP, told Law360 that the "FDA recognizes that there could come a time when you would be able to provide a scientific justification of no need for switching."

Elsewhere, the final guidance eliminated terminology had left some observers scratching their heads. For example, it no longer references "fingerprint-like similarity," a term the FDA has been using for years to describe similarity that is demonstrated using extremely sensitive techniques.

"It created a lot of confusion among people in the field as to what exactly that meant," Betti said Friday.

The draft version of the interchangeability guidance had directed readers to other guidances for descriptions of the fingerprint-like characterization, but the Association for Accessible Medicines has called that directive unhelpful, writing that the concept "is insufficiently described in other guidance documents."

Lyndsay Meyer, an FDA spokeswoman, told Law360 on Friday that 16 drugmakers as of May 1 had publicly announced the submission of 29 pending biosimilar applications. Although the agency isn't allowed to divulge specifics that companies haven't themselves divulged, there has been "robust interest in the interchangeability pathway," she said.

In a notable move, FDA Commissioner Ned Sharpless on Friday mentioned that, beginning next year, the agency will be able to approve insulin products as biosimilars. The products, which are essential to diabetes treatment, have seen their prices soar in recent years and face relatively little competition.

"The agency is being very clear about its focus on paving the way for interchangeable, pharmacy-substitutable insulin products," Fox said.

Looking ahead, a clearer path has been opened for interchangeable biosimilars in general, with the caveat that every product will still face its own challenges and ultimately have to find its own way to market.

"Maybe overall there's a more simplistic aspect to it," Kevin Nelson, a Schiff Hardin LLP partner, said of

Friday's guidance. "[But] it's really going to be product dependent and really going to be depending on the type and the amount of data that's provided."

--Editing by Adam LoBelia.