THE NATIONAL LAW JOURNAL

MARCH 21, 2016

An ALM Publication

BIG PHARMA | A SPECIAL REPORT

Big deals abound in Big Pharma, and with them comes an array of antitrust implications that attorneys are grappling with. At the same time, rapid scientific developments mean that laws addressing innovation and availability of new drugs must keep up. Inevitably, all the movement, whether on the business side or the science side, demands a global approach to the laws governing the pharmaceuticals sector.

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Biosimilars Market Is at a Critical Turning Point

Congress enabled their speedy approval in 2010, but courts and the FDA will determine how fast they move.

BY CARLOS ANGULO

The next 12 to 18 months are likely to be a critical time for an industry at the forefront of 21st century health care—biosimilars. Congress enacted landmark legislation in 2010 creating an expedited FDA approval pathway for these products, and the biosimilars industry has begun to grow rapidly.

But the U.S. Food and Drug Administration and the courts are now considering several important aspects of the biosimilars statutory and regulatory framework, and their decisions will determine the industry's full potential as it comes of age.

Biologics, which are large-molecule medicines derived from living organisms, are among the most expensive drugs in America and account for a growing share of prescription drug costs. On average, biologics cost $45 per day, as compared to $2 per day for traditional small-molecule drugs. Certain biologics cost tens or even hundreds of thousands of dollars per patient per year.

To address this, Congress in 2010 passed the Biosimilars Price Competition and Innovation Act (BPCIA) as part of the Affordable Care Act. The BPCIA created an expedited FDA approval process, under which the agency may approve a biosimilar based on the agency's previous approval of another biologic, called the "reference product."

This approach both reduces biosimilars' development costs and facilitates quicker FDA review, expediting competition and consumer access to affordable life-saving medicines. One recent study estimated that increased competition from biosimilars would save the U.S. health care system more than $44 billion over 10 years.

AP PHOTO/J. SCOTT APPLEWHITE, FILE

EXPEDITED: President Obama signed the Affordable Care Act in 2010. It included the Biosimilars Price Competition and Innovation Act, legislation providing fast-track approval for biosimilars.

The recent year has witnessed significant developments in the area of biosimilars. The FDA approved the first biosimilar—Sandoz Inc.'s version of Amgen's filgrastim product Neupogen—in March 2015. Several more applications have been filed with the FDA, and companies are heavily investing in biosimilars development. This progress, along with the potential for enormous health care savings, may be significantly impacted by the coming decisions from the FDA and the courts.

Among the key issues that the FDA is currently considering are the criteria for determining whether a biosimilar is "interchangeable" with its reference product. Under the BPCIA, the FDA may deem a biologic to be biosimilar to a reference product if it is shown to be highly similar to, and without meaningful clinical differences from, the reference product. A biosimilar may be deemed "interchangeable" with the reference product if, among other things, it produces the same clinical effect as the reference product in any

given patient. The key consequence of an interchangeability determination is that interchangeable biosimilars, like standard small-molecule generic drugs, would be covered under state automatic substitution laws. Therefore, pharmacies would be required to automatically fill, without physician intervention, a prescription for a reference product with the less expensive interchangeable biosimilar—thereby dramatically increasing patients' access to critically needed medicines and dramatically lowering health care costs.

FDA is currently developing regulatory criteria for proving interchangeability—for example, whether a biosimilars applicant will need expensive, time-consuming clinical studies to prove the same clinical effect. Biosimilars companies and other stakeholders, as well as Congress, have argued that the FDA is moving too slowly in this area, and this delay is impeding the development of a robust biosimilars market. For its part, the FDA has said that it is essential to get the science right at this early stage in biosimilars' regulatory history.

The FDA's decision, when it is made, will go a long way toward determining the cost of obtaining an interchangeability designation and therefore the economic incentives for drug companies to develop these products.

Another key issue facing the FDA is whether a biosimilar product should be given the same international nonproprietary name as its reference product. The BPCIA itself is silent on this issue, leading to what has been a multiyear debate.

Supporters of unique international nonproprietary names for biosimilars, such as the brand biologics industry, argue that biosimilars should have different names because they are in fact different products (in other words, similar but not identical to their reference products) and that different nonproprietary names will ensure proper tracking of postmarketing drug safety issues (known as pharmacovigilance). Advocates for same international nonproprietary names—including the biosimilars industry, pharmacists, retirees lobby AARP and others—argue that differential naming will chill use of, and therefore competition from, biosimilars; will cause confusion among prescribers, patients and pharmacists, thereby compromising patient safety; and are unnecessary for effective drug safety monitoring given other available tools.

Last fall, the FDA issued a proposed rule and draft industry guidance on the naming issue, proposing that a random, distinguishing four-digit suffix be added to the international nonproprietary name of each biologic product—including both reference products and biosimilars. Interchangeable products would share a suffix. The FDA explained that it believes "shared nonproprietary names are not appropriate for all biological products," and it expressed "a need to clearly identify biological products to improve pharmacovigilance and, for the purposes of safe use, to clearly differentiate among biological products that have not been determined to be interchangeable."

THE COURTS ARE ALREADY BUSY INTERPRETING CRITICAL ASPECTS OF THE BIOSIMILARS PRICE COMPETITION AND INNOVATION ACT, SUCH AS PROCEDURES FOR RESOLUTION OF PATENT DISPUTES.

The FDA proposed rule and guidance have been the subject of extensive comment and criticism. One such critic is the Federal Trade Commission, which contends that the FDA's proposal could cause prescribers to incorrectly believe there are clinically meaningful differences between a biosimilar and the reference product and therefore be reluctant to prescribe biosimilars, harming product development and competition.

There is no indication when, if at all, the FDA will issue a final naming rule or guidance—or then whether the FDA's proposal will be challenged in court.

For their part, the courts are already busy interpreting other critical aspects of the BPCIA, such as the statute's procedures for resolution of patent disputes between a biosimilars applicant and the sponsor of the relevant reference product—procedures referred to as "the patent dance." The courts have been asked to consider whether certain "patent dance" steps are mandatory or merely voluntary, and what remedies are available in the event that a party chooses not to take part in the patent dance at different stages.

One such step provides that a company seeking to market a biosimilar shall give 180 days advance warning before marketing. Last year, the U.S. Court of Appeals for the Federal Circuit held that such notice can only be given after FDA approval, and that notice can be compelled by the reference product sponsor through an automatic injunction. The effect of this holding would be to delay the marketing of an FDA-approved biosimilar by six months and to enable the reference product sponsor to enforce this delay automatically in court.

Sandoz, the biosimilar manufacturer in this case, has asked the U.S. Supreme Court to review this decision, arguing that Congress did not intend for the notice provision to cause a six-month delay in patients' access to approved biosimilars and that an automatic injunction conflicts with the remedies Congress chose in the "patent dance" provisions. (Disclosure: The author has filed amicus briefs in support of Sandoz's position on behalf of biosimilars trade associations.) Whether the court takes this case, and what it decides if it does, will shape the landscape for the biosimilars industry for years to come.

Biosimilar naming, interchangeability, and the "patent" dance provisions are just three of the critical BPCIA issues that have the industry and policymakers watching closely. It is no exaggeration to say that what the FDA and the courts decide will go a long way toward determining if we can realize Congress' goals of making affordable life-saving medicines available to patients quickly and of achieving dramatic cost savings to the U.S. health care system.

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