CRA Insights: Life Sciences

CRA Charles River Associates

February 2014

When a copy is not a copy: biosimilars v. generics

In economic analyses of antitrust issues, damages assessments in intellectual property disputes, and other forms of commercial litigation, it is often necessary to assess the structure and conduct of the marketplace at issue. In this respect it may be tempting to rely on the past experience of generic small-molecule drugs to predict how the introduction of biosimilar copies of biologics may affect the market. This would be a dangerous assumption. Biosimilars are large-molecule drugs with an evolving regulatory pathway,[1] complexities in the development and manufacturing processes, and different legal hurdles for patent challenges than those typically confronting generic versions of small-molecule drugs. Accounting for the differences and understanding the appropriate way to model the marketplace for biosimilars, as opposed to generics, may have significant consequences for economic analyses in the context of litigation. This *CRA Insights* probes some of those differences and their implications.

A different marketplace

The competitive environment for large-molecule biosimilars is likely to be quite different than that for typical small-molecule generics. For example, a lack of mandatory substitution for biosimilars would mean that they may not be able to rely on existing demand for the reference drug and pharmacist substitution to gain sales.[2] Further, many biosimilars would be physician-administered drugs with no opportunity for intervention at a pharmacy. As a result, companies with biosimilars may have to engage in their own marketing and product support efforts to gain share, leading to an environment analogous to the behavior among branded products in the same therapeutic category rather than the typical generic experience.

In further contrast to generics, biosimilars will generally have higher development costs, a more uncertain approval pathway, and a more expensive and difficult manufacturing process. Fewer pharmaceutical players have the capabilities to successfully develop a biosimilar, potentially

---

[1] The US Food and Drug Administration (FDA) draft guidance supports treating each biosimilar application on a case-by-case basis, taking into account the particular circumstances surrounding each biologic and adopting a flexible approach to biosimilar approval.

[2] With biologics there is the additional hurdle of achieving "interchangeability" to meet thresholds for mandatory substitution. This pathway remains unclear, with recent FDA guidance primarily focused on biosimilarity and the FDA still determining what evidence would be required for interchangeability.

leading to a lower threat of competitive entry. Complicated manufacturing processes also likely mean that there will be more patents protecting the product and the manufacturing process, potentially raising the likelihood and complexity of patent litigation. Due to the complexity of the molecules, companies may pursue different clinical strategies to demonstrate biosimilarity including decisions on which indications to address.

These differences between biosimilars and generics will have implications for competition, reimbursement, product lifecycle management, and patents, as we discuss below.

Competitive issues

- ***Price erosion:*** As a consequence of fewer competitors and less mandatory substitution, we expect less price erosion than the typical generic experience. There will be more opportunities for meaningful product differentiation (perhaps biobetters rather than biosimilars) and hence increased non-price competition.

- ***Complementary products and services:*** The complex nature of biologics and the conditions that they treat often require complementary products/services (e.g., diagnostics, physician provided services, etc.). For example, the Centers for Medicare & Medicaid Services (CMS) recently began a Bundled Payments for Care Improvement (BPCI) initiative. Under this program, Medicare reimburses care providers based on an entire episode of care instead of individual services and administered drugs. As bundled payment opportunities spread into the commercial market, one could anticipate further investments in physician services and complementary products by biologics manufacturers seeking to secure a competitive advantage. As a consequence, one might also anticipate additional antitrust scrutiny and challenges.

- ***Exclusivity:*** Unlike the 180-day exclusivity period granted to the first generic on market, there is no current market exclusivity for the first drug to achieve biosimilarity. The first biosimilar to achieve *interchangeability* has a one-year exclusivity period, which is substantially longer than for small-molecule drugs and will certainly affect market dynamics. The FDA has not yet released definitive guidelines regarding the type of information necessary to prove interchangeability, leaving considerable uncertainty over the difficulty of the process.

Reimbursement

- ***Biologic and biosimilar product coding:*** The classification of biologics and biosimilars has significant implications for reimbursement. Innovators want biosimilars to have a separate product/billing code from the originator drug to allow for different reimbursements for the products while biosimilar makers want the same code for all drugs in the same class.

- ***Medicare reimbursement of biosimilars:*** Biosimilar reimbursement is expected to be set at the average sales price (ASP) of the biosimilar drug plus six percent of the amount determined for the reference biologic. The structure of incentives between the reference biologic and the biosimilar will have a large impact on physician and patient uptake.

Product lifecycle management

- ***Product changes and biobetters:*** The development, success, and frequency of new versions of existing biologics have a significant impact on the incentive to develop biosimilars. To the extent that product modifications are relatively common, it creates greater uncertainty for biosimilar manufacturers. Instead, competitors may produce their own biobetters, with competition focused more on product and service attributes than on price.

- ***Licensing agreements:*** Historically, branded manufacturers have reached agreements with generic entrants to produce "authorized generics" for sale in the market. The extent of analogous "authorized biosimilars" may be reduced. Branded biologics will be less inclined to manufacture biosimilar products for potential competitors as long as their proven history and manufacturing processes provide a competitive advantage in the marketplace and due to the regulatory difficulty in proving bioequivalence of independently produced biosimilars.

Patent issues

- ***Patent challenges:*** IP litigation will surround the relevant governing patents protecting a biologic. The FDA has proposed a process that involves an exchange of patent lists between the innovative manufacturer, the biosimilar applicant, and third-party patent holders that is significantly more complicated than the existing process for small-molecule drugs. This suggests a more burdensome process that may deter some biosimilar entry.

- ***"At-risk" launches:*** Biosimilar launches before the conclusion of patent litigation (similar to small-molecule, at-risk generic launches) will face a more burdensome process in identifying the protecting patents.[3] However, the expectation of less price erosion after biosimilar entry reduces the potential damages that an "at-risk" entrant faces while also affecting the potential profitability.

- ***Large molecule patents:*** Biologics are more complicated molecules with the potential for a greater number of patents over the compound and manufacturing process. There will be increasing attention paid to the value of the individual patents in a large molecule. Recent judicial decisions regarding the use of the "Entire Market Value Rule" in determining the appropriate royalty base may be especially relevant in determining damages in such matters.

Conclusion

In this *CRA Insights*, we have highlighted some key issues surrounding biosimilars. Any analysis of the economic impact of biosimilar entry cannot rely solely, or even primarily, on historical precedents of small-molecule generic entry and must account for the novel market environments that are expected in light of biosimilar entry. The lack of historical antecedents underscores the importance of rigorous economic analysis in litigation settings where characterizing alternative market outcomes are critical. These issues will gain increasing attention as biosimilars begin to enter the market over the next decade and we will be following their developments closely.

---

[3] There currently is no Orange Book equivalent for biologics and the proposed FDA pathway for identifying relevant patents is more time consuming and burdensome.

Contact
Peter Rankin
Vice President
Washington, DC
+1-202-662-3935
prankin@crai.com

Andrew Tepperman
Principal
Toronto
+1-416-413-4084
atepperman@crai.com

About CRA and the Life Sciences Practice

CRA is a leading global consulting firm that offers strategy, financial, and economic consulting services to industry, government, and financial clients. Maximizing product value and corporate performance, CRA consultants combine knowledge and experience with state-of-the-art analytical tools and methodologies tailored to client-specific needs. Founded in 1965, CRA has offices throughout the world.

The Life Sciences Practice works with leading biotech, medical device, and pharmaceutical companies; law firms; regulatory agencies; and national and international industry associations. We provide the analytical expertise and industry experience needed to address the industry's toughest issues. We have a reputation for rigorous and innovative analysis, careful attention to detail, and the ability to work effectively as part of a wider team of advisers. To learn more, visit **www.crai.com/lifesciences**.