



Newport Premium

## **Generics companies, responding to tough times, steer towards higher-risk portfolio strategies**

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These are tough times financially and strategically for many generics companies, particularly in the U.S., the world's largest pharmaceutical market. Manufacturers are experiencing falling net prices driven by customer consolidation and increasing competition, coupled with a lack of operational flexibility and a landscape of new product opportunities significantly different from those of the past. Additionally, these factors are creating an environment of greater uncertainty for generic portfolio managers. Given these challenges and resulting uncertainty, many generics manufacturers are responding by pursuing higher-risk portfolio strategies to differentiate themselves and grow their businesses.

### The distribution channel consolidates

One fundamental challenge generics companies are responding to is consolidation of the purchasing groups and drug distribution channels. Today, the market is defined by the strategic alignment of the major retailers with the largest wholesalers. Essentially three or four main buying groups of generic drugs in the U.S. procure some 90% of the prescription volume in the U.S. This is a tremendous amount of pooled buying power, which is putting pressure on the generics companies to cut prices or face losing significant market share.

### Hyper-competitive markets

One key reason for this pricing leverage is that hyper-competitive generic drug markets are developing every day and often at an unpredictable cadence. Just as emerging generics companies are looking for growth by filing more applications in regulated markets, the U.S. FDA has been simultaneously committed to increasing the number of generic approvals in first-time and established product markets. Many of these new generics manufacturers are situated in low-cost-base countries like India and are often vertically integrated as well; thus they have a very competitive pricing structure, adding yet another layer of disruption to the market. This trend – of new approvals and aggressively priced launches – is so widespread that it is causing overall negative growth in the portfolios of established generics manufacturers.

### Changing nature of new product opportunities

Another important factor roiling generics companies is the focus and productivity of innovative pharmaceutical R&D. The future pipeline opportunities for generics manufacturers increasingly come from lower volume (higher-priced) specialty products, including large molecule biologic medicines. This is associated with a significant change in capacity requirements, affecting particularly those larger established generics companies. Now they need different capabilities internally or through partnerships to bring a new generic drug to market. Secondly, true clinical breakthroughs are quickly changing

the standards of care in many therapy areas, often displacing or entirely replacing established branded drug or whole classes of drugs. Combined, the dynamics of innovative R&D are rapidly and continuously altering the landscape of available new product opportunities for generics and the capabilities needed to develop and market these new products.

### Products can disappear virtually overnight

The hepatitis C space is an excellent example of how innovation is influencing generic portfolio management. Until 2014, hep C was mainly treated by one of two antiviral drugs – one from Merck and one from Vertex – Victrelis (boceprevir) and Incivek (telaprevir). Then Gilead launched Sovaldi and Harvoni, and within months the incumbents, Merck and Vertex, realized that demand for their drugs had disappeared, virtually overnight, and they consequently discontinued them. For generics companies, in North America at least, this also meant the loss of two product markets and the nullification of several years of investment into their copycat versions.

This is just one example of how it is increasingly difficult to predict which branded therapies will still be on the market, let alone generating growing revenues, by the time a generic drug is approaching first approval. This also underscores the present challenges for generics manufacturers in identifying and subsequently launching new products that will generate sustainable sales, particularly in the face of increasing numbers of aggressive competitors.

### Generics companies seek differentiation

Many generics manufacturers are reacting to these changing market dynamics with a strategy to differentiate themselves from competitors as a way to create new value and sustain growth. Of course, differentiation can be especially difficult in a generics market where, by definition, the products of one company are the same as those of the next company. Thus, standing apart from the competition requires speed in execution and an increasing tolerance for uncertainty and risk. In practice, this means diversifying product lines and revenue sources.

### New channels

The first diversification strategy is to sell into new channels, thus reaching new customers. For example, a manufacturer might expand from a focus on retail pharmacies to institutional or government channel customers. Lately, the hospital channel in regulated markets especially has been a strategic target, particularly for Indian manufacturers, like Cipla and Glenmark, seeking to move beyond their roots in traditional oral solids. Again, maintaining growth rates under current market

conditions and limiting exposure to hyper-competitive products practically requires such expansion.

Superficially, this approach might seem relatively easy, simply a matter of leveraging an existing set of products. However, serving new channels with new customer types can add complexity to a portfolio and to business operations. This is because successfully serving a market like hospitals or clinics can require adding new products, such as sterile injectables, that require new R&D or manufacturing technologies, not to mention different sales and marketing capabilities. Notably, some hospital injectable products have experienced chronic shortages highlighting the difficulties with reliably and consistently manufacturing these formulations to high quality standards. There can be other obstacles. New customers might require new packaging configurations, like blister packs instead of bottles. Manufacturing and marketing in new channels can also mean complying with different regulations like local manufacturing mandates in the case of government purchasing programs. All these factors increase complexity and thus risk – risk of delays, of compliance, of loss of focus – and expose the business to new unknown situations.

Increasingly, however, growth-oriented firms are taking on these risks to reach new customers.

#### New launch strategies

For the next approach to diversification – various new product launch strategies – there are very clear tradeoffs in risks and benefits. Pursuing a Paragraph IV (PIV) patent challenge in the U.S., for example, can offer six months of market exclusivity and the opportunity to capture significant market value and volume share. But, this opportunity necessitates accepting additional complexity, particularly in the formulating of a new generic product where the chosen formulation must not only meet bioequivalence and stability standards but also be aligned to a corresponding non-infringement and/or invalidity legal strategy. Moreover, there are additional, often substantial, costs associated with patent litigation, along with a higher risk of delays for approval and launch. The first wave patent challenger therefore has to tolerate greater uncertainty in outcomes and engage legal resources beyond standard freedom-to-operate determinations in order to maximize PIV exclusivity opportunities.

A less risky and somewhat less costly option can be to challenge patents but wait for the litigation outcome of another (presumably first wave) challenger. In this scenario, a generics sponsor pursues a Paragraph IV challenge, either as a first wave firm eligible for exclusivity or as a subsequent 180-day entrant, and then petitions the court to stay the litigation pending the outcome of another generic sponsor's patent litigation with the brand company. More specifically, the firm can bind its litigation outcome to that of the other firm, assuming that the facts of the cases, particularly the proposed generic formulations and thus patents under challenge, are analogous.

An alternative strategy is to forego a patent challenge altogether yet plan for the relevant constraining patent(s) to be defeated by another generics company and thus be ready to launch after the successful PIV challenger's exclusivity period. This is distinct from the least risky, and least profitable, option of waiting for the last patent to expire naturally. Of course, the risk with anticipating the defeat of patent, whether a company is in the first or subsequent wave of entrants, is the potential sunk cost in product inventory should the constraining patents remain in effect and prevent a generic launch.

Data compiled by Clarivate Analytics clearly shows that more and more generics sponsors are pursuing Paragraph IV strategies in the U.S. Again, this underscores how manufacturers are accepting more complexity and risk as they look to capture more sustainable value and growth. Another implication of this trend is that it means product markets are becoming much more competitive more rapidly than even a few years ago, which in turn further fuels the need to quickly refresh the pipeline to sustain growth. (See Figures 1 and 2.)

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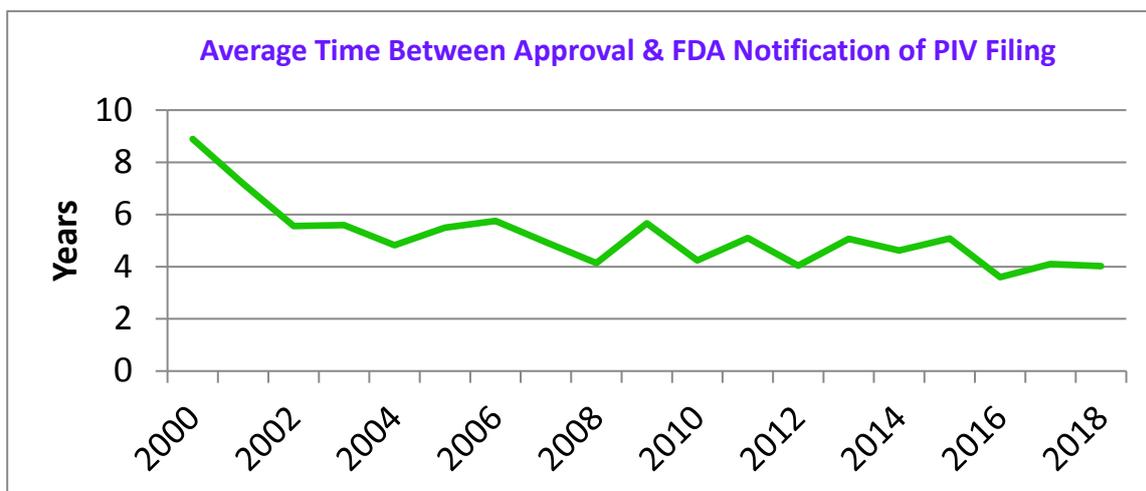


Figure 1: Source : Newport Premium, Clarivate Analytics

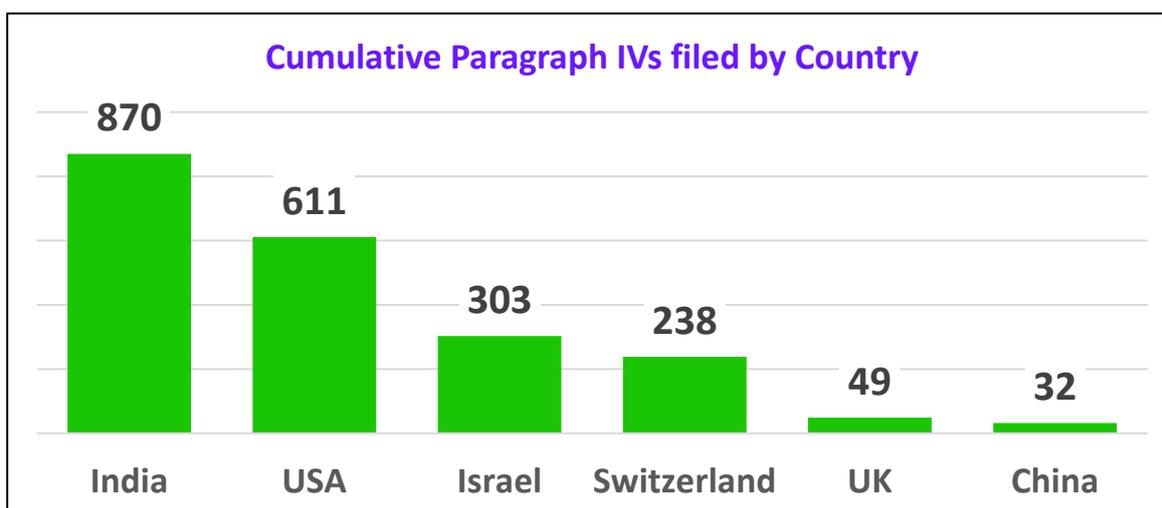


Figure 2: The large number of PIV patent challenges from Indian companies indicates a rapid change in portfolio strategy to accept more risk in order to capture more value. Source: Newport Premium, Clarivate Analytics

**Moving up the value chain**

The third way that companies are going about protecting their margins or growing their businesses is to move up the product value chain. (See Table 1.) The generics market for many years was easily defined by “little white pills” – high volume, low complexity oral solids. Because of the hyper-competitive nature of these low-complexity markets, many companies are adding to their pipelines and portfolios more complex types of formulations and dose delivery technologies; presumably, the higher (technical and regulatory) barriers to entry mean more sustainable profits for a longer time.

Higher-complexity, higher barrier-to-entry products have no specific definition though they can be generalized to a few broad categories, including:

- controlled release or long acting formulations (e.g., emulsions or microspheres)
- sterile injectables or otic and ophthalmic administrations
- drug-device combinations (e.g., auto-injectors, respiratory devices and transdermal patches and film)
- proteins, peptides and other structures that straddle the small molecule chemical and large molecule biological space from a production and regulatory perspective.

Beyond 'Little White Pills'
Many generics companies are adding more complex formulations and dose delivery technologies to their portfolios, including:
<ul style="list-style-type: none"> <li>controlled release or long acting formulations (e.g., emulsions or microspheres)</li> </ul>
<ul style="list-style-type: none"> <li>sterile injectables or otic and ophthalmic administrations</li> </ul>
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**Table 1: Source: Newport Premium, Clarivate Analytics**

Generics firms most hungry for growth are interested in any area where differentiated or specialized formulation and manufacturing capabilities can manifest enduring barriers to entry and thus sustainable value creation. So far, however, these manufacturers have had only limited success with the most complex (and thus most valuable) products. There are some stand-out examples of so-called “complex” generics coming to market and remaining in relatively low competition environments. One would be Copaxone, or glatiramer acetate. The 20 mg and 40 mg versions of Copaxone have now both gone generic. Glatiramer is a very complex molecule, difficult to characterize, and the drug is paired with an auto-injector device. Moreover, the product requires special handling procedures and distribution chains. Another example is Lovaza omega-3 gel caps. It’s a highly refined prescription fish oil product that was called out by the FDA as a “complex” generic – a product that is notably difficult to formulate and manufacture consistently within agency bioequivalence requirements.

Conversely, there have also been stumbling blocks on the path toward marketing other high-barrier-to-entry generics. Some brand products still have not seen generic competition even though their constraining patents have expired. One prominent, long-standing example was the EpiPen. There had been no FDA-approved substitutable alternative from another company on the market to offer true price competition. Companies such as Teva and Sandoz had long sought to bring a substitutable product to market. Despite waiting for the approval of its generic EpiPen for several years, Teva suggested that the launch of its product would be taking place during the “coming months,” rather than immediately after its approval by the FDA on August 16, 2018.

Another example is the Advair Diskus inhaler. The relevant drug patents expired a few years ago, but so far there has been no generic approved as a substitute for that product. Mylan, Sandoz and Hikma have each received Complete Response Letters on their generic applications. Again, FDA approval timing is uncertain for these proposed generic products. This just underscores the challenges with drug-device combinations and high-complexity formulations even for the most sophisticated generics companies. These types of “complex” products might be high reward, but they are certainly high risk from a launch success and ROI standpoint.

**Conclusion: Manage risk with market insight**

We have seen in this paper that many generics companies, especially in the U.S., have begun to embrace profound changes in their portfolios in response to market challenges. Generics companies seeking competitive differentiation by diversifying their product portfolios necessarily must accept more complexity and risk as they extend beyond their traditional capabilities. These risks, particularly those involving uncertainty, can be mitigated with a well-informed view of the future market environment. Players that make the right preparations – so that they understand the capabilities and pipelines of competitors, develop insight into the chemistry and technologies of new product opportunities (both on the market and in clinical trials), and forge a clear view of the IP landscape surrounding brand products – put themselves in the best position to navigate today’s rough market shoals and succeed.

## Who we are

Clarivate Analytics accelerates the pace of innovation by providing trusted insights and analytics to customers around the world, enabling them to discover, protect and commercialize new ideas faster.

We own and operate a collection of leading subscription-based services focused on scientific and academic research, patent analytics and regulatory standards, pharmaceutical and biotech intelligence, trademark protection, domain brand protection and intellectual property management.

Clarivate Analytics is now an independent company with over 4,000 employees, operating in more than 100 countries and owns well-known brands that include Web of Science, Cortellis, Derwent, CompuMark, MarkMonitor and Techstreet, among others.

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