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**Generics boom set to drive
transformation of the sector**

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Executive Summary

The generic drug market continues to grow. Despite consolidation, competition between manufacturers is fierce. However, for those with capacity to differentiate their products there is significant opportunity.

Some try to find an edge by reformulating products so they are more convenient and otherwise beneficial for patients. Others choose to compete by using modified regulatory strategies. In the US, the 505(b)(2) pathway is becoming increasingly popular.

In Europe, the likely introduction of the Supplementary Protection Certificate (SPC) manufacturing waiver will further expand the market for generic drug firms and their suppliers. Allowing generics firms to manufacture for export and stockpiling while the SPC is in place will accelerate market entry on patent expiry.

European industry groups argue that generic manufacturers need to be incentivised to make legacy drugs. For manufacturers able to navigate the complex regulatory landscape and secure supply agreements there are significant opportunities.

Demand for generic medicines continues to grow, driven by mounting patent losses, efforts to cut healthcare spending and the increased incidence of age and life-style related diseases.

For manufacturers, particularly those able to modify finished dosage forms (FDF), there is a real opportunity says Dr Jonathan J. Darrow from Harvard Medical School, who told us “Overall, the generics market is very robust.

“Currently, approximately 90% of all prescriptions in the US are filled with generic drugs, a fraction that has been rising steadily for over 40 years. As patent expirations continue, the number of drugs eligible for generic copying will continue to increase.”

A similar pattern is seen in Europe according to Adrian Van den Hoven, Director General of generics industry group Medicines for Europe.

“The majority of patients with chronic diseases are using generic medicines daily as part of their treatment course. In addition, generic medicines are big contributors to the sustainability of healthcare systems in Europe. They represent 67% of prescription medicines dispensed in Europe

while only accounting for around 4% of the healthcare budget.”

Competition and consolidation

Market growth has driven a wave of consolidation with suppliers seeking to expand capacity and reach by buying rivals. ^[1]

For example, since 2006 Teva Pharmaceutical Industries as acquired IVAX, Nycomed and Actavis, Alergan's generics business, in a series of billion dollar deals. In the same period Endo bought Par and Pfizer snapped up Hospira. ^[2]

But despite the M&A frenzy, the dynamic nature of the market and its opportunities mean there is still significant competition among manufacturers.

Van den Hoven said, “The sector is not very consolidated in terms of the number of manufacturers and their market share. There is no dominant player in the European generic market. However, there is consolidation occurring in the manufacturing of older, declining products. This is leading to a smaller number of suppliers for essential older molecules like many anti-infectives.

He told us consolidation is driven by pricing and procurement policies that result in the selection of single suppliers.

“This obviously creates supply risks for Europe and there is a need to reconsider these policies to incentivise more manufacturers to participate in the market.”

“The impact of expensive new regulatory requirements like the falsified medicines directive, which cost the whole pharmaceutical industry over €1 billion, or like Brexit which required the industry to transfer and duplicate a huge number of dossiers and activities to the EU. It is clear that these additional costs will weigh most heavily on products whose sustainability is already marginal on the market.”

Dosage form diversification

Generics companies try to sustain and grow market share using a range of approaches informed by both their own cost bases and the dynamics of the markets they serve.

In the US, for example, competition for a share of the country's expanding generics market has prompted many manufacturers to rethink regulatory strategies says Dr Darrow.

“Competition in the generic industry can be intense, reducing profitability. The volume of ANDAs approved each year has increased substantially from a decade ago. Some generic firms have sought to increase profitability by diversifying into modified products using the 505(b)(2) pathway.”

Traditionally, generics firms have sought US market entry via an abbreviated new drug application (ANDA). The process requires them to prove their product performs like the reference listed drug (RLD), but permits them to use existing preclinical and clinical data. An ANDA provides 180-days of market exclusivity during which rivals cannot sell versions of the same product.

The 505(b)(2) pathway, in contrast, is not specifically intended for generics. Instead, it is designed to encourage development of modified versions of

approved drugs that provide additional benefits. Sponsors must show the product is safe and effective, but, like ANDA applicants they can use data generated by other parties. ^[3]

However, the major difference between an ANDA and approval via the 505(b)(2) pathway is that the latter affords three to five years of exclusivity. ^[4] In effect, generics firms using it will be competition-free for longer.

Finished dosage forms

Increased interest in the 505(b)(2) pathway has been accompanied by a diversification of finished dosage forms and the technologies used to produce them.

Varying a formulation so it changes how a drug's active pharmaceutical ingredient is released is precisely the type of modification the 505(b)(2) pathway is designed to encourage.

Likewise, producing a finished dosage form that requires fewer pills than rival products is another strategy generics firms are using to try and differentiate themselves from competitors.



Healthcare spending

Efforts to reduce public healthcare spending by governments around the world are also impacting the generic drug industry.^[5]

The rationale is that encouraging the use of non-branded pharmaceuticals in place of branded products will result in significant saving.^[6]

Dr Darrow told us “For a given product, the discount of the generic product's price relative to the brand product's price is directly related to the number of generic firms competing in the market.

“Products with a single generic manufacturer show a 13% discount relative to the branded product, while those with three manufacturers show a 40% discount, on average” he added.

Whether the savings have been large enough remains a point of debate. Some accuse both innovators and generic drug manufacturers of colluding to keep prices artificially high^[7], while others suggest prices have eroded too far.^[8, 9]

More recently, in the US, there have been suggestions the Government should begin

manufacturing generic drugs in order to ensure they are available at the right price.^[10]

Regulatory changes

In addition to encouraging use of generic drugs, the US Government is also trying to support development of non-branded products.

In January, Food and Drug Administration Commissioner Scott Gottlieb outlined the agency's efforts to advance the development of complex generics to improve patient access to medicines.^[11]

Complex generics, as the name suggests, are drugs that as a result of their formulation, delivery systems or their active ingredients, are harder to “genericize” under traditional manufacturing approaches.

Gottlieb's concern is that “there are a number of complex drugs that are no longer protected by patents or exclusivities that would forestall generic approval, yet they continue to face no generic competition owing to the difficulty of developing generics.”

A lack of competition will mean that prices remain



at their current level. To address this the FDA will issue specific guidance documents for complex generics outlining the scientific challenges involved.

It also plans to make “recommendations on establishing active ingredient sameness and help advance the development of new analytical tools able to reduce development time and cost and inform regulatory decisions.”

SPC waiver

Regulatory changes on the other side of the Atlantic are also impacting the generics sector. In February, the Council of the European Union reached an agreement on the text of a manufacturing waiver for Supplementary Protection Certificates (SPC).^[12]

In the EU, an SPC granted to branded drug firms will extend product patents to compensate for delays during the approval process.

At present generic manufacturers are not permitted to manufacture or sell non-branded versions of the innovator drug in the EU or elsewhere while the SPC is in force.

If introduced, the waiver will remove this restriction,

enabling EU generics firms to manufacture for export to markets where patents have already expired. It will also allow them to manufacture and stockpile products ahead of patent expiry in the EU, thereby accelerating market entry.

The plan is supported by Medicines for Europe, the group representing the generics industry in the European Union.^[13]

Van den Hoven told us “The European Parliament will adopt an important piece of legislation – the SPC manufacturing waiver – that will increase manufacturing opportunities for Europe massively. We are going to leverage this legislative change to increase our manufacturing footprint in Europe.

But European legislators and policy makers need to do more according to Van den Hoven, who cautioned that incentivising manufacturers is key.

“It is important for the EU to consider the importance of manufacturing supply in its pharmaceutical policies for essential medicines. Most pricing and procurement policies are based on absolute lowest price with no regard for security of supply. This is hardly an incentive for manufacturers to invest in new plants for these essential medicines. This is becoming a major risk for Europe and it needs to be addressed thoughtfully.”

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