

# Assessing the impact of proposals for a Supplementary Protection Certificate (SPC) Manufacturing Exemption in the EU

**Ramya Logendra**, Engagement Manager, Supplier and Association Relations

**Per Troein**, Vice President, Strategic Partners



# Assessing the impact of proposals for a Supplementary Protection Certificate (SPC) Manufacturing Exemption in the EU

---

Within the European Economic Area (EEA), a Supplementary Protection Certificate (SPC) confers the same rights as a patent, meaning that manufacturing or marketing of a generic pharmaceutical product cannot begin in an EEA country until the relevant SPC has expired. SPCs were introduced in the European Union (EU) to maintain and stimulate pharmaceutical research in the EU, compensating innovators for insufficient effective period of patent protection due to long and costly development timelines.

The European Commission (EC) is currently working on an evaluation of the SPC Regulation. As part of that exercise, the EC is considering proposals to allow manufacturing in Europe during the SPC protection term, notably for export purposes. QuintilesIMS has looked at the historical evidence to assess what the potential impact of this could be.

Proponents of an “SPC Manufacturing Exemption” argue that if the European based industry were able to begin manufacturing (not selling) products in European countries where an SPC is still in place, these products could be exported to markets outside Europe where IP protection has expired or has never existed, thereby bringing an economic benefit to Europe.

In this report we outline three evidence-based arguments which highlight some of the potential impacts of such a policy for Europe.

The study is based on independent research and analysis undertaken by QuintilesIMS that was funded by EFPIA.

---

## A. There are potential losses to European originator companies and decreased export value for the EU if an SPC Manufacturing Exemption is introduced

### **Summary**

- It is argued that if the European based generic industry were able to begin manufacturing (not selling) products in European countries where SPC's are still in place, these products could be exported to markets outside Europe where IP protection has expired or has never existed, bringing a potential economic benefit to Europe. This would also enable companies to stockpile generics and launch from day 1 in Europe.
- Analysis shows that today, in some instances originator products are able to retain sales in countries outside of Europe after patent expiry, while the generic market is dominated by domestically produced products. Generics manufactured in Europe are more likely to compete for market share with the original brands (capitalizing on the notion of European brand value), rather than with cheaper, domestically manufactured generic products. These factors indicate that an SPC Manufacturing Exemption could result in substituting the export value of originator products for lower value generics, potentially decreasing the export value for Europe.
- Furthermore, countries outside the EU often provide incentives for domestic manufacturing and the cost of production, distribution etc. of generics manufactured in these countries is often less than generics manufactured in Europe. Therefore large, international generic manufacturers may opt to produce domestically within the non-European market rather than in Europe to be able to compete with domestic generic manufacturers. Smaller companies may not have the option to produce domestically due to scale.

# 1. Do European-based generic manufacturers have success in non-European countries?

## Methodology

The aim of this analysis is to investigate the evolution of value sales market share between domestic, European and other generic companies for a selection of molecules. Molecules were selected based on a number of criteria. Firstly, the top 30 generic molecules were ranked by value of sales in the 8 non-European countries combined. Next, molecules with generic entry after 2005 in at least 2 of the 8 countries were selected. This list was further narrowed down by selecting molecules where SPC expiry in Europe was earlier, or the same year as generic entry in at least 2 of the non-European countries. This was to ensure the analysis covered a selection of generic molecules which could be manufactured (because of SPC expiry) by European, Domestic or Other companies in the time period assessed. Similar to the 2014 study conducted for Medicines for Europe by the University of Coimbra, only small molecules were assessed in the analysis.

**Country scope: non-European countries – Australia, Brazil, China, Canada, Japan, USA, Russia, Turkey**

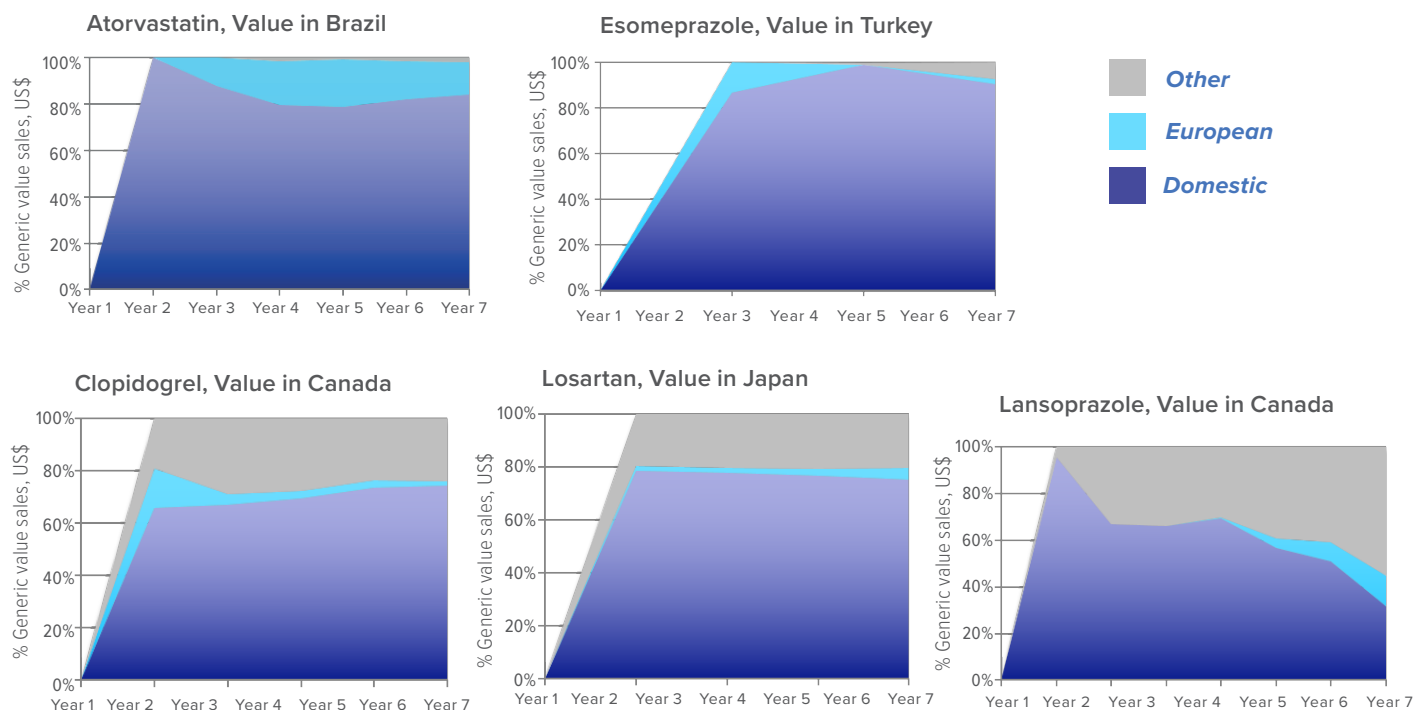
**Molecule scope: Esomeprazole, Atorvastatin, Clopidogrel, Lansoprazole, Losartan**

Country groupings:

- Corporation nationality used to determine groupings
- Domestic - e.g. in Brazil, generics sold by a Brazilian company
- European - company with European corporation nationality
- Other - International corporations (e.g. Canada, India, Israel, Japan, South Africa, Turkey, US)

## Analysis

Case Study Examples (Source: QuintilesIMS, MIDAS MAT Dec 2015, Brazil retail only)



- In most non-European countries, local companies win the majority of generic sales, both initially and in the long term. In these countries, European corporations, such as Sanofi (Medley) and Novartis (Sandoz), win some of the generic business but tend to also manufacture domestically. This is because some of the non-European countries provide incentives (often as a requirement) for domestic manufacturers, and additionally, the cost of production and distribution is often cheaper.

## Conclusions

- There are many environmental factors impacting a potential export strategy to the target countries, such as trade barriers, price levels, ability to manage local commercial relations based on local environment, pharmacy and patient attitudes and increasingly, incentives for domestic producers.
- Domestic companies in countries like Brazil, Russia, and Turkey often win the majority of business both initially and in the longer term. Other (International) companies, which manage to compete, normally establish local manufacturing.
- Ultimately, these dynamics leave very little export potential for European generic manufacturers with or without an SPC Manufacturing Exemption.

2. If European generic companies are successful in non-European countries, will this impact export of innovators?

## Methodology

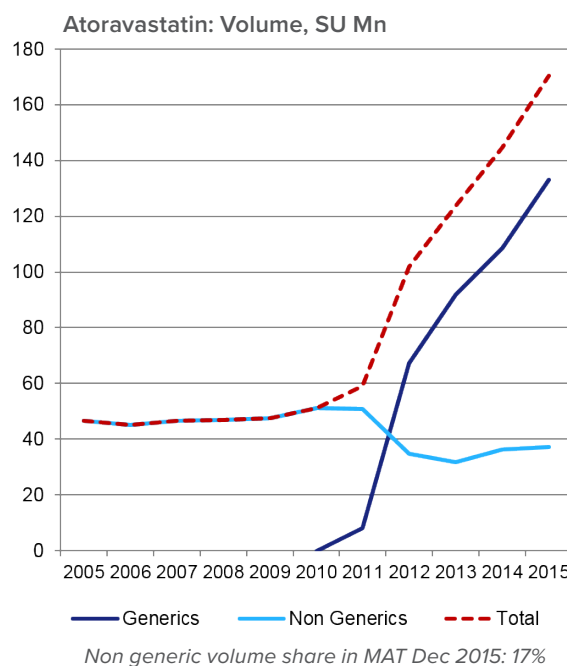
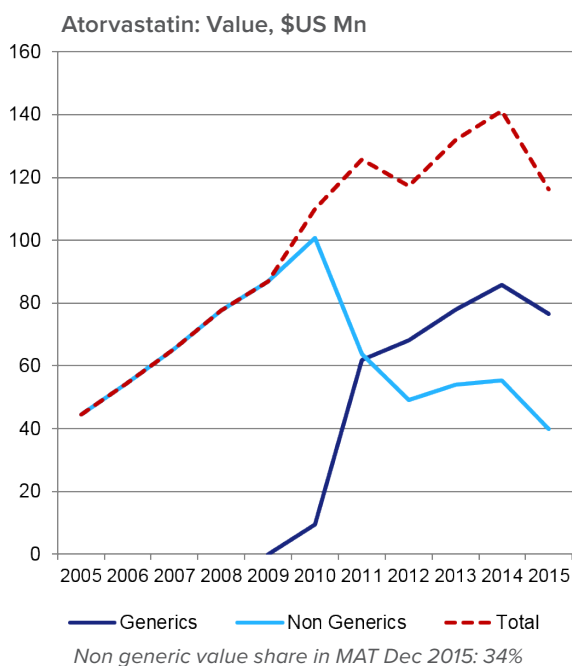
This analysis investigates the evolution of value sales and volume for a selection of molecules. Molecules were selected based on a number of criteria. Firstly, global non-biologic molecules were ranked by value sales. Next, molecules which were launched before 2005 were selected, to ensure there was a long enough time period to assess the impact of generic entry. Finally molecules which had generic versions launched in the last 10 years in at least 6 out of 8 of the non-European countries were selected.

Country scope: Australia, Brazil, China, Canada, Japan, USA, Russia, Turkey

Molecule scope: Atorvastatin, Esomeprazole, Rosuvastatin

## Analysis

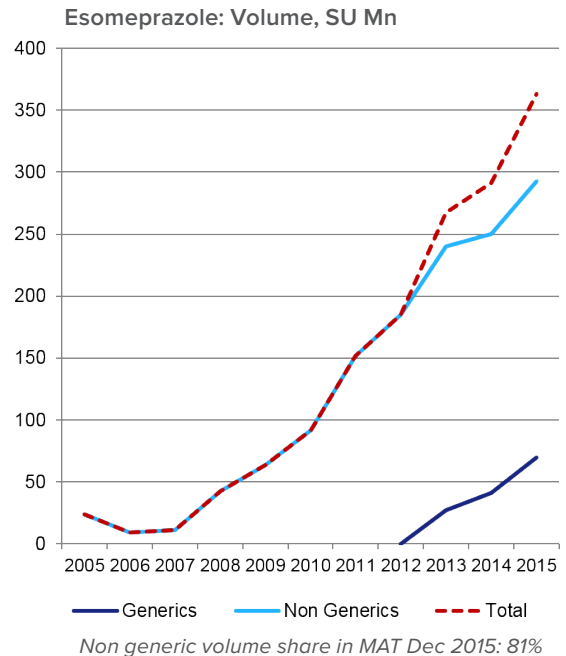
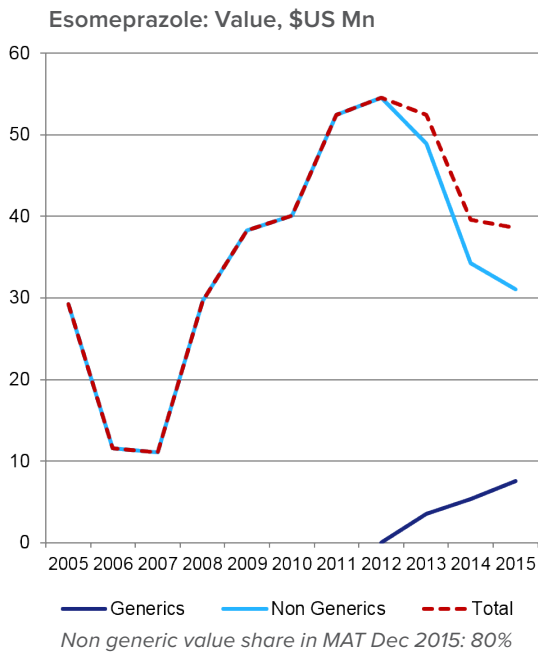
Case study 1: Atorvastatin in Brazil (Source: QuintilesIMS, MIDAS MAT Dec 2015, Brazil retail only)



- The case study of Atorvastatin in Brazil shows that, although the value fell, the volume of the original brand stayed relatively flat. The generics with much lower prices expanded the market. 84% of the 2015 Atorvastatin generics sales in this example were sold locally by Brazilian companies (Sales US\$, QuintilesIMS, MIDAS MAT Dec 2015). The finished generic products are also usually produced locally.

- The original brand Lipitor API is manufactured in Ireland, and the finished product is produced in Germany.
- The Rosuvastatin case study in Brazil (not shown in the document) looks very similar to Atorvastatin, with the volume of the original brand remaining relatively flat post generic entry.

Case study 2: Esomeprazole in Turkey (Source: QuintilesIMS, MIDAS MAT Dec 2015)



- The case study of Esomeprazole in Turkey shows that, although the value fell, the volume of the original brand continued to rise following the entry of generics.
- 90% of the 2015 Atorvastatin generics sales in this example were sold locally by Turkish companies (Sales US\$, QuintilesIMS, MIDAS MAT Dec 2015).

## Conclusions

- The analysis demonstrates that original brands retain some brand equity in a number of non-European countries several years after generic entry.
- Most of the generics shown in these case studies are produced locally. In some markets, generics manufactured in Europe are more likely to compete for market share with the original brands (capitalising on the notion of European brand value), than with low-priced domestically manufactured generic products, with which it would be much harder to compete.
- If both the originator (often manufactured in Europe) and European generics are competing for market share outside the EU, a potential consequence could be fewer original brand exports from Europe to non-European countries, as these are replaced with European generics. This could therefore cause employment losses to innovators in Europe, and also a reduction in trade value level caused by the shift to exporting cheaper generics instead of original brands.

## B. The arguable benefits to European generic manufacturers of an SPC manufacturing exemption are very limited in some cases, as the European SPC / patent expiry is often either earlier, or not significantly later than SPC expiry in other markets

### Summary

An argument has been made that if the European based generic industry was able to begin manufacturing (not selling) products in European countries where SPC's are still in place, these products could be exported to markets outside Europe where IP protection has expired or has never existed, bringing an economic benefit to Europe.

For this proposal to have an impact, it would require the SPC expiry date within European countries to be significantly later than in other markets.

There is a large diversity in SPC / patent expiry dates between non-European countries and European countries. In addition, SPC expiry dates in Europe are not always significantly later than in the export markets – and, in many cases, are actually earlier than these non-European markets.

- SPC patent expiry dates in Europe are often before target export markets, therefore leaving limited additional benefit from an SPC Manufacturing Exemption as it would not be possible to sell generic products in the target export markets.
- In cases where the first European SPC expiry date is later than the first non-European SPC or patent expiry date, there could be some export opportunity should an SPC Manufacturing Exemption be granted. However, the window of opportunity is limited when it comes to time and number of countries.

### Methodology

The product selection was made using the top 25 original branded products based on ranking by size of sales MAT Dec 2015 US\$, limited by traditional products that are no longer protected in some countries. The Estimated Protection Expiry date (referred to as the “SPC / patent expiry date” in this document) used for the analysis is a prediction of when QuintilesIMS believes individual products will become susceptible to generic competition. Factors used to derive the estimated protection expiry data include the SPC expiry date, patent information, journal and information around litigation.

*Countries in scope: Europe Group (France, Germany, Italy, Japan, Norway, Poland, Slovenia, Spain, Sweden & UK) and Non-Europe Group (Brazil, China, Russia, Turkey & USA).*

### Analysis

Case study examples of 3 selected molecules & recorded SPC expiry dates (Source: QuintilesIMS MIDAS MAT Dec 2015 )

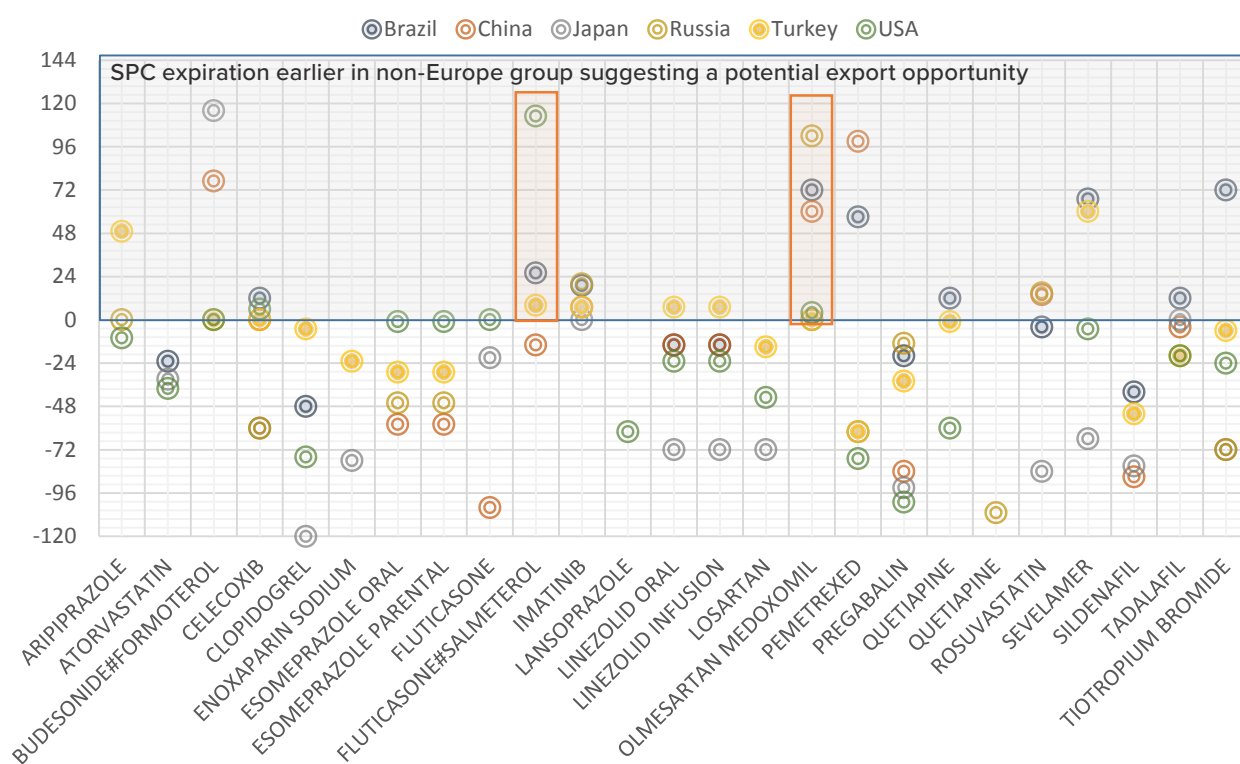
|              |          |        |        |        |         |        |         |         |        |        |        |        |        |          |          |        |
|--------------|----------|--------|--------|--------|---------|--------|---------|---------|--------|--------|--------|--------|--------|----------|----------|--------|
|              | Country  | Turkey | Norway | Poland | Russia  | France | Germany | Japan   | Spain  | Sweden | UK     | Italy  | USA    | Slovenia | China    | Brazil |
| ARIPIRAZOLE  | SPC_date | May-10 | Jun-14 | Jun-14 | Jun-14  | Oct-14 | Oct-14  | Oct-14  | Oct-14 | Oct-14 | Oct-14 | Apr-15 | Apr-15 | /        | /        | /      |
|              | Country  | Norway | Spain  | Brazil | Japan   | USA    | UK      | Germany | Italy  | Sweden | France | Turkey | Russia | Poland   | Slovenia | China  |
| ATORVASTATIN | SPC_date | Sep-08 | Jun-09 | Aug-10 | Jun-11  | Nov-11 | May-12  | May-12  | May-12 | May-12 | May-12 | /      | /      | /        | /        | /      |
|              | Country  | Poland | Russia | Brazil | Germany | UK     | USA     | France  | Norway | Spain  | Sweden | Italy  | Japan  | Slovenia | China    | Turkey |
| CLOPIDOGREL  | SPC_date | Feb-03 | Jul-03 | Feb-07 | Jul-08  | May-09 | Jun-09  | Sep-09  | Oct-09 | Oct-09 | Oct-09 | Mar-10 | Feb-13 | /        | /        | /      |

Notes:

- SPC expiry dates are ranked from earliest expiry to most recent
- “/” shown in countries where data is not available (because the product was not sold in that country, or because its SPC / patent expiry date was not captured)
- Countries highlighted in blue are the potential export markets, those in white are European markets

The graph below shows the potential number of months between the first SPC / patent expiry date in the non-Europe group compared with Europe Group. The negative number of months represent the countries where SPC expiry dates for the molecules are available in the Europe Group before the non-Europe Group.

Chart showing number of months between first SPC expiry in non-Europe group compared with Europe group (Source: QuintilesIMS MIDAS MAT Dec 2015; Circles represent individual countries)



- There is a large diversity in SPC expiry dates between non-European countries and European countries in the sample.
- The chart above highlights that the highest concentration of circles are within the negative scale, which represents an earlier first SPC expiry in Europe compared to non-Europe countries.
- The scale in positive shows some potential opportunity as 14/25 molecules (at pack level) have a first SPC expiry in a non-European country before Europe. However in the case of each molecule (at pack level), it is clear that the potential is only isolated to selected countries.
- Of the 14 examples, there is only a significant opportunity across 2/25 molecules where there are 3 or more countries with first SPC expiry in a non-European country before Europe (shown in red boxes in the chart above).

## Conclusions

The timing of SPC expiry dates in Europe is not always significantly later than in the target markets – and, in several cases, is actually earlier than in non-European markets.

Since European SPC / patent expiry dates are often before target export markets, this leaves limited additional opportunity or benefit from an SPC Manufacturing Exemption, as it would not be possible to sell generic products in the target export markets.

In cases where the first European SPC expiry date is later than first non-European SPC expiry date, there could be some export opportunity should an SPC Manufacturing Exemption be implemented, however, the window of opportunity is limited.

---

## C. The effect of the early launch production of generics on employment in Europe would likely be limited due to the present ability of European corporations to win most of the initial generic business in Europe

### Summary

- As noted above, the opportunities for European companies in relation to export markets are limited in light of the small or non-existent window that would be created by an SPC Manufacturing Exemption.
- Within the European generics markets, the most attractive business is the market in the first 6 months post-loss of exclusivity. This is because the regulated generic prices are often higher in the initial period post-loss of exclusivity, and also because there is often less competition on the market. These factors mean that the discounts which generic manufacturers have to give to win the generic business are lower in this initial period.
- Findings show that despite the SPC Regulation, it is often European generic companies that are first to market in the EU, winning this attractive, initial business.
- Opportunities for European generics to use an SPC Manufacturing Exemption to locally manufacture API are also extremely limited. API are currently sourced the most cost-efficient way, with India and China being the primary sources of API manufacturing. Reliability, experience and price are the main determining factors impacting the choice of API providers. European API manufacturers could potentially only compete in low volume, niche product markets.

1. Are the winners of the most attractive initial generic business in Europe often based in Europe?

### Methodology

The Generic Market Share, by corporation nationality, in the first 18 months of generic entry across European countries is reported through the analysis. Molecules were selected by ranking European generic molecules by MAT Dec 2015 value sales and then selecting the top 2 molecules with a generic launch after 2005.

*Country scope: Germany, France, Italy, Spain*

*Molecule scope: Pantoprazole, Atorvastatin*

Country groupings:

- Corporation Nationality used to determine groupings
- Top 5 global generic: (MIDAS Dec 2015 Sales, \$US): Teva, Novartis, Mylan, Allergan, Pfizer
- European: company with European corporation nationality
- Other: International corporations (e.g. Japan, India, US, Canada, Israel and Brazil)



## Analysis

Case study example: Pantoprazole (Value, \$) (Source: QuintilesIMS MIDAS MAT Dec 2015; \*as determined by first 6 quarters of sales in Europe)

| Country | Generic Market Share in first 18 months of generic entry* |                              |               |
|---------|---|------------------------------|---------------|
|         | European Company  | Top 5 Global Generic Company | Other Company |
| FRANCE  | 47%   | 44%                          | 9%            |
| GERMANY | 15%   | 34%                          | 51%           |
| ITALY   | 47%   | 48%                          | 5%            |
| SPAIN   | 78%   | 21%                          | 0%            |
|         |   |                              |               |
| Average | 47%   | 37%                          | 16%           |

- In the examples analysed, European companies, Top 5 global generic and other companies all took share of the initial generic market in Europe. In the case of Pantoprazole, European companies took 47% market share, on average, across the European countries analysed.
- Whilst the API production location cannot be determined, it is clear that for the examples analysed, most of the top 5 Global generic companies, will actually be manufacturing generics from a European manufacturing base already. Therefore, in reality, the proportion of generic market share manufactured in Europe will be higher than stated here.
- In most of the countries, the European and top 5 global generic companies take majority generic share.

## Conclusions

- The winners of the most attractive initial generic business in Europe can often be European corporations. In addition, generic business is already often manufactured in Europe (either by European corporations or top 5 global generic companies). Therefore the employment opportunities around generic manufacturing in Europe may not change significantly if an SPC Manufacturing Exemption is introduced.
- As documented in the first section of this report, introducing an SPC Manufacturing Exemption could also result in an increased uptake of European generics in countries outside the EU to the detriment of originators. Potential consequences are that there are fewer original brand exports from Europe to non-European countries, as these are replaced with European generics. Therefore this could also cause employment losses to innovators in Europe.

## 2. Is API currently sourced the most cost-efficient way, outside of Europe?

### Methodology

We interviewed 5 different companies: one top 5 Global Company, one mixed brand and generics company, and three regional/local European companies. The people interviewed held various different positions in the organisations but all have a good insight of the API sourcing strategy.

The key starting questions were: how do you decide how to source API? Is it produced by yourself, or is it bought from a producer from a lower cost manufacturer?

## Insights

There was some diversity in the responses; a typical statement was: “it is not just about price, it is as much about reliability of supply and quality”. Another common statement was “certain molecules will very quickly get a lot of alternative suppliers for the API. Prices will become very low. It is almost more interesting to look at more niche, smaller volume business opportunities, which generate less competition”.

It was clear that companies have different experiences from using API vendors: “We tend to work with an Indian vendor that we have had very good success with”, “we normally source more complex products from China based on our good experience. True commodities we source from India”.

From interviews we learnt:

- Each company tends to use their own strategy based on their experience; in the end reliability is likely to overshadow the very lowest price.
- India is the main source for very low cost/high volume API.
- China accounts for 30 - 40% of all API but is focused on more complex and specialty API.
- Originators often place the API manufacturing with a partner in a low cost country very early to get cost advantages.
- “Blockbusters” typically get several Indian (or Chinese) API manufacturers offering the API. Competition drives prices down.
- “Specialty products” will have less competition as the skills required to produce API’s for these products are more unique. While the reliability rule stands, it is highly likely that they are most efficiently sourced from a specialised API provider in China.
- In Europe, the opportunity may exist with “niche” products that are small in volume and where the majority of sales are derived from Europe.
- Early SPC expiries in certain European countries (commonly Norway, Poland and Malta) have not had a major influence on location of API sourcing so far.

Companies will consider several factors when assessing manufacturing location:

- Existing infrastructure and skill base
- Home market advantage: local manufacturers often have strong brand equity with patients, pharmacists, and prescribers, as well as a better understanding of the local environment
- Tax efficiency: markets have differences in tax rates and incentives to establish production
- Regulatory advantages

## Conclusions

- API is currently sourced the most cost-efficient way.
- Large volume API are likely to continue to be produced in places with the lowest cost which are India and China.
- More niche oriented API could potentially increasingly be produced in Europe when the volumes are so small that it is not likely to attract competition. Given that these areas will be niche and small in volume terms, this is unlikely to have a major influence on employment opportunities in Europe.
- Company’s choice of manufacturing location will be determined by several factors, some of which are currently more favorable outside of Europe.

