BioSpectrum
the business of Bio & Health Sciences
ASIA EDITION

The Changing API Industry

17 December 2018 | Opinion | By Priyanka Bajpai

The spending on healthcare has grown at a rapid pace in recent years worldwide and this has directly benefited the Active Pharmaceutical Ingredients (API) market. According to Stratistics MRC, the Global Active Pharmaceutical Ingredients market is expected to grow from $129.12 billion in 2015 to reach $198.8 billion by 2022 with a CAGR of 6.4%.

Growth in healthcare adoption has benefited the API market immensely. There is greater focus on accessibility to affordable healthcare and this has led to increased surge for access to medicines, in turn driving the growth of the market as a whole. Sanjeev Kumar, Industry Manager, Transformational Health, Frost & Sullivan, Asia Pacific comments, “Innovator APIs which were traditionally the largest segment are continuing to grow much more slowly in comparison with generic APIs, which constitute the fastest growing segment. With several key brands going off-patent, and as and consolidation in the pharmaceutical Industry, the demand for branded APIs has gone down significantly over the years. Consequently, generic APIs have witnessed a boom, and are expected to continue growing steadily, with further expected patent expiries and a subsequent increase in generic production capacities globally.”

Trends in API market

Patent expiration of prominent drugs, government initiatives, regional penetration and increasing aged population are some of the factors that are driving the market growth. Strict validation and safety guidelines stated by WHO and fragmented market are the factors that are hampering the API market growth. “The trend is shifting toward outsourcing the manufacturing of advanced APIs, such as biotech-based APIs, biopharmaceuticals, and advanced bulk drugs required for the production of dosage forms of new chemical entities in high-end therapy areas, such as oncology”, says Mr Kumar.

Over the next five years, the global market for active pharmaceutical ingredients (APIs) will be driven by increased demand for pharmaceutical products such as generics and biological drugs.

- **Specialty medicines driving the market**

A higher generic adoption rate in developed countries that ranges from 27% to 32% is driving global medicine spending and aiding greater access to improved, lifesaving healthcare services. The adoption of branded generic drugs is predicted to be higher in emerging economies such as China and India and generic drugs accounted for nearly 80% of the total drugs sold by value in these fast-growing nations in 2016. Rising use of specialty medicines is anticipated to grow the pharmaceutical spending worldwide with quicker growth in richer, developed nations as compared to their emerging counterparts. This is

primarily because the former have adequate manufacturing units, a higher spending power, and greater emphasis on transparent pricing by assessing measuring effects on the population. Karen Wai, Chief Operating Officer, Biofourmis says, “In general in developed markets the regulations are clearly defined or there are ample resources to keep regulations relevant to technological advances. In developed markets due to the reduced ability to spend on healthcare in general you are looking at places that are playing on the ability to manufacture at a cost effective price point versus a market that will drive revenue from the sales of the product.” Mr Sanjeev adds, “Due to the current restructuring of the pharmaceutical industry, API CMOs are expected to witness a strong upsurge in demand, particularly in the generics sector. However, in the innovator drugs segment, a major portion of the manufacturing process is still controlled by big pharma and the role of CMOs is limited.”

API Market in Asia-Pacific

Asia-Pacific is an important geographical region and has a number of emerging countries in terms of API manufacturing. Even though the proportion of healthcare spending in the APAC region is comparatively low, the growth rate in this strategic region has outpaced that of mature markets in North America and Europe. Rising healthcare spending has led to quality healthcare becoming accessible along with a higher demand for pharmaceutical products across APAC. The pharmaceuticals consumed here are mostly produced in onshore manufacturing units. Furthermore, contract manufacturing organizations are key outsourcing allies for pharmaceutical companies that supply their wares to North America and Europe. With increased competition, pricing pressures and regulatory changes, drug manufacturers are resorting to outsourcing raw material procurement and manufacturing activities. Asia-Pacific and RoW are the fastest-growing markets for APIs (8.0% and 7.2% CAGRs, respectively) due to increases in consumption, healthcare expenditures and access to medicines. In the global API and intermediates industry, Asia-Pacific accounted for 27.9% of the market share by revenue in 2015, and this is expected to grow to more than 33.2% by 2020. Sanjeev Kumar says, **“**Although the overall cases of poor quality and unsafe APIs are relatively low, an increase in the number of cases is likely to have a negative impact on the entire region. However, with generics accounting for over 50.0 per cent of the overall API production, contract manufacturers in Asia are estimated to account for over 80.0 per cent of the overall small molecule API production globally. In addition, India features the highest number of FDA-approved units next only to the United States, and several hundreds of companies are involved in the production and supply of APIs, formulations and finished dosage forms to the regulated markets. The challenge for regulatory authorities from advanced markets is the continuous physical inspection of hundreds of these units to ensure product quality and safety.”

The vast majority of anti-inflammatory and antibiotic drugs are manufactured in Asian nations such as China and India. The lower labor cost and abundant raw material availability needed to make API are the critical factors responsible for the massive growth in the APAC API market. In addition to this, regulatory support and government encouragement to establish API manufacturing hubs by way of favorable tax policies are helping drive the APAC API market. The large patient population base that consumes non-controlled drugs over the counter is also a key factor leading to the boom in APAC in-house API consumption.

Patent cliff and API

Apart from increased healthcare expenditure by the urban populations across the world and rapid increment people aged over 60 years, the global API market stands to gain addition traction from the increase in drug master file (DMF) filing from Pharma companies. That being said, patent expiry of lucrative biological drugs is expected to open new opportunities in this market during the forecast period of 2017 to 2023 (business intelligence study).

There has been an increasing emphasis on biopharmaceuticals API. Manufacturing of biopharmaceuticals is a capital-intensive, complex and highly technical process in comparison to that of small molecules. The outsourcing of biopharmaceuticals manufacturing is becoming increasingly attractive, driven by the lack of captive manufacturing capacity with mid and small biotechnology companies that drive the research and development pipeline. Talking about the business strategy for pharma companies to respond to API industry landscape given the patent cliff and opportunities it has opened up for generics, Ms Wai says, “Some have gone the way of developing biosimilars (e.g. Novartis through Sandoz) to combat the erosion by generics. Some have built generic arms (with varied success) Merck, Sanofi. Others have increase the value proposition for their drugs by chasing patient related outcomes on top of the standard clinical trial safety and efficacy. Another new value differentiation is incorporating digital technologies that are tied to the demonstration of outcomes for the pharma brand and aid in medication adherence and monitoring – e.g. through digital biomarkers.”

Mr Kumar adds, **“** The business model of contract manufacturing organisations (CMOs) is rapidly evolving to suit the changing demands of biopharmaceutical innovation, with over 50.0 per cent of biopharmaceutical companies outsourcing some form of their biopharmaceutical production. CMOs have also adapted well to the change by offering value-added services such as packaging, logistics and anti-counterfeiting in addition to traditional manufacturing, making outsourcing

increasingly attractive option.”

Quality Control and API

The ICH guidelines and FDA recommendations about how to effectively manage quality risk in drug manufacturing are clear and plentiful. However, the amount of qualification and validation that take place is really left to the discretion of drug manufacturers and their CMOs. Mr Kumar believes in the process. **“**In 2016, warning letters were issued by the US FDA to several Chinese pharmaceutical manufacturers for GMP non-compliance, resulting in a denial of entry of the latter's products into the United States. Following this, the US FDA has opened affiliate offices in Chinese cities such as Beijing, Shanghai and Guangzhou to conduct periodical inspections to ensure that standards are met. Recent efforts have been made by the CFDA to address issues of IP protection and development of innovative drugs which will have a positive impact on innovative API manufacturing”, he notes.

Similarly, during 2015-2016 Indian manufacturers have faced quality issues, which have raised regulatory concerns from importers. The issues are being addressed by both the Indian governing bodies and FDA. The governments in APAC are implementing favourable funding regulations that promote the development of high-quality pharmaceutical products.

Product-Offering Expansion and Cost Reduction

For the manufacturers of drugs, active pharmaceutical ingredients (APIs) are of great essence as their quality defines the effectiveness of the products. However, not all pharmaceutical companies possess in-house API manufacturing capabilities and it is not feasible for a single company to produce all the APIs required for their formulation offerings. An intense focus on commercializing drugs and reducing operating costs by outsourcing R&D activities can improve the organizational efficiency substantially. Outsourcing at later stages of development through the appointment of strategic partners can potentially improve operational efficiencies throughout the value chain. A balanced portfolio approach goes a long way in expanding sales and simultaneously reducing risk. Karen Wai notes, “Cost effectiveness might not be the only key sales & marketing points with the tightening of regulations, higher cost for compliance. Now they must look at differentiation through potentially niche specialization due to the changes in the healthcare environment where due to increased knowledge of diseases there are better molecular targets and we can now get into the subtype of a disease and make an impact there.”

This could be by possessing branded generic drugs, branded drugs, and unbranded drugs within the same portfolio. In addition, clearly defined forward linkages in the supply chain can garner greater market share in different regions. Mr Kumar, looks at the potential, **“**As the API manufacturing industry becomes more competitive, there is an increasing onus on technologies that enhance manufacturing efficiencies. Several leading API participants, particularly those in the Asia-Pacific region, are taking measures to improve equipment utilisation and product yield, as well as to reduce process time and harmful emissions and increase reuse and recycling. From a geographical perspective, Europe-based participants cater to the innovator sector in the US and Western European markets because of their proven capabilities. On the other hand, Asian companies are major suppliers to the generics industry in the Western markets.”

Looking into the future

In order to keep pace with the industry, many generics-focused companies will continue to gain capabilities through acquisition. Innovator companies are building their own facilities to pursue new therapeutic areas of interest while others are trending toward outsourcing the development, scale-up and commercial production of API to custom development and manufacturing organizations with diverse capabilities that can offer a one-stop shop.

With the continuous growth and shift in the market, we can expect more mergers, acquisitions and investment as companies strategize in order to be competitive and relevant in the industry.