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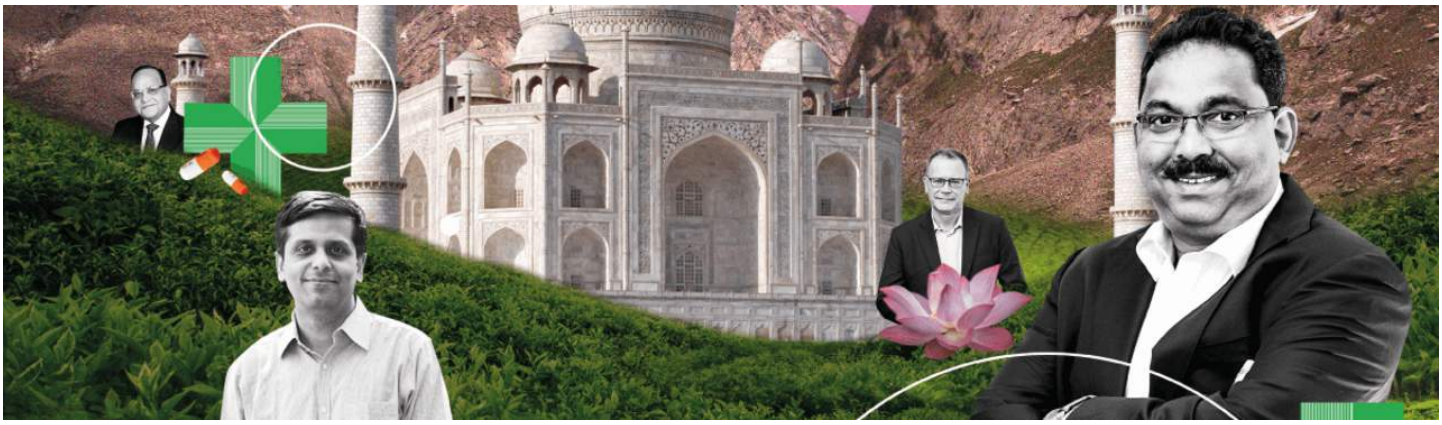

MANUFACTURE |
Standards & Regulation, Small Molecules, Facilities, Technology and Equipment, Business Practice, Formulation, Ingredients

A Blossoming Market

India is emerging as an economic powerhouse. The growth of its pharmaceutical sector – particularly small molecule APIs – has certainly contributed to its domestic and international success, but what opportunities and barriers does the flourishing sector face?

Maryam Mahdi | 09/08/2020 | Longer Read

the Small Molecule Manufacturer

This article was published in our sister publication, The Small Molecule Manufacturer, which celebrates the field of small molecule drug development and manufacturing with interviews and articles focusing on success stories, equipment, and new processing techniques. ***Read more about The Small Molecule Manufacturer here.***

With an estimated value of US$41 billion per year and a CAGR of eight percent (1), India is the world's largest supplier of generics. The country – dubbed "the pharmacy to the world" – provides medicines to over 200 countries (2), but the market dominance it now enjoys is relatively recent. Prior to 1970 (3), there was

little pharmaceutical infrastructure in place, which made the country reliant on foreign imports.

“Though India has a long history of traditional medicine use, its journey with allopathic drugs is fairly new,” says Selwyn Noronha, CEO at ACG Capsules. “Almost all drug patents held in India in the 1950s and 1960s were held by foreign companies. And domestic drug prices were among the highest in the world, meaning that only a privileged minority could afford them.”

New attitudes began to take hold in the late 1960s (3). The nation wanted to become self-reliant, producing medicines for its own population as well as for international markets. And by the 1970s, this shift in attitude coupled with the introduction of new legislation prompted the launch of most of India’s pharma companies. The Patents Act of 1970 allowed companies to develop generic versions of patented drugs so long as they were manufactured using novel approaches (4). This sparked a new trend in the industry and companies began to focus their energy on reverse-engineering the latest medicines –creating their own manufacturing processes to compete in the pharmaceutical marketplace. The FDA’s Drug Price Competition and Patent Term Restoration Act, or Hatch Waxman Act, also helped generics manufacturers bring products to the US market (5). Offering companies a 180-day exclusivity period for abbreviated new drug applications (ANDAs), the law incentivized the production of cheap alternatives to common brand-name drugs.

Since then, Indian pharma has grown rapidly and cemented its place in the industry. In the US, for example, one in three drugs is reported to have been developed by an Indian generics company (1). According to Noronha, the cost of these medicines also contributes to the nation’s competitive advantage. “India first began exports to the international markets in the 1980s,” he says. “APIs were the first products sold abroad but the sale of formulations quickly followed. This new direction caused an upheaval in the global supply chain and the prices of myriad drugs (including NSAIDs like Ibuprofen and acetaminophen) were slashed to a quarter of prevailing market prices.”

The low costs of Indian products certainly contributed to their attractiveness – but that alone was not enough to secure their position in the market. Could other aspects of the manufacturing process also be improved to help India break into more highly regulated markets?

Selwyn Noronha,CEO at ACG Capsules.

A question of equipment

Throughout the 1980s, heavy import taxes prevented Indian companies from acquiring the equipment they needed to comply with cGMP (**6**). As a result, many turned to local suppliers, but generally the equipment lacked the sophistication needed for high yields and efficiency.

“The growth of the export market prompted an important change in the attitude of India’s equipment manufacturers. Many companies were increasingly focused on the pharmaceutical markets of the West and needed superior machinery that could enhance process control, mitigate human error, and yield products compliant with their regulations,” says Richard Stedman, CEO at ACG Engineering.

Equipment manufacturers quickly responded by developing machinery with superior process control technology. Stedman says, “To be considered viable, companies needed to demonstrate their ability to mitigate the risk of human error in their operations. The mounting pressure from their Western industry partners was a clear incentive for change.”

Richard Stedman, CEO at ACG Engineering.

Falling import duties in the early 1990s meant that companies could finally consider purchasing foreign manufacturing equipment (6). And the increased competition forced the hand of domestic manufacturers, who began to develop machinery with equal or superior capabilities. “Though our local equipment manufacturers were able to meet industry expectations in the past, overall equipment efficiencies (OEE) is the crucial measure in manufacturing productivity today,” Stedman says. “Pharma manufacturers are no longer satisfied with equipment that delivers desired product quality with adequate process controls; they are looking at improved efficiencies, higher uptimes, faster cleaning, and higher OEEs. But past experience proves that our equipment manufacturers don’t settle for the status quo. I’m confident that they will deliver new technologies to meet the industry’s growing demands.”

Clearing up misconceptions

Though India has made significant contributions to the global generics market and has the highest number of FDA-registered facilities outside the US, quality issues have led to negative perceptions. In 2019, for example, it topped the list of countries with the most FDA-issued warning letters for manufacturing quality. Of the agency’s 43 letters, 20 were aimed at Indian facilities and cited control issues, lack of written procedures inside plants, insufficient laboratory records, poor sanitation, and data security as common violations (7). Although Noronha agrees that the warning letters

can't be refuted, he argues that concerns about the quality of Indian facilities stem from "Bolte of lies: The Inside Story of the Generic Drug Boom" by Katherine Eban. In his opinion, the book made broad generalizations about Indian generic products, depicting them as "cheap ripoffs" and products of gross process violations.

"Bad press always attracts more attention than good," he says. "The industry is now working to lay these misperceptions to rest. One example is that several recently launched contract research and clinical research laboratories have established global partnerships – testament to the credibility of the industry."

Sudarshan Jain, Secretary-General of the Indian Pharmaceutical Alliance.

Crisis management

According to ACG's Noronha, the COVID-19 pandemic has provided Indian pharma with an unusual opportunity to prove itself on the global stage. The pharmaceutical industry is facing an unprecedented challenge – and Indian pharmaceutical companies now have the opportunity to reassess their operations and work with international partners to deliver therapeutic solutions. "Indian companies have quickly been identified as partners to manufacture potential oral and vaccine-based solutions – palpable proof of India's relationship with companies and organizations worldwide," Noronha says. "I hope that our response to the crisis will have lasting effects on our global perception."

Though COVID-19 may be driving a shift in how India is perceived, it also raises a new challenge: India receives 60-70 percent of some of its API requirements from China, but the pandemic has significantly disrupted the flow of supply (1). Noronha explains that several Indian companies have reported interruptions in production schedules, partial shutdowns, and supply chain disturbances as a result of China's border closures. Such logistical challenges have prompted many to evaluate whether a single API source is still a viable option for drug manufacturing. "The availability of raw materials has been uncertain. Many businesses have reported an exponential increase in operational costs and service prices," says Noronha. "The COVID-19 outbreak is bound to spark a change in mindset across India's pharmaceutical community as the need for self-reliance in manufacturing bulk drug ingredients becomes increasingly obvious."

> ***"I hope that our response to the crisis will have lasting effects on our global perception."***

Sudarshan Jain, Secretary-General of the Indian Pharmaceutical Alliance opined that the Indian government and Indian pharmaceutical industry have risen to the challenge, continuing to supply medicines to patients across the country. "COVID-19 has given us the opportunity to usher in a new era for the country's healthcare and pharma ecosystems. We're already seeing how well industry and government can collaborate to find solutions," he says. "When the pandemic began, many companies across the country were able to maintain an inventory of critical APIs and key starting materials despite the shutdown of China's borders."

The Indian government also recently passed the Bulk Drug and Medical Devices policy, which focuses on increasing domestic manufacturing of APIs and key starting materials (8). The policy will give India the chance to scale up its ingredient manufacturing capabilities and challenge China's position in the market. The country has already identified a key opportunity to reduce manufacturing costs and reduce its "dependency on other countries for bulk drugs" (8). Drug manufacturers will receive incentives for manufacturing 53 critical bulk drugs prioritized for development by the government.

Beyond bolstering its manufacturing capacity, India is embracing new practices to ensure business continuity and employee safety amid the crisis. Pharmaceutical manufacturers were exempt from the country's stringent lockdown, so employers had to explore new ways to prioritize the health of their workforce. Under legislation

issued in May (9), the government required companies to encourage remote working wherever possible and urged employers to enforce social distancing practices on their premises (10). Noronha anticipates that the implementation of social distancing will drive digitization and automation in all manufacturing processes. “The severe restrictions on movements will usher in different ways to connect, engage, and serve global customers using the latest digital platforms,” he says. “This will redefine the way the pharma industry carries out marketing activities for decades.”

For the future

Though COVID-19 will have a lasting impact on pharma, the industry had already begun to change to meet the needs of its stakeholders. Vision 2030, India’s plan for cross-sector growth, outlines four key areas of development for the pharmaceutical industry (1):

improved accessibility and affordability of drugs in the domestic market

investment in the development of breakthrough drugs

continued growth in the USA

Increased presence in large, unpenetrated markets like Japan and Latin America

Jain believes these targets are achievable for Indian companies that are keen to prove they can offer more than generics to their customers. “Until now, the Indian pharmaceutical industry’s success has largely been in generics – but India was one of the first markets in the world to initiate biosimilar development and has seen the launch of many biologic products,” he says. “Though this a positive step, the sector has had limited success in developing other product classes, such as gene therapy and specialty drugs. Spurring innovation in these types of complex drugs can usher in the next leg of growth for pharma in India.”

> ***“As the world begins to embrace Industry 4.0 concepts, continuous manufacturing, and additive technologies, we must also consider their benefits for our continued success.”***

But, for ACG, the industry’s growth will be defined by its ability to embrace technologies that offer improved process and data control. “Technologies that improve overall efficiency need to be given more attention. As the world begins to embrace Industry 4.0 concepts, continuous manufacturing, and additive

technologies, we must also consider their benefits for our continued success. We have to keep an ear to the ground to keep up with changing times," says Stedman.

Whatever strategies they use to increase their market presence, Indian companies are proving their ability to adapt to market needs and reliably partner with companies worldwide. And it's this "can-do" attitude that will underpin India's future success.

References

About the Author

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After finishing my degree, I envisioned a career in science communications. However, life took an unexpected turn and I ended up teaching abroad. Though the experience was amazing and I learned a great deal from it, I jumped at the opportunity to work for Texere. I'm excited to see where this new journey takes me!