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More than manufacturing: India's homegrown COVID vaccines could transform its pharma industry

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India is known as "the pharmacy of the world," and the nickname is well-deserved. The second-most populous country is a drug manufacturing powerhouse. One in three pills consumed in the U.S. is made in India. Its factories churn out more than half the globe's total vaccine supply and produce more generic drugs than anywhere else.

Already, India is likely to be an essential player in the manufacturing of a COVID-19 vaccine. One of the country's pharmaceutical giants is starting to produce hundreds of millions of doses of a leading contender.

But in the race to defeat the coronavirus, India wants to do more than be the world's workhorse; it also wants to harness science to bring the pandemic to an end. At least seven Indian pharmaceutical companies are working to develop a vaccine and two have progressed to human trials, an achievement Prime Minister Narendra Modi has touted as a source of national pride.

An indigenously-developed vaccine with a rapid rollout could be crucial for India, where nationwide lockdowns failed to prevent India from becoming the country with the fastest-growing number of coronavirus cases in the world, with over 68,000 deaths and more than 3.9 million confirmed infections.

If an Indian pharmaceutical company is able to bring a COVID-19 vaccine to the commercial market, it could transform the industry's reputation, giving India a globally-distributed coronavirus vaccine that's not just made or tested in India, but developed there, too.

Generic expertise

India's pharmaceutical industry is best known for producing generic drugs, which are identical to brand-name drugs but less expensive because they're made after the patent on the branded version has expired.

A government push in 1970 to wean India off costly imports and manufacture cheaper medicines for its own citizens led to legal reforms that kickstarted growth of India's generics industry. A new law allowed patents on manufacturing processes, but not the end product, which incentivized Indian pharmaceutical firms to develop alternate ways to produce existing drugs.

Those reforms proved especially prescient a decade and a half later, when the U.S. Hatch-Waxman Act relaxed generic drug regulation in the U.S., a "crucial" development for India's generic industry, said Sudarshan Jain, secretary-general of the Indian Pharmaceutical Alliance. The law made it easier for generic drugmakers to enter the U.S., and India was well-positioned for the resulting ramp-up of generic drug production worldwide.

"By the time you got to the 1990s you already had a very...well-developed pharmaceutical industry, which was very good at the manufacturing side of producing drugs. So literally anything that was out there, India was capable of making those combinations," said Sujay Shetty, India pharmaceuticals leader for professional services firm PricewaterhouseCoopers.

Today, the pharmaceutical sector is responsible for 2.5 million jobs in India. It's a significant contributor to GDP and the third-largest contributor to reducing India's trade deficit, said Sathya Prathipati, senior partner and leader of the pharma practice in India for McKinsey.

An employee checks a vaccine vial labeling machine at a Serum Institute of India pharmaceutical plant in Pune, India in 2015. The Institute working with AstraZeneca to produce a COVID-19 vaccine developed by Oxford.

Sanjit Das—Bloomberg/Getty Images

The cost of producing drugs, including vaccines, in India is relatively low because of cheaper labor and the nation's large-scale manufacturing facilities. A rotavirus vaccine by Indian pharma giant Bharat Biotech, for example, cost one-fifteenth as much as rotavirus vaccines developed outside of India.

"A [coronavirus] vaccine developed in India would be far cheaper than a vaccine developed anywhere else," said Chandrakant Lahariya, a vaccinologist and public health expert who has published research on the history of vaccines in India. The affordability of a COVID-19 vaccine is paramount; if doses are prohibitively expensive, it could hamper distribution, prolonging the pandemic and costing lives.

The largest vaccine maker in the world is the Serum Institute of India, a private family-run drug company founded in 1966 and headquartered in the western Indian city of Pune. It's partnered with pharmaceutical giant AstraZeneca to produce the Oxford University COVID-19 vaccine, which a World Health

Organization (WHO) official dubbed the world's most advanced coronavirus vaccine candidate. The company did not respond to a request for comment.

Serum plans to price one dose at $3 for India and other emerging economies, Reuters reported on Aug. 25.

In comparison, Pfizer and German biotech firm BioNTech SE made a deal with the U.S. government to charge $19.50 per vaccine dose, and Moderna said in August it is charging between $32 and $37 in some deals for its vaccine. The Pfizer vaccine is being manufactured in the U.S. and Germany; Moderna's vaccine is being manufactured at sites in the U.S. and Switzerland.

Serum chief executive Adar Poonawalla has said half the doses will go to India and the other half will go to the rest of the world, especially poorer countries.

'Very good at the D side'

India's drug manufacturing prowess is unparalleled, but its pharmaceutical research and development (R&D) lags behind by comparison.

"It's a big industry and the industry is less into research to develop new vaccines, it's more geared towards producing ... vaccines in a very cost-effective manner," said Shaheed Jameel, a virologist and chief executive officer of the Wellcome Trust/DBT India Alliance, a public charity that funds biomedical and health research in India.

India's pharmaceutical industry as a whole spends around 6% of total earnings on R&D, versus 20-25% among global pharmaceutical firms, said Reji K. Joseph, an associate professor at the Institute for Studies in Industrial Development in New Delhi who researches patents and India's pharmaceutical industry.

For example, R&D spending as a percentage of sales was 26% for AstraZeneca in 2019. (Firms in India also spend a smaller share of their revenue on R&D because related costs like labor and building construction are generally cheaper, according to Joseph.)

Many Indian firms focus exclusively on generics; the leading Indian firms that do invest in R&D tend to focus on developing and improving on generic drug formulas. Multinationals in the U.S. and Europe, meanwhile, tend to focus on creating new chemical entities for new drugs.

The strength and success of India's generics industry has meant that there isn't as much incentive for generic drugmakers to diversify into riskier—and more expensive—research of new chemical entities.

"Most companies [in India] have not ventured into the development of new medicines. They are still in the production of generics...so they don't need to invest heavily in R&D," Joseph said.

"India's very good at the D side, the development side," Shetty said. "It's more like incremental innovation, so in terms of broad innovation or [research], it's relatively small."

R&D expenditure is increasing slowly, Joseph said, but technological and financial constraints have kept it from growing at a faster pace. "The development of new drugs involves a lot of investment and [many] companies cannot sustain such investments" on the scale of American and European pharmaceutical giants, he said. "Even the largest Indian firm is small compared to western [multinational corporations]."

Normally, said Jameel, the emphasis on manufacturing over R&D isn't a drawback for India's pharmaceutical industry, but "one lesson that Indian R&D is learning from [the coronavirus pandemic] is that you must have platforms that you can very quickly repurpose to make vaccines for a new pathogen that has emerged," Jameel said.

Having existing vaccine platforms reflects prior investment in research. Oxford used existing technology, a chimpanzee adenovirus vaccine vector, to make its vaccine. Moderna, another global frontrunner for a coronavirus vaccine, made use of its experimental zika virus mRNA vaccine platform to develop its vaccine candidate. Zydus Cadila, one of the Indian companies working on a COVID-19 vaccine, created its experimental DNA vaccine platform from scratch; Bharat Biotech, another Indian vaccine player, developed its coronavirus vaccine on a Vero-cell platform.

Three vaccine contenders

The Zydus Cadila and Bharat Biotech vaccine candidates are two of 37 potential coronavirus vaccines currently undergoing human trials around the world.

"Everybody today is concerned about coronavirus. Everyone wants to know when the vaccine will be available. Our scientists are working tirelessly." Modi said in a national address on the ramparts of Delhi's Red Fort on Aug. 15.

Indian Prime Minister Narendra Modi discussed coronavirus vaccine candidates in a national address on India's 74th Independence Day on Aug. 15 in Delhi.

Xinhua/Getty Images

"Not one, not two, as many as three coronavirus vaccines are being tested in India," Modi said, referring to the vaccines indigenously developed by Bharat and Zydus. He also counted in his tally the AstraZeneca-Oxford vaccine that the Serum Institute is set to manufacture.

Bharat Biotech, based in Hyderabad, is a known commodity in India's vaccine sector, having launched an H1N1 influenza vaccine in 2010 and successfully developed and launched vaccines for Japanese encephalitis in 2013 and rotavirus in 2015.

For its coronavirus vaccine, called Covaxin, it's collaborating with the Indian Council of Medical Research, University of Wisconsin-Madison virologists and U.S. biotech firm FluGen. Covaxin is an inactivated vaccine, meaning it contains "dead" particles of the coronavirus, SARS-CoV-2, that are no longer disease-producing, but will still prompt an immune response from the inoculated person.

Bharat conducted phase one trials of Covaxin across 12 sites in India, and will likely start phase two trials this month, according to local media reports.

"Most of the vaccines come from the Western world. But I am happy to share that the two vaccine candidates from India are actually in the lead with the rest of the world," Suchitra Ella, joint managing director of Bharat Biotech, told the *Times of India* on July 30.

Bharat Biotech declined to comment.

Zydus started its phase 2 human clinical trials on Aug. 6 at multiple sites across India. Its vaccine candidate, ZyCoV-D, is a DNA-based vaccine. It contains genetically-engineered DNA molecules called plasmids that resemble those of the coronavirus. Inactivated vaccines are the easiest to make, while DNA vaccines—which the WHO describes as a "radically new approach to vaccination"—have never been approved for human use anywhere in the world, Jameel said.

Headquartered in Ahmedabad, a city in the western coastal state of Gujarat, Zydus is one of India's biggest pharmaceutical companies and a large generic drugs manufacturer. It also has a track record of vaccine winners, including an immunization for a seasonal influenza, one for chickenpox, and one for rabies. Zydus did not respond to request for comment.

"I'm very hopeful that at least one, if not both of these will do well, and if that happens then we'll be spoiled for choice," Jameel said.

Every country for itself?

As the pandemic wears on and scientists around the world race to develop a safe and effective cure, some experts have expressed a fear of 'vaccine nationalism'—of countries developing vaccines with an eye to inoculate their own citizens first, rather than working towards global distribution.

A health worker collects a swab sample from a woman to test for the coronavirus at a primary health center in Hyderabad on Sept. 4, 2020.

NOAH SEELAM—AFP/Getty Images

India's government hasn't yet struck official procurement deals with its domestic vaccine makers, but in mid-August, a government committee met with the three firms whose vaccines are undergoing human trials in India, to discuss a potential distribution deal and find out how soon, and at what price, the firms can produce vaccine doses.

Serum's Poonawalla told the *New York Times* that although he plans to send half of the Serum-produced vaccines to poorer countries around the world, India's government "may still invoke some kind of emergency if they deem fit or if they want to."

India's government has previously blocked companies from exporting potential COVID-19 treatment drugs, reportedly to ensure Indian citizens had access to the medications. (The government later lifted the restrictions.) So far, India's government has not objected to Serum's distribution plan.

Global collaborations led by agencies like the WHO and the Coalition for Epidemic Preparedness Innovations will play an important role in global vaccine distribution and stockpiling doses for poorer countries, Lahariya said. At the same time, he added, "There's already a sort of consensus developing that if any country develops a vaccine, of course they'll keep a higher proportion for within their country."

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