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Canada

Hindered by policy, Canada's pharma industry pushes to build on its solid foundation

By Karen Langhauser, Chief Content Director

One of the great medical discoveries of all time was born from innovative Canadian research.

When four Toronto researchers (Banting, Best, Collip and Macleod) discovered, developed and tested insulin, they created the first effective treatment for diabetes — revolutionizing the standard of care and undoubtedly saving millions of lives.

The development of insulin was a bright spot in Canada's rich history of scientific discovery.

But if the country is going to reach the ambitious goals laid out by the federal government two years ago — doubling the size of the health and biosciences sector and becoming a top-three global hub by 2025 — the pharma industry will have to push beyond its core competency.

"When you look at our ecosystem it's done a fantastic job of generating a lot of early stage companies, but unfortunately we've failed to take a lot of those companies across the finish line," says Andrew Casey, president and CEO of BIOTECanada, a national association whose mission is to lead the advancement of the Canadian biotechnology ecosystem.

Hindered by a complex regulatory environment and conflicting policy direction regarding drug pricing, the pharma industry has its work cut out for it. But many believe the industry — described by Casey as "diverse and deep in its nature" — is up to the task.

The Canadian pharma industry supports 34,000 jobs in Canada

Source: Innovative Medicines Canada

LOFTY GOALS

Announced in 2017, the Canadian government's Innovation and Skills Plan was focused on making the country a world-leading center of innovation by supporting economic growth in six key sectors, health and biosciences being one of them. Part of this plan included a new model for industry-government collaboration, which in turn produced the Health and Biosciences Economic Strategy (HBEST) in 2018.

At the time, Canada ranked fourth in global health and biosciences hubs, behind the U.S., U.K. and Germany.[1] The HBEST action plan laid out several economic growth targets for the Canadian pharma industry including doubling health and biosciences exports to CA$26 billion (~$20 billion USD) and doubling the number of companies to 1,800.

According to Casey, even pre-COVID, these HBEST objectives were a "stretch target." But given the industry's strong foundation — a globally recognized capacity for scientific research — he still believes the goals are within reach.

"The plan recognizes some fantastic existing strengths in the Canadian ecosystem and the desire to push the industry even further," says Casey. "It is a way of challenging every part of the ecosystem to do a better job recognizing that we do have a very strong foundation upon which to build."

GETTING TO MARKET

A well-known obstacle when it comes to bringing drugs to the Canadian market is the country's lengthy marketing approval timeline. And while Health Canada's drug approval process is frequently criticized for being slower than its American or European counterparts, the regulator is just one part of a sequential, time-consuming process.

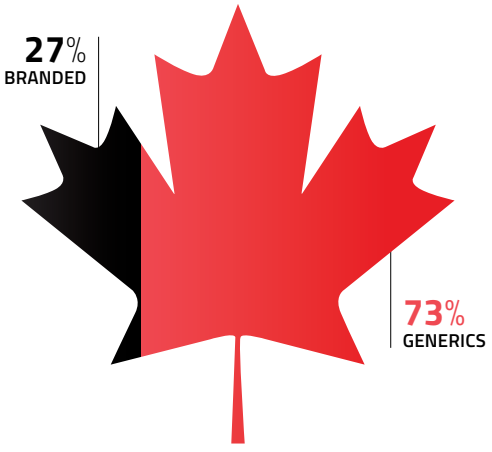
After Health Canada evaluates a drug candidate for safety and efficacy, the approved drug must then undergo a health technology assessment through the Canadian Agency for Drugs and Technologies in Health (CADTH). Established by the federal government, the small but powerful independent agency is responsible for making recommendations to the provinces and territories about treatments accepted for public drug plans.

Following the CADTH review, the pan-Canadian Pharmaceutical Alliance (pCPA), an

alliance of provincial, territorial and federal governments, steps in to conduct joint negotiations for drugs (both brand and generic) in order to achieve the best value for publicly funded drug programs and patients.

"Getting these steps compressed has been difficult. It's getting better but still could be significantly streamlined. There's movement afoot to deal with it but as long as it remains separate entities, it's always going to be a challenge," says Casey.

Prescription drug market in Canada



SOURCE: IQVIA. CANADIAN COMPUSCRIPT. MAT DECEMBER 2019

PHARMA HATES UNCERTAINTY

But a labored drug approval process is not what is holding the industry back from achieving the government's economic goals. In fact, many argue that government itself is handcuffing the industry with new price control measures.

Last year, the Canadian government passed what is being touted as the biggest reform to the country's drug pricing policy in over 30 years. A hotly debated policy issue, the amendments to the Patented Medicines Regulations are currently set for implementation on Jan. 1, 2021, after COVID pushed the original July 2020 date.

The Patented Medicine Prices Review Board (PMPRB) conducts ongoing reviews and, if necessary, investigations of individual patented drug prices to make sure they are not excessive. In short, the reform will change how the federal agency calculates the fair price of branded prescription drugs (notably excluding countries with high prices, such as the U.S., as price comparator countries) and enable the agency to consider the cost-effectiveness of new medicines. Proponents say the adjustments will reduce the list prices of current and future branded meds in Canada by an average of 20 percent, saving patients US$10 billion over the course of a decade.

But critics — among them, the pharma industry — says this siloed approach to reducing health care spending is limiting Canadian's access to innovative medicines, as well as creating an inhospitable environment for investment.

"Uncertainty created by policy process, like the amended PMPRB regulations, gives companies pause when or if they bring products to the Canadian marketplace," says Casey. "Pharma hates uncertainty."

$3 billion a year = Economic impact of the pharma industry on Canada's economy

Source: Innovative Medicines Canada

Perhaps more concerning is the indirect effect that pricing uncertainty could have on the overall pharma ecosystem in Canada. The majority of large branded pharma companies in Canada are foreign multinationals with Canadian subsidiaries. Of the top 20 selling drug corporations in Canada, only Apotex, Bausch Health (formerly Valeant), Pharmascience and Teva Canada (formerly Novopharm) are Canadian-based.[2]

The presence of commercially active multinational companies looking to replenish pipelines creates opportunity, as they provide a vital source of capital and support for smaller, early stage companies in Canada. Pharma-led investments and partnerships have led to the maturation of several significant Canadian companies with a number now poised to become commercially active.

But these investments and partnerships taking place in Canada are at risk through the new pricing dynamic.

"If you make this market uncomfortable and unattractive for large multinationals, they will change their business practices. They will likely decrease their investments and partnerships in Canada — and that's problematic. Maybe clinical trials start slowing down as well. It's a slippery slope," says Casey.

RIPPLE EFFECTS

The government push to drive drug prices down to the lowest possible price line in Canada is creating an effect felt beyond the Canadian borders. Critics of the new pricing policy see it as a disservice to the global pharma industry as a whole.

"Our drug prices have to stay aligned with the global marketplace," says Casey. "In some ways, what is happening in the U.S. reflects the fact that we are allowing the Trump administration to point us out as bad actors."

What Casey is referring to is an executive order, part of four orders designed to lower the price of prescription drugs for U.S. patients, signed by President Trump in late July. If implemented, the Executive Order on Increasing Drug Importation to Lower Prices for American Patients will allow for the commercial importation of certain prescription drugs from Canada.

While the real-world implications of this order may be fairly limited — only a small subset of drugs are able to be imported under the statute — it does highlight a large disparity in prices between countries.

For years, Americans have routinely skirted federal law by tapping online pharmacies in Canada to buy prescription drugs at a fraction of the price they would pay at home. While the Trump EO does not address personal importation, this practice has led to considerable concerns about drug safety, exposing American patients to nefarious characters as drugs travel across borders — an issue that critics of the new EO say could be seen at the wholesale level as well.

Wholesale imports of drugs from Canada also raises supply concerns for the Canadian pharma industry. The country already has a pharmaceutical trade deficit: In 2019 Canada imported US$13.9 billion worth of drugs, versus the $8.4 billion it exported.[3] A previous study predicted that if 20 percent of U.S. prescriptions were filled using Canadian sources, the demand from the U.S. for patented drugs would deplete the Canadian branded drug supply in just 201 days.[4]

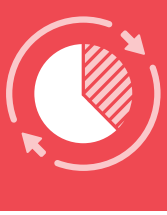
In addition to causing supply shortages for Canadian patients, importing drugs from Canada would likely do little to ease the price burdens in the US.

"Let's say, hypothetically, you were able to take every single pill out of Canada, I'm not sure you'd have enough to address the problem in a county in Florida, let alone the entire U.S.," says Casey.

THE TIMING IS RIGHT

The Canadian pharma industry continues to push back on the Patented Medicine Prices Review Board's modernized regulatory framework, contributing alternate proposals that the industry feels can address health care fiscal challenges while also supporting pharma's business model. So far, the industry has been unsuccessful in achieving the type of change it wants to see and many fear the extent to which the new regulations will impact the country's ability to attract investment to commercialize Canadian innovation.

However, the pandemic, as we all know, has changed much in the world. Unfortunately, some economic sectors that previously generated high amounts of revenue may be



Canada is the 10th largest pharma market in the world

Source: IQVIA. Canadian CompuScript. MAT December 2019

slow to recover, if at all. And many are wondering how countries will compensate for this loss in revenue.

"I look to innovation and biotech, certainly the pharma and biotech industries, as potential replacements for some of that," says Casey.

Economic recovery and a return to any semblance of normalcy hinges on testing, treatments and vaccines — and the global pharma and biotech industries have mobilized at unprecedented speeds to make this possible.

Casey hopes that pharma's progress will create a new appreciation for the value the industry brings, and that, in turn, may influence policy in Canada.

"In this paradigm is there an opportunity for a new discussion that is a bit more holistic and not so narrowly focused on pricing? I hope so," he says.

Overall, if the Canadian pharma industry wants to achieve big goals by 2025, it will take a combined effort from industry and government. Government policy can help or hinder the pharma industry's ability to attract the investment and capital needed to support a thriving market for pharmaceuticals.

"If a good idea isn't attracting investment where it is, that good idea will go to where that investment is and we will lose out on the commercialization of that product," says Casey.

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Brazil

Brazil's pharma industry has long been held down by high taxes and bureaucracy — but the weight could soon ease

By Meagan Parrish, Senior Editor

As the behemoth of Latin America, Brazil has long been a sought-after market for pharma. Although most of the world associates Brazil with sprawling coastlines and tropical forests, the country is an attractive destination to pharma for another reason: its large population.

As the world's sixth most populous country, Brazil represents the biggest market opportunity in Latin America for multinational pharma companies. Valued at around $23 billion by EY, a global consulting agency, Brazil represented the seventh largest pharma market in the world in 2018.

Growth has also been steady. According to EY, the pharma industry has grown by about 7 percent year over year (in Brazilian Real terms) for the last five years, and withstood a recession that lasted from 2014 to 2017.

Nelson Mussolini, the executive president of Sindusfarma, a pharma industry trade association for Brazil's Sao Paulo region, says that the coronavirus pandemic is making estimates for future growth tricky, but that preliminary predictions indicate that commercial pharmaceutical sales will increase by about 5.5 percent in 2020 and grow to 8 percent next year.

"Pharma was isolated from the previous recession and there is potential to keep growing despite a COVID-related recession that could be coming," explains Fabio Schmitt, a Brazil strategy and transactions partner at EY.

Yet, significant barriers still remain when it comes to gaining access to this large pool of patients, for both global and local pharma companies. Despite its size, the industry has long had its wings clipped by high taxes, a burdensome bureaucracy, price controls and a high rate of API imports. And without sustained and significant investments in innovation, Brazil has been stuck in the grind of generics manufacturing, unable to produce notable advancements in R&D.

However, the industry could be approaching a turning point. With the coronavirus pandemic raging in Brazil, public and political will to bolster the country's access to health care resources is rising. And if regulatory changes roll pharma's way, the industry could shake off some of its chains and soar even higher.

AT A GLANCE

"The pharma market in Brazil is really divided between generics and patent," explains Schmitt.

According Sindusfarma, the Brazilian Ministry of Economy registered 418 pharma manufacturing plants in the country in 2018. EY estimates that nearly half of the industry's revenue is concentrated in its top 10 companies. Of those 10, six are Big Pharma companies and the other four are local. Generally speaking, Schmitt points out that while Big Pharma companies control the market for branded medicines in Brazil, almost all of the local companies stick with the generics market.

With access to free health care guaranteed by a program known as the Unified Health System (SUS), Brazil's government and hospitals gobble up a 30 percent chunk of the local low-cost drug market while the other 70 percent of drugs are sold through commercial pharmacies.

"Local companies have been successfully managing in this environment," Schmitt says. "But it's not a very easy market to play in."

The tax burden

Although Brazil's corporate tax rate is 15 percent, the country levies taxes on companies in many other ways including taxes on imports, exports, transactions, properties,

> **The pharma market in Brazil is really divided between generics and patent.**
>
> Fabio Schmitt, a Brazil strategy and transactions partner at EY

services, income and more — adding up to a system that's far more burdensome than most other countries.

"This is a very complex system…maybe the most complex in the world," explains Eliane Kihara, a partner with PwC.

According to Mussolini, taxes correspond to nearly 32 percent of the amount paid by drug consumers.

"In the global context, the weight of drug taxes in the country remains an aberration," he says.

With such a high tax burden, Kihara says that pharma companies often have to invest a significant amount of money in human capital to support the tax system and avoid penalties.

"If Brazil did tax reform…that would be fantastic news and make the country more attractive for investments," she says.

Price controls

"Perhaps the greatest challenge [to the pharma industry] is the review of drug price controls," Mussolini says.

Every year, drug price increases are limited by CMED (Câmara de Regulação do Mercado de Medicamentos), an arm of Brazil's health regulatory body known as ANVISA. According to Mussolini, price controls were eased for some OTC drugs in Brazil, but discounts were largely maintained, which showed that the market is competitive enough to keep prices down.

"There is ample evidence that a series of drugs in Brazil can be freely priced, due to the excellent market competition. It is the case with generic drugs, which still have controlled prices despite having dozens of players in the various therapeutic classes," he says.

Mussolini also argues that price controls are denying pharma companies the ability to invest in innovation. Sindusfarma estimates that the country's entire private pharma market (excluding public sales to hospitals

Supreme Court watch

Brazil's highest court is currently deliberating on a case that could have major implications for the country's generics sector. In the case, the constitutionality of Brazil's 10-year minimum extension on 20-year patent terms is being challenged. Those in favor of the extra 10-year term argue that it protects property rights and encourages innovation, while those against the rule say that it violates free competition and hinders industry development. If the Supreme Court rules against the 10-year extension, Licks Attorneys estimates that 22,000 patents for pharmaceuticals in Brazil could be eliminated.

and the government), is worth about $17 billion, which, Mussolini says, means that "...the investment in R&D of a single large international laboratory is higher than that of the Brazilian private pharma industry as a whole."

Brazil's top 10 pharma companies by revenue

Pfizer
$1.28 billion

Sanofi
$1.22 billion

Roche
$936 million

Hyper Pharma
$931 million

Eurofarma
$925 Million

EMS
$906 Million

Novartis
$805 Million

Aché
$796 Million

Cristália
$469 Million

Abbott
$464 Million

—Data compiled by EY

API imports

It's a familiar story for many countries around the world. With Brazil relying on generic manufacturing to supply its demand for lower cost drugs, the industry has become wedded to API imports from India and China. EY and PwC both estimate that Brazil currently imports about 90 percent of its APIs, leaving the supply chain vulnerable to disruptions in the quantity and quality of its drug ingredients.

So far, Kihara says that Brazil has not experienced any supply disruptions during the coronavirus pandemic, but the situation has exacerbated concerns about shortages, and increased pressure on the industry and government to find solutions.

A CORONAVIRUS PUSH

As a general rule, the pharma sector in Brazil has never been a major contributor to the world's advancements in R&D, save for one exception — vaccines. While the world reels from the coronavirus pandemic, Brazil is poised to play a starring role in the quest to bring a vaccine to market.

Part of its importance in this epic push for a vaccine is apparent. Brazil is now the country with the second most confirmed cases of the coronavirus and the sixth most populous country, making it an easy market to find participants for large-scale studies. One late-stage trial of a vaccine candidate

> **It takes much longer to register a drug in Brazil than in the U.S. or the EU.**
>
> Nelson Mussolini, the executive president of Sindusfarma

developed by University of Oxford and AstraZeneca is already underway in Brazil.

Its clinical research infrastructure is also primed for the task. Historically, Brazil has housed a number of major studies for vaccines including Zika and dengue fever, which has helped create the right environment for studying a vaccine. Several major institutions have partnered with Big Pharma companies in the past and have laid the groundwork for the next big shot with ample labs, testing clinics and professionals in place.

According to Schmitt, the pandemic has also "fast-tracked" the push for modernizing the country's pharma industry as a whole.

"COVID-19 has exposed barriers we have in the country to develop and distribute drugs," he says. "It was already on the government's playbook to improve the country's pharma infrastructure and health care access. Now the demand for this is getting a boost, and I think the government will lean toward this."

OPTIMISM FOR CHANGE

Since President Jair Bolsonaro took office in January 2019, Mussolini says that there have been promising talks between the pharma industry and the government, and that the industry's proposals have been "well received."

"The government's willingness to know and resolve issues related to health and the pharmaceutical industry is evident," he says.

Sindusfarma is pushing for several key changes including relaxed price controls, the elimination of taxes on the production of medicines and less red tape around drug approvals.

"It takes much longer to register a drug in Brazil than in the U.S. and the EU," he says. "Meeting the rigorous standards of a modern regulatory agency such as ANVISA is fundamental for developing the pharmaceutical industry. However, it is necessary to reduce the bureaucracy of processes and procedures to give more agility to companies and thus provide lower costs, more profit and investments in research."

Mussolini says that Sindusfarma is also pushing for a less restrictive environment for clinical trials.

"The current regulations create serious problems, which frequently make drug research unfeasible to the detriment of Brazilian patients and applied research in the country," he says.

When it comes to APIs, Kihara says that the government is expected to begin providing incentives to bolster local production by the end of this year. She says that the incentives could be tied to building new production facilities for APIs and are being discussed alongside the issue of lowering or streamlining taxes.

Given the current government's openness to considering changes and rethinking processes in the pharma industry, all of the experts interviewed for this article expressed optimism that although no new regulations have emerged yet, they are on the way.

"There is political will," Kihara says. "It is a now a matter of survival that there are changes within the next couple of years."

global dose

Russia

After building its domestic infrastructure, Russia's pharma industry looks to go global

By Meagan Parrish, Senior Editor

It was hardly a blip in the news last month when the director of one of Russia's leading research institutes said they could be ready to start a mass vaccination campaign against the coronavirus by fall. Plenty of other pharma companies in the hunt for a Sars-CoV-2 vaccine have stolen headlines around the world in recent months, but the work of Russian scientists combatting the pandemic has largely remained in the shadows. Now, it's possible that's about to change.

While the eye-popping claim that a new coronavirus vaccine could be ready for roll-out within a few months was clearly ambitious (and most likely overly optimistic), the efforts illustrate a rising aim in Russia to make a bigger mark on the global pharma scene.

Although Russia has long been a leader in other scientific fields, its pharma segment has failed to become a hotbed of technological advancements. Instead, the industry has been dominated by state-controlled policies, a high rate of imports and low-cost generic manufacturing. However, Russian leaders are now on a quest to bolster R&D investments in pharma and put the industry on track to increased independence and innovation. To achieve these goals, the industry will have to clear several major hurdles.

GOVERNMENT INVOLVEMENT

On the surface, Russian pharma patients have been given a sweet deal. Under the country's state-controlled health care system, Russian citizens have been guaranteed access to all inpatient drugs as well as

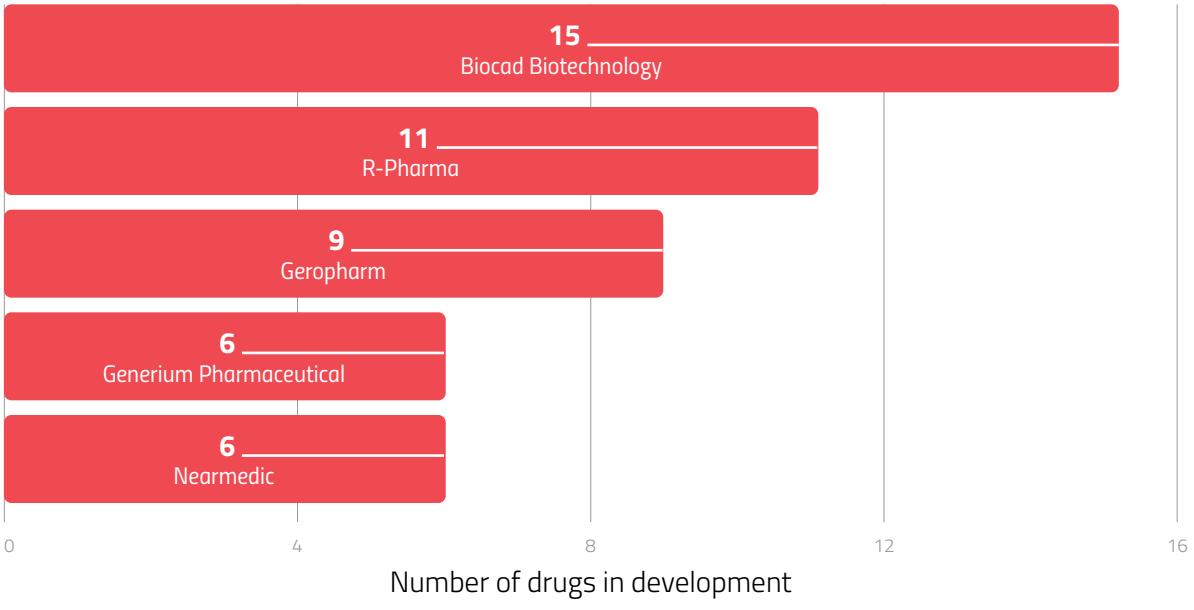
many outpatient drugs for free. Naturally, the government wants to procure these essential medicines on the cheap. However, this has created other challenges in the market.

For example, price caps determined by the government for essential drugs have made it difficult for local manufacturers to make money on drug production, despite prices being set to allow for 30 percent in profit (maximum). The emphasis on getting low-cost drugs has also contributed to the country's reliance on generic medicines. And because there are not enough local producers of APIs on the domestic market, the industry is also heavily reliant on API imports for manufacturing from China and India.

So, in 2011, the Russian government launched an initiative called Pharma 2020 to lay the groundwork for more domestic pharma production. At the time, about 90 percent of the drugs on Russia's market were imported and the goal was to reduce that figure to 50 percent. Nearly 10 years later, Russia is headed in the right direction but is still importing about 70 percent of its drugs.

Meanwhile, growth in Russia's pharma market appears to be increasing each year, but only modestly, and the growth has been slowing. According to Oleg Berezin, a partner and the head of the Life Sciences and Healthcare group at Deloitte, the country's pharma industry grew by 9.5 percent (in Russian ruble terms) in 2019, but after adjusting for inflation for drugs, the real growth was only about 7 percent. This year, the market is set to

Russian pharma companies with the biggest pipelines



The Russia government's use of financial instruments such as tax benefits and subsidies has helped breathed some new life into the pharma market.

grow more, but mostly due to inflation and government spending.

"We don't have double digit growth like we had five years ago," Berezin says. "Currently the market is not just stagnating — there is small growth."

Still, the Russia government's use of financial instruments such as tax benefits and subsidies has helped breathe some new life into the pharma market. In 2018 alone, 12 new large production sites were opened in Russia.

The cash flow has also helped buoy scientific progress in drug development. In the last few years, Russian pharma companies have introduced several new drugs onto the market including a next-generation protease inhibitor for hepatitis C developed by R-Pharm, and the world's first approved biosimilar for dornase alfa, a cystic fibrosis treatment, made by Moscow-based Generium.

Yet, low drug prices are continuing to create roadblocks for local drugmakers. In April, a group of seven manufacturers informed Russia's Industry and Trade Ministry that they may have to stop making about 50 essential medicines because the cost of production now exceeds the sale price, partly due to the devaluation of the ruble and rising API prices caused by COVID-19.

THE NEXT MOVE

Now that more infrastructure has been built to produce pharmaceuticals, the Russian government is looking to take the next step and invest in long-term industry growth and globalization. Today, a new initiative called Pharma 2030 is in the works, which Berezin says will attempt to make the country's pharma industry more competitive and innovative.

Berezin says that Russia has enough facilities for finished dosages to make most essential drugs onshore, so the focus is now on decreasing imports of APIs.

"We already have some incentives for local producers of APIs," he says. "There are specific benefits and incentives with respect to drugs that are sold to the government and produced locally, which are even larger if a drug is produced out of local APIs."

The bigger challenge, Berezin says, is going to be boosting the development of

first-generation therapies and transforming the industry into a high-performing export-oriented sector, which is another goal of Pharma 2030.

"There is not enough financing for R&D from Russian pharma companies or Big Pharma companies, which generally don't have R&D activity here except for clinical trials," he says.

One mechanism that could be created by Pharma 2030 is the support of more joint ventures for pharma companies looking to enter emerging markets. A specialized venture fund could also further support pharma innovations.

The trick will be balancing Russia's historic isolationism and emphasis on the domestic production of low-cost drugs with the desire to be competitive on a global level.

It's also unclear to what extent the initiative will make Russia an attractive destination for investments from multinational pharma firms. Although several Big Pharma companies — such as Novartis, AstraZeneca and Sanofi — operate in Russia, the current emphasis is on producing drugs for the local market in a wide range of therapeutic areas such as oncology, diabetes and cardiology. However, Berezin says that some, especially those that do not have local manufacturing facilities, lose market share due to the preferential treatment given by Russian government contracts to local manufacturers.

THE DIGITAL LANDSCAPE

Modernizing the country's pharma sector is top-of-mind for Russia's industry. To that end, Russia has mandated new track and trace regulations that are currently scheduled to go into effect on July 1 (although the deadline could be postponed). Similar to other programs around the world, Russian pharma manufacturers will have to report every step their products take through the supply chain, as well as pricing information. Ultimately, the goal is to reduce the presence of any counterfeit drugs or other illegal practices on the market.

And Berezin says that if producers and market authorization holders have all of their drug data reported by the entire supply chain to the system, it will create a big opportunity to use and analyze this data.

In general, however, the pharma industry in Russia has been slow to adopt digital tools. Only about one-third of Russian companies who responded to a recent survey conducted by Deloitte said they have implemented a digital strategy. Although companies understand that there are advanced solutions available, many still rely on websites and social media as their only digital tools.

To date, Russia has the third highest number of coronavirus cases in the world

"In this particular area, the Russian market has a long way to go, but recent regulatory developments, such as a green light for OTC online sales, will likely boost it," Berezin says.

THE COVID-19 EFFECT

The effort to be the first country that successfully secures a coronavirus vaccine has echoes of the old space race. Will Russia pull off another Sputnik?

Russia's deputy prime minister for Social Policy, Labor, Health and Pension Provision, Tatyana Golikova, has stated that the country has 47 coronavirus vaccines in development, although just 10 have been recognized by the World Health Organization. Clinical trials on at least two candidates are set to begin this month, and the hope is that at least one candidate could be registered with local regulators by fall.

The country has plenty of reasons to want to rush progress. To date, Russia has the third highest number of coronavirus cases in the world, and securing a vaccine will be a crucial step for the country's recovery.

Russia is also working on new treatments for the coronavirus, and the CEO of the Russian Direct Investment Fund made a bold claim in May that its scientists have developed "perhaps the most promising COVID-19 drug in the world." The drug, called Avifavir, is based on an existing flu treatment that Russian researchers have enhanced. Early results from a study of 330 participants showed that it can reduce the duration of the coronavirus to just four days in some patients.

Developing a game-changing treatment or being the first country to approve a coronavirus vaccine would make a definitive statement about the capabilities of Russia's pharma industry. As the country moves to bolster its ability to be an innovative force in pharma, its efforts to fight the coronavirus could help put Russian drugmakers on the global pharma map.

global dose

Ireland

Moving beyond its reputation for low taxes, Ireland's pharma industry aims for new frontiers in manufacturing

By Meagan Parrish, Senior Editor

Every so often, one of pharma's kookiest stories bubbles up from the quaint, coastal town of Ringaskiddy, Ireland and makes the rounds in the global press.

There's something in the air that's making people and animals feel frisky, locals like to tell reporters. The culprit? A Pfizer plant that has been situated in Ringaskiddy since 1969 and for decades, has been manufacturing Viagra. The belief by some is that byproducts from the blockbuster arousal medication have been making their way into the town's water and air, and turning residents into "walking stiffs."*

Rumors have also swirled that local tourism officials have pushed the tales from "Viagra village" as a way to drum up interest in visiting Ringaskiddy. And for a few days, the story inevitably does put Ireland's pharma manufacturing sector on the public radar. But for those inside the industry, Ireland has a much different reputation.

With a marginal corporate tax rate at 12.5 percent (one of the lowest in the EU), major companies, including all of the top players in pharma, have long flocked to the lush hillsides of Ireland to set up shop. In recent years, however, Ireland's business economy has evolved beyond simply being a

* Pfizer, of course, has denied the long-standing rumors, telling The Irish Sun most recently in December that its facilities "all have environmental licenses that strictly regulate air emissions and water discharges" that are in accordance with local environmental law.

About 62 percent of Ireland's exports were pharma products during the first nine months of 2019.

so-called tax haven. Today, the country's pharma industry is becoming known as a hub of cutting-edge facilities geared toward process innovation.

IT'S NOT JUST LUCK

Ireland may be dwarfed in size and population by many of its cousins in the EU, but the country nevertheless commands a mighty manufacturing footprint.

More than 85 pharma companies (including nine of the top 10) operate over 100 facilities in Ireland. All told, the industry exports around $85 billion worth of products each year and is now one of the largest exporters of pharmaceuticals in the world.[1]

Investments in Ireland's pharma manufacturing capacity have also remained steady in recent years. According to Tommy Fanning, head of Biopharmaceuticals & Food of IDA Ireland, the country's economic development organization, the industry has been injected with an average of about $1 billion in annual capital investments over the last five years.

Some of the country's biggest biopharma wins in recent years include a planned vaccine production facility by China's WuXi Biologics that will be located in Dundalk and create about 200 jobs. Merck announced three investments in 2017 and 2018, including a new biologics drug substance facility in Dublin to produce its blockbuster immunotherapy drug, Keytruda. Shire, now owned by Takeda, has also announced two major investments in the last few years, including a new cell therapy facility in Dublin. And the list goes on.

Fanning says that all of this has added up to the creation of a sector with an expertise in molecule development and manufacturing.

"We've moved from being yes, a low tax location, to being very innovative in the context of getting the product to market and making sure that's done efficiently with no break in the supply chain," he says.

Although many pharma firms may have originally been wooed by Ireland's low tax rate, Fanning says that once rooted there, companies find other reasons to stay.

"The big attractor for Ireland today is very much around the regulatory culture and skilled workforce," he says.

Close to 25,000 people work directly in the country's pharma industry, over half of which are third-level graduates.[2] Leveraging the country's skilled workforce remains a top-of-mind for the industry, especially as the sector positions itself to stay relevant in the next era of manufacturing.

TOWARD THE LEADING EDGE

Small and large molecule manufacturing capabilities remain robust in Ireland. But according to Philip Hannon, the communications and public affairs manager of the Irish Pharmaceutical Healthcare Association, Ireland's pharma industry is up against several key challenges including generic production offshoring and a potential loss of competitiveness.

"Potential benefits from next-generation therapeutics will be difficult to capture without significant investment," Hannon says.

Now, laying the groundwork for those investments is exactly where the industry is focused.

"We're looking at what we need to do to make sure we have the infrastructure to support investments in areas like cell and gene therapies," Fanning says. "So we've upped the ante in terms of building skills."

Investments in up-and-coming therapeutic classes, such as cell and gene therapies, are still in the early phases in Ireland. To help turn Ireland into a more attractive location for the kinds of cutting-edge facilities that will be needed for these new therapies, Fanning says that the country's National Institute for Bioprocessing Research & Training (NIBRT) is now pivoting to cell and gene therapy training for pharma employees. The aim is to give Ireland a healthy supply of manufacturing professionals who are poised to propel the country's pharma industry forward.

"These institutes work closely with the industry to understand the needs of the industry and provide the right skills," Fanning says.

Companies in Ireland have also been at the forefront of digitization. Several pharma sites in Ireland are considered "lighthouse projects" in terms of "industry 4.0" adoption and are supported by Ireland's large IT industry. Some companies, such as Novartis and Eli Lilly and Company, are

A big win

Last year, Ireland's own Jazz Pharmaceuticals became the first company to ever win FDA approval for a dual-acting dopamine and norepinephrine reuptake inhibitor to improve wakefulness in adults living with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea.

using their facilities in Ireland to implement next-generation platforms and data analytics operations.

"This has led to a cross fertilization between life sciences, pharma and the IT sector," Fanning says.

The emphasis on digitization has also helped attract a large number of clinical research companies and contract research organizations.

"The idea of digital clinical trials, for example, is going to be even more important with events such as the spread of COVID-19," Fanning explains.

Yet, there are a few issues hanging over the region that are leaving the industry on edge.

REGULATORY UNCERTAINTY

Brexit — it's a word that elicits so much unease in the EU that Fanning refers to it as the "B word."

Despite officially leaving the EU on Jan. 31 and promising to hammer out a deal by the end of this year, the UK has yet to formalize a plan for its departure. Talks among negotiators have been ongoing, even amidst the coronavirus lockdowns, but so far, have mostly ended in frustration on both sides. Thus, the exact terms of the UK's departure and what it means for trade, security and regulations, is still being left to speculation.

Even without a Brexit deal, Ireland's pharma sector has started making adjustments to prepare.

"The concern is to ensure continuity of the supply of medicines to the population," Hannon says. "Because 70 percent of medicines coming into Ireland pass through the UK, particular attention has to be given to transport, customs and other logistics issues."

Hannon also points out that because it's still unclear what the new trade terms will be between the EU and UK, some pharma companies have invested in changing their supply routes to avoid the UK all together.

A "hard" Brexit could also mean that drugs manufactured in the UK or imported into the UK for distribution into the EU might have to be re-tested under the EU's regulatory guidance. According to Fanning, some pharma companies have therefore moved regulatory licenses for drugs they were planning to launch in the UK to Ireland, which will maintain its regulatory clarity under the auspices of the European Medicines Agency.

Overall, Hannon says that the focus in Ireland is on not letting Brexit deliver a blow to the industry.

"The biopharmaceutical industry in Ireland, along with the government and other key stakeholders, has been engaged in intense work to mitigate the impact of Brexit," Hannon says.

Multinational companies in Ireland are also now facing an evolving tax environment. Ireland has long dealt with public outrage over its various tax breaks for large corporations. Now, what's known as the "double Irish" loophole, which has allowed companies to shift some non-U.S. profits to Ireland to avoid higher taxation, is set to be phased out this year. But Fanning says that support for the country's low effective corporate tax rate remains steady.

"Everybody in Ireland understands the benefits we have from a lower tax rate," he says. "It's not going to change."

THE COVID-19 FACTOR

Like the rest of the world, Ireland has been in the midst of a nation-wide lockdown due to the spread of the novel coronavirus. So far, this disruption has not impacted work at the country's pharma plants or caused any shortages in the supply chain. According to Fanning, Ireland's pharma companies have been taking proactive steps to limit the spread, such as implementing staggered shift changeovers to ensure that teams are not exposed to each other, and creating "contact diaries" so that workers can keep track of whom they have been in contact with.

Meanwhile, pharma companies in Ireland have been in talks to see how they can support the global push to manufacture a COVID-19 vaccine once one is approved.

"There is no doubt that we will hear about some part of a COVID-19 vaccine being manufactured in Ireland because we are such a big part of the global supply chain," Fanning says.

It's this importance to both its local economy and the global supply chain that Fanning says will continue to give Ireland a prominent position on the industry's map in the years to come.

"Pharma is hugely important to the economy of Ireland," Fanning says. "The biopharma sector is very strong — and will continue to be."

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global dose

Iraq

Corruption and political unrest create a challenging — but not impossible — pharma environment

By Karen Langhauser, Chief Content Director

Manufacturing and distributing safe, effective and affordable pharmaceuticals is a challenge within itself — add political upheaval and widespread corruption to the scenario and the situation becomes extremely complex.

What many in the U.S. know of Iraq is mired in extreme political conflict, centered around efforts to defeat the Islamic State in Iraq and Syria (ISIS). Former Iraqi President Saddam Hussein, who was executed in 2006, lives in infamy as one of the most brutal dictators in history. In recent news, the U.S. carried out airstrikes against multiple Iranian-backed militia sites in Iraq in retaliation for a rocket attack near capital city, Baghdad.

Yet, in the late 80's, Iraq, which is only about twice the size of the state of Idaho, boasted the largest pharma market in the Middle East — larger than Egypt and Saudi Arabia, which both more than double Iraq in geographical size. At the time, the Iraqi government was investing heavily in health care, aided by a flourishing oil sector. But decades of corruption, inappropriate policies and economic sanctions, now compounded by the coronavirus pandemic, have taken a toll on the country's wider economy.

Iraq's health care system is a mixed initiative of the public and private sectors, and many believe that the strong private sector has the capacity to supplement the struggling public sector. To that end, there exists an opportunity especially for foreign pharma partners to invest their expertise into the market, resulting in a growing

Pharma companies in Iraq must be registered with the MOH Department of Pharmacy

competitive market that will edge out corrupt practice, bettering the health care sector for the Iraqi people.

THE MARKET

Iraq was established as an independent state in 1932, on land that was home to ancient Mesopotamia civilizations. Up until the 1950's, Iraq, with a portion of its land mass part of the historical Fertile Crescent, had an economy dependent on agriculture and farmlands. The discovery of oil nearly a century ago began shifting the country's economy heavily towards petroleum exports.

Iraq's GDP was $225.50 billion in 2019, according to World Bank figures, placing the country just within the top 50 global economies. The GDP is driven by industry — mainly the oil sector, which provides roughly 85 percent of government revenue. Less than 4.5 percent of the country's GDP is spent on the health care sector, giving Iraq one of the lowest percentages of pharma spending as a proportion of GDP among countries of the same economic class (for comparison, the U.S. spending percentage is around 18).[1]

Despite this, the pharma sector in the Middle East as a whole has observed remarkable growth over the last few years. Iraq's pharma market today is worth around $3.5-4 billion. Business Monitor International estimates that the Iraqi pharma market grows about 10-15 percent per year.[2] Ali Mosawi, founder and chairman of Al Hayat Scientific Office — one of Iraq's oldest pharmaceutical agents and trusted partner to many of the world's leading pharma companies — is inspired by current happenings.

"There is a vibrancy in the country and our market which I have not seen for some time, driven by the enthusiasm of the young population. Before the current pandemic, the cities were again becoming exciting centers of intellectual and academic study, with medical and scientific academies overwhelmed with applicants and corrupt practices being put under ever greater scrutiny," he says.

REGULATORY STRUCTURE

Iraq's Ministry of Health (MOH) is broadly responsible for ensuring the availability of safe and effective drugs. Drugs are approved by the special committee for the

National Board of Drug Selection (NBDS) operating under the MOH.

The speed of drug approvals in Iraq is improving, with timelines estimated at around two years and as quick as six months for drugs going through the accelerated review pathway. Iraq is increasingly supportive of approvals from regions with stringent regulatory authorities (such as the EU's EMA or the U.S. FDA) for fast track approval.

Pharma companies in Iraq must be registered with the MOH Department of Pharmacy. Once registered, every product needs to be tested and licensed. It is possible for international companies to bypass the prerequisite of company registration if they do business through a local partner who imports the product from them. Al Hayat, for example, is AstraZeneca's exclusive agent in Iraq, providing market access, facilitating participation in pharmaceutical tenders, and ensuring the reliable and compliant distribution of AstraZeneca drugs.

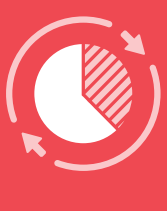
Iraq's NBDS derives an Essential Medicine list which indicates the medicines that hospitals and pharmacies should stock at all times. Getting products on the list is beneficial for pharma companies, but, according to Mosawi, the process isn't easy.

"You must explain why there is an essential need for that drug in the country, as well as the cost efficiency of adopting it. Once you have approval, you go through a registration process. You will get an import license during the registration process so that the drug can be made available to the private sector."

COUNTERFEIT DRUG PROBLEMS

Most assessments rank Iraq as the "highest risk" when it comes to political and business climates. Much of this is attributed to ongoing political unrest. Anti-government protests reached a peak last year, as demonstrators took to the streets in mass to protest corruption, unemployment and what they saw as government failure to use oil revenues on public services, such as health care.

Corruption is also a contributing factor to increased risk. For years, scattered, anecdotal accounts have been trickling out of



There are ~8,600 trade drugs registered with the MOH, and Iraq has 28 national pharmaceutical companies

Source: Open Access Rheumatology: Research and Reviews 2019:11

Iraq about the severity of the health care situation — stories about patients lashing out, sometimes violently, at doctors for misdiagnosis or prescribing medicine that had caused complications, only to find out later that counterfeit medicine was to blame.

In 2014, Iraq's counterfeit drugs industry had an estimated worth of $1 billion a year — a fifth of all pharmaceutical sales in the country.[3] A more recent Reuters report claimed that 40 percent of medicine in the market is smuggled from countries including Turkey, Iran, Jordan, Lebanon, India and China, according to public statements from health officials.[4]

Mosawi contends that the situation is difficult but not impossible. "Yes, there are unscrupulous actors who seek to take advantage of the Iraqi market and this remains a constant challenge for us." Al Hayat, however, has found success by working with international partners who insist on strict compliance standards.

"We now view our regulatory responsibilities through the same lens as the international ones of partners like AstraZeneca, Sanofi and Pfizer, who are beholden to the Foreign Corrupt Practices Act and European directives on anti-money laundering and corruption," says Mosawi.

Each batch of medicine distributed by Al Hayat is marked by a secure double hologram system, reassuring pharmacists that the drugs are 100 percent genuine. In addition, Al Hayat stores its medical products in state-of-the art warehouses at which strict quality control procedures as defined by the World Health Organization are enforced.

FUTURE HOPE

As the world battles the health and economic implications of the coronavirus pandemic, progress on preexisting challenges within Iraq's pharma sector may understandably be slowed. But gradual pushes by the government are helping to rebuild an ailing system.

In 2019, the MOH enacted reforms to allow private businesses to own hospitals. On the regulatory side, the MOH has driven forward the need for stricter compliance requirements in the sector, supported by growing expertise coming from the country's medical schools.

"This, with the requirements of global companies entering the market, has created pincer pressure which has driven the expectation ever higher," says Mosawi. "The sector is making great strides in the right direction. As international partners continue to grow in the market, their standards of safety and compliance can only further promote this growth."

For a full list of references, visit pharmamanufacturing.com.