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Putting COVID learnings into practice

Market focus: Canada

SEPTEMBER 2020

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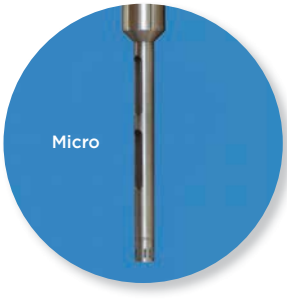

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FEATURES

DEPARTMENTS

Meagan Parrish
Senior Editor

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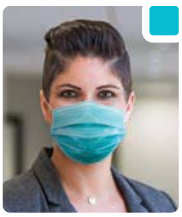
Karen Langhauser
Chief Content Director

Manufactured patriotism

The government wants to reshore generics, but the drug industry isn't celebrating



I was recently involved in a debate amongst friends over whether or not Labor Day should be considered a "patriotic" holiday.

Labor Day honors the American labor movement and pays tribute to the contributions and achievements of American workers. Stemming from the Industrial Revolution, the labor movement and subsequent rise of unions created a way for common workers to achieve collective bargaining power. These early factory workers not only played a key role in transforming our country into an industrialized nation, but through protests, strikes and negotiations, their unions fought for shorter work weeks, safer working environments, health benefits and an end to child labor.

But deciding what falls within the definition of patriotism may simply come down to individual opinion.

Consider the push to "buy American." While the concept dates back to President Hoover and has been applied to many segments of manufacturing throughout history, the Trump administration's recent executive order targets the drug industry specifically, ordering federal agencies to purchase (FDA-deemed) essential drugs and medical supplies from U.S. factories.

In many ways, this was a long-time coming. Pre-COVID, drug ingredients from China had triggered several prominent recalls, calling into question the safety of drugs made with foreign ingredients. The emergence of a pandemic out of China brought about supply shortages in the U.S., and with that came revelations about the vulnerability of the U.S. supply chain and a growing anti-China sentiment among lawmakers.

On the surface, focusing on the resiliency of American drug supply chains was warranted. The executive order aims to reduce U.S. overdependence on foreign nations and attempts to guard against shortages of critical supplies.

But the plan lacks specifics and perhaps more importantly, universal buy-in from the pharma industry. As the industry knows all too well, the economics of making generic ingredients and finished products are not on America's side. The high costs of labor, adhering to environmental standards and keeping up with FDA regulations are often cited as major obstacles to reshoring.

And yet some companies — like the one that nabbed one of the largest BARDA contracts in history — say reshoring is feasible. Phlow, a Virginia-based startup, plans to use its BARDA bucks to utilize automated continuous manufacturing methods to produce APIs. The company also says it has been tweaking the process to make it more efficient and environmentally friendly.

Still, not everyone in the industry is convinced, and the overarching concern is that moving production to the U.S. will eliminate redundancies and actually increase supply chain risks — and may end up driving up the cost of drugs.

Circling back to the discussion of patriotism, this situation begs the question: Is patriotism the act of using U.S. labor to produce drugs on U.S. soil or is it making sure that all Americans have access to the highest quality, affordable drugs?

Perhaps real victory will come in figuring out how to do both. Rather than one-off grandiose measures, the government can help build a foundation for a long-term plan to make reshoring more attractive to companies. Meanwhile, the industry can more rigorously vet its international supply chain partners.

With the government as a financial partner, the pharma industry can find a balance that best benefits American patients — and that's something worth celebrating with fireworks and flag waving.

industry dose

Meagan Parrish
Senior Editor

Pharma's warp drive

The key factors helping drugmakers develop a vaccine in record time

In the world of sci-fi fandom, a debate has long simmered about the possibility of traveling in hyper-speed like the Star Trek Enterprise, which could blast through space in "warp drive" — or, faster than the speed of light.

So when the time came to decide if pharma could move faster than ever before to develop a coronavirus vaccine, it's perhaps no surprise that one of the industry's top regulators drew from that idea and dubbed the White House's vaccine initiative Operation Warp Speed (OWS).

Since being announced in April, OWS has doled out billions of dollars to help companies develop candidates, ramp up manufacturing and prepare distribution to meet the government's lofty goal of delivering 300 million doses of a SARS-CoV-2 vaccine by January 2021. But as several drugmakers approach the finish line, concerns are also mounting that the industry could be moving *too* fast.

Although the flurry of action is aimed at shrinking the typical 10-year timeline for developing a new vaccine down to less than 18 months, Phyllis Arthur, vice president of Infectious Diseases and Diagnostics Policy at the Bio-technology Innovation Organization (BIO), argues that the process shouldn't be called "rushed." Rather than speeding through the clinical trials that test safety and efficacy, Arthur says that the FDA has come up with new efficiencies that streamline the often lengthy regulatory process.

Be on the lookout for next month's cover story where *Pharma Manufacturing* will explore pharma's role in combating an alarming rise in vaccine hesitancy.

Here are some of the key factors Arthur says are helping pharma along:

Master protocols: Instead of having each individual vaccine developer work directly with the FDA to create a protocol for their clinical trials, the agency has created a "master protocol" for all companies developing a SARS-CoV-2 vaccine. According to Arthur, the master protocol establishes uniform criteria for assays and primary endpoints that makes it easier to compare vaccines without having to do a head-to-head trial.

Earlier this year, the FDA also released a guidance to the industry called "Development and Licensure of Vaccines to Prevent COVID-19," that explains what the requirements will be for a SARS-CoV-2 vaccine to be approved. In the guidance, the agency lists the parameters for chemistry, manufacturing and controls, toxicity studies and licensing, and standardizes primary endpoints for clinical trials.

With hundreds of coronavirus vaccines in development, Arthur says that these efforts to streamline the development of a vaccine have been critical to speeding the regulatory review process for companies in the hunt.

"Having regulators gain agreement across industry and across regulatory agencies on what all the companies would do the same [in clinical trials] was certainly helpful in speeding the research process," Arthur says.

Clinical trial networks: Setting up clinical trials is an "arduous and complex set of activities," Arthur says. In addition to finding trial sites and health care professionals, pharma companies also have to recruit enough participants.

So, the National Institutes of Health (NIH) has set up clinical trial networks that have helped streamline this process for vaccine developers. By working with a network of contract research organizations and other government agencies, the NIH has propped up a coronavirus vaccine trial network that now spreads to every corner of the country. Collaboration between the major arms of the government under OWS — including the NIH, the CDC, the FDA, BARDA and others — is also playing a critical role in creating a network of support for drug developers.

The NIH has also made it easier for drugmakers to find volunteers, which Arthur says is one of the longest parts of the clinical trials process. To sign up for a clinical trial, volunteers can now fill out an online application through the NIH website.

Arthur says that the NIH has also increased its outreach efforts to make sure that trials include volunteers with different ethnic backgrounds and underlying health conditions. These efforts have not only helped companies find enough volunteers to move them quickly through the different phases of clinical trials, it could also play a role in getting more people to take a coronavirus vaccine once one is approved.

"Doing outreach to communities of color and showing how clinical trials are done is one of the most important things to building trust and having the broadest reach," Arthur says.

Long-term follow-up: Although the industry has been aided by these new efficiencies, there's no getting around the fact that in order to develop, test, manufacture and distribute a vaccine by the target date set by OWS, pharma companies won't be able to conduct long-term safety studies before approval.

"There is going to be less long-term safety data than what you would see with vaccines in the past," Arthur admits.

But serious side effects associated with vaccines are rare. Companies will also be expected to conduct post-market safety analysis of their vaccine if it's approved, and Arthur says there is a "very strong commitment among regulators to robustly follow-up on these vaccines."

Arthur also argues that people should consider the unique nature of the situation.

"It's important to note that this is a pandemic," she says. "You have to think about it in terms of a risk/benefit ratio, and especially consider the risks of an unknown pathogen and its bad outcomes on individuals, the community and the economy."

Although Arthur acknowledges that questions and concerns about safety should be addressed, she also contends that approving a vaccine before long-term safety studies can be conducted is not a "short cut" — it's a tradeoff.

"I think that people are right to ask these questions," she says. "But my question is: How long do you want to live in this pandemic state? That is the tradeoff that needs to be made."

Canada wants to double the size of its health and biosciences sector and become a top-three global hub by 2025 — can it get there?

READ OUR GLOBAL DOSE FOCUS ON CANADA ON PAGE 16

Meagan Parrish
Senior Editor

Bring

Inside the movement to put generic drug production back on America's shores

it home

Without the coronavirus pandemic, it's possible that the impact of Rosemary Gibson's work would have mostly been felt inside the policy and industry circles of pharma. But in the topsy-turvy world of COVID-19, experts have suddenly been propelled to a new kind of notoriety as they've been called upon regularly to explain the various issues in our health care system — Gibson among them.

Since publishing her book, "China RX: Exposing the Risks of America's Dependence on China for Medicine," in 2018, Gibson has been kicking up a storm about our over-reliance on drug imports — particularly active pharmaceutical ingredients (APIs) for generic drugs. And evidence of our vulnerability to China's control of the drug supply was on display even before the coronavirus.

In 2018, a massive recall of blood pressure medications swept through the industry, triggered by tainted APIs from China. By the end of 2019, the push to improve the quality and security of America's global supply chain was gaining bipartisan steam in Congress.

Then, the pandemic struck. As U.S. hospitals reeled, shortages of personal protective equipment and essential medicines gripped the public consciousness and revealed weaknesses in our health care supply chains. The finger pointing and calls for change were swift — and the revelations about America's vulnerable supply chains collided with coronavirus frustrations and an anti-China drumbeat growing louder among some lawmakers.

Cue the "China virus." Cue an increasing sense of nationalism about America's drug supply. Cue the calls to put drug manufacturing back on home soil. Cue Rosemary Gibson.

"It's a great day for our country," Gibson said in mid-May on a prominent daily radio show.

Her appearance was scheduled within days of the U.S. government announcing an agreement worth up to $812 million with Phlow Corp., a startup in Virginia promising to provide end-to-end manufacturing capabilities for a host of essential generic medicines.

"Tomorrow morning, Americans will be going to work to make critical medicines that we need to help people with coronavirus recover. Those medicines will be made right here, in the United States of America," she said.

The movement to reshore generic drug manufacturing to the U.S. was truly underway.

The case for reshoring

In the months following the Phlow announcement, the efforts to support American generic manufacturing gained momentum. In addition to quality and supply concerns, the implications for America's national security continues to play a dominate role in calls for reshoring.

China hasn't withheld drugs from America yet, but as trade tensions rise, turning off the drug spigot remains an option for Beijing. In late August, as if to prove the point, the *South China Morning Post* reported that a high-profile economist and government advisor in China suggested that Beijing should weaponize its exports of drugs if the U.S. cuts off its supply of semiconductors.

"We will not take the lead in doing this, but if the U.S. dares to play dirty, we have these countermeasures," the Chinese advisor, Li Daokui, said.

Impact of the CARES Act

In March, Congress passed sweeping legislation aimed at providing economic relief during the pandemic. The CARES Act also included key provisions for drugmakers designed to mitigate coronavirus-related shortages that could also reveal more about America's supply chain for generic drugs including:

- Expanded reporting requirements for potential shortages, including projected API shortages and reasons for the shortage
- New volume data on the "amount of each drug … that was manufactured, prepared, propagated, compounded, or processed … for commercial distribution" in the U.S.

The new reporting requirements were supposed to take effect on Sept. 23, but the FDA recently stated that the electronic portal it is creating for data submissions isn't up and running yet.

With these threats looming, arguments for moving production away from China have found a welcome home in the White House.

In August, President Trump signed an executive order with provisions that require that certain government agencies begin buying "essential medicines" — which will be determined by the U.S. Food and Drug Administration — from companies in America. The so-called "Buy American" order exempts certain drugs if they are already in abundant supply or if procuring them in the U.S. would increase the cost by more than 25 percent.

Yet, a major problem has been hanging over the White House's approach — the pharma industry isn't exactly enthused.

With each new executive action, blowback from trade groups has intensified. Although industry discontent started with widespread acknowledgement that the U.S. has lost too much manufacturing ground in the market for generic drugs, concerns about the deals the government has struck and the mandates being handed down are creating friction in the efforts to bring essential medicines production back home.

Rising China

Behind the scenes, Gibson is humble and thoughtful as she describes China's "deliberate strategy to drive Western companies" out of the generic drugs business.

Despite the fact that her work plays into the suspicions and hostility towards China that has seized political discourse on the right, Gibson maintains that she isn't aligned with any special interest — and that, in fact, being an outsider has allowed her to more openly speak the truth.

"I've been doing briefings to people in the legislative and executive branches to help them better understand this space," she explains. "I think people know I don't have an axe to grind, and that gives me a very valuable role to play. I'm honored to do it."

Although she has become a leading voice on the issue and has testified before Congress, Gibson was by no means the first to report on it. For over a decade, the story of penicillin has often been cited as a grim case-in-point.

After World War II, penicillin was mass manufactured in plants around the U.S. But in the 1980s, China upended the market by making major investments in penicillin fermenters, which sunk its price on a global scale. In 2009, *The New York Times* reported that Bristol-Myers Squibb had shuttered the last plant in the U.S. that manufactured APIs for antibiotics like penicillin, leaving the U.S. exposed to any supply chain disruption that could arise.

Within a few years of BMS' plant closure, lawmakers began to express anxiety about America's over-reliance on China for several essential drugs and the FDA's lack of adequate data on exactly how much APIs the U.S. is sourcing from abroad. Over 10 years later, the story is much the same.

Although the FDA knows the number of API facilities in the U.S. and abroad, the agency still doesn't track the exact volume of imports for APIs into the U.S. supply chain. In "China RX," Gibson claims that China controls 80 percent of the U.S.'s supply for core generic drug components — an estimation that is now frequently cited as proverb by lawmakers and often in the press. In reality, the exact volume is anyone's best guess.*

There is substantial evidence, however, that generic API manufacturing capacity is growing overseas. Every year in the Federal Register, the FDA releases its outline of fees being levied under the Generic Drug User Fee Amendments (GDUFA). In addition to collecting fees for new generic drug approval applications, the FDA also sets a rate for API plants based on the number of facilities calculated from generic drug submissions.

In the last few years, the number of generic API facilities identified in the U.S. has remained stagnant — 81 for fiscal year 2021, 76 in 2020, and 79 in both 2019 and 2018.

Internationally, however, the number of generic API facilities continues to climb — 583 were identified for fiscal year 2021, up from 548 in 2020, 534 in 2019 and 513 in 2018.

"With the GDUFA fees, one of the things that has come to light is the smaller number of facilities that manufacture APIs in the U.S.," explains John DiLoreto, executive director of the Bulk Pharmaceuticals Task Force, a trade organization representing API manufacturers. "The smaller the universe of domestic API manufacturers you have, the more pressure there is to bring more manufacturing capacity back to the U.S."

When looking further up the supply chain at key starting materials (KSMs), the needed precursors for APIs, the situation could be even worse.

"A lot of these are both basic commodity and specialty chemicals," DiLoreto says. "There might be a few key suppliers in the U.S.…but KSM manufacturers are scattered around the world and centered in China."

Much like APIs, the economics of making KSMs are not on America's side. Manufacturing KSMs is widely considered a dirty affair that can generate a large amount of toxic byproducts and waste, making China — where environmental regulations are generally not as strictly enforced as in the U.S. — a more desirable locale for production.

For generic APIs, the high cost of keeping up with FDA regulations also continues to play a strong role in diminishing the appeal of American manufacturing. While U.S. facilities have to prepare for FDA inspections that occur — often without warning — at least every two years, overseas companies are not investigated as often and always know when the FDA is on the way.

"API manufacturers want a level playing field," DiLoreto says. "It takes a lot of resources to put a quality program in place."

But despite this backdrop of challenges keeping generic drug manufacturing out of the U.S., Jonathan Kimball, the vice president of Trade and International Affairs at the Association for Accessible Medicines (AAM), the U.S. generics industry's largest trade organization, argues that the supply chain issues may not be as bad as they seem.

Is reshoring even necessary?

When asked if the concerns surrounding China's control of the generic drugs may be overblown, Kimball doesn't hesitate.

"Definitely," he says. "When you look at how the generics industry has performed since COVID, for the vast majority of products, the market has operated very well."

One of the biggest concerns since the coronavirus pandemic began is that supply chain disruptions could trigger drug shortages.

For years, the FDA has leveraged a number of tools to help mitigate drug shortages and the efforts have paid off. In the last decade, the number of new shortages reported each year has fallen dramatically. (The total number of drugs on the FDA's shortage list, however, has stubbornly hovered each year around 100.)

In late February, Stephen Hahn, the FDA's commissioner, tweeted that no drug shortages had been reported — even for the 20 drug products sourced solely from China — because of COVID-19. Some shortages did arise in spring, especially as demand spiked suddenly for certain medicines, such as hydroxychloroquine. Yet, many of those shortages were quickly resolved.

"In the instances where there have been shortages, it's because companies could not have predicted the necessity of the COVID-related drugs," Kimball maintains.

Rather than reshoring production, Kimball and others argue that if America wants to bolster its generic drug supply chain, there is a better way.

Alternate supply chain fixes

"Reshoring sounds for some like a silver bullet," says Vincent Colicchio, vice president and head, Supply Chain and External Manufacturing — North America Generics at Dr. Reddy's. "But at Dr. Reddy's, that is not a foregone conclusion.

* Some have publicly questioned the validity of Gibson's 80 percent estimate, which includes KSMs and APIs, that she says was based off a comparison between the U.S. market and an estimate made by the Indian government, who stated that they receive about 70 percent of their KSMs from China. "If India is in that situation then the U.S. must be in at least the same situation," she says. "Add on top of that the substantial percentage of APIs we get from China, and that's how I came up with 80 percent." That figure is also in line with estimates from other major countries — such as Russia — about the volume of generic API imports they receive from China.

We will evaluate reshoring on a holistic basis and determine the benefit over the long term."

Based in India, Dr. Reddy's is one of the world's largest generic drug manufacturers. Currently, Colicchio says that Dr. Reddy's manufactures 70-75 percent of its finished dosage forms for the North American market in India and the U.S. Because India is also a purchaser of APIs sourced from China, the country has been affected by many of the same supply chain concerns as the U.S. To make sure that the company does not experience severe disruptions, Colicchio says that Dr. Reddy's is taking several measures to "de-risk" its supply chain.

The idea, Colicchio says, is to always do a bit of doomsday prepping in order to make sure that any sudden shift in demand will not quickly deplete stocks.

"We strive to maintain sufficient finished goods inventory levels with at least two to three months on hand. That's why it's critical to procure sufficient levels of APIs and other raw materials." he explains. "In pandemic conditions, it is advantageous to target having at least three to four months of API supply available to deal with potential disruptions, which will also help stabilize your cost of goods in the event that suppliers increase API costs."

Colicchio also argues that reshoring in America could put patients at risk by potentially causing dramatic price increases.

"If the federal government mandated that companies had to produce a high percentage of pharma products in America within the next 10 years in order to minimize the dependence on India and China, that ultimately will cost them more — not 10 percent more, but potentially 30-40 percent more."

To be further prepared for sudden API supply shortages, Colicchio says that companies should also ensure they have secondary suppliers lined up.

"Let's say the FDA inspects one of your API suppliers and identifies there are significant compliance gaps at their production facility. They could halt API production — for weeks to months — until the compliance violations are remediated," he says. "You need to have a secondary API supplier in place to ensure business continuity."

DiLoreto also argues that moving production to the U.S. isn't going to eliminate supply chain risks.

"It would be great if we could identify all of the KSMs and APIs and bring them back to the U.S., but then you don't have redundancies," DiLoreto says. "What if you were manufacturing in the U.S., let's say in Florida, and there was a hurricane coming? Then what would you do?"

Kimball also points out that despite the threatening rhetoric from Beijing, there are major financial disincentives in China to cutting America off.

"China is an important part of our industry, so we hope that they will continue to play a responsible role in delivering medicines," Kimball says. "But the real goal is ensuring that there are redundancies so that if there are disruptions, other countries are able to stand up and produce more of what's needed."

Yet, despite the efforts from regulators and industry to shield the generics supply chain from hiccups, and the arguments that the market is generally performing well, the push to reshore production — at least for "essential" medicines — is clearly on course. Now the question is: How can the industry get in on the action?

100 billion = Generic drug doses manufactured annually in the U.S.

Association for Accessible Medicines

Engaging the industry

For proponents of reshoring, the generics manufacturing deal with Phlow was the first victory on a road being built to create jobs, provide economic stimulus, and reduce our reliance on API imports. Months later, another deal to make generic APIs was announced — this time it was a $765 million loan with long-time camera and chemicals maker, Eastman Kodak.*

But inside the generics industry, many were scratching their heads. Why did the first major contracts created to reshore essential medicines production go to companies without a proven track record in generic drug manufacturing?

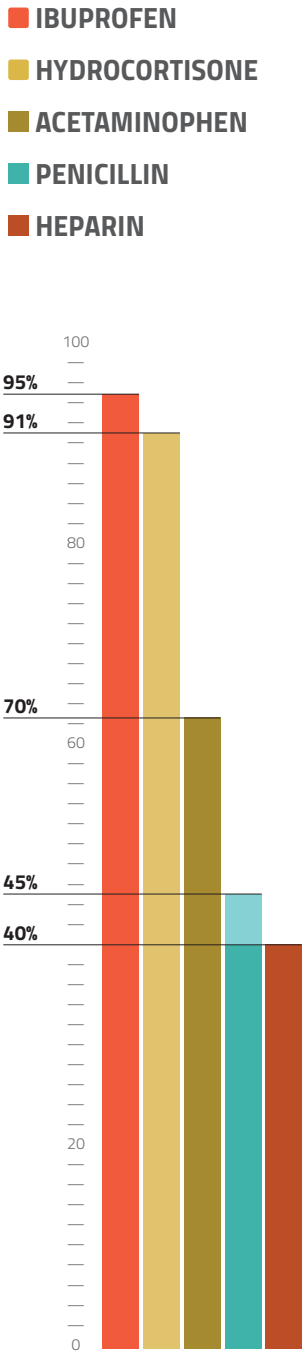
"Almost every one [of the manufacturing companies] said, 'How do we get considered for a deal like that?'" explains DiLoreto. "As existing API manufacturers, they were dismayed by not having an opportunity to be a part of any government effort to increase API manufacturing."

This lack of engagement from the White House didn't set a cooperative tone. As far as DiLoreto knows, the generics industry was not approached before the

* Within days of the Kodak announcement, the loan was put on hold after the Securities and Exchange Commission (SEC) launched an investigation into potential wrongdoing associated with trade and executive stock purchases made around the time the deal went public. The loan will remain on hold until the SEC completes its probe, which could take months.

China's chokehold

The amount of imports from China into the U.S. for key drugs



—2018 U.S. DEPARTMENT OF COMMERCE DATA

Phlow or Kodak deals were finalized and there was no apparent bidding on the contract.

"I think there was a lot of concern that these contracts were given to any existing manufacturer…without looking at how [the government] could get a good deal by inviting competition," DiLoreto says. "It was a fire, shoot, aim approach. They are jumping into the river but don't have a boat yet."

Kimball would not comment on whether or not AAM was contacted by the White House ahead of the Phlow announcement. But, he said that AAM is in talks with a number of people in the Trump administration about what can be done to attract additional investment for its member companies.

"Our policies have received strong support from the Trump administration," Kimball says. "We've had a number of good discussions and we hope that as policies develop further we will continue to engage in those conversations and they will be supportive of broad-based generics manufacturing."

The policies Kimball is referring to were included in AAM's "Blueprint for Enhancing the Security of the U.S. Pharmaceutical Supply Chain," which was created by the organization to demonstrate how the White House should use more carrots than sticks to make reshoring attractive.

Show me the money

Since the "Buy American" policy was first floated by the White House this spring, the issue has riled the entire pharma industry — from branded to generics. Although there is support for some of the measures in what became Trump's executive order in August — such as identifying vulnerabilities in the supply chain — many contend that mandating government purchases from U.S. suppliers could do more harm than good.

In June, Stephen Ezell, vice president of Global Innovation Policy at Information Technology and Innovation Foundation, a Washington think tank, published an in-depth smackdown of the order, concluding that "Buy American policies…could unwittingly reduce supply chain resiliency, while doing little to boost U.S. innovation competitiveness."

"A better solution would be to use financial incentives," Ezell says.

Among the policy initiatives that Ezell recommends are more investment in R&D for advanced manufacturing processes and leveraging the tax code to encourage greater levels of drug manufacturing.

"America needs policies that encourage but don't compel the reshoring of production," Ezell wrote in his analysis.

AAM's "Blueprint" involves similar policy recommendations, including a 50 percent tax credit to "offset the costs of manufacturing medications on the priority medicines list."

"Our proposal involves everything from tax incentives to grants to an international trade agreement that recognizes the value of the global supply chain," Kimball explains.

Overall, Kimball says that the U.S. should focus on ways to make reshoring a safe bet for manufacturers.

"How do you create a system in the U.S. that encourages generic production that is competitive and doesn't lead to higher prices? That is the equation that we think is going to be very difficult to answer," he says.

Yet, as the deal with the U.S. government shows, Phlow Corp. thinks they have an answer.

Intensifying the process

Despite the eyebrows that were raised after the Biomedical Advanced Research and Development Authority (BARDA) announced that it had tapped a newcomer on the generics scene to receive the massive manufacturing contract, Dr. Frank Gupton, one of Phlow's co-founders, says that having a bit of outsider perspective has given the company an edge.

Launched with CEO Eric Edwards — who previously co-founded a pharma firm called Kaleo —Phlow has been willing to approach generics manufacturing with fresh eyes to see how the system can be improved, says Gupton, a long-time pharma and chemical engineer.

Originally, Edwards and Gupton had set their sights on manufacturing hospital treatments for pediatric patients struggling with rare, genetic diseases. But Edwards was also struck by another problem: hospital patient deaths due to drug shortages. With Gupton at his side and the coronavirus spreading, the pair eventually sharpened their focus on manufacturing essential medicines. Recognizing that they could help provide a solution to shortages, Edwards contacted the U.S. Department of Health and Human Services (HHS) and pitched an idea for end-to-end manufacturing. Through this relationship, the BARDA deal with Phlow was born.

Now, the name of the game at Phlow is process intensification. In addition to using automated continuous manufacturing methods to produce APIs, Gupton says the company has been tweaking the process to make it more efficient and environmentally friendly.

Congress is weighing several bills banning government drug purchases from China including the "Protecting our Pharmaceutical Supply Chain from China Act."

"One of the areas I was always concerned with is catalysts," Gupton explains. "There is one that is used a lot in API manufacturing that is made from heavy metals that are highly toxic. You have to do multiple operations to purify the drug."

Using a new technology, Gupton says that Phlow is able to "immobilize the catalysts on a solid support to separate them," which he says improves the process, reduces waste and "has a much smaller footprint than in the past."

"No one has committed to this kind of low-cost, automated manufacturing," Gupton says.

As part of the four-year $354 million contract BARDA (which includes a potential $458 million option after the base period to maintain long-term sustainability), Phlow will set up end-to-end capabilities to manufacture essential generic drugs for the strategic national stockpile using KSMs sourced from AMPAC Fine Chemicals, APIs made by Phlow, and finished dosages produced by Civica RX, a nonprofit created in 2018 to manufacture generics for a consortium of health systems and hospitals. Gupton says that if a particular KSM is not available in the U.S., AMPAC will find a workaround by using a different chemical or engineering process.

Under another deal with HHS, Phlow has already delivered more than a million doses of five different drugs for the national stockpile. Gupton says that Phlow, which is registered as a public-benefit corporation, doesn't know exactly when it will start cranking out essential drugs for the BARDA agreement, but that it could be a few years.

"We've got our heads down," he says. "We're working hard every day."

Gupton says that Phlow plans to price its drugs lower than other generics on the market, but doesn't know how much lower that price will be yet.

"Our goal is to be competitive," Gupton explains. "We will look at every aspect to make sure that we've identified every opportunity [to keep prices low]."

One thing that is for certain: Even without the U.S. government investing in reshoring, the tide could be turning against Chinese drug manufacturing.

America or bust

The way Harry Moser tells it, American industries have been "spoiled" by China for far too long.

"China is now looking to clean up its environment, so over time, they will not be as enabled for low-cost manufacturing," Moser, president at Reshoring Initiative, a think tank/trade association aimed at bringing manufacturing back to the U.S., says. "If [the generics industry] thinks they'll be saving money by having the Chinese dump their chemicals into a river, that won't happen forever. That advantage is going to be taken away."

Gupton also sees the market shifting away from favoring China in the long-run.

"The current issues associated with sourcing health care out of China are quite obvious," Gupton says. "However, over the long-term, the federal government is in the process of creating a more level playing field for U.S. manufacturers to effectively compete with Chinese health care providers for formulated products and active ingredients, as well as key building blocks to produce these materials."

The current landscape may still be tilted in China's favor, but Moser is unmoved by arguments that America can't rebuild its generic manufacturing infrastructure.

"Can it come back in five years if companies get started now? Or would you rather still be dependent on China?" Moser posits. "Or are you willing to put in the effort, money and work to be self-sufficient again?"

Although Republicans have wholeheartedly embraced the issue of wrestling manufacturing out of China's hands, bipartisan support for

producing essential medicines in the U.S. remains strong. None of the experts interviewed for this article think that the results of the 2020 presidential election will hinder the momentum towards reshoring.

"We wouldn't lose steam under [Joe] Biden," Moser says.

Yet, there is hope in the industry that instead of one-off measures, the government will come forward with a comprehensive, long-term plan to make reshoring more beneficial for companies here.

"The government hasn't yet engaged the generics industry the way they have with [coronavirus] vaccine manufacturers like Moderna, Pfizer, AstraZeneca, GSK, etc., and also with new alliance corporations to provide COVID-19 pandemic medicines," Colicchio says. "Engaging generics companies now to open a dialogue to provide affordable medicines is an important step that will help." DiLoreto agrees.

"If the whole point of reshoring is to ensure that we have essential medicines in the U.S., then we should know what those drugs are, how we get them here and start laying the groundwork for how we can manufacture them in the U.S.," DiLoreto says.

Going forward, Kimball says that the industry will need the government to be a financial partner in the efforts to bring generic manufacturing back.

"What the Phlow contracted demonstrated is that you need government investment," he says.

As for Gibson, she'll still hold a front row seat in the efforts to reshore for the foreseeable future. Now a member of Phlow's board of directors, Gibson says she'll use her role to help ensure that the company continues working "in the public interest." She also points out that it will be up to other companies in the generics industry to demonstrate that they're willing to do their part to secure America's supply of generic drugs.

"We have had drug shortages in this country for 20 years and nobody stepped up to the plate to offer to help fix them. Nobody," she says. "You have to show that you're willing to help — not just to take, but to give."

Karen Langhauser
Chief Content Director

Focus on: Canada

Hindered by policy, the pharma industry pushes to build on its solid foundation

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.

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."

The Canadian pharma industry supports 34,000 jobs in Canada

Source: Innovative Medicines Canada

Getting to market

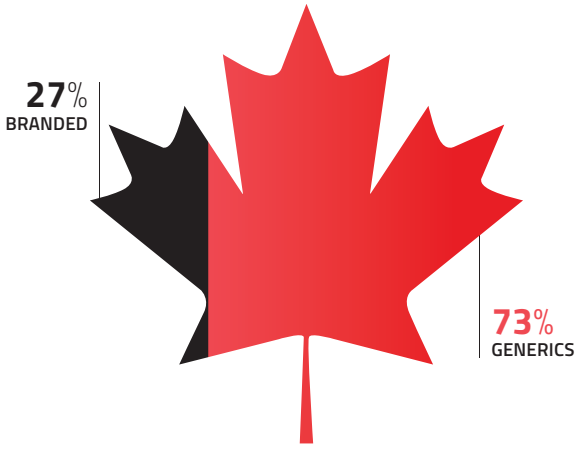
A well-known obstacle when it comes to bringing drugs to the Canadian market is the country's lengthy marketing approval timeline. And while Health Canada's drug approval process is frequently criticized for being slower than its American or European counterparts, the regulator is just one part of a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

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 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.

References

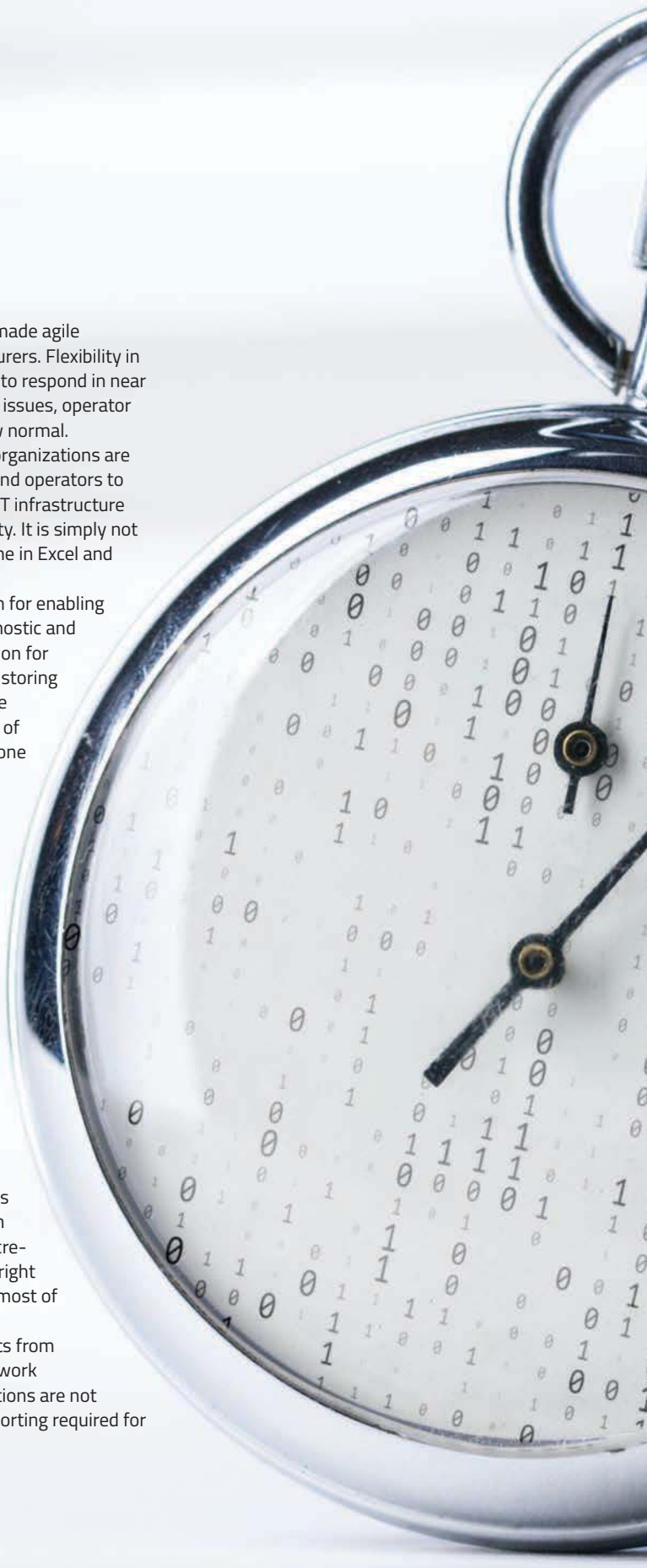
1. *The Innovation & Competitiveness Imperative: Report of Canada's Economic Strategy Tables — Health and Biosciences. September 2018.*
2. *Canada's pharmaceutical industry and prospects. Government of Canada. Accessed Sept. 1, 2020*
3. *Workman, Daniel. Canada's Top 10 Exports. World's Top Exports. Aug. 18, 2020*
4. *Shepherd M (2018) U.S. Drug Importation: Impact On Canada's Prescription Drug Supply. Health Econ Outcome Res Open Access 4:146.*

The unprecedented market conditions of 2020 have made agile operations the new imperative for pharmaceutical manufacturers. Flexibility in scheduling and manufacturing capacity, as well as the ability to respond in near real-time to constraints — whether in raw materials, quality issues, operator availability or asset reliability — are requirements of the new normal.

From primary research to production (Exhibit 1), pharma organizations are seeing an increased need to empower scientists, engineers and operators to make data-driven decisions. However, the existing data and IT infrastructure for many companies does not support this level of adaptability. It is simply not possible when data is trapped in silos, analyses are being done in Excel and collaboration is happening via email.

Cloud-based data storage and analytics present a solution for enabling access to data across the tech transfer stages, creating diagnostic and predictive insights, and harnessing machine learning innovation for production optimization at scale. This addresses the issue of storing petabytes of available data, the variability of this data and the problems that need to be solved at "the speed of now" — all of which add up to too much complexity for humans working alone with spreadsheets.

As organizations adopt cloud-based innovation for advanced analytics — the benefits include improved cycle times, reliability and yield — along with quicker time to market for faster returns on R&D investments. Some of the common use cases for analytics at various stages of scale-up include quality by design modeling, verifying quality with golden profiles, continued process verification and batch monitoring and reporting. Finally, pharma manufacturers are focused on achieving and exceeding corporate sustainability goals including waste reduction, energy consumption improvement and securing the health and safety of their workforce as more employees work from home and teams are distributed.



Defining the issues

The first challenge that global manufacturers need to tackle is data access. On-premise data, while large in volume and with potential value, is stored at the plant level in data silos. This creates significant barriers for making this data available to the right people at the right time to act based on trends and insights, most of which are currently hidden from view.

Beyond siloed storage, there is the issue of getting insights from data. Applications for data historians have been designed to work with real-time process control systems, but trending applications are not designed for the advanced analytics or global operational reporting required for agile operations.

Megan Buntain
Director of Cloud Partnerships, Seeq Corp.

Solving problems at 'the speed of now'

How pharma can leverage the cloud to make data-driven decisions quickly

Pharma companies typically rely on business intelligence (BI) applications to extract more value from relational data, but BI applications aren't purpose-built to handle process time series data. And spreadsheets aren't ideal for global operational reporting or near-real time decision-making (Exhibit 2). Therefore, none of the existing application solutions are sufficient to meet today's needs.

To address these challenges, pharma manufacturers have turned to the cloud for data storage — bringing data from business, lab and manufacturing systems together in a cloud data lake to address access issues. This allows data access to be democratized across an organization by putting all the data in one spot, leveraging the scale and global availability of the cloud.

This approach supports the goal of many chief information and digital transformation officers to generate value chain efficiencies with a common data model for optimizing every stage of the manufacturing process, from raw material to product shipment. That said, the initial IT investment required to achieve data movement and aggregation in the cloud can be high. In some cases, IT-driven initiatives to create cloud data lakes are met with resistance from operational technology (OT) teams concerned about data protection and security.

There are also issues with leveraging advanced analytics to improve operational performance by finding insights in the aggregated data. Advanced analytics requires three attributes for implementation success:

1. Access to any and all relevant data associated with investigation;
2. Applications to enable process engineers and subject matter experts (SMEs) to tap their knowledge of the plant, processes and assets;
3. Support for collaboration and distribution of insights across the organization to enable rapid data-based decision making.

Solving problems using modern cloud technology

Adoption of the cloud is not one-size-fits-all: There are different stages of cloud adoption across the industry. The most advanced companies are using industrial data lakes combined with self-service analytics applications, empowering employees to solve production problems creatively and rapidly. There are four additional models for leveraging cloud-based computing.

The first is quick start analytics where analytics applications, purpose-built for process data, are deployed in the cloud, accessible to users from a web browser and connected to on premise data historians.

Next is "lift and shift," or moving archival historian data to the cloud so the data is more accessible and available for users anywhere in the organization.

Third is continuous process data movement to cloud, sometimes called streaming data processing. In this scenario, a near-real time flow of process data from the historian is ingested into the cloud, enabling updated production monitoring dashboards across dozens of sites and hundreds of batches.

Last is pure Industrial IoT, where sensor data is piped directly from the assets or a production line to the cloud with no on-premise storage of data.

Whichever method works best for an organization, the need for self-service analytics applications that empower SMEs — those employees who know

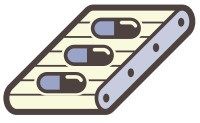
EXHIBIT 1

Effective pharmaceutical technical transfer with advanced analytics

Manufacturers are challenged to scale up quickly from the lab to full production.

Lab
Scientists and engineers design the process

Pilot
Engineers develop process to scale-up manufacture



Commercial
Engineers and quality analysts manufacture product at commercial scale

Knowledge capture through tech transfer

Understand relationships among variables

Verify assumptions and optimize scalability

Monitor process variability and quality

the data and processes best — is essential for all of these scenarios. Otherwise, an organization may have moved data to a more accessible place, only to find no value was created.

Specific examples of requirements for advanced analytics solutions include the ability to connect to data, find tags quickly, cleanse and contextualize data, diagnose issues and predict future asset and process performance. Then with insights in hand, users need to easily share their work and collaborate with colleagues across different business units and distributed teams. In today's world of remote work, this is made easier if each user is working with a browser-based, secure application, with no need to use a VPN for connection to a corporate network.

A critical requirement is the ability to connect to all data sources from the same application, across all tech transfer stages, so product lifecycles can be accelerated and improved (Exhibit 3). The goal is to empower teams so they can generate insights quickly — in minutes or hours instead of months. This degree of acceleration is only possible by simplifying the integration of existing systems, and by using the compute horsepower and scalability of the cloud.

As insights are generated, it is also important to implement knowledge capture systems. Analytics applications must enable user annotation, journaling of analysis steps and documentation of text-based notes or diagrams so knowledge is shared easily and does not get lost when employees change roles or leave the company.

Finally, modern cloud solutions need to democratize machine learning innovation. There is tremendous benefit to be gained by empowering engineers with point and click-based prediction models, and with regression or other statistical methods, all transparent to the user. These solutions must be easy to apply because without industrial context in the form of SME insights, their value may be lost, or the results not trusted by the people who are supposed to take action.

Today, many engineers coming to industry directly from universities already have coding skills in Python, R and other advanced languages. These new employees want to apply

those skills to advanced analytics, a desire that should be encouraged and enabled. At the top end of the continuum, data science and centralized analytics teams want access to process data, and process teams need to work collaboratively and scale out the impact of their efforts across the enterprise.

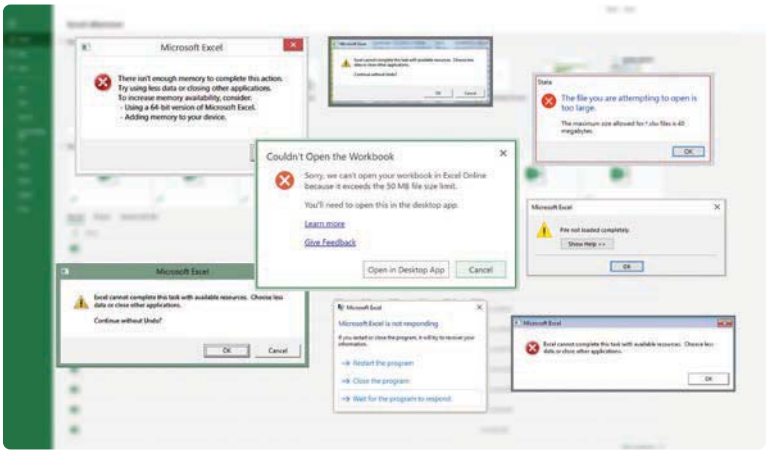


Exhibit 2: Spreadsheets weren't designed to handle the data volumes and complexities inherent to advanced analytics efforts.

Analytics in action

One example of accelerating speed to market is a large molecule pharma company that was finding it difficult to reduce the time involved in pinpointing which pilot drug batches had the best opportunity for commercial production.

Batches do not always maintain integrity as they scale from R&D to pilot to commercial production, and the company's scientists were struggling to predict cell growth at scale, especially using laboratory and pilot data from different historians and databases. They needed a way to accelerate the scale-up process for promising new monoclonal antibodies.

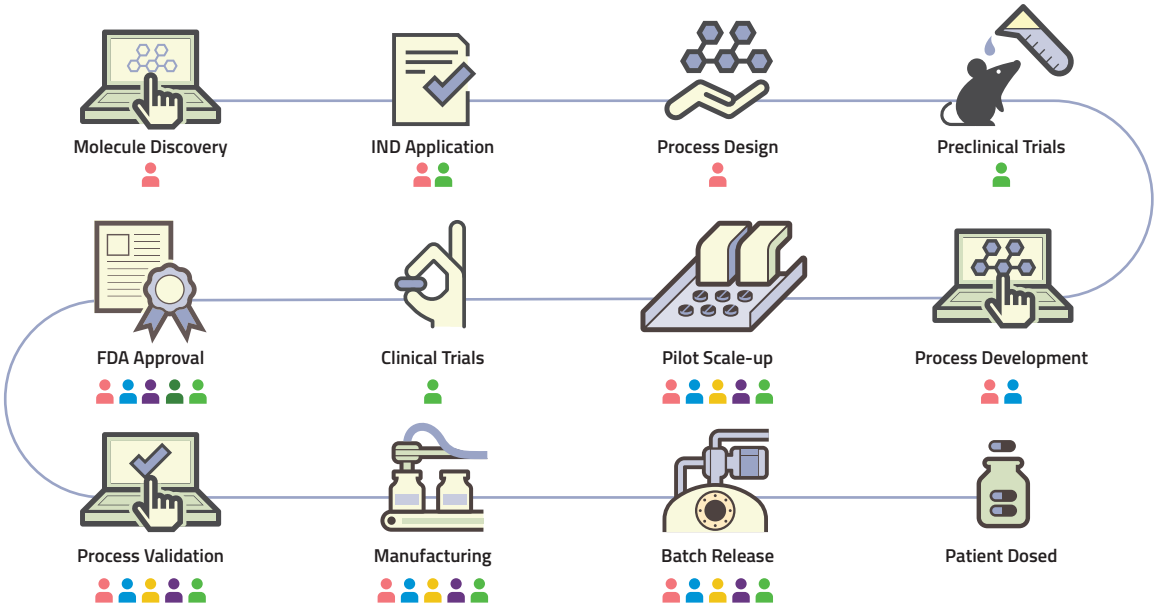
Previously, the engineers would export all the data from the different sources into Excel spreadsheets and try to overlay it, a very time-consuming process. Then, they would calculate scale-up factors such as agitator power per unit volume or oxygen sparging rate. Using spreadsheets for this analysis was too difficult and cumbersome.

Using cloud-based analytics, company engineers were able to combine lab and pilot plant data from different historians to visualize trends. They were also able to

EXHIBIT 3

Empower product evolution life cycle

Employees working across the product life cycle need data access to accelerate drug development.



quickly calculate scale-up metrics, batch KPIs and performance measurements for each experiment.

The team was able to efficiently determine differences among batches, compare results of various measurements and experiments and document all findings in electronic journals. This enabled easy collaboration to refine results, improve designs for future experiments and compare results during scale-up.

For example, the technology transfer team can now integrate oxygen sensor measurements to calculate cell-specific oxygen uptake rates for the laboratory and pilot scale to predict the cell growth curve for scale-up. Those values, coupled with other scale-up factors such as oxygen sparging and agitation power, define the scalability of the cell culture as it moves toward commercial production. Cloud-based analytics applications can now flag deviations in the scale-up batches compared to the expected trends to identify potential process limitations.

Faster process development means pharma firms are better able to meet clinical timelines. In this case, a reduction in development time equated to a bottom-line increase of more than $1.5 million.

Use best practices to get started

Getting started with cloud-based analytics begins with defining use cases and working backwards to the required technologies, applications and data infrastructure. Once these use cases and user stories are defined, pharma firms should start small by gaining buy-in for one analytics success on a single batch. This will enable the team to iterate, and to then drive decisions on data governance such as asset hierarchies, so the analytics can be scaled, for example to all batches or all assets in a class.

Finally, it is best to start analytics efforts using existing data, wherever it is stored. Moving, copying or aggregating data shouldn't be the first step because this can create an overly complicated technology infrastructure. Better decisions regarding infrastructure can be made after a few use cases are proven and a keen sense of requirements is gained. Ideally, advanced analytics efforts should begin before data movement to prove the value of the proposed endeavor.

Bryan DeBois
Director of Industrial Artificial Intelligence, RoviSys

David Sprinzen
Director of Marketing, VANTIQ

Plugging the manufacturing cracks

How to ensure COVID learnings are put into practice for good

COVID-19 has shined a spotlight on the cracks in pharmaceutical manufacturing. Even before the pandemic, life sciences experts had warned about the risks of a globally concentrated supply chain where pockets of raw materials and active pharmaceutical ingredient (API) suppliers in other regions of the world left pharma companies and patients particularly vulnerable to a sudden manufacturing stoppage. Any production disruptions, they said, could have catastrophic effects on human health.

Their concerns were borne out with the sudden emergence of the novel coronavirus, which not only disrupted manufacturing but also led to widespread supply chain shortages as the pharma sector was focusing its attention on developing new therapeutics and vaccines for COVID-19. However, in an industry where companies make drugs that are life-saving, downtime is not an option.

Technology that can make data actionable in real-time has been a boon to pharma companies during COVID-19. It has helped them keep employees healthy and safe, adjust to smaller teams and react to issues faster. But that technology should not be tucked away in a server closet once the pandemic subsides. It solves issues that pharma manufacturers can no longer ignore.

Initial effects and lessons

COVID-19 dealt a blow to pharma manufacturers that were already facing a skilled labor shortage and running reduced crew shifts. As the virus spread, these reduced work crews became skeleton crews as many employees either became sick or were hesitant to come into facilities because they feared infection. Manufacturers were forced, for social distancing reasons, to reduce staffing even further, keeping non-laboratory and plant-floor workers at home.

The new distance requirements, while a safety necessity, inevitably slowed down production processes. A McKinsey poll of more than 300 research and development functional leaders, including chief medical officers from over 50 global companies in the sector, estimated that productivity has declined by 25-75 percent due to remote working.[1] As companies adjust to remote work environments along with reduced lab capacity, clinical and product development pipelines are suffering.

Pharma companies continue to scramble to come up with employee protection solutions to mitigate health risks so their people can return to work safely.

In the face of a virus that spreads rapidly when people work in close quarters, pharma companies improvised an assortment of stopgap protection measures such as routine temperature checks, staggered shifts, and limits on personal interaction where sites remained open. This was trial-and-error in real time because employees working in laboratories and manufacturing sites were on the front lines with the pandemic threatening their own health.

Real time is the new normal

As the industry looks to apply lessons learned, one clear takeaway is the need for solutions that will improve business resiliency. It's no longer enough to rely on traditional safeguards companies put in place during "normal times" to ensure general safety standards and protect workers doing the delicate work of biologic manufacturing against standard illnesses. COVID-19 has reminded us there is nothing standard about a pandemic.

In the past, pharma companies weren't under such pressure to respond to issues in real time. They were accustomed to taking the necessary time required to collect and review data on their products or the performance of their equipment. In the face of challenges like COVID-19, that timetable needs to speed up. An employee with a fever that goes undetected risks triggering an outbreak that could lead to a total shutdown of the manufacturing site. Such information is critical, and manufacturers need to be able to have it immediately so they can respond quickly and with agility.

For comparison's sake, consider the unfortunate example of the meat-packing industry which was relatively slow to react to the new health risks posed by COVID-19. Several meat and poultry processing facilities suffered multiple outbreaks that led to closures as thousands of workers got sick with the virus.

Had those sites been equipped with effective contact tracing

5 Benefits of working in real time

1. Workforce health and safety
Businesses making use of real-time data now have a way to ensure the wellbeing of their workforce. Instead of waiting until an employee falls ill before sending them home — at that point, you're already behind the infection curve. IoT-based monitoring solutions that send back real-time data allow managers to track the health of employees, based on up-to-the-minute data. Managers can act preventively to send home employees showing early signs of fatigue or illness.

2. Workplace health and safety
Real-time data also allows the early detection of any hazardous conditions that could potentially harm the safety of the workforce. In the event of an incident, such as a carbon monoxide leak or a fire, management can gather instantaneous updates on the status of the problem and location of workers in the facility. Real-time information also helps with the oversight of more routine safety-related norms around the maintenance and sanitization of equipment.

3. Minimizing production downtime
Instead of waiting for something to break, companies can now spot early signs of technical malfunction, mobilizing repair teams as needed to intervene before a situation worsens and systems and machines break down. Organizations reap additional cost and health benefits since they no longer need to staff as many technicians on site. At the same time, they reduce potential health risks that may arise since fewer employees are required to work in a facility.

4. Integrated maintenance
Manufacturers often find themselves running disparate systems where it's hard to communicate and share data internally. But with real-time data, the deployment of sensors and devices around a site will immediately inform managers of any urgent operational decisions they need to make — from DEFCON-1 emergencies down to nuts and bolts situations, such as whether to keep the power on in a room or shut off a piece of equipment for the night.

5. Resource management and efficiency
In any complex factory, there are so many steps in production that a single change can affect operations at all the other points on the assembly line. Based on real-time data collected along each point on that line — for instance, an alert that a particular piece of equipment needs maintenance — managers can adjust any step or multiple steps in order to improve performance.

technology, they would have been able to understand how employees were moving through their environment. Technology would have helped them learn where people had been, who they interacted with, which rooms they spent time in, and whether they adhered to physical distancing rules.

Further, they would have been in a stronger position to enforce safety compliance, making sure that employees wore masks or were sanitizing their hands correctly.

Many companies are now connecting thermal imaging cameras into their Internet of Things (IoT) network to measure body temperatures and monitor employees as they enter the facility. As people walk through the door, the systems can flag anyone with a high temperature for further evaluation. Importantly, this occurs in the moment, not after someone has been walking around for an hour and interacting with other workers. The upshot: Facility managers will be able to detect and respond to potential trouble in minutes, not hours.

All in all, such a system contributes toward achieving the larger goal of creating a safer, more secure environment for employees.

Situational awareness

Situational awareness isn't just for pandemics, however. It is no easy feat, as it depends upon collecting information from the environment, focusing on events taking place in real time and then converting that data into actionable insights.

As the pharma industry considers how to develop better business resilience in the post-COVID-19 era, situational awareness needs to remain a critical component of any recovery strategy.

Real time is part of the broader digitalization trend underway the last few years as more organizations connect to IoT and deploy sensors and devices that collect information from their environments. Even gateways and edge devices now have logic running anywhere and everywhere. With this extraordinary amount of data, companies can apply artificial intelligence to extract meaningful understanding to be more proactive when it comes to operations and strategy.

That means any organization can now receive alerts for everything from an industrial accident to an active shooter on site, to the previous example: identifying someone who may be carrying a virus onto the plant floor. This situational awareness can be connected to DEFCON-style modifications in plant operations, orchestrating near-instant changes to policies, systems, and workflows with a single button click.

With the right IoT technology monitoring their workplace and workforce, managers at a pharma facility can sense, analyze, and act upon data in a single view – and all in real time.

All of these developments are shifting the capabilities of businesses as they enter a new age of the real-time enterprise. The inputs can come from current existing enterprise business systems, mobile devices, web browsers or other inputs. These myriad pieces of sensory data reveal a lot about the work environment. It might be about a particular machine's status or conditions related to the broader business environment. The information gets contextualized, combined and correlated so that the organization can apply best practices and truly operationalize its data.

What's more, these new applications don't require a database and so, don't suffer performance hits that might arise if they were required to store data for subsequent analysis. And since they are built to leverage IoT, AI and edge technologies, they can literally sense and react to events as they take place.

Paper is dead — or it should be

Digital is still a long way from becoming central in life sciences interactions.

Indeed, many pharma manufacturers still rely on paper records for batch processes. However, paper can get lost, and a batch without a record cannot be sold. Currently, a review of paper records requires someone to be present at the facility. That's not a recipe for increased speed and agility.

Moving to real-time technology systems does not require ripping out or completely replacing enterprise systems. But manufacturers need to be able to cross-pollinate and better orchestrate their current systems to foster smarter coordination and accelerate average response times. As we reimagine work processes in a post-COVID world, anything that can reduce unnecessary physical contact is worthwhile. Ideally, companies should be able to build an alert that notifies a reviewer when a completed batch record's exceptions are ready to be reviewed digitally. However, as the future takes shape, it will feature increasing reliance upon digital tools that provide greater situational awareness.

Doing more with less

Another lesson learned from COVID-19 is technology's ability to do more with less. That must continue, even as staff come back on site. Nowhere is this need more pronounced than when it comes to maintenance teams. While pharma manufacturers have traditionally counted on their maintenance teams being able to travel to multiple facilities, the quarantines, lockdowns and limitations on travel has hampered flexibility.

Here's where technology compensates for the loss of physical manpower. Solutions that allow remote monitoring of assets and bring together data associated with those assets will transform how maintenance teams do their jobs. They'll now have clear insight into how the machines on the plant floor are functioning. What's more, operators on plant floors will be able to use mobile forms built into the platform to augment the total picture — including descriptions of what they're hearing, seeing, and even smelling from their equipment. All of that feedback would get routed to the appropriate maintenance team.

Pharma learned hard lessons in the past several months. But while this pandemic may be unique, the experience vividly underscores the need for comprehensive solutions that combine automation and human interaction.

There's been much conversation about what adapting to the new normal will require as manufacturers shift to recovery mode. Pharma companies that are equipped to respond quickly and take the proper steps are going to be the winners — and smarter, situational technology solutions will be key.

References

1 *McKinsey & Company. "COVID-19 implications for life sciences R&D: Recovery and the next normal." May 13, 2020.*

product focus

Meagan Parrish
Senior Editor

Machine-guided manufacturing

AI and VR solutions that are transforming operations

Machine learning is no longer a fringe concept. From artificial intelligence (AI) to virtual reality (VR) tools, machine learning solutions have invaded processes throughout pharma facilities.

And with new therapies becoming more complex to produce, the need to utilize high-powered tech to aid operations is growing as well.

"Pharmaceutical manufacturers are under increasing pressure to deliver more productivity," says John Vitalie, chief executive officer of Bigfinite. "With almost half of new drugs approved being single-batch, personalized medicines, the average tenure of market-leading drugs has halved, and along with new biotech processes, this all contributes to a rapidly changing manufacturing landscape."

Here is a look at some of the AI- and VR-powered solutions that are transforming every phase of pharma processing from early drug discovery to manufacturing on the pharma plant floor.

A new way of researching

According to Shohei Imamura, strategic project manager, Olympus Corporation of the Americas, AI technology is enabling groundbreaking analyses of cells that, until recently, seemed impossible to achieve.

"Deep learning enables many things that are difficult to realize in traditional image analysis, such as the prediction of the position of the nucleus in label-free cells," Imamura says. "With deep learning technology, this prediction becomes simple to do."

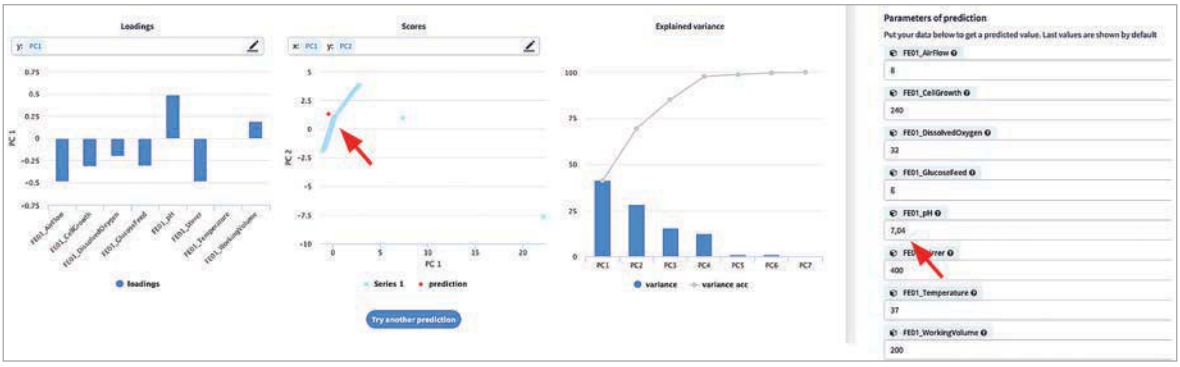
To utilize AI in cell imaging, Olympus launched its scanR high-content screening (HCS) station that combines self-learning microscopy — reducing photobleaching and improving speed, accuracy and measurement sensitivity — with high-throughput deep-learning analysis technology based on a dedicated convolutional neural network architecture. The company says that the scanR system excels in drug discovery applications, showing the biochemical effects of compounds on the cellular level and drug-induced changes at gene expression levels.

"Additionally, deep learning makes it easy to predict fluorescence signal from extremely low exposed images," Imamura says. "These advantages help contribute to improved throughput, reduced photo-damage, and lower costs."

Transforming training

AI and VR tools are by no means a replacement for employees. But, of

Emerson's Mimic Field 3D provides a realistic way to develop operations skills without the need for actual unit operations exposure.



course, they can help make operators better at their work, especially when they're in training.

"The pharmaceutical and life sciences industry is undergoing immense change, and the amount of information employees are expected to retain is ever increasing," says Graham Provost, global director, AVEVA Unified Learning. "The mounting information means people can't always remember the critical things right in the moment of need. This can be especially damaging to a manufacturing division, as it can cause safety and compliance issues as well as lower equipment availability."

To help improve worker performance, AVEVA partnered with Axonify, a B2B SaaS company, to offer adaptive microlearning powered by AI as part of its Unified Learning solution. According to the companies, the program includes a single, integrated platform encompassing simulation for training with extended reality capabilities; tools for designing learning and development programs; flexible deployment enabling customers to choose cloud, hybrid, or on-premises implementation; and AI to fill knowledge gaps with personalized training.

Overall, the companies say that the training program helps drive measurable outcomes for organizational competency needs.

Emerson has also released a VR-based learning solution called Mimic Field 3D that provides an immersive environment for planning, training and operations support.

"A key element of the pharma 4.0 digital transformation is to ensure organizational readiness for newly deployed products and advanced applications," explains Bob Lenich, director for global life sciences, Emerson. "If operators don't effectively use new work practices and technologies, the facility won't achieve its performance goals."

Emerson says that Mimic Field 3D provides a realistic way to develop operations skills without the need for actual unit operations exposure or the plant to be built. Specifically for the life sciences industry, Mimic Field 3D enables critical training and maintenance experience in areas such as gowning, sample taking, facility awareness, asset tracking, and emergency facility training in a safe environment without affecting production.

Ultimately, Emerson says that "Mimic Field 3D empowers new workers to acquire knowledge and experience at a faster pace as they learn from each immersive experience, enhancing safety and overall operational performance."

Understanding data

Principal Component Analysis (PCA) is a commonly used way of navigating large data sets and seeing the relationships between variables. In manufacturing, it can help companies visualize trends in operations. But much of this process has typically been achieved manually — until now.

> The Bigfinite GxP PCA application leverages AI to transform complex relationships in data sets.

Recently Bigfinite released its GxP AI-powered platform, which Vitalie says was designed to help manufacturers navigate these new challenges.

"The Bigfinite GxP AI powered cloud platform…and the new PCA application is the first real-time, cloud-based PCA available on the market," Vitalie says.

According to the Bigfinite, its PCA application is a ready-to-use component of its GxP AI-enabled cloud platform, and provides root cause analysis and predictive deviations capabilities for pharma and biotech manufacturing. The company says that the new PCA application uses advanced, multivariate statistics combined with AI to help manufacturers better analyze and control their processes.

"Combined with AI, pharma manufacturers have unprecedented access to transform complex relationships in data sets to versions with fewer dimensions to easily identify variances in data," Vitalie says. "Ultimately our PCA application can enable more accurate data-driven decision-making, which will result in higher productivity."

John Noble
VP Life Sciences, Jacobs

A catalyst for transformation

A gradual transition in project delivery has morphed into an acceleration as biopharma fights COVID-19

The COVID-19 pandemic is the biggest single challenge facing society, with academia, the scientific community and private enterprise all doing what they can to help control the global spread. As part of this effort, the biopharma sector is responding to the urgent need to develop a vaccine and treatments to tackle a pandemic that has, to date, infected more than 27 million people across the world.

This mobilization by biopharma is not surprising; by its very nature, it is a resilient, innovative sector that has purpose at its core. That purpose has never been more pronounced as its key players bring all of their expertise and innovation to bear in the fight against COVID-19.

Pre-COVID, the biopharma sector was already grappling with a series of disruptors. The commercialization of novel cell and gene therapies requires a shift in thinking to address emerging operational and regulatory challenges. Adding to this is the need to address pricing issues and access for potentially transformative treatments as well as the ongoing, industry-wide battle for the best talent. These factors were combining to make investment decisions more challenging. They also put the efficient use of capital and shorter delivery times under increasing scrutiny.

Now, as biopharma companies around the world work at pace to bring life-saving products to market, solutions providers for biopharma facilities are delivering COVID-related projects within schedules that would have been deemed unthinkable a few years ago.

A leaner approach

Even before the pandemic, the manner in which biopharma projects were delivered was being transformed with solution providers developing leaner, and more integrated and innovative solutions to address increasingly complex needs.

One such approach is integrated project delivery (IPD). The IPD approach blurs the lines of traditional project delivery and ensures that the best person or company is assigned to each task, resulting in an optimized, leaner solution. IPD also ensures that projects are delivered in a way that gives the best value to the client in terms of optimal safety, quality, cost and schedule.

What had been a gradual transition in the approach to project delivery has morphed into an acceleration as the biopharma industry — like many other related industries — steps up in the fight against COVID-19.

Solution providers are deploying the most effective and impactful elements of IPD to support the urgent need for the biopharma sector to deliver vaccines and treatments on a global scale — in record time and to the highest quality standards.

For biopharmas, this shift is being driven by the need for rapid retrofits to enhance the flexibility of existing facilities. The goal is for these retrofits to be made operational in one-quarter of the time that a conventional new build can be safely delivered, with the aim of fast-tracking production of COVID-19 therapies, vaccines and testing.

The reality is that the coronavirus has fast-tracked some of the dominant and most impactful traits of IPD, including a relentless focus on safety and quality; flexible capacity; deeper collaboration with project partners; and an agile approach to overcoming evolving challenges.

The pandemic has introduced unique challenges in ways of working, and as such, existing initiatives that put on-site safety at the heart of workplace culture and technologies that help to maintain physical distancing have become more relevant.

The response to the coronavirus has also led to deeper collaboration among project partners. This is an area where IPD comes into its own. Using this approach, the focus shifts from a task-focused environment to one where people come together to collaborate to deliver the project.

IPD ensures all partners have an equal opportunity to bring value. Deeper collaboration allows unique skills to come to the fore and allows companies to move from solving complicated problems to quickly delivering solutions, while maintaining the highest quality and integrity of the manufacturing process.

Through COVID and beyond, new challenges are emerging which require that project delivery teams remain agile and innovative. A team's ability to think outside the box is what will continue to unlock new possibilities for biopharmas and indeed, across all industries.

While there are challenges ahead, the potential to reimagine tomorrow resonates now more than ever. And the progress being made in project delivery will live on, reaping benefits for long into the future.

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Mike Blankenstein
Senior Director, Patient Supply Operations Manufacturing and Supply Chain, Adaptimmune

Because patients can't wait

How autologous cell therapy companies can adapt planning processes to maintain operations amid supply chain disruptions

The COVID-19 pandemic has affected life sciences organizations across the world and has led them to adapt in various ways. This is especially true for companies working on autologous cell therapies, which are dependent on complex supply chains for coordinating patients, practitioners and manufacturers. Autologous cell therapies require a flexible manufacturing capacity and a highly skilled workforce, which places these intricate supply chains at risk of disruption in the current uncertain climate.

The chain of custody for these live cells is critical to ensuring the safe and timely treatment of patients. Outside of cell collection and shipping to and from the treatment center, the "one patient, one batch" manufacturing process requires a broad range of materials and consumables. Furthermore, little of this work can be completed remotely. From cell collection at the clinical sites to administration of the engineered cells at the clinical site, people are needed to complete the work. With the challenges imposed by the risk of COVID-19, extra steps and diligence are required to ensure all processes are carried out properly.

Expecting the unexpected

The COVID-19 pandemic has created unique challenges for the manufacturing process behind autologous cell therapies, such as its impact on the availability of raw materials due to the additional need for personal protective equipment (PPE). In addition, suppliers may be experiencing reduced manufacturing capacity because employees may be out sick or caring for others during the pandemic. There is also uncertainty concerning delivery dates for materials because some suppliers source from countries that may be particularly hard hit by COVID-19. To mitigate potential shortages, companies need to increase their inventories of critical materials and implement secondary source planning.

In terms of logistics, shipping of the cellular starting material and final drug product is typically done via air with time limits due to the stability of the material being transported. With the pandemic limiting travel, flights have been cancelled on a moment's notice, leaving companies with no choice but to source last-minute alternatives. This scenario should drive companies to consider road transit, when possible, to mitigate against unexpected flight cancellations. In addition, contingency plans should be prepared with logistics partners to transport cells via chartered flights if no other transport solutions are available.

Additionally, the imposed quarantines and restrictive measures needed because of the COVID-19 outbreak have affected internal operations. Autologous cell therapy companies need to manage employees' schedules and work environments to make certain essential employees are safe while conducting critical operations. In tandem, companies must mitigate the risk of employees contaminating the drug product with the virus. This can be achieved by implementing a work-from-home policy for employees when feasible, executing social distancing measures on site, enhancing cleaning routines, and adding PPE and temperature checks for employees that must be on location.

The patient perspective

Companies must also be conscious of the issues raised by the COVID-19 outbreak as they relate to the patient journey. Current circumstances may leave patients unable to travel to the clinical site and forced to social distance out of fears for their health. Ultimately, these challenges mean companies need to work on a site-by-site, patient-by-patient basis to do everything they can to supply autologous cell therapies to people who are particularly vulnerable, such as patients undergoing treatment for cancer. Alternate treatment sites are being utilized to provide a location closer to the patient and not as heavily impacted as large institutions. This can make the patient journey easier in a way that also mitigates potential exposure to COVID-19 at large treatment centers.

During these unprecedented times of global uncertainty, there are a multitude of factors affecting every aspect of the supply chain for these autologous cell therapies. It is vital that autologous cell therapy companies quickly and efficiently adapt planning processes to ensure they are able to maintain operations and manufacturing — because we know patients can't wait.

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