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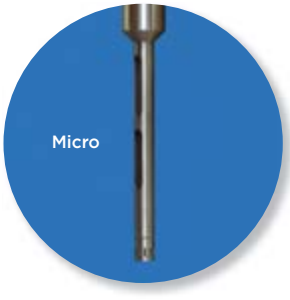

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Karen Langhauser
Chief Content Director

Cyber scares

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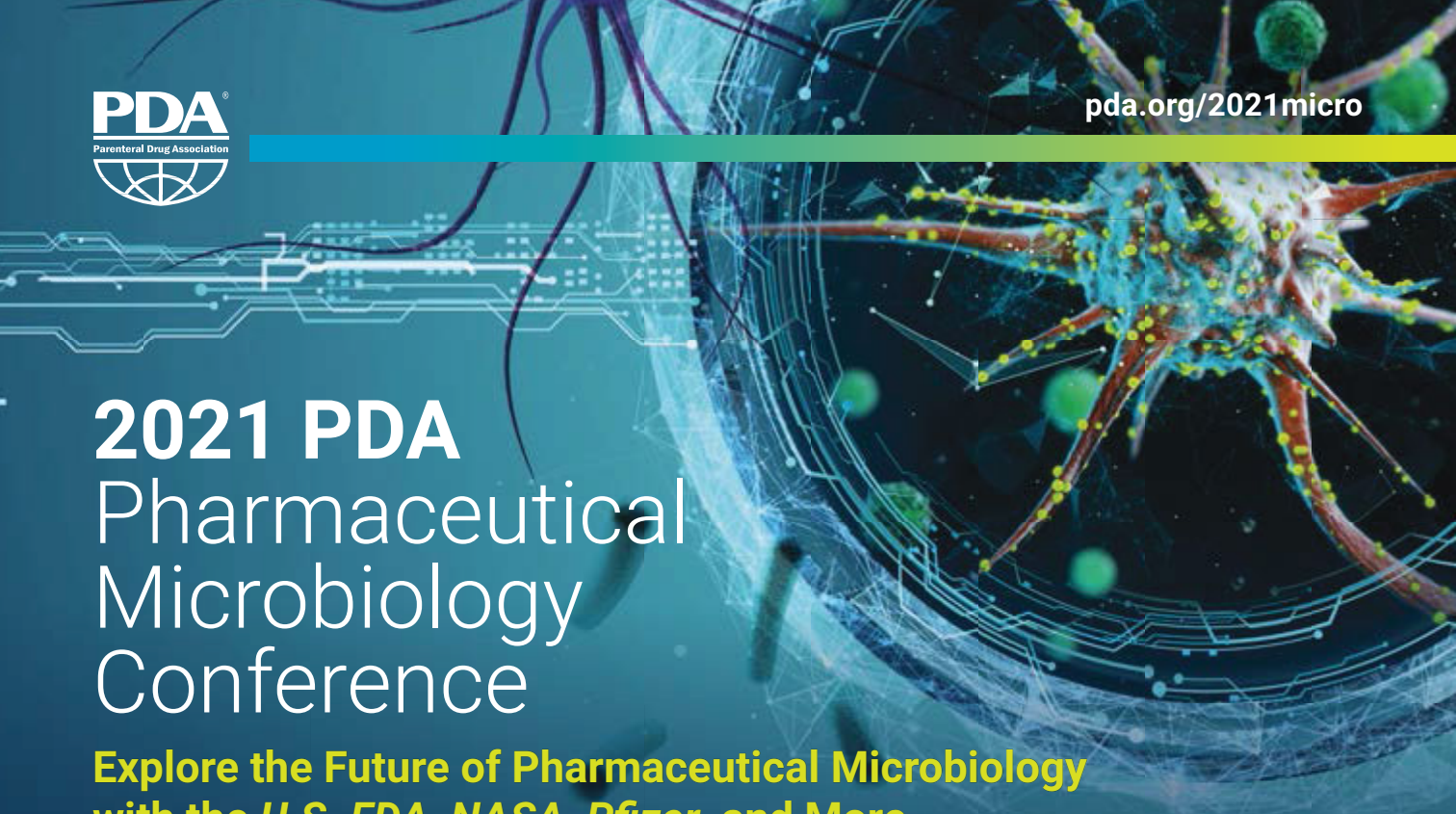

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Karen Langhauser
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Cyber stories to tell in the dark

Pharma is facing a scary truth about cybersecurity

Confession: I was usually the kid at sleepovers who was responsible for giving all the other kids nightmares.

I've always had an insatiable appetite for scary stories. As a child, I was especially fond of urban legends: alligators populating city sewers via toilets, travelers waking up one kidney short in a bathtub of ice and of course, the woman who didn't realize there was a homicidal maniac hiding in the backseat of her car.

Urban legends tend to stick with you. The good ones strike the perfect balance between inconceivably terrifying and yet concerningly relatable. The most compelling urban legends are usually cautionary tales — painful reminders of a worst-case scenario resulting from a friend of a friend's failure to stay vigilant about what's going on inside her own car.

Cybersecurity warnings can have a similar chilling effect. Back in 2012, then-Defense Secretary Leon Panetta gave a particularly dire speech, warning that cyberattacks had the potential to cripple the nation's power grid, transportation system, financial networks and government.

"A cyberattack perpetrated by nation states or violent extremist groups could be as destructive as the terrorist attack of 9/11," Panetta said during his speech at the Intrepid Sea, Air and Space Museum in New York. He warned that such groups could "derail trains loaded with lethal chemicals," "contaminate the water supply in major cities" or "shut down the power grid across large parts of the country."

Scenarios like those could prompt even the bravest of security professionals to sleep with the cyberlights on.

Yet, the cybersecurity field has always had a bit of a reputation for alarmism and threat inflation, consistently warning of the potential for catastrophic events. But cybersecurity experts' affinity for doomsday talk doesn't mean warnings should be haphazardly flushed like unwanted baby alligators.

Urban legends with the most staying power offer some level of plausibility in their threats. The "killer in the backseat" story has been kicking around in different forms since the 1960s. Despite the fact that the chances of being murdered in your own car by a serial killer are pretty low, muggings and car jackings are very real crimes and women, especially women alone at night, assume an inflated risk of such crimes.

While cybersecurity warnings can at times be hyperbolized, the threats are very real for pharma. As you'll read in this month's cover story, the pandemic has brought with it a 50% uptick in cyberattacks on the bio/pharma industry. Not only are attacks becoming more frequent — pharma companies are fending off multiple attacks on a daily basis — they are more targeted and sophisticated. And if you don't want to take the word of private cybersecurity companies, look no further than the FBI, the Department of Homeland Security, INTERPOL or the United Nations — all of which have been flashing their metaphorical high beams to warn pharma of lurking predators.

Though the pharma industry has placed a collective foot on the accelerator to get vaccines and treatments into the hands of patients as quickly as possible during a global pandemic, the industry's continued efforts to stay aware of who is coming along for the ride are more vital than ever — and will help everyone sleep more soundly at night.

Meagan Parrish
Senior Editor

Robots to the rescue

University/industry collab leads to innovative syringe-filling system

It's no secret that working long hours in a cleanroom environment can be grueling. The bunny suits can get sweltering and the hours doing monotonous tasks can drag. On top of that, staffing cleanroom techs for an around-the-clock operation can be a major challenge for pharma companies.

With the hope of overcoming these issues, South Carolina-based Nephron Pharmaceuticals recently went looking for a way to automate syringe-filling for small batch manufacturing and turned to the brainpower nearby.

Within the University of South Carolina, the Office of Innovation, Partnerships, and Economic Engagement (OIPEE) provides a way for companies to engage with students and faculty to solve vexing industry problems.

"The university can bring a client in, and we'll create a solution for that client with advanced manufacturing," Bill Kirkland, executive director of OIPEE, explains.

For Nephron, that solution was robotics. After striking up a partnership, students and researchers from UofSC eventually innovated a new automated syringe-filling system that utilizes flexible, high-speed robots provided by Yaskawa Motoman and processing power developed by Siemens. According to Kirkland, the system's robotic arm that works under a single hood is part of what makes it unique. It was also designed specifically for small-batch operations, and importantly for Nephron, the new technology will help eliminate manufacturing downtime.

The UofSC student-designed syringe-filling machine was installed at Nephron Pharmaceuticals earlier this year and is undergoing commercial validation.

"We have a workforce issue in that we have lots of trained sterile pharma techs, but expecting them to show up every shift 24/7 is challenging," Lou Kennedy, CEO of Nephron, says. "So, for example, if someone calls in sick, this allows us to do many steps using robotics, and it keeps us from having to shut down."

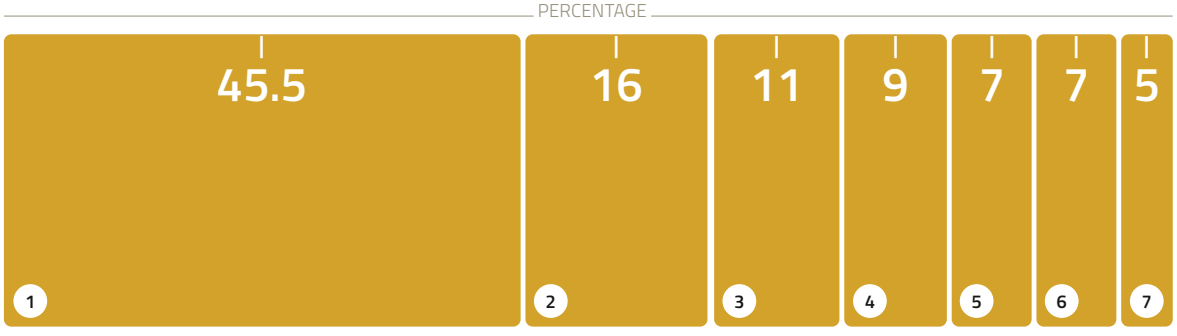
Although there are other robotic syringe-filling solutions on the market, Kennedy says she has never seen a system as small and nimble as the one built by UofSC.

"It operates underneath a flow hood in a cleanroom and that's important because we are working with injectables," Kennedy says. "And it's compact and can move from one cleanroom to another."

After the technology was developed, the system was installed in a Nephron facility earlier this year, where Kennedy says the company is perfecting the tech and it is being commercially validated. Once they find the manufacturing

see more results from our annual Smart Pharma Survey on page 19

Pharma manufacturers: What area would see the most benefit from increased use of digital tools?



1. Plant floor production **2.** Drug development, including clinical trials **3.** Quality control **4.** Supply chain management **5.** Equipment maintenance and repair **6.** Packaging **7.** Drug discovery

"sweet spot" and it wins regulatory approval, the companies plan to license and commercialize the technology. Ultimately, the plan is to target biopharma facilities and hospitals in need of small-batch manufacturing solutions.

"By virtue of its previous relationships with Yaskawa and Siemens, UofSC faculty and OIPEE pitched this solution to Nephron, who agreed to bear some of the initial cost of setting up the research facility in the McNAIR [Aerospace] Center," Kirkland said in a statement this spring. "All three companies, as well as the university, will benefit greatly from the introduction of this system into the commercial space."

In addition to being a boon for the Nephron, the collaboration also showcased how industry partnerships can be a stepping stone for engineering and manufacturing students — including those who were not considering a career in pharma before. According to Kirkland, one of the students involved in the collaboration went on to score a job at Siemens, and another did the same at Nephron.

"Partnerships like this one are a win for patients, employees and students, not to mention for companies like ours, that continue to grow and expand our capacity to help others," Kennedy said in a statement this spring.

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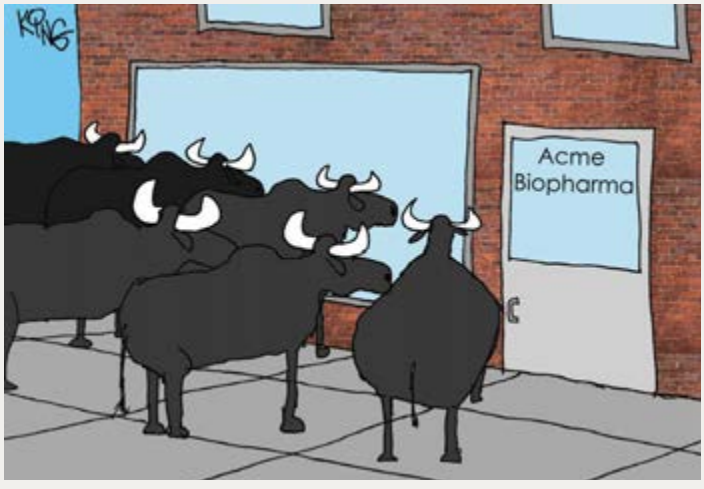

"The stock market bulls are awaiting their next unicorn to court."

—**Michael Brown**

Funny Pharm comics are drawn by professional cartoonist Jerry King. Readers submit suggested captions to win. Above is a recent cartoon and winning caption.

Jacqueline Barberena
Sr. Director, Global Marketing and Product Management, STARLIMS Corporation

Data management for the entire product lifecycle

The right LIMS can enable the pharmaceutical industry to improve the quality and safety of products from concept to consumer

Today's pharma manufacturers are finding they need more robust tools to meet modern regulatory expectations around data integrity.

Pharma requires a data management infrastructure that allows labs to work faster and more productively, with greater transparency. This digital transformation will allow the industry to derive more intelligence from their data, ultimately improving product and process safety, and enabling faster regulatory audits and approval timelines.

In the pharma industry, Laboratory Information Management Systems (LIMS) have become a mission critical application that supports this digital transformation from the ground up.

Pharma Manufacturing recently spoke with Jacqueline Barberena, Sr. Director, Global Marketing and Product Management at STARLIMS Corporation to get a better understanding of the vast benefits of implementing and deploying a LIMS in the pharma sector.

Q: The term "Laboratory Information Management System" can be misleading because in practice, these systems help manage data beyond laboratory testing. How does a LIMS improve day-to-day operations across the entire enterprise?

A: You are correct, a Laboratory Information Management System typically expands beyond laboratory data management. It is a comprehensive solution that not only manages data but helps with quality, regulatory compliance and safety throughout the entire product lifecycle.

LIMS solutions have the ability to integrate with existing systems, while also identifying opportunities to improve processes so that organizations can bring high quality and safe products to market faster. For a pharma/biotech organization, this means automation and secure data management for the entire product lifecycle, from R&D to production to quality assurance.

Q: What are some common barriers to implementing a LIMS in pharma, and how can they be overcome?

A: There's never a great time to implement sophisticated software in any industry, particularly industries that are as highly regulated as pharma and require intricate workflows. It takes proper planning, an excellent roadmap, resources to take time away from their day to day responsibilities, and funding. It's a big undertaking, but it's well worth it especially if an organization is still paper based. Two of the most significant barriers to innovation are outdated informatics tools and inefficient manual workflows. Moving from paper-based and outdated methodologies to automated digital solutions can breathe new life into the day to day operations of a lab.

The success of a LIMS project depends on several factors. One of the most important factors is creating accurate and useful laboratory workflows within the LIMS, ensuring that staff is involved, understand the benefits of the system, and will therefore work with and not against the system. Overcoming barriers and successfully implementing and deploying a LIMS requires:

- A clear understanding of the business and user requirements.
- A user-friendly interface that ensures a high-level of user adoption.
- LIMS workflows that match, or improve on, the existing laboratory workflows, enhancing efficiency and productivity.
- A clear understanding of the role of the laboratory and proper data management to the success of the overall organization, to name a few.

Q: What type of infrastructure is needed to ensure the success of a data management solution such as a LIMS within an organization?

A: I don't believe a specific type of infrastructure needs to be in place for a LIMS to help an organization. We have customers now that range from start-ups who were completely paper-based in their operations to mid-sized organizations who were partially paper-based and utilizing a combination of legacy informatics systems, to large global enterprises who were fairly automated but whose systems did not have the latest informatics innovations. All of these types of organizations with different infrastructures can benefit from a LIMS if it is properly implemented with the correct functionality and requirements to address the needs of the business.

Transform your lab
The STARLIMS Unified Solution is a powerful combination of offerings, using our world-class LIMS as the foundation.

Q: As companies continue their digital transformation journey, they often run into an issue referred to as "technical debt." What does this mean and how does STARLIMS address this problem?

A: The term technical debt can have a few different interpretations, however, essentially it means that as a lab's instruments, platforms and software are updated and replaced, outdated systems are retired from use, but many will still need to be maintained at significant cost in order to access data held in proprietary formats. It's a fact of laboratory life that has existed within the LIMS industry for decades.

As labs are chasing the latest revolutionary technologies, some may promise to support digital transformation in the short term but may result in technical debt five or ten years down the line. STARLIMS, however, is an application that supports this digital transformation from the ground up, while addressing the issues of technical debt.

As a corporation, we have taken an evolutionary approach to technological development, so that it can grow and adapt in parallel with the data requirements, formats and needs of labs taking on new analytical technologies and workflows. It's about empowering manufacturing, R&D and testing labs with the ability to stay ahead of the rapidly evolving technological and data landscape, so that they can protect their investment and derive maximum insight from data, enterprise wide. STARLIMS aims to constantly innovate. In the world of technology especially data management, staying ahead of the innovation curve and anticipating future customer needs is key to staying in business.

Q: What is on the horizon for STARLIMS and what does the future hold for LIMS?

A: This year has been an exciting one for STARLIMS and now as a standalone software organization, we are uniquely positioned to innovate faster than ever.

In July we announced the latest release of our Technology Platform V12.2. This highly anticipated release was a major step forward in the modernization of STARLIMS. The new technology platform features a powerful Electronic Lab Notebook (ELN) system, which allows for the execution of test workflows without interruption, using modern HTML5 technologies. HTML 5 is a more modern-looking, flexible, powerful, and efficient application which improves the performance, integration, and usability of STARLIMS.

On the business application layer, in 2018, STARLIMS released its first 100% HTML5 systems for clinical and quality manufacturing customers such as pharma and biotech. HTML5 is also most compatible with newer web browsers such as Google Chrome, which is key as older browsers such as Internet Explorer are becoming un-supported.

This year, STARLIMS also launched a new SDMS product (Standalone Scientific Data Management System) and STARLIMS LES (Lab Execution System). With STARLIMS LES, customers can ensure standard operating procedures are being followed and tasks are being developed in a compliant manner for regulated labs.

Looking ahead, to support customers on their journey, futuristic technologies are essential, including IoT, AI/AR etc. For STARLIMS, an example of this is the Digital Assistant. This technology provides the ability to interact with the STARLIMS HTML5 solution using user voice. Customers can utter commands using the microphone, launch applications and KPIs, conduct hands-free workflows while away from their desks and build their own skills to meet individual business needs. The tool leverages advancements in AI and NLP (Natural Language Processing), allowing the user to interact with the system using only voice. With continual and consistent product releases and innovations, STARLIMS will stay ahead of the technology curve.

Karen Langhauser
Chief Content Director

Cyber scares

THE THREATS ARE REAL — AND CRIMINALS ARE PREYING ON PHARMA

Alan Brill didn't strike me as an alarmist. During our interview he was pleasant and calm, patiently explaining to me the ins and outs of cybersecurity.

But you shouldn't mistake Brill's composure for a lack of urgency.

With over 30 years of experience dealing with cybercrimes, Brill, who now serves as a senior managing director with Kroll's Cyber Risk practice, has been in some high-pressure situations.

In 1991, on the fifth day after coalition forces re-took Kuwait from the Iraqi army, Brill led a small team on the ground seeking intelligence from computers left behind by retreating Iraqi forces. In 2008, when a foreign intelligence service penetrated the computer networks of the Obama campaign, it was Brill who was tapped to lead the effort to remove the hackers and prevent them from re-entering.

So when Brill refers to the cybersecurity problem in the pharma industry as "existential," it's probably a good idea to take heed.

"This is a real issue. You can't simply say, 'Talk to the CIO, it's a technical problem' or 'Talk to the COO, it's an operations problem,'" says Brill. "It has come down to the fact that what you're dealing with is very often an existential problem — the company may live and die based on what happens."

And Brill is not the only one trying to get the word out.

Last year, the Federal Bureau of Investigation (FBI) and the Department of Homeland Security's Cybersecurity and Infrastructure Security Agency (CISA) jointly issued a stark warning: China-affiliated cyber actors were caught trying to obtain valuable intellectual property and public health data related to COVID vaccines, treatments and testing. Pharma companies were among those targeted, and officials urged them to maintain dedicated cybersecurity because the delivery of treatment options — at a time when COVID was ravaging the world — was in jeopardy. Similar warnings have recently been sounded about hackers from both Russia and North Korea.

There is no shortage of data backing these warnings. According to a report from cyberthreat intelligence company BlueVoyant, cyberattacks on the biotech and pharma industry increased by 50% between 2019 and 2020.[1] Black Kite, a cyber-risk management company, recently found that one in 10 global pharma manufacturers are at a high risk of suffering a ransomware attack.[2]

Individual pharma companies are speaking out as well. During an online panel at the Aspen Cyber Summit last December, Johnson & Johnson's Chief Information Security Officer (CISO), Marene Allison, said J&J had seen a 30% uptick in cyberattacks during the pandemic and that health care organizations are fending off attempted penetrations by nation-state threat actors "every single minute of every single day."

With many experts warning that the attacks on pharma are not only more frequent but more sophisticated, the message is clear: Cybersecurity threats have become a very real part of doing business in pharma and the industry's continued success — as well as the lives of millions of patients — depend on pharma's ability to kick its cyber vigilance into high gear.

> **"As a professional in this field, I'm constantly amazed at the speed with which hackers adapt."**
>
> — Alan Brill

The lure of pharma

Among security professionals, 1930s bank robber Willie Sutton has become somewhat of a mythical figure. As the story goes (the incident was later refuted by Sutton himself in his autobiography), when a reporter asked the prolific thief why he robbed banks, Sutton replied, "because that's where the money is."

As one of the largest and most profitable industries in the world, pharma has long since been a darling of cybercriminals. To begin with, the industry is ripe with valuable intellectual property data on drug formulations and technologies.

"The 'bad guys' today know the pharma industry has trade secrets. The industry has information that they can monetize — that they can threaten to release and get money, or that they can encrypt and get money or some combination of the above," says Brill.

The pharma industry is also the gatekeeper to massive amounts of personal health data collected during clinical trials. One analysis found that a patient's full medical record can sell for up to $1,000 — nearly 10 times the going rate for social security numbers and credit card information.[3]

One of cybersecurity's most cautionary tales involves the 2017 NotPetya ransomware attack that hit, among many organizations, Merck & Co. Often touted as one of the most devastating attacks in cyber history, the virus infected Merck through a server in Ukraine and quickly spread. The attack led to a disruption of worldwide operations, ultimately resulting in a $1.3 billion insurance claim.

As was the case with Merck, the global nature of the pharma industry makes it a broader target for cyberattacks.

"If I'm a criminal and I think I've found a weakness in your plant in Malaysia or your plant in Turkey or wherever, why not hit there?" says Brill. "It's all cyber-connected. They [cybercriminals] look for weak links — and they've gotten very efficient at exploiting them."

Hitch-hacking pharma's digital journey

Pharma Manufacturing's recent Smart Pharma Survey (read more on page 19) found a positive climate for digital innovation in the industry. Over 88% of respondents believe that, even if the manual processes used in their plants were seemingly effective, their companies would choose to automate processes if given the option. A similar percentage of respondents indicated that digitalization is an important part of the discussion when their companies are upgrading manufacturing facilities.

Digital innovations such as cloud computing, artificial intelligence and connectivity via industrial IoT are enhancing every aspect of pharma, from speeding up drug discovery to making plant floor operations easier and more efficient.

Despite all its benefits, digital transformation, if not handled carefully, also carries with it new cyber-risks.

For example, IBM Security's Cost of a Data Breach report found that misconfigured clouds were a leading cause of cyber breaches. For pharma, more than half of the industry's cyber incidents happen during this move to the cloud — and to make matters worse, breaches that happen during cloud migrations are the most expensive.[4]

While the pandemic has had a positive impact on pharma's digital progress, forcing the industry to drop a lot of its traditional constraints, it also has created more opportunity for cyberattacks.

"The pandemic undoubtedly exacerbated the rise of cyberattacks," says Liz Mann, EY Americas Life Sciences and Health Cybersecurity leader. "The shift to remote working facilitated an abrupt change to corporate network traffic patterns and to the degrees of controls implemented in a work-from-home environment."

Last year, hundreds of thousands of workers in the pharma industry pivoted to remote work virtually overnight, which resulted in, among many things, an influx of personal devices on corporate networks.

During Aspen's Cyber Summit, Meredith Harper, CISO at Eli Lilly, noted that the drugmaker's decision early on in the pandemic to allow some 16,000-17,000 global team members to work remotely substantially increased the footprint of the cyberattack surface.

According to Harper, Eli Lilly went to great lengths to quickly roll out an educational awareness program about how to better protect against cyberthreats in a home environment, including offering employees financial allowances to properly secure their workspaces.

The impact of the pandemic on cybersecurity wasn't exclusive to the pharma industry. Overall, the pandemic increased the threat of cyberattack for companies across all industries. Kroll and partners surveyed 500 security and risk leaders at large organizations — those with more than $500 million in revenue — on matters related to their cybersecurity programs, specifically threat detection and incident response. What they discovered was that the vast majority (93%) of organizations suffered a compromise of data over the past 12 months.[5]

New attack models

The pharma industry is frequently heralded for its life-saving innovations in human health. But like drugmakers, cybercriminals are also fast evolving.

"As a professional in this field, I'm constantly amazed at the speed with which hackers adapt and come up with new ways of working that actually work," reflects Brill. "You know, it's the kind of thing where if they would apply themselves to good things, we'd have great breakthroughs."

Wishful thinking aside, no industry is immune to attacks by nefarious actors, and despite its mission to save lives, this rule includes pharma. While it's concerning enough that attacks on pharma have become frequent, it's even more troubling that the attacks are more targeted and sophisticated.

While the ransomware approach with the end goal of financial gain remains the most popular method of attacking pharma companies, experts are warning that the spectrum of attacks is widening.

"The thing about cyberthreats is that old experiences fuel new ideas, and the landscape is always changing. Threat actors continue to demonstrate patience, creativity and determination in the process," says Mann.

Ransomware-plus

Ransomware — a form of malicious software ("malware") designed to block access to a computer system or data — makes up almost half of all reported attacks on the pharma industry.[1]

In its most basic form, ransomware works like this: Criminals encrypt a company's data or systems and then force the company to pay a ransom in exchange for decrypting the information or restoring access to systems.

But according to Brill, criminals have also started "double-dipping" in the ransomware pool.

"Kroll's internal intelligence group is seeing that in about half of our cases, before the ransomware is actually launched and everything is encrypted, the hackers steal the data," says Brill. "The hackers say, 'Pay me the ransom or you'll never get your data back.' And then after you pay the ransom, they say, 'By the way, I stole a copy of your data. And if you don't pay me more, it's going to be made public on the internet.'"

Brill says that Kroll has also recently seen an influx of attacks bypass the ransomware altogether. In these cases, attackers go beyond simply disabling systems; instead they steal sensitive data and hold it for ransom, threatening to sell it if the ransom isn't paid.

Digital espionage

Stories of suspected nation-state cyberespionage, sometimes reminiscent of old spy film plots, frequently light up the news headlines. Their intrigue is compounded by the fact that they are often shrouded in mystery — confirmed

by "unnamed government sources" and lacking details regarding the perpetrators, whether the attacks were successful and what data may have been compromised.

Brill ran point on one of the most high-profile cases of suspected cyberespionage in history.

During the 2008 U.S. presidential election cycle, the FBI and U.S. Secret Service determined that both the Obama and the McCain campaigns were being targeted by hackers. A team of experts from Kroll, led by Brill, was dispatched to Obama's campaign headquarters and to the Democratic National Committee to identify the infection, cleanse infected systems and bolster defenses. Kroll investigators determined the compromise occurred through a phishing email made to look like the outline of a meeting agenda and containing a malicious .zip file attachment.

U.S. officials later attributed the attack to hacking units backed by the People's Republic of China. Dennis Blair, who served as President Obama's director of National Intelligence from 2009-2010, told NBC News that the hackers were, "looking for positions on China…surprises that might be rolled out by campaigns against China."

While espionage isn't the top cyberthreat faced by pharma companies, the pandemic has created an ideal scenario for nation-state attacks. The amount of valuable, proprietary information being generated by drugmakers during COVID vaccine development, combined with an international scramble for information and supplies, and the rise of vaccine nationalism, make vaccine data an almost irresistible target.

Early on in the pandemic, U.S. federal agencies accused both Chinese and Russian cyberespionage groups of attempting to steal COVID vaccine information from drugmakers.

Then, in December of last year — when the U.S. was just days away from authorizing its first vaccines — The Wall Street Journal reported that North Korean hackers targeted at least six pharma companies* working on coronavirus treatments and vaccines in the U.S., U.K. and South Korea. A few months later, South Korea's intelligence agency claimed that North Korea had attempted to steal information on vaccines and treatments by hacking Pfizer.

Supply chain attacks

As the pharma supply chain becomes increasingly global and complex, cybercriminals are capitalizing on new opportunities.

"One of the approaches we see today is what's referred to as a 'supply chain' attack," says Mann. "In this case, supply chain refers to a 'one to many' attack, where the attack is launched at a third party or a technology manufacturer, but the intent is to reach the companies in its supply chain."

Hackers look for a weak link in cybersecurity protocols and use it as an entry point.

*According to a Dec. 2, 2020 WSJ report, AstraZeneca, Johnson & Johnson, Novavax, Genexine, Shin Poong Pharmaceutical and Celltrion were all targeted by North Korean hackers.

Recent pharma-related cyber events

** Dates correspond with when incidents were made public*

March 2020

U.S.-based CRO ExecuPharm revealed that "unknown individuals" deployed ransomware to its IT systems and sought payment for a decryption key. Attackers may have accessed and/or shared select personal information from ExecuPharm personnel, as well as from personnel at parent company, Parexel.

May 2020

The FBI and CISA issued a public service announcement warning health care, pharma and research sectors working on COVID response that they were the "prime targets" of hackers. Per the statement, China-affiliated cyber actors had "been observed attempting to identify and illicitly obtain valuable intellectual property and public health data."

May 2020

Several media sources reported that hackers linked to Iran targeted staff at Gilead Sciences, amid the company's scramble to develop COVID treatments. It was reported that hackers attempted to compromise email accounts of Gilead staff by using messages that impersonated journalists.

July 2020

The U.K.'s National Cyber Security Center revealed that a "cyberespionage group" associated with the Russian intelligence services attempted to hack into coronavirus vaccine research in the U.S., Britain and Canada.

July 2020

The U.S. DOJ indicted two Chinese men for spying on U.S. companies conducting coronavirus research. Prosecutors said that the hackers, who received some support from Chinese intelligence agents, had stolen "hundreds of millions of dollars' worth of trade secrets, intellectual property, and other valuable business information."

October 2020

Dr Reddy's Labs announced that it had isolated all its data centers in the wake of a cyberattack. The incident forced the Indian drugmaker to briefly shut down several production facilities in the U.S., U.K., Brazil, India and Russia, right as Dr. Reddy's was gearing up for late stage trials on Russia's Sputnik V vaccine.

10

November 2020
Sources told Reuters that North Korean hackers tried to break into AstraZeneca's systems as the drugmaker was working on its COVID vaccine. The hackers posed as recruiters on LinkedIn and WhatsApp to approach AstraZeneca staff with fake job offers, the sources said.

December 2020
WSJ reported that North Korean hackers targeted at least six pharma companies working on coronavirus treatments and vaccines in the U.S., U.K. and South Korea.

December 2020
IBM X-Force released a report on malicious cyber actors targeting the COVID cold chain. The phishing campaign spanned across six countries and targeted organizations working with Gavi, The Vaccine Alliance.

December 2020
Pfizer and BioNTech announced that documents related to the regulatory submission of their COVID vaccine had been accessed in a cyberattack on the European Medicines Agency. The EMA later confirmed that some of the stolen data was released online and Dutch newspaper De Volkskrant reported that both Russian and Chinese intelligence agencies were behind the attacks.

February 2021
South Korea's intelligence agency said North Korea attempted to steal information on coronavirus vaccines and treatments by hacking Pfizer.

March 2021
Cyber intelligence firm Cyfirma said that a Chinese state-backed hacking group targeted the IT infrastructure and supply chain software of two Indian vaccine makers — Bharat Biotech and the Serum Institute of India, the world's largest vaccine maker.

May 2021
The FBI and the Australian Cyber Security Centre warned of an ongoing global Avaddon ransomware-as-a-service campaign targeting multiple sectors, including the pharma industry.

"Cybercriminals attack once, land in many places, and see what can be accomplished. A lot of damage can be done quickly in this manner," says Mann.

The pandemic has further extended the pharma supply chain and by doing so, created more potential points of attack. The need to transport millions of doses of vaccines with unique cold storage requirements has introduced new partners to the pharma supply chain. And these new partners bring new security issues.

A recent BlueVoyant logistics report found that attacks on shipping and logistics firms tripled between 2019 and 2020.[6] While most pharma companies have robust cyber defenses in place, that is not always the case with delivery and logistics companies. Connecting systems via GPS and digital apps exposes all partners in the chain, warns Brill.

As a case in point last November, Americold, the world's largest owner and operator of temperature-controlled warehouses — and one of the companies tapped to provide the specialized cold storage required for the Pfizer vaccine — disclosed that its computer network was affected by a cyber incident, later revealed to be a ransomware attack.

The attack on Americold wasn't an isolated incident either. A month later, the cyber teams at IBM and the Department of Homeland Security's CISA warned of a phishing campaign spanning across six countries that targeted multiple organizations associated with Gavi, The Vaccine Alliance's Cold Chain Equipment Optimization Platform — a program put in place in 2015 to help improve the global availability and installation of high-performing cold chain equipment.

Insider threats

Insider threats come in various forms, and they don't always have to be malicious.

As the pandemic took hold, the combination of a hasty transition to remote work, a high-stress climate and the need to work quickly created an environment where even the most well-intentioned employee could inadvertently enable a cyber breach.

In September 2020, cybersecurity experts at Positive Technologies investigated an elaborate social engineering attack against a major pharma company. The attack involved North Korean hackers using a fake LinkedIn profile with hundreds of connections and bogus job offers to trick employees into running code that eventually compromised the corporate network.

There are also occasions where, as the famous line goes, "the call is coming from inside the house." Aside from occasional data breaches perpetrated by a disgruntled employee, experts at Kroll have spotted a new trend whereby criminals enlist the help of pharma insiders to pull off their attacks.

"In recent weeks, we've seen some of the cybercriminal gangs reaching out to people inside an organization and saying, 'If you will plant some malware for us, we'll give you a percentage of whatever we get in ransoms,'" says Brill.

To this end, experts have warned of the rise of a new business model used by ransomware developers, referred to as Ransomware as a Service (RaaS). Essentially, criminals are

Cyberattacks on the biotech and pharma industry increased by 50% between 2019 and 2020.

— BlueVoyant

selling kits on the dark web that allow wannabe-hackers who lack the tech skills to develop their own ransomware to simply buy what they need to launch attacks. The ransoms are then shared between the buyer and the RaaS company.

Don't turn your back

For pharma companies, dealing with cyberthreats is part of doing business. But despite the robustness of systems in place, Brill argues that it must always stay top-of-mind.

"The way I look at it, if you're in the pharma or biotech business, you may not like to think about it, but you're in the cyber business," says Brill. "Whether you like it or not, the risks are there. The only choice is whether you're going to ignore them or you're going to understand them."

As threats change and become more advanced, being proactive has become more crucial.

"What we've seen is an evolution in our client base — from 'protect the perimeter and hope for the best' to active monitoring, where you really have people looking at what's going on and trying to get as near to real-time feedback when things go wrong," says Brill.

Being proactive also extends to situations such as upgrading to new, more connected technologies on the plant floor. The digital plant can offer tremendous benefits, provided manufacturers make cybersecurity part of the discussion from the start.

"The magic lies in recognizing that cybersecurity needs to be embedded in emerging technologies from the outset, and by design," says Mann. "The mistake organizations make is in introducing new technologies first, and then trying to secure them later. It is better, faster, smarter and less expensive to embed security into the process from the beginning."

Making cybersecurity a top initiative means starting conversations from the top.

Big Pharma has seen the rise of in-house chief information security officer positions and increasingly, according to Mann, these leaders have a seat at the boardroom table. "The movement from the back office/IT to front office/business strategy, is occurring, albeit slowly," says Mann.

For the smaller companies who may not have the means to have a dedicated cybersecurity executive, there are experts for hire, like Brill and his colleagues working in Kroll's Global Cyber Risk practice, offering end-to-end cyber-risk solutions. Mann notes that some pharma companies may also opt for a part-time or "on-call" CISO.

"We recognize it's not always feasible to have a dedicated executive, but the threat is significant, therefore organizations all need to figure out a way to address it," says Mann.

Brill stresses that cybersecurity can't happen in a bubble. Recognizing patterns and methods of attack can help defend against breaches. It's here that experience and exposure makes a big difference.

"We handle several thousand cases a year. And as a result, we're able to collect a lot of data on what's happening right now, this week, last week, last month, etc." says Brill.

Collaboration, or "crowdsourced cyber security" is also a viable method of broadening experience.

The Health Information Sharing and Analysis Center (H-ISAC) is a global, non-profit organization offering health care stakeholders a forum for coordinating and sharing physical and cyberthreat intelligence. The community — which consists of clinicians, payers, pharma, academia and health IT — is focused on sharing intelligence on threats, incidents and vulnerabilities as well as advice and best practices for mitigation.

"As an industry, pharma recognizes that a threat to one is a threat to all," says Mann. "In my experience, I have seen pharma CISOs help one another during cyberattacks. When human or animal life is at the center of the business, perhaps it inspires better collaboration."

Ultimately, eliminating cyberattacks entirely is not possible, so it comes down to a familiar concept in pharma — managing risk.

"In a nutshell, no one can protect everything with equal rigor. This is a fact. Therefore, risks need to be assessed and defenses implemented based on the likelihood of a breach and the potential for harm," says Mann. "The cyberthreats are significant and ever-changing, so the equation is one of balancing risk with resources."

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Pharma's digital prowess put to the test

Positives, negatives and mixed results from this year's Smart Pharma Survey

Pharma Manufacturing's fifth annual Smart Pharma Survey separately asked drug manufacturers and equipment and services vendors* their thoughts on the pharma industry's digital maturity.

While results from our 2019 survey generated concern that the industry's enthusiasm for the digital "revolution" was waning, last year's survey results — fielded six months into the pandemic — were brimming with digital positivity.

With the pandemic persisting, what has become of pharma's digital journey?

As pharma professionals around the globe wait to see what post-pandemic industry will look like (and when it will arrive), this year's mixed bag of survey results reflect that sentiment.

The positives

Pharma companies are proactively choosing to automate.

Just over 88% of pharma manufacturers — the highest percentage in survey history — said they believe their company would choose to automate processes if given the option.

The pandemic has propelled change.

More than half of pharma manufacturers surveyed said that the COVID pandemic has led to more automation and less personnel on the plant floor; increased interest in digitalizing the supply chain and better integrating partners; and an increased use of technology to collect and analyze data in real-time.

For the 5th consecutive year, pharma vendors believe that the No. 1 issue holding back their customers' digital progress is fear of regulatory backlash

The negatives

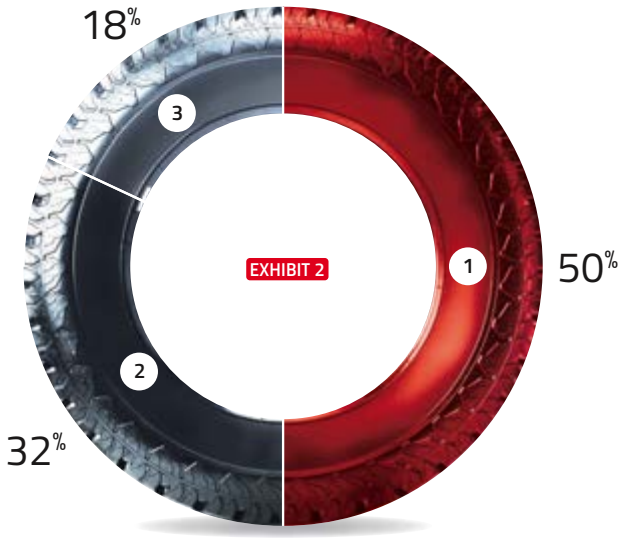
Less than 80% of pharma manufacturers can decisively say the pharma workforce is becoming more comfortable with automation. This is trending way down from last year's 93%.

Are we going backwards, or has it just been a tough year? As companies work through the kinks of rapidly deployed digital solutions, frustration is inevitable.

This year, 27% of equipment vendors claim that when their pharma customers are designing/upgrading their facilities, digitization is "rarely" part of the discussion.

While the majority of pharma manufacturers say digitalization is part of their facility design discussions (Exhibit 4), pharma vendors don't quite agree.

And according to ISPE's Pharma 4.0 Special Interest Group, which has been working since 2015 to translate how Industry 4.0 impacts the pharma industry's unique requirements, this could hold pharma back. ISPE has stated that while smart factory transformations are not a "must," they provide a competitive advantage to the extent that missing out could be a business risk.



Which of the following statements best describes your company's progress on digital transformation/IIoT initiatives?

1. At the starting gate, with focus on learning and exploration
2. We are now identifying early applications to pilot
3. We have identified specific applications and made investments to match

What changed

More pharma manufacturers and equipment vendors felt that the responsibility of pushing the drug industry to automate belongs to equipment manufacturers and software providers.

According to survey results, 38% of pharma manufactures and 54% of vendors think that equipment manufacturers and software providers should be proactively leading the charge by offering innovative products and education.

One of the many issues the pandemic has highlighted is the importance of reliable, trusted supply partners. Pharma's core competency is discovering innovative treatments, so an increased reliance of partners to provide the necessary tools could free up the industry to do what it does best.

EXHIBIT 3

Top concerns about smart equipment and technology in plants

PHARMA	VENDOR PERCEPTION OF PHARMA
Integration	Integration
Education	Regulatory hurdles
Regulatory hurdles	Big data

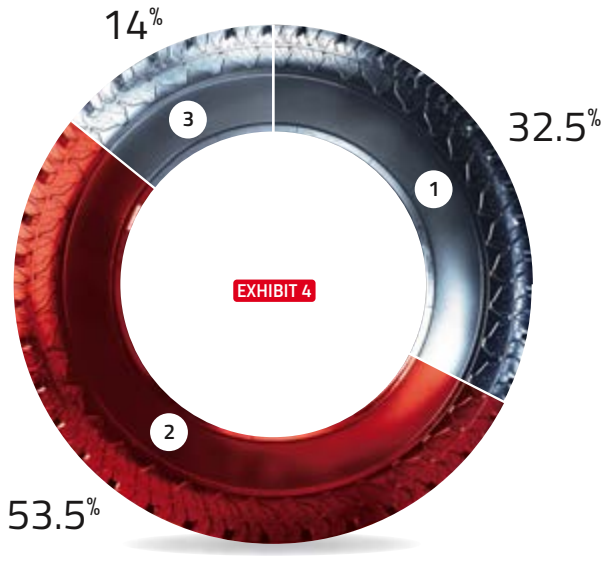
What stayed the same

Half of pharma companies are still at the starting gate when it comes to progress on digital transformation/IIoT initiatives.

This finding (Exhibit 2) is consistent with results from the past five years of pharma surveys.

To see how pharma compares on a broader industrial stage, we can look to Smart Industry's most recent State of Initiative report, which compiles results from surveyed

*For the purposes of this survey, "vendors" are defined as companies who offer pharma processing equipment, lab equipment, controls or software, as well as contract researching, consulting or related services. There were 36 vendor responses. "Pharma manufacturers" are defined as those who manufacture pharma or biopharma drugs, make APIs or excipients or offer contract manufacturing services. There were 43 manufacturer responses.



When your company is designing or upgrading its manufacturing facilities, how important is digitization to the discussion?

1. It is a leading priority
2. It is important, but not the biggest priority
3. it is rarely part of the discussion

professionals from across manufacturing, processing and related industries. When asked about their company's progress on digital transformation initiatives, only about 10% purported to still be at the "starting gate."

And yet, the variability in pharma's survey answers can partially be attributed to the lack of a standard, unified method for evaluating a company's digital transformation progress. In short, everyone defines digital success differently.

Pharma's top concerns surrounding smart equipment and technology in plants haven't changed since 2018.

Integrated, defined as, "difficulty integrating new technology with existing lines or equipment" continues to hold the number one spot for both pharma manufacturers and equipment vendors. (Exhibit 3)

This persistent and pervasive hurdle stems from the many legacy systems in operation on the pharma plant floor that lack the capability to connect to high-level automation systems or devices, as well as pharma's need to connect technologies from different suppliers to develop fully integrated processes.

Regulatory hurdles, specifically a lack of regulatory buy-in or understanding of new processes, continue to be cited as an obstacle by both pharma manufacturers and equipment vendors.

This comes in spite of considerable strides made by the U.S. Food and Drug Administration towards shaking the agency's reputation as innovation blockers.

of pharma manufacturers say the pandemic hasn't changed the industry's perspective towards digitalization

During this year's Parenteral Drug Association annual meeting, Jeffrey Baker, deputy director, Office of Biotechnology Products, Center for Drug Evaluation and Research, challenged the pharma industry's wiliness to modernize in the manufacturing space. According to Baker, although more than 90% of FDA submissions are supplements to Biologics License Applications, very few, if any, reflect modernization or deployment of new manufacturing technologies.

Baker pointed out that despite the fact that regulators are often blamed, the reality is that the FDA has encouraged the development of advanced manufacturing technologies for 20 years through strategic plans, working groups, partnerships and programs.

The pharma industry relies on balancing risk. In the digital sense, this means deciding what risks are worth taking. The most successful digital strategies have often challenged the historical understanding of regulatory policy.

Bob Lenich
Director of Global Life Sciences, Emerson Automation Solutions

Slow rush to the cloud

Strategic cloud deployment is critical to achieving business and operational results

From supply chains to the mobile workforce to technology transfer, the pharma industry is figuring out where it makes the most business and operational sense to leverage cloud technologies. Many production systems today can be implemented in the cloud, but there are still very good reasons for keeping some of them on-premise for the foreseeable future.

As organizations consider which systems to move to the cloud and which to keep on-prem, they must consider how to protect both data and process control, while still making it easy to get critical data out of the system to enable enterprise-wide business decisions. Network latency, security and the role of individual systems in business processes should guide any strategy.

A new approach

For years, the Purdue Model — an industrial control systems architecture reference model — has been the gold standard for separating enterprise and control system functions into hierarchical zones for improved security and performance. More recently, however, the rapid expansion of IoT devices, along with edge and cloud technologies, has disrupted this hierarchical structure of data flow.

Today, manufacturers rely on data sharing between different levels of the organization and need an architecture to support data flow. The best solutions are tiered —with a mix of local, cloud and hybrid architectures — driven by the needs of plant systems and functions.

A three-tiered system, consisting of an on-prem control layer, a hybrid real-time production layer, and a cloud-based enterprise layer helps promote successful and secure operations while ensuring data is not trapped in silos, which impede business decisions and technology transfer.

The on-prem control layer

Control components and systems must be fully protected because any incidents occurring at the control level will have the highest impact on safety and production. All components operating at the control layer benefit from low-latency, high-speed and fully redundant networking solutions. Because these are the most mission-critical and time sensitive systems — usually residing on the plant floor — cloud hosting is generally not a reliable or secure enough option. The control layer is typically hosted on-prem to ensure software and equipment have the fastest, most reliable and most secure connections.

Closed-loop process control

Process robotics, machine and equipment control typically reside in the control layer. As the heart of operations for production, the control system always needs a high-speed, low-latency connection to plant equipment and personnel.

Moreover, in continuous control and batch executive operations, many plants use coordination and advanced control strategies, which directly impact lab and production equipment. Continuous operation strategies such as cross-unit coordination drive production processes to a desired state and ensure successful lot production. This cross-unit coordination provides feed-forward and feedback events and triggers, where timing is critical. Keeping the control system in the same physical location as plant equipment ensures network latency or internet outages do not create problems in coordinated responses.

Safety and equipment health

High-speed, low-latency operation is also essential for safety, and for functionality specific to machinery health. The fast network operation available locally at the control layer enables processes and equipment to communicate state changes to trigger interlocks — essential functionality that cannot risk delays from a network outage.

In addition, executing health management functions for critical or hazardous equipment at the control layer enables fast response or trips on machines experiencing faults before they can cause damage or create safety risks.

Easily moving data

Nearly all process data flows through the control layer. Even though the control layer will not be hosted in the cloud, organizations still need a method to gather process data, and to pass it securely across the site and enterprise for better business decisions.

Typically, plants do not want to send control data thousands of miles away to a data center for processing, nor do they want to introduce the security risk of opening the control layer to external internet-connected systems. Edge computing solutions solve this problem by bringing

computation and data storage closer to the devices generating data in the control layer.

One key component for implementing edge communication, the edge gateway, provides a solution to securely collect data from the control system, without impacting its performance or uptime (Exhibit 1).

Dedicated security features like one-way data diodes with encrypted messaging can deliver essential data from the plant to enterprise systems without exposing control technologies to the internet. In addition, they remove the need for the complex configuration and the context loss created by sending data to a third-party system such as a historian.

Secure edge gateway configurations function as a one-way IT/OT bridge to pull production data to higher levels of the enterprise. These solutions can also be scaled to support edge analytics, or to contextualize and deliver data from multiple control systems to a hybrid cloud or cloud for enterprise-wide analysis.

The hybrid production layer

Many pharma production systems rely on real-time data to allow systems and personnel to quickly respond to incidents. These systems perform real-time or near-real-time manufacturing automation and optimization directly impacting production. As a result, they require the security and low latency most easily provided by on-prem technology.

However, real-time production systems also regularly need fast and intuitive connectivity to cloud enterprise systems. These solutions provide access to the corporate-wide material, as well as laboratory and planning information, along with the site-based dashboarding and inventory management necessary to make strategic decisions. Access to these systems must be tightly secured but does not require the low latency of production systems (Exhibit 2).

With a hybrid production layer, these systems can be hosted locally on virtual machines to ensure real-time data connectivity, while still providing background cloud connectivity, with front-end interfaces replicating cloud systems.

Manufacturing execution

Many of the real-time systems essential to improved manufacturing execution benefit from stable, low-latency connectivity to plant hardware and systems. In systems like order execution, real-time material management and real-time equipment state management, a delay of even a few seconds can create complications in production, and impact quality or safety.

EXHIBIT 1

Edge gateways provide a secure way to move data from the control system to the cloud.

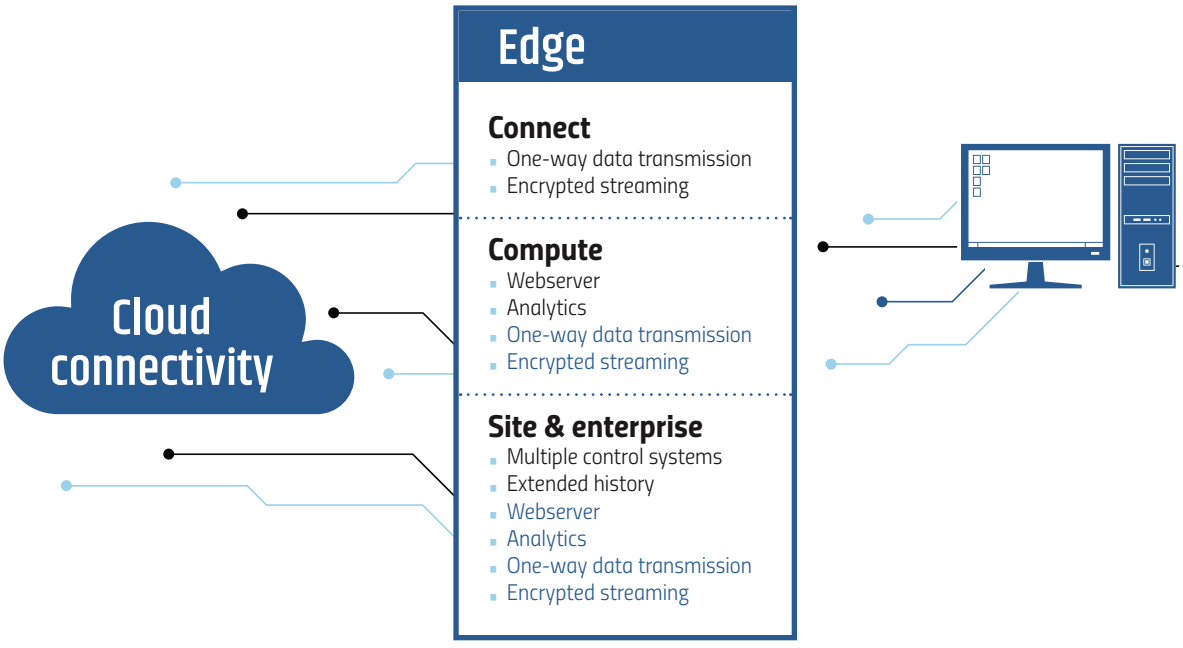
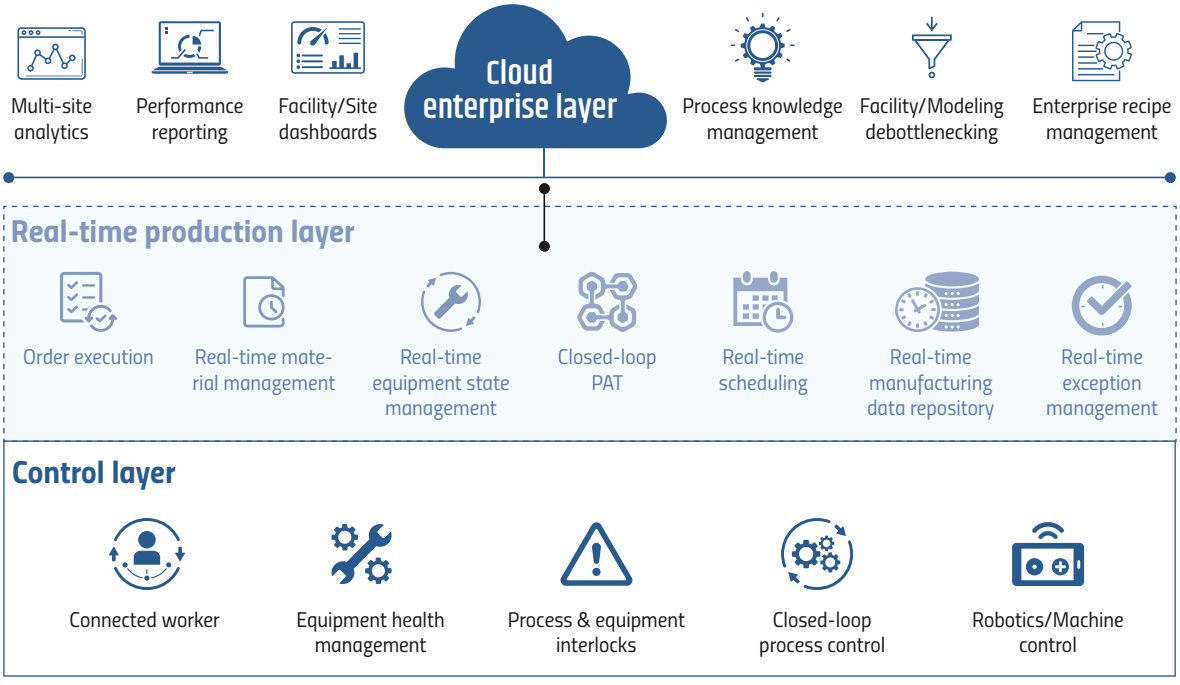


EXHIBIT 2

A three-tiered architecture eliminates data silos while preserving security.



Today, most production facilities run real-time systems at the production layer to provide low-latency performance, while still making it easy to transfer critical data to enterprise systems in the cloud for more centralized management and performance evaluation.

Continuous monitoring and predictive maintenance

Closed-loop process analytical technology (PAT) and real-time exception (RTE) management also run best on local hardware with access to cloud systems. Like manufacturing execution systems, real-time quality control applications are constantly connected to plant hardware, and they often require real-time alert delivery and response. Plant personnel rely on PAT and RTE systems to deliver critical messages to mobile devices as soon as they occur, enabling staff to respond and intervene before an anomaly impacts production.

In addition, enterprise personnel need the same data — though not in real-time — to track and trend performance of individual production centers across multiple locations. As a result, maintenance and production optimization systems typically perform better in a hybrid environment where they are hosted on local hardware for fast notifications to on-site personnel, but can seamlessly connect and deliver data to cloud systems. Cloud connectivity drives enterprise analytics and predictive modeling — information that is no less critical but far less time sensitive.

Scheduling

Modern digital scheduling tools offer powerful, real-time scheduling to monitor current production and automatically adjust future production. For high-volume, low-margin plants, this scheduling often necessitates instantaneous status updates, where delays due to network outages or latency cannot be tolerated.

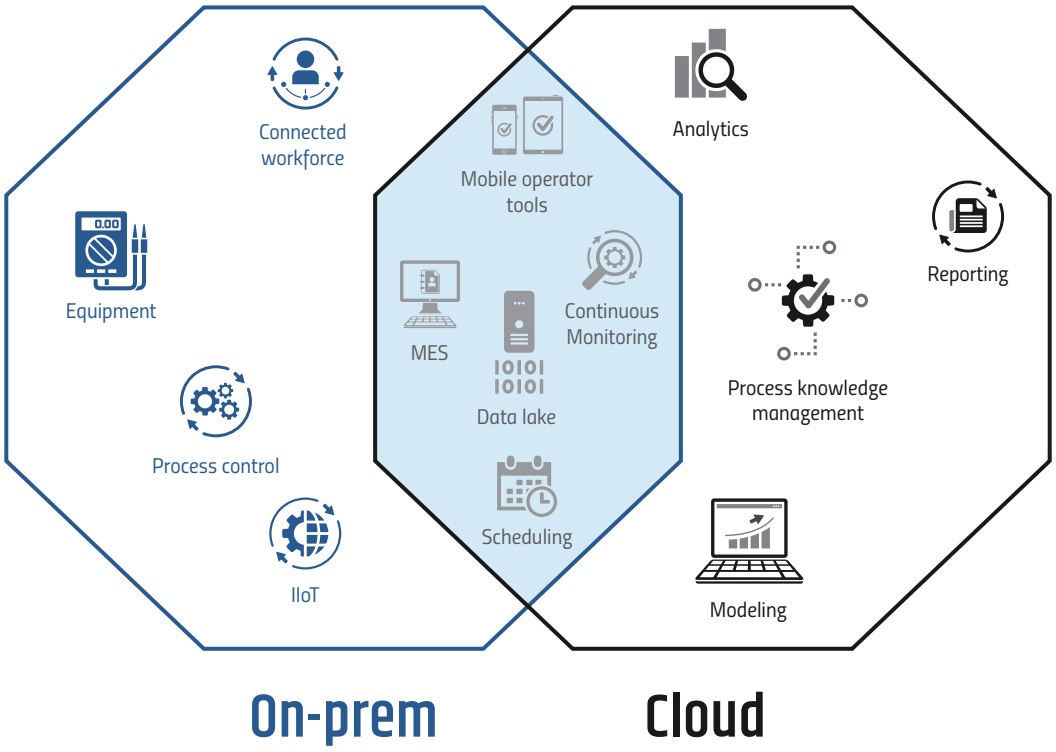
Scheduling software hosted virtually with on-prem equipment offers the best of both worlds, providing the performance necessary to continually update scheduling accurately, while also providing fast cloud connectivity to schedule data for monitoring, trending and adjustment at the enterprise level.

Data lakes

Pharma manufacturers rely on real-time manufacturing data repositories to facilitate easier technology transfer. Research, reliability, operations, maintenance and other departments may all need to collect and use OT data. Data lakes connect the wide variety of software packages used by different departments.

EXHIBIT 3

Knowing which systems should and should not touch the cloud is essential to designing a secure but supportive architecture.



They are used to store, standardize and share data in real-time across every stage of a product, from development to production.

Many organizations opt to host data lakes in the cloud. However, other organizations are hesitant to store data in a cloud repository for security and time-sensitivity reasons. These organizations often look to on-prem data lake solutions to improve connectivity and contextualization of data, without relinquishing control of sensitive information.

Such an approach allows organizations far greater control over the data available inside and outside of the corporate network. This ensures continuous access to real-time data without limiting the effectiveness of key enterprise technologies such as advanced analytics, process knowledge management (PKM), and enterprise resource planning (ERP) systems.

The cloud enterprise layer

Enterprise expertise takes a long-term view of operations across time and multiple plants. As a result, data for these tasks does not typically need to be on-site, nor is it heavily reliant on real-time delivery.

Full cloud-based solutions are particularly valuable at the enterprise level, where systems perform less time-sensitive tasks. While cloud systems are highly stable and often boast uptime of higher than 99.9%, scheduled or unscheduled service outages will likely still occur. These outages are more easily tolerated by business-level systems, which are important but won't cause production, safety or quality issues in the event of downtime.

Analytics

Advanced analytics systems use multi-source data coupled with artificial intelligence (AI) and machine learning (ML) to create the powerful predictive technologies enabling speed-to-market.

For analytics systems performing non-real-time multi-site analysis, hardware requirements tend to increase quickly. As a result, investing in on-prem equipment to run models and engines is often cost prohibitive. Cloud systems, however, scale quickly, easily and affordably to keep pace with the needs of complex AI and ML models. Moreover, analytics software in the cloud is regularly updated, ensuring users always have access to the latest and greatest

models to drive better production and higher quality.

Cloud hosted applications make it easier to integrate across systems such as performance reporting, facility and site dashboards, ERP and laboratory information management systems. In a growing number of facilities, cloud connectivity continues down to systems in the hybrid space, like electronic lab notebooks and manufacturing execution systems.

Process knowledge and management (PKM)

PKM applications improve technology transfer and collaboration across the enterprise. These systems thrive in a cloud environment, where anyone in the organization — regardless of location — can quickly access data they need from any stage of therapy development. Process development, material science, technology and other personnel can collaborate to scale recipes and more easily execute technology transfer from anywhere in the world.

Facility modeling and debottlenecking

Manufacturers use modeling and digital twin simulation for a variety of production needs, from testing process changes and eliminating production bottlenecks, to performing predictive maintenance tasks, to training operators to improve performance, quality and safety.

High-fidelity simulations, which start large and continue to grow as new process areas and models are added, are ideal for cloud hosting, where storage and processing power are easily and affordably scalable at a moment's notice (Exhibit 3).

Picking the right architecture

While not all systems need to be hosted on-site, neither is every system ready to run in the cloud. Fortunately, organizations don't need to choose one solution or the other. Instead of rushing to the cloud, organizations should focus on security, performance and safety needs to select an array of architectures supporting equipment and personnel, while maintaining a secure, productive environment.

With the wide range of cloud, hybrid and edge solutions available, it is easy to find the right mix of hosting technologies to improve performance, throughput, and speed to market — while still protecting key elements of development and production such as quality, runtime and security.

Meagan Parrish
Senior Editor

Focus on: Australia

Already a leader of biotech research, Australia looks to rebound in manufacturing

There's a phrase insiders like to use to describe Australia's pharma industry: punching above its weight.

Although the country is home to just under 26 million inhabitants, Australia ranks in Scientific American's top five countries for biotech activity. And its roughly 230,000 employees in pharma — according to 2017 estimates from trade organization AusBiotech — are known for their world-class skills in scientific research.

"Australia's great strength is that we have very highly skilled professionals in our industry, and an exceptionally great talent pool," Gisela Mautner, president of the Australian Pharmaceutical Professionals Association (APPA), says.

The science-fueled environment has helped bolster a healthy clinical trial landscape. Between 2010-2018 Informa Pharma Intelligence estimates that the number of new trial starts in Australia grew each year by about 4.1%, outpacing the global compounded annual growth rate of 2.5%.

The emphasis on leading-edge treatments has also trickled down to clinicians in Australia, who are resourceful and adept at delivering modern, high-tech therapies to patients.

"Our clinicians look to the world," Mautner explains. "The U.S. and EU both have their own approach. But our clinicians look to the U.S. as well as the EU and pick whatever's best. So we get to apply the best of these various treatment options, and we have modern facilities to do them in."

But while the R&D and clinical world has stayed on the cutting edge of modern medicine, the country's manufacturing industry has slipped through the cracks of Australia's economy. Naturally, COVID-19 has heightened awareness of the growing problem, and now the country is looking to funnel the same kind of support it has created for R&D into manufacturing as well.

$13 billion =
The size of Australia's pharma market
— IBIS World

Manufacturing erosion

"It's been a slow death of drug manufacturing," Mautner says. "This is maybe why the government didn't realize it and didn't see the urgency to do anything about it. COVID opened their eyes, so now things will change."

Like many countries, drug manufacturing in Australia has slowly but steadily diminished over the years as companies have found cheaper alternative locations, particularly in Asia. Estimates by Statista in 2021 showed that Australia's pharma sector now imports about four times as much as it exports, leaving it highly vulnerable in the global supply chain.

But as the pandemic has dragged on, talk of bringing it back has increased. Last year, the country's former Industry Minister, Nick Minchin, wrote in The Australian Financial Review that, "It is tragic that manufacturing has more than halved as the share of our economy in just the last 20 years."

Government backing of R&D has been strong in Australia since 2011 when the R&D Tax Incentive — which offers companies a refundable 38.5-43.5% tax credit for research conducted in the country — went into effect. Now, the focus is shifting to ways the government can bolster the manufacturing sector as well.

Early strategies in the pandemic involved repurposing existing facilities for critical medical supplies, which led gin distilleries to shift to hand sanitizer and packaging companies to suddenly make surgical masks. Yet, federal funds are now flowing in the direction of longer-term solutions.

Between 2014-2020, the country's Advanced Manufacturing Growth Centre (AMGC) pumped $47.9 million into 78 different manufacturing projects, creating more than 2,100 jobs. And in July, the country announced a plan aimed directly at pharma. Called the Modern Manufacturing Initiative (MMI), the plan will provide $36 million in investments for Australian pharma manufacturing companies to help reduce the country's reliance on overseas suppliers. The MMI is part of a broader $1.5 billion plan called the Modern Manufacturing Strategy developed to restore a high-quality, sustainable manufacturing sector in the country.

So far, the MMI initiative has doled out money to support a number of companies including Vaxxas, which produces a vaccination device that delivers doses with a "Band-Aid" like patch, and Noumed Pharmaceuticals, which plans to construct a new $85 million facility for drug manufacturing.

Don't forget about Australia

Despite its reputation for burgeoning biotech activity, Mautner says that Australia's far-off location can make it seem less attractive for multinational pharma companies scouting trial locations.

"Most of the Big Pharma companies are located in America or the EU, so whenever they start projects or studies it's much easier to do them there," Mautner says. "So it's a constant effort to keep reminding them that we are here. That is a major challenge — to stay front of mind for global pharma headquarters."

Because of the cost involved in getting a drug approved for the country's government-funded Pharmaceutical Benefits Scheme, which provides free medication to Australia's residents, some companies may even forgo seeking approval for their drugs in Australia altogether — a situation that has, in some cases, hampered access to potentially life-saving treatments.

"The cost of submissions is higher because you need a team of experts who do nothing but prepare those submissions," Brigid Waite, an executive committee member with APPA, says. "It is one of the most robust processes in the whole world, and very few countries have as stringent of a process as we do."

Although there are currently no initiatives aimed at lowering the cost of new drug submissions, Waite says the Australian government has identified pharma as a key area of needed growth and that the country will continue to woo pharma companies to its borders in other ways.

"The government has realized that there's a major gap for manufacturing in general and then for pharma, so it will need to have [public/private] collaborations," Waite says. "That is how we will work together going forward."

COMPANY SPOTLIGHT

Provectus Algae

An innovative Australian startup unleashes the power of algae for biopharma

In the landscape of Australian biotech startups, Provectus Algae has emerged as one of the buzziest — and they have a unique pitch for biopharma.

Traditionally, the production of recombinant pharmaceutical proteins for products such as vaccines and antibodies has relied on mammalian cells, bacteria or yeast for cell expression. Instead, Provectus has innovated a proprietary biomanufacturing platform called Precision Photosynthesis that uses algae in cell culture, and unlocks its numerous advantages over other methods. Nusqe Spanton, CEO and founder of the company, says that algae is cost competitive with mammalian cells, and has the unique ability to produce more complex molecules than bacteria and yeast.

"We like to take advantage of those opportunities where algae is differentiated," Spanton says. "Especially for products that might not see the light of day because of their manufacturing limitations."

Although algae is abundant in nature and in fact, considered one of the world's oldest organisms, its value in commercial manufacturing has been limited by the difficulties involved in its growth. But with its platform, Spanton says

that Provectus has developed a unique way to use light when growing algae that scales-up well and offers finite control of the cells.

"With the way we use light, we can control the DNA of the cells, and we can switch genes on and off just by changing the type of light we give the algae," Spanton says. "This is a step change for biomanufacturing."

The applications for algae in biomanufacturing stretch beyond pharma. So far, Provectus has found applications for its manufacturing platform in multiple industries including food and beverage, agriculture and animal therapeutics. Provectus has formed commercial partnerships to pilot and eventually commercialize high-value products grown with algae.

"We have identified key areas where we see huge potential in algae's entry point," Spanton explains.

In pharma, Spanton says that ultimately the company plans to license its platform technology — made with a range of novel bioreactors fit with machine learning, AI and automation controls — to cGMP manufacturers. For now though, the technology is still being validated in partnership with several companies and its lead pharma product is in animal health — a strategy that might help ease the pharma industry into the idea of using algae.

"In pharma, there are fermentation systems that have been used for hundreds of years. And the conservative nature of the industry means that companies often don't like to take risks," Spanton says. "So, rather than going head-on into the pharma market, we're validating in a lower-risk market — the non-human market — so that we can prove the technology rapidly."

The company's potential for success hasn't gone unnoticed by investors. In October, Provectus raised $3.25 million in a round of seed financing. Last year, the company also scored a $250,000 grant from the federally funded Advanced Manufacturing Growth Centre to help commercialize its tech, and all told, has received about $400,000 in government backing.

"The government has been a fantastic supporter of the manufacturing market in Australia," Spanton says. "The shift in Australia's political landscape is enabling the growth of biomanufacturing and giving us the opportunity to provide huge solutions in many large and life science markets."

Emmanuel Ligner
President and CEO, Cytiva

The race to scale

How standardization and flexibility helped speed efforts to manufacture COVID-19 vaccines

As the industry well knows, bringing a new product to market is a painstakingly long process. Generally, it takes about a decade to develop a new vaccine and typically between two and five years to develop the manufacturing process for a new product. Then, to build a stainless steel facility from scratch and get it commissioned? That's usually about another three years.

Very few people, therefore, thought we would see a viable COVID-19 vaccine in use before 2022. Yet here we are in mid-2021 with approximately 3.5 billion vaccine doses administered globally at the time of writing — a truly remarkable achievement for the thousands of people worldwide who have worked tirelessly to make it possible.

This success would not have been possible with traditional methods. We needed rapid, proactive, disruptive innovation to open up new possibilities — not just in developing the vaccine itself, but in being able to manufacture it on an industrial scale and at a speed never before seen in the biopharma industry.

Two Danaher operating companies— Pall Corporation, which specializes in filtration, separation, and purification technologies; and Cytiva, a global provider of technologies and services for therapeutic development and manufacture — have been intimately involved in the race to develop viable COVID-19 vaccines and have experienced firsthand the breakthroughs and innovations that have gone into this remarkable success.

Here are their stories.

The blueprint for a billion doses

In the spring of 2020, the University of Oxford contacted Pall to enlist their help with what would become one of the greatest biopharma manufacturing challenges of all time: To design the process that would enable them to produce billions of doses of their new viral vector in a fraction of the time it had taken for similar products previously. Not only did it need to deliver speed, but this process also needed to be simple, scalable and easy to implement in many different manufacturing sites to achieve the same product no matter where it was manufactured in the world.

It's possible to standardize key elements to accelerate process development and manufacturing — a balance that we as an industry have not been able to strike until now.

Pall had significant expertise in viral vector manufacturing, having already developed over 30 large-scale, viral-vector-based processes in the biopharma industry prior to the pandemic, creating a blueprint that could be used for the manufacture of many future viral vector therapies, including standardized manifold designs, equipment lists and processes. The team at Pall applied their process development expertise and production know-how to design and establish a process for the Oxford/AstraZeneca COVID-19 vaccine.

This combination of technical expertise and experience of scaling production processes with Pall's integrated manufacturing solutions for gene therapy and vaccines turned out to be vital in accelerating the speed at which the COVID-19 vaccine process could be developed. Instead of starting from scratch, the Pall team had already created a repeatable template for viral vector manufacturing that covered 80% of what would be needed with the Oxford/AstraZeneca vaccine — they simply then needed to customize the equipment, consumables and workflows based on the specific requirements of this project.

This automated, end-to-end integrated, platform solution was developed to tackle the challenge of scaling up manufacturing for gene therapy. The scalable platform can also address issues that arise when genomic products are manufactured using individual manufacturing steps. For instance, single-use technologies allow for easy scale-up from the laboratory scale to full current Good Manufacturing Practice (cGMP) commercial operation. The company's single-use platform achieves this by keeping the materials of construction the same for its comprehensive range of disposable solutions for upstream through downstream to formulation and filling processes. This approach can provide the same robustness, reliability and batch records required for commercial manufacturing.

Because of such standardization, the team was able to configure the equipment solutions and manifold designs without needing to go through lengthy validation processes — reducing risk and cutting out what normally takes up a huge portion of the process development timeline.

Taking manifolds as an example: There are over 20 contract manufacturing organizations (CMOs) working to manufacture the vaccine, each using more than 50 different manifolds in each bioprocess. This could potentially lead to hundreds or even thousands of different manifold designs being used around the world. Thanks to the standardized processes deployed on this project, the same manifolds were used across the entire project — simplifying the supply chain and adding certainty and consistency for manufacturing teams, wherever they are in the world.

And because of the application of single-use technologies, the Pall team was able to develop a scalable manufacturing process for the COVID-19 vaccine in just eight weeks. This allowed for the first commercial batch at one of Oxford/AstraZeneca's contract manufacturing partners in the UK to be run only 60 days after starting to work on the process itself — a remarkable turnaround time on a truly groundbreaking global project.

Scaling up with flexible factories

In January 2020, the Coalition for Epidemic Preparedness Innovations (CEPI) — considered one of the most influential organizations in the fight against COVID-19 — asked

Australia's University of Queensland to generate the raw materials for clinical trials of a vaccine that had not even been developed. What's more, they planned to start clinical trials for the vaccine in just 16 weeks — an exceptional timescale for something of this nature. The university quickly turned to Cytiva, a long-time collaborator, for help on this vital project.

By Feb. 8, with Cytiva's experience and hands-on assistance, the University of Queensland had a plan in place to speed up the timeline to a matter of months, rather than the usual one and a half to three years. This was despite the fact that this particular vaccine included an innovative structure called a molecular clamp.

To achieve this in time, multiple processes had to run in parallel. Cytiva started by providing key process development expertise to build the first-generation purification approach, and a scalability plan that included technology transfer to the Cytiva site in the U.S. where the clinical material for next phases of clinical trials would be used. The entire process was coupled with a strict supply chain plan, disposables and chromatography resins, ensuring critical material would be available to progress through the clinical steps.

Cytiva also had to rapidly innovate and speed up its own development processes to meet the timescales. They developed, in real time, a new chromatography resin that was not yet commercially available and introduced it into the process. This helped optimize product purification and accelerate to process scalability.

But what really made a difference in this vaccine development project was the decision to take an end-to-end approach that made the factory incredibly flexible. It provided fast deployment and accelerated access to production with adaptable, scalable processes. Each step of the plan was re-imagined, from the bench to future manufacturing.

This end-to-end, single-use technology-based manufacturing process approach was fully automated and integrated. Cytiva used its flexible manufacturing platform, which made it possible to "copy and paste" the manufacturing process to multiple sites around the world, with speed and reliability in order to get the same result — a consistently effective vaccine.

For the future

There is a great variety of ways vaccines can be produced for COVID-19 or any other infectious disease. Each one is unique, and there is no single silver bullet solution to manufacture every vaccine in the most effective way. But it is possible to standardize key elements to significantly accelerate process development and manufacturing — a balance that we as an industry have not been able to strike until now.

The shift from stainless steel to single-use has been crucial. Now, by embracing new innovations in manufacturing — whether using a flexible factory approach, or by standardizing key aspects of the manufacturing process — we believe we can rapidly advance biopharma's ability to bring vaccines and other new therapeutics to market faster.

This year demonstrated how industry-wide collaboration enables innovations in drug development and greater speed to market. Major and complex challenges require a diversity of experience, backgrounds, and cultures to foster solutions. We must embrace a collaborative spirit to develop the life-saving treatments the world needs.

Scientists manufacturing biologics at Cytiva's Fast Trak lab in Westborough, Mass.

Avantor

Claudia Berrón
Senior VP, Clinical Services

Radha Krishnan
Global Head, Biorepository Operations & Strategy

Mastering the sample management ecosystem

A holistic, flexible approach to managing critical research assets can be a drug development game-changer

The pharmaceutical industry is challenged more than ever to produce effective therapies faster. Any first-to-market strategy must include consideration of research assets, whether plasma or tissue, or even informed consent data. These vital assets play a key role in active drug development today — and the therapy innovations of tomorrow.

Critical to the validity of research, biological and nonbiological samples require meticulous care. But managing the massive sample management ecosystem requires more than deciding where samples will be stored long-term after the clinical trial ends. Rather, an effective sample management strategy requires a holistic approach from the beginning that offers the flexibility scientists and clinical trial managers need to move discovery forward for life-changing treatments.

Piecemeal is not ideal

Often, sample management is a patchwork of solutions developed in siloes. For example, large pharma companies might run hundreds of trials worth billions of dollars, involving thousands of study managers and teams — with each trial's sample services supported by different third-party vendors, such as central labs and contract research organizations (CROs). Different vendors lean on different sample management processes and different technology, often with different subcontractors managing key elements.

Whether the size of the pharma company is small or large, the use of many different vendors can lead to:

- Lack of sample visibility: Clinical teams may not fully know what inventory they can access across an organization. Mergers, acquisitions and changing personnel — and the confusion those shifts often bring — can also hamper transparency into available research assets.
- Increased costs: Managing a wide range of vendors requires additional time to manage everything from requesting samples to paying multiple invoices.
- Higher risk of errors: Every additional touch point from multiple vendors — from account managers to order management systems — creates more opportunity for errors that can lead to lost samples, research delays and even a poor patient experience.
- Uncoordinated approach: When multiple stakeholders across various vendors are involved in decision making it can lead to a disjointed management approach that increases costs and risks.

Samples deserve more thorough consideration than they sometimes receive. Consider the amount of time, money and resources clinical trial teams put into recruiting patients, as well as sample collection and analysis. The intrinsic value of even a single sample is significant.

What's more, researchers want — and need — to focus their energy on developing new treatments and vaccines instead of worrying where their samples are or if they're being stored properly. A flexible, holistic infrastructure with streamlined processes takes this unnecessary pressure off scientists' shoulders so they can focus on what matters most: the development of life-changing and commercially viable products.

Comprehensive sample management can reduce inefficiencies. Samples stored onsite at a lab take up valuable storage space and require lab teams to

spend time managing that inventory. The ability to move samples seamlessly and quickly on- and offsite — between a lab and a storage facility — creates more efficient processes, boosts scalability, increases onsite storage capacity and decreases the day-today management burden on researchers and other in-house staff.

A poor sample management strategy can impact patient care as well. The trend toward individualized medicine that's driven by biomarkers makes it critical to ensure samples are available when needed. Lost, delayed or compromised samples can damage the patient experience.

Creating a life cycle sample management strategy

Each sample must be properly stored and tracked through clinical trials and beyond, making long-term sample management an essential strategic consideration. Developing a holistic approach that maximizes these critical research assets and allows scientists more time to focus on science requires consideration of three key elements:

Storage

Good storage practices are a critical part of the sample management process, helping to maintain study integrity and long-term sample viability. During active trials, any samples compromised before analysis can put the study at risk, while compromise in post-study storage can impact the ability to leverage the sample for additional analysis or even future studies.

A flexible sample management strategy will consider the full chain of custody, from collection to lab to storage to disposal. It encompasses well-established operational workflows, as well as oversight and reporting for every stage of the sample's shipping, handling and storage both onsite and offsite. Consolidating sample management with end-to-end traceability helps mitigate risk and makes it easier to monitor the sample across the full storage ecosystem.

Considerations may include whether the samples require the biorepository to perform high-level indexing or conduct individual itemization, sorting and storage. Sample management strategy must also consider standard operating procedures, GxP and regulatory compliance, and 21 CFR Part 11 technology validation to support physical and digital sample chain of custody traceability. In addition, it's important to evaluate scalable solutions that offer the flexibility to scale with the trial's needs as well as provide access to specialized resources.

With sample management, a secure, compliant space that is temperature- and humidity-controlled is a primary concern. While the majority of samples require standard storage conditions, like controlled room temperature or cryogenic storage, others may require the flexibility of a freezer reconfigured to minus 30 degrees Celsius. Regardless of the trial samples' precise needs, access to secure, temperature-controlled storage monitoring systems is essential to maintaining sample integrity and mitigating risk.

Consider what type of related capabilities will be needed over the full life cycle of the sample as well. For example, if aliquoting will be needed, using a one-stop-shop biorepository eliminates transportation risk and ensures audit trail integrity by creating aliquots under the same roof.

A flexible sample management strategy will consider the full chain of custody, from collection to lab to storage to disposal.

In terms of short-term storage, during an active clinical trial, a sample might be retrieved, shipped and returned to storage hundreds of times over a two- to five-year period. Researchers need the flexibility to access samples quickly and seamlessly during active clinical trials. To facilitate those quick turns, labs have two options: onsite freezer farms so scientists can retrieve samples quickly or offsite storage facilities that can properly support active trials by shipping samples within 24 hours.

Medium and long-term storage is often an issue that isn't fully addressed until the study closes. Retention requirements for samples also vary, even from state to state, as well as continuously evolve, so it is critical to plan compliant storage in advance. This helps avoid the additional cost, time and stress that comes with making a last-minute decision.

Compliant, easy-to-access long-term storage also plays a critical role in advancing discovery quickly. Consider that samples previously used in SARS research helped catalyze the rapid development of a COVID-19 vaccine. Moving beyond COVID-19, flexible long-term storage of the sample — and its related data — will help fuel exploration research.

Data

Data is an increasingly important part of sample management — and data storage is only one component. Data collected with a physical sample often includes specific and valuable attributes, like the sample source, the indication and the drug administered.

A sample management strategy should include data inventory consolidation, as well as the collection of the required attributes. This ensures regulated data

An effective sample management strategy requires a holistic approach that offers the flexibility scientists and clinical trial managers need to move discovery forward for life-changing treatments.

can be tracked and traced across the full ecosystem, allowing researchers and clinical trial managers to quickly access study reports, raw data and clinical trial master file records.

Effective data management also increasingly includes informed consent information, which can be used to facilitate future clinical trials. These data systems must be compliant with a host of data privacy regulations across the world whether the lab is storing digital sample information itself or contracting with a third-party vendor.

When developing a sample management strategy, it's important that the biorepository offers a sound technology infrastructure. The ability to integrate associated data quickly is essential to successful clinical research. In addition, the ability to capture and access specific attributes help make trials more efficient, whether it's identifying a sample at the end of its life or selecting specific samples for a new research study.

Logistics

The sample ecosystem is complex, and holistic research asset management requires logistics able to handle the complexity. For active trials, consider a strategy that includes the flexibility of 24-hour sample return that keeps scientists on track and on time. The so-called Amazon effect plays a role, too, as researchers and clinical trial managers want a more transparent experience that features the easy ordering and fast shipping common in consumer transactions.

In well-established markets, regulations continue to shift, requiring sample logistics with the flexibility to adjust to new standards, such as the EUMDR regulation that came into effect in May 2021. Transporting samples across emerging regions like the BRICS block (Brazil, Russia, India, China and South Africa) and the Middle East can present different challenges that must be considered carefully. For example, different transportation modes within a single area might require specific types of paperwork to maintain compliance and allow for seamless shipments.

Another consideration is whether specialized logistics will be required, from freight forwarding to site relocation. A sample management strategy may require logistics personnel trained and licensed to manage a secure cold chain or dispose of hazardous, radioactive or controlled substances.

Moving sample management into the future

Technology will become more efficient, and the related infrastructure will scale in a way that can manage the full data picture. It will become increasingly important to map movement of a single sample across the full ecosystem, even when it involves multiple vendors.

As regulations continue to evolve, biospecimen tracking and management will continue to play a critical role requiring adherence to high standards. Samples collected must be of high quality with detailed annotations and proper consent tracking. This digital data connected to the sample is key to unlocking accurate and timely information that leads to medical discoveries. Data-driven research will lead to discoveries in translational research and personalized medicine, paving the way to next-generation biobanking.

Just as researchers and clinical trial managers are leveraging advanced technology to feed research models, they will look to digitalization to play an essential role that fully addresses sample management's evolving needs.

With sample visibility across multiple trials, digitalization can more efficiently — and more cost-effectively — help structure new trials for innovative therapies. For example, technology can provide the insight that a sample collected for Indication A can also be used for Indications B and C. These capabilities will be a significant game-changer in the future of clinical trials, research and development. Using those attributes across all trial inventories can eventually map and examine patient population pools and indications to help accelerate future trials.

As clinical trials move with the future of medicine, it will be more important than ever for researchers and clinical trial managers to develop solutions that manage samples from pre-clinical research to long-term archiving. Whether outsourcing to third-party vendors for select services or partnering with an end-to-end solutions provider, a holistic, flexible approach will boost efficiency, lower costs and reduce risk — allowing scientists to fully focus on the next life-changing innovation.

product focus

A ROUNDUP OF THE LATEST INNOVATIONS MAKING R&D EASIER FOR PHARMA MANUFACTURERS

Real-time spectroscopy analysis

Although spectrometers provide a wealth of useful data about chemical composition measurements for drug developers, there are still a host of limitations associated with their use. In particular, Raman spectrometers have required separate computers to house the software needed to convert raw measurements into data.

Now, Kaiser Optical Systems, an Endress+Hauser company, has released an embedded Kaiser Raman Rxn analyzer suite that helps manufacturers overcome that challenge and more. According to the company, the Kaiser Raman embedded analyzer collects *in situ* measurements, which allows for real-time monitoring and control. The Rxn2 and Rxn4 models in the suite also have flexible installation options for different lab and manufacturing settings, and are able to self-calibrate when needed. In addition, the models connect with external systems around the clock without sacrificing data security.

"With this 24/7 automation, companies can maintain a continuous pulse on the safety, quality and efficiency of their operations — whether in laboratory or manufacturing settings," Kaiser said. "Data may be collected manually, continuously or periodically — with support for embedded predictors. The analyzers' controller technology is designed for inherent security as a fixed-purpose device to minimize inadvertent or malicious user interaction."

Increased precision in life sciences research

With the goal of keeping workflows moving at a smoother pace, Avantor has launched a line of robotic tips that improve precision in lab robotic and liquid-handling systems. The J.T.Baker robotic tips can be used in a range of applications — from genomics and cell biology to proteomic workflows — and are designed to work for even small volumes of liquid.

Manufactured in Germany under certified cleanroom conditions, the tips are also tested for a range of potential contaminants to ensure high-quality standards. The transparent tips allow for the visual recognition of foam to ensure proper sampling.

Overall, the company says that the robotic tips help researchers move from drug discovery to delivery at a faster pace.

"Our new, high-quality J.T.Baker robotic tips help researchers get the reliable, repeatable results required to keep critical life sciences work moving forward," Rohit Shroff, senior vice president, Global Lab Products, Avantor, said. "Our tips provide customers the precision and reliability they need to support their dynamic requirements."

Laser technology for R&D settings

Although tablet and capsule laser markers are well established in large manufacturing settings, there is still a need for smaller versions of the tech in R&D labs. With that goal in mind, Tri-Star Technologies has introduced a Desktop Tablet and Capsule UV Laser Marker that's portable and small enough for R&D spaces.

Weighing just 32 pounds, the laser marker is designed to fit onto desktops, tables or any space near an electrical outlet. Once installed, the laser marker is an ideal solution for pilot runs or the small-volume production of tablets and capsules of any size and shape. The system, which incorporates the high-resolution technology used by leading pharma companies, can be upgraded to include automatic part feed and a part inspection camera.

The software also includes a complete set of English characters with the option to add special fonts or other languages.

Speeding biomarker discovery

In the quest to discover medications more indicative of disease, traditional separation technologies that lack high-resolution and throughput make it difficult for researchers to identify clinically significant molecules.

To improve disease prediction, diagnosis and treatment, MOBILion has released its High-Resolution Ion Mobility Mass Spectrometry (HRIM-MS) instrument aimed at improving biomarker discovery. Based on Structures for Lossless Ion Manipulation (SLIM), the instrument provides high-resolution separations to improve the characterization of biomarkers. The instrument is also designed to work quickly and allow researchers to more reliably analyze critical quality attributes of complex analyte classes, including glycans and lipids.

"This fast, efficient, super-high resolution separation technology makes it easier to separate and identify the most challenging molecules that are difficult to detect but that have analytical significance," the company said in a press release.

According to the company, the deeper characterization that's enabled by the platform helps reveal more than what is available with conventional approaches while also accelerating the drug development process.

Enhancing analytics of LIMS data

Data collection is prevalent in pharma, but harnessing useful data analysis remains a hurdle for many companies. To help pharma labs overcome this challenge, LabVantage Solutions has released LabVantage Analytics, a full-featured solution that the company says allows users to more easily explore, analyze and visualize LIMS, enterprise and external data.

Designed to integrate with the LabVantage LIMS platform, the new solution uses an AI engine and machine learning to analyze structured and unstructured data from several sources — including data ingestion, pre-processing and storage — in one application. An easy-to-use interface with a customizable dashboard then allows companies to quickly access data reports that drive business insights.

All told, LabVantage says the new solution helps companies pinpoint and leverage key data that can lead to profitable decision-making.

"LabVantage Analytics represents another milestone in our support of digital transformation — turning scientific, business and external data into accessible knowledge that speeds new discoveries, increases lab productivity, improves quality, and reduces consumables waste and instrument downtime," Robert Voelkner, vice president, Sales and Marketing at LabVantage, said.

Brian Ribnicky
Cell Therapy & Bulk Biologics Drug Substance SME, Jacobs

A flexible future

Overcoming operational challenges in cell and gene therapy production

The global cell and gene therapy (CGT) sector is set to experience strong growth in the coming years, and is projected to reach $14 billion by 2025. A combination of factors is driving expansion including ongoing acquisition activity, significant investment in production and a growing pipeline.

With an increasing number of therapies receiving approval, the companies working in this highly specialized area of medicine must address complex and evolving operational challenges in order to keep pace with growing demand.

With production moving from small, lab-style facilities to larger operations, more CGT manufacturers are turning to a planning roadmap to address how they will scale out. In other instances, the absence of a coherent long-term plan is posing challenges for manufacturers, and may lead to delays of up to two years as companies seek to renovate or retrofit existing space or build new facilities.

While the challenges of scaling out CGTs are multi-faceted, flexible facilities offer a path to future-proof operations.

Scale-out specifics

Challenges arise when companies focus solely on production capacity and do not look at the needs of related upstream processes that feed into manufacturing.

For example, when planning to scale out, CGT manufacturers need to consider providing greater QC lab space so staff can update and maintain multiple pieces of specialized equipment simultaneously. Companies must also consider how additional warehouse space can be deployed; that is, not only focusing on GMP activity, but also staging and kitting of single-use bags, tubing and process kits.

Manufacturers face issues in transferring knowledge and tech expertise from existing lab-style facilities to larger manufacturing sites. This is evident on two fronts: First, there is a finite number of staff with the requisite skills and expertise to manage the transfer of technology and processes. Second, CGT companies need to ensure that while transfers take place to new manufacturing sites, there are adequate people to maintain operations and production at their existing facilities.

Each piece of cell and gene therapy lab equipment is specialized and requires highly trained, skilled individuals to maintain. If a specialist is deployed as part of a scale-out operation, the company must ensure that there is an equally skilled colleague who can maintain equipment at the existing facility.

With production ramping up, manufacturers also face challenges in areas such as viral vector production, kitting, media and buffer production, and data integrity. Typically, CGT manufacturers work with one viral vector supplier, but because of greater demand, some companies in this sector may consider sourcing and working with a second supplier. This elevates concerns around sharing intellectual property with another third party in this highly specialized area and is prompting some CGT companies to look at the possibility of bringing viral vector production in-house.

Flexible solutions

Manufacturers looking to ramp up production in a seamless manner must plan for the long term and look at operational requirements that will arise during the next five to 10 years. Flexible facilities play a central role in overcoming these challenges.

For example, companies bringing viral vector production in-house will need to provide segregated QC labs as the need arises, and that capability can be enabled by the flexible facility approach. To accommodate more expansion bioreactors or incubators, facilities can be designed with large ballrooms or smaller suites with removable walls.

Similarly, flexible facilities can support CGT companies when it comes to scaling out and ramping-up production capacity. Modular structures can be deployed quickly to facilitate tech transfer, provide QC lab space and ensure staff can update and maintain multiple pieces of specialized equipment, while also providing warehouse space for GMP activity and related upstream manufacturing processes.

Looking ahead, flexible facilities will continue to play a significant role in supporting the cell and gene therapy sector's requirements, with rapid reconfigurations and new builds underpinning growing demand.

With the CGT market predicted to experience exponential growth, flexibility will be a key driver into the future.

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ad index

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Sanjay Sharma
CEO, Roambee

Got (vaccine shipment) data?

How an early warning system can help secure pharma cold chains

The Suez Canal blockage incident — the latest "black swan" event in a year filled with them — has exposed weaknesses in the global supply chain. Suppliers with goods on the Ever Given certainly knew where their shipments were located — but did they know the condition of their products?

The event was a wake-up call to suppliers worldwide stressing the vital need for data-rich, real-time supply chain visibility.

This need is particularly evident in the global distribution effort of COVID-19 vaccines, due to unprecedented scale and urgency, as well as cold chain requirements.

With more moving parts and therefore, more scope of breakdowns, a cold chain is the most vulnerable kind of supply chain. It's especially vulnerable in pharma, as stringent compliance requirements make the cold chain vital to avoiding exposure to risk. Things can go wrong despite the various risk management plans and techniques applied. For example, even a drop of half a degree in temperature could impact efficacy or stability of COVID-19 vaccines.

Thus, the best practice is to find a way to identify and mitigate these risks before facing the worst-case scenario. This is where a pharma cold chain monitoring system comes in.

Pharma cold chain monitoring technologies have progressed in leaps and bounds, evolving from manual data collection to data loggers with automated logging but manual extraction, to Bluetooth devices that sync with wireless networks.

While the latest pharma cold chain technologies have resolved the data availability problem to a point, they still leave some gaps. The biggest of these gaps is the lack of real-time, relevant data that provides actionability in the true sense — in short, an early warning system.

A cloud-based, wireless monitoring solution, when well-executed with good global connectivity, will track the temperature of shipments in transit in real-time. This type of system gives usable signals that you can act upon, instead of scrounging through spreadsheets. The information automatically reaches the right person at the right time. This helps the person responsible respond to early warning signals and contain damage as soon as it begins.

> "Active cold chain monitoring gives usable signals that you can act upon, instead of scrounging through spreadsheets.

Filling the gaps

An active pharma cold chain early warning solution can provide companies with relevant and actionable data with real-time visibility, while traditional data loggers can only give information about the condition (usually just temperature). An early warning system provides the combination of live sensor data and preemptive actionability, which helps reduce preventable losses due to damaged goods, resulting in better supply chain performance, better market share, and ultimately a much better brand image.

Investing in active cold chain monitoring becomes critical when dealing with pharma goods. Pharma companies not only need to know something has gone wrong, but also need to develop contingency plans for those anomalies on-the-go, so quick decisions based on insights before something hits the bottom line are key.

Active pharma cold chains can help businesses and governments not only by saving the cost and effort that goes into re-ordering contaminated pharma packages due to events such as temperature excursions, theft and delays, but also from the absolute agony of having indirectly put human life in danger.

In short, the "old school" pharma cold chain tracking techniques (e.g., data loggers that only give you limited post-event information) are like hunting for an Uber at 8:45 a.m. when your office is 30 minutes away. An early warning system is like your daily morning alarm that saves you from being late for work, and enables you to do what needs to be done, at the right time.

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