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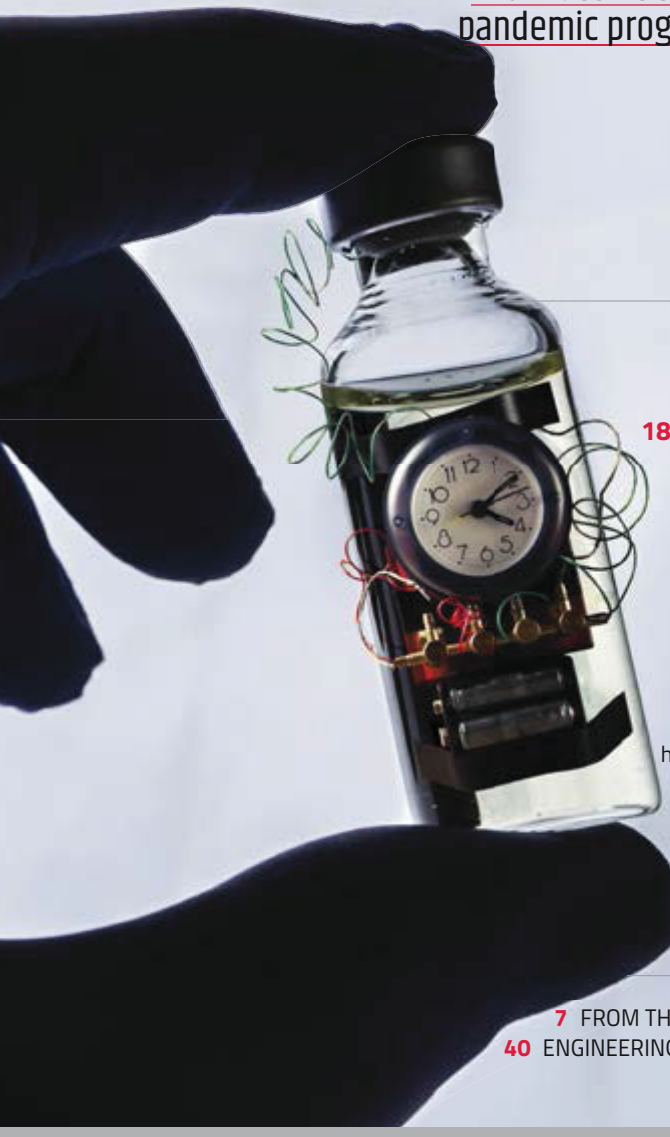
Chief Content Director

ONE SHOT

With vaccine skepticism threatening to shatter pandemic progress, pharma can't afford to falter

page 8



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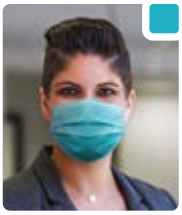
Defusing vaccine skepticism

Public trust is set to explode, taking pandemic progress with it



It's a familiar cinematic trope: The hero (or in some cases, the poor sucker in the wrong place at the wrong time) is trying to remain calm as the clock conspicuously ticks down. The ominous music builds. Sweat beads down his face, as his shaking hands clutch a pair of wire cutters and he ponders the familiar conundrum: "Which wire do I cut?"

Any misstep, of course, would end in catastrophe.

As I explored the topic of vaccine skepticism for this month's cover story, I couldn't help but picture the wire cutters in the hands of the pharma industry. While it's true that public health campaigns fall largely under the purview of government, pharma has a lot riding on the success of COVID-19 vaccines. Beyond the time and money drugmakers have poured into vaccine development, public health, industry reputation and future acceptance of vaccines hang in the balance.

According to numerous polls, public trust is waning — and the clock is ticking. As several late-stage trials edge towards the finish line, it's now or never when it comes to convincing the majority of Americans that COVID-19 vaccines are safe.

But much like defusing a bomb, hesitation is not the only mistake to be made. Rushing a vaccine that ends up being ineffective or unsafe is the equivalent of hastily cutting the wrong colored wire…a move that could be lethal for vaccine confidence and even more literally, people.

During a time when we can't possibly use the term "unprecedented" enough, a different type of vaccine skepticism has emerged. Instead of pharma's familiar foe — the fervent anti-vaxxer watching "Plandemic" on repeat and refusing to believe in science — today's skepticism is penetrating the circles of those who have historically supported vaccination.

Why would people who typically trust vaccines refuse one at a time when the need is so urgent? The answer is a complicated mess of tangled wires.

For some, the idea of warp speed vaccine development — cutting a decade-long timeline down to less than a year — generates fear that vital safety steps will be skipped. For others, the dangerous collision of politics and science that has characterized much of this pandemic has polarized their views on vaccines. President Trump, touting his administration's success, has repeatedly promised that the American people will have a vaccine before Nov. 3., even though every health official in the country seems to disagree with this possibility. Drugmakers — some more vocally than others — have insisted that clinical trials aren't designed to follow the U.S. election timeline.

Add to that, the FDA's Emergency Use Authorization, an authority granted to the agency specifically for use in times of public health emergencies, has been dragged into the political warzone, bringing the agency's credibility with it.

Pharma is faced with a near impossible situation when it comes to contributing to the national dialogue about vaccines: push too hard and they seem opportunistic, stay quiet and they lose control of the narrative on vaccine safety. We have seen historic pledges, open letters, op-eds and candid interviews, as the pharma industry and public health agencies alike struggle to get the voice of science to rise above the noise.

It is my opinion that drugmakers have stepped up and emerged stronger than ever. The pandemic has birthed a more transparent pharma industry. One that is open about its clinical trial process. One that is willing to explain the intricacies of drug development to the public. One where CEOs speak up and speak out.

Rarely in movies do the bombs explode. In the nick of time, the hero prevails. And in this case I think pharma, backed by science, will save the day.

industry dose

Pharma's 2020 Influential Women in Manufacturing

The story behind one of this year's honorees

JoyL Silva's career has long been marked by bold leaps.

After landing her first role at Pfizer, Silva worked her way through a number of positions — from health care sales to global operations and into leadership. Some colleagues advised that if she wanted to go further maybe she should go back to business school or perhaps work abroad on an international assignment. Instead, when an opportunity arose in 2018 to take on a leadership position as the general manager for Pfizer CentreOne, a leading pharmaceutical contract development and manufacturing organization embedded within Pfizer, Silva — who had no formal experience or training in manufacturing — dove into the role.

"I didn't know if I would be able to take what I knew from a marketing and commercial perspective and learn the manufacturing language, which is so critical to building credibility," she explains.

But Silva did exactly that. Not only did she forge strong business partnerships that helped unlock potential customers and new streams of revenue, Silva also instituted a number of operational and digital changes, restructured the company to have a clearer geographical and technology focus, and helped Pfizer CentreOne win an award for its customer service. All told, Silva led Pfizer CentreOne during its highest period of revenue in its 40-year history.

"[Taking that role] really was the most important moment in my career because I was able to prove to other people, to myself and to other women that you don't have to know everything or have grown up in a certain function to take a new job," she says. "If you surround yourself with experts and establish yourself as credible professional, you can move forward and lead."

A leading example

With the same level of confidence, Silva recently took on an entirely new role — this time as the vice president, global franchise lead for hematology at Pfizer. Now, with her new job focused on both marketing and developing a portfolio of assets for Pfizer's hematology portfolio, Silva will once again be involved in a completely different side of the business. Silva says that taking on this position has been a game-changing decision.

What advice would she give to other women in manufacturing who might be looking to shake up their working life? Be unafraid of asking questions.

2020 IWIM Winner
JoyL Silva, vice president, global franchise lead for hematology, Pfizer

"Whenever I've met other professionals, I would always hear their title, yet I wanted to know more about what they actually do on a day-to-day basis," she explains. "I feel like that curiosity could be seen as a weakness, but that is how you find out what other types of roles you could see yourself in."

By forging these kinds of new connections, Silva says that women can help blaze a new trail in their career.

"When people give you advice and offer something, take advantage of it. Even if it's something you don't think you're interested in. Be curious," she advises.

We launched a podcast!

Pharma Manufacturing's new podcast series, Off Script, offers in-depth interviews and discussions with industry experts about hot-button topics in pharma, and goes behind the scenes of our print and online coverage to follow the industry's biggest issues surrounding scale-up, technology innovations, regulations and more.

Check out our first episodes at PharmaManufacturing.com:

- **Episode one:** The intriguing backstories behind our September cover story on reshoring generic drug production. (Available now)
- **Episode two:** A look at the complex challenges with distributing a coronavirus vaccine and what's being done to turn vaccines into vaccinations. (Coming in October)
- **Episode three:** A deeper dive into the central question from our October cover story: With vaccine skepticism threatening to dismantle pandemic progress, will the industry's efforts be enough to defuse the situation before public trust explodes? (Coming later in October)

Each year, *Pharma Manufacturing's* parent company, Putman Media, recognizes women effecting change in industrial production spaces with the Influential Women in Manufacturing awards. This year's class of winners included five note-worthy veterans from pharma:

- **JoyL Silva**, Pfizer
- **Colleen Herczak**, Grand River Aseptic Manufacturing
- **Barbara Juncosa**, MiraCosta College
- **Dafni Bika**, AstraZeneca
- **Jennifer Blanchette**, Baxter Healthcare

Read their stories at PharmaManufacturing.com

ONE SHOT

With vaccine skepticism threatening to shatter pandemic progress, pharma can't afford to falter

Even in today's most uncertain times there are many things of which people are certain.

Ask any American who they are voting for in November, how they feel about federal mask mandates, or if schools should reopen for in-person learning and the majority will answer without hesitation.

And yet, when it comes to what could be one of the most important public health developments in modern history — SARS-CoV-2 vaccines — and more specifically, whether or not people will choose to get the shots once they're available, millions of Americans begin to equivocate.

"Well, it depends…" is the common sentiment from many — even from some inside the pharma industry. The stipulations vary by individual, with approval timing and the type of regulatory approval granted topping the list of concerns.

Throughout the pandemic, numerous polls conducted across the U.S. have attempted to gauge public trust in hypothetical COVID-19 vaccines. While the results have varied, the polls decisively depict a troubling trend: Trust is shifting in the wrong direction. Springtime polls found just a quarter of Americans hesitant about the safety of potential vaccines. Now, as several late-stage vaccine trials edge

towards the finish line, skepticism surrounding vaccines continues to spread at a rate faster than the coronavirus itself — and recent polls are reporting that as many as 50 percent of Americans say they will not get a vaccine when one is available.

Unlike the more traditional "anti-vax" movement, coronavirus vaccine skepticism has permeated the circles of health professionals and scientists alike, elevating the issue to more than just an unfounded concern conjured up by fringe conspiracy theorists.

Pharma, backed by billions of dollars of government support, is putting forth an extraordinary effort towards the development, testing, and manufacturing of vaccines, but the perfect storm of politics, misinformation and "warp speed" progression continues to cast waves of doubt over vaccine safety. In a flurry of op-eds, open letters and pledges, leaders of government health agencies and pharma companies have repeatedly tried to assuage fears by swearing allegiance to science and safety.

But trust, as they say, is earned in drops and lost in buckets. With everything on the line — public health, company reputations, future acceptance of all vaccines — pharma only has one shot to get this right.

How did we get here and, more importantly, can the industry defuse the situation before public trust explodes, taking vaccine progress with it?

49% of U.S. adults say they definitely or probably would not get a COVID-19 vaccination at this time

— A national survey by Pew Research Center, conducted Sept. 8-13 among 10,093 U.S. adults

Explaining vaccines in context

Vaccine makers have always faced opposition from anti-vaxxers. When smallpox outbreaks in the late 19th century led to vaccination campaigns across the U.S., opponents founded the Anti-Vaccination Society of America. Additional leagues were formed; protests, anti-vaccine publications (old-school social media) and court battles ensued.

But during the present-day pandemic, anti-vaxxers are not the main faction the pharma industry is contending with in the battle to increase vaccine confidence. In fact, they are rarely part of the discussion.

"If you remove those folks that have unfortunately landed in the anti-vaccine category for all vaccines, I think that the group the pharma industry is trying to communicate with more concretely are the people who actually support vaccines. They vaccinate their kids, they get the flu shot," says Phyllis Arthur, vice president, Infectious Diseases and Diagnostics Policy at the Biotechnology Innovation Organization (BIO). "What we are trying to do is differentiate between this group and that narrow set of the population that is concerned about all vaccines, no matter how long-term the data."

This newly emerging group of vaccine skeptics are, according to Arthur, "struggling with the difference between the vaccines they support, which they support because they have lots of data, and the potential COVID-19 vaccine, which will come with some unknowns."

"And I think that's perfectly rational," says Arthur.

It might be surprising to hear a vaccine policy expert with a 20-year career championing vaccines use the term "rational" in a discussion about vaccine wariness, but Arthur is quick to explain the novelty of the current situation.

"I think what's happening is we're not explaining or putting the vaccine in the context of a solution to a pandemic," says Arthur. "The coronavirus vaccine is different because it's a pandemic vaccine."

There is no denying the pharma industry's traditional vaccine development has been completely upended by the urgency of the pandemic. Racing a virus that continues to cause thousands of deaths around the world on a daily basis, the industry is attempting to safely condense a process that typically can take a decade, down to a matter of months. Arthur points out that because the industry's approach to vaccines is unique, the industry's approach to addressing vaccine confidence during a pandemic should be unique as well.

"We're in the middle of a major global infectious disease event. We can't travel. We can't go to work. These are very different times. And when you think of it that way, then you would think about the approach to explaining the vaccine differently," she says.

*Pfizer is the only drugmaker involved in the Operation Warp Speed program who has recently expressed the possibility of an October timeline. As of Sept. 28, 2020, Pfizer reported having enrolled 35,369 participants across four countries for its phase 3 coronavirus vaccine trial. CEO Albert Bourla says the company could have "a conclusive readout" in late October and that if the results are positive, the company will immediately seek FDA approval.

Skepticism: Now available in many flavors

The new strain of vaccine skepticism that has emerged during the pandemic has multiple and varied points of origin.

"You have a variety of different flavors here; it's not just all one thing contributing to vaccine hesitancy," says John LaMattina, senior partner at PureTech Health, author and former president of Pfizer Global R&D. "And if each of those add up — to say 50 percent of the population — then it could really slow down progress."

Why would people who generally support vaccines refuse one at a time when the need is so urgent?

For starters, the SARS-CoV-2 vaccine approval timeline has become an election flashpoint. While championing his administration's aggressive vaccine push, President Trump has repeatedly promised the American people a vaccine before Election Day — a timeline that has been refuted by top level health officials and the majority of drugmakers involved in Operation Warp Speed.* Democratic leaders, including vice president nominee Kamala Harris, have responded by raising concerns about taking Trump's "word for it" on the safety of a pre-election vaccine. Trump, in turn, has accused Democrats of spreading "reckless anti-vaccine rhetoric."

While partisan divide alone is enough to dent vaccine confidence, the pandemic has dragged the U.S. Food and Drug Administration — the 100+ year old agency heralded for its gold standard work in protecting public health — into a political warzone. The perception of political interference has caused many to doubt the agency's credibility when it comes to drug approvals.

"Another element that enters into this of course ties into the FDA, and what the FDA has been doing so far in terms of COVID-19," says Stewart Lyman, who has worked as an independent biopharma consultant for more than 15 years. (Lyman is also known for voraciously and colorfully taking on Twitter trolls who spread false information about vaccines.) "Political interference in the process is only making things worse."

At the center of much of the controversy has been the agency's issuing of Emergency Use Authorizations (EUAs), a pathway that was thrust into the public eye during the pandemic after the agency

Operation Warp Speed frontrunners

Pfizer and BioNTech

Vaccine: mRNA (BNT162b2)

Status: Phase 2/3 trial launched July 27

Target enrollment: 44,000

Moderna

Vaccine: mRNA (mRNA-1273)

Status: Phase 3 trial launched July 27

Target enrollment: 30,000

Johnson & Johnson (Janssen)

Vaccine: Adenovirus vector vaccine (JNJ-78436735)

Status: Phase 3 trial launched Sept. 23

Target enrollment: 60,000

AstraZeneca and the University of Oxford

Vaccine: Recombinant viral vector vaccine (AZD1222)

Status: Phase 3 trial launched Aug. 31, currently on clinical hold as of Sept. 8 in the U.S.

Target enrollment: 30,000

Novavax

Vaccine: Recombinant protein (NVX-CoV2373)

Status: Phase 3 UK trials launched Sept. 24; phase 3 U.S. trial to be launched in October

Target enrollment: 30,000

*DATA AS OF OCT. 4, 2020

issued two heavily debated EUAs — one for the malaria drug hydroxychloroquine, the other for blood plasma from recovered COVID-19 patients.

Hydroxychloroquine, for which the EUA was revoked two months after it was issued when the science didn't hold up, was (and still is) ardently promoted as a COVID-19 treatment by President Trump and many of his supporters. The second controversial EUA decision, for convalescent plasma, was made on the eve of the Republican National Convention. President Trump and FDA Commissioner Stephen Hahn came under fire for what many interpreted as a misrepresentation of data during the press conference announcing the EUA.

For Lyman, the tipping point for FDA credibility actually came the day prior to the convalescent plasma EUA, when President Trump accused the FDA of being part of the "deep state," directly calling out Commissioner Hahn.

"The deep state, or whoever, over at the FDA is making it very difficult for drug companies to get people in order to test the vaccines and therapeutics. Obviously, they are hoping to delay the answer until after November 3rd. Must focus on speed, and saving lives! @SteveFDA," Trump tweeted.

While Commissioner Hahn later commented in press interviews that he had never seen anything that resembled the "deep state" at the FDA, Lyman — who doesn't mince words — feels the agency head should have had a much stronger reaction, and that the credibility of the entire agency was tarnished because Hahn did not do so.

"When Trump accuses the FDA of being part of the deep state and says they are working to slow down the progress of making the vaccine … to not have the head of the FDA counter this clearly and vigorously — I thought this was disgraceful and unconscionable," says Lyman.

"I think Stephen Hahn needs to step down," he concludes.

If it's possible to put politics aside, a vaccine made available under an EUA may also invoke concern that vaccines are being approved too quickly. While historically there has only been one vaccine issued under an EUA,* the possibility of using the pathway for a COVID-19 vaccine has not been ruled out by the FDA or drugmakers. Top officials at the FDA have repeatedly promised (via published op-eds and interviews) that no shortcuts will be taken, even if an EUA is granted.

"We don't have any intention of using EUA to take a vaccine of sub-optimal effect or an unproven vaccine forward," Dr. Peter Marks, director of the Center for Biologics Evaluation and Research (CBER), stated during a mid-August press event.

Yet, many health experts continue to voice concerns surrounding the perception that a vaccine is being "rushed" to approval. In an Aug. 26 letter to Commissioner Hahn and Marks, the Infectious Diseases Society of America (IDSA) and HIV Medicine Association (HIVMA) strongly recommended the full licensure of a vaccine rather than an EUA, stating that "meeting the requirements for

*The first use of the EUA authority was in 2005, when an EUA was issued for the military to use an anthrax vaccine, Anthrax Vaccine Adsorbed.

full approval is the surest route to maximum public trust and vaccine uptake."

"It's interesting how the speediness of the approval works against buy-in from the public to take the vaccine. There's already a lot of misinformation out there, and getting through that is going be difficult enough — but I think if vaccines do come out under EUAs, it could be difficult to convince the public at large to take them," says Chad Landmon, who chairs Axinn, Veltrop & Harkrider's IP and FDA Practice Groups, frequently counseling on food and drug law.

reaching a somber one million lives lost, a return to some semblance of normalcy rests on safe and effective vaccines — and, more specifically, people willing to take these vaccines.

But the issue at hand is not about defending the merits of vaccination — the vast majority of those who are expressing hesitancy about COVID-19 vaccines support vaccination in general. Instead, the implicit danger of this situation comes in the prospect of potentially losing people who may only be hesitant

> **In my mind, the absolute worst outcome here — worse than having no vaccine — is to come up with a vaccine that turns out to be not safe or not effective — or even both.**
>
> — Stewart Lyman

in this one particular situation, to the "other side" — and once people fall down the rabbit hole of anti-vaccination, they may be lost to science forever.

With vaccine confidence already historically low, a misstep by vaccine developers this far into the game could be catastrophic — having a ripple effect beyond the current coronavirus pandemic.

"In my mind, the absolute worst outcome here — worse than having no vaccine — is to come up with a vaccine that turns out to be not safe or not effective — or even both," says Lyman. "Because that is going to cause people to doubt vaccines big time and pharma big time. And you're going to see a dip in the number of people who are vaccinating their kids for measles and other illnesses. And that is going to result in a much greater increase in sickness and death across the country."

Arthur agrees with the potential for serious repercussions.

"I think everyone is worried about that. I worry about there being a blowback on regular vaccines that have lots of data to them. I certainly worry that it undermines public health in general," says Arthur.

Although wavering trust in vaccines is creating a tenuous situation for pharma, it's a situation that could also break in pharma's favor.

"The pharma industry's reputation has suffered and this is a golden time for them to reverse public opinion by coming up with something effective in record time. That would do a tremendous good to resuscitate the industry. But if they screw it up, well…it will just further trash a reputation that's already struggling," says Lyman.

Perhaps no one recognizes reputational inflection points for the pharma industry more aptly than John LaMattina. In 2013, after touring the country

For the pharma industry and government agencies alike, addressing the issue of vaccine skepticism and its spiderweb of causes has become a complex problem with no easy solution.

Imagining what's at stake

"What is at stake is beyond imagination," said Pfizer CEO, Albert Bourla, in a recent interview about developing COVID-19 vaccines.

The gravity of the situation on the surface is serious enough: With the pandemic death toll recently

Drugmaker's historic vaccine pledge

On Sept. 8, 2020, in order to ensure public confidence in the scientific and regulatory process by which COVID-19 vaccines are evaluated and may ultimately be approved, the CEOs of AstraZeneca, BioNTech, GlaxoSmithKline, Johnson & Johnson, Merck, Moderna, Novavax, Pfizer, and Sanofi pledged to:

- Always make the safety and well-being of vaccinated individuals our top priority.
- Continue to adhere to high scientific and ethical standards regarding the conduct of clinical trials and the rigor of manufacturing processes.
- Only submit for approval or emergency use authorization after demonstrating safety and efficacy through a phase 3 clinical study that is designed and conducted to meet requirements of expert regulatory authorities such as FDA.
- Work to ensure a sufficient supply and range of vaccine options, including those suitable for global access.

for his first book and coming across so many people filled with anger about the pharma industry, LaMattina wrote a second book, "Devalued and Distrusted: Can the Pharmaceutical Industry Restore its Broken Image?"

"When I wrote 'Devalued and Distrusted,' pharma's reputation was really in the pits," says LaMattina.

"And while they've been slowly improving, things seem to have really turned around for them last March when a lot of companies basically dropped what they were doing and devoted resources to COVID-19. And what was fascinating was people suddenly started to get it. In this crisis, who's going to come up with the therapeutics and vaccines? When you really want to gear up and run a clinical trial of tens of thousands of people and manufacture a billion doses of vaccines, only one place does that. And that's the pharmaceutical industry," says LaMattina.

While he is a self-proclaimed cheerleader for pharma's response to the pandemic, LaMattina is quick to acknowledge that the industry needs to continue to confront misconceptions if it wants to gain back public trust, and much of this can be accomplished through transparency.

Ask and you shall receive

In many ways, the pharma industry has exceeded expectations — in some cases even granting items on hypothetical wish lists opined by industry experts — putting forth historic levels of transparency when it comes to COVID-19 vaccine development.

For example, several industry veterans have penned articles urging COVID-19 vaccine developers to adhere to the strictest of scientific standards when it comes to vaccine safety and efficacy. LaMattina was among those to make this request publicly. In an opinion piece published in Forbes, LaMattina stressed that it was imperative that biopharma companies unite behind the mantra, "We will issue no vaccine before its time."

Just days later, industry vets (including LaMattina) got exactly what they asked for when nine vaccine makers released a joint pledge to continue to make the safety and well-being of vaccinated individuals the top priority in the development of the first COVID-19 vaccines.

The media was quick to label the pledge as "historic," and those in the industry agree with this assessment. "I don't remember anything of this nature ever," says LaMattina.

The pledge, which included a bulleted list of four specific promises, was intended to provide reassurance to both health professionals and the general public that vaccine makers are committed to science and safety.

"I'm sure people recognize this is unusual. Drug companies coming out and saying 'We're not going to cut corners here. We're not going to be forced into getting approval on something before it's ready.' It's kind of hard not to notice that — certainly with doctors it had to resonate pretty well," says LaMattina. "And it was the right thing to do."

In another example, BIO, the biopharma industry's largest trade association, published an open letter from several biopharma CEOs calling on their peers and the federal government to commit

> **“If you’re a pharma company and you make too heavy of a push, you risk all the credibility you’ve earned.”**
>
> — John LaMattina

themselves to transparency when it comes to clinical trial data. “We believe that public health, and the public’s trust in new medical products, are dependent upon the integrity, transparency and objective assessment of new data as they emerge,” the letter stated.

Pharma’s most dramatic response to these calls for transparency came in mid-September when Moderna and Pfizer/BioNTech — both of which are involved in the government’s Operation Warp Speed push to produce 300 million doses of vaccine by January 2021 — released their phase 3 clinical trial protocols to the public. Days later, two more drugmakers tapped into the OWS initiative, AstraZeneca/University of Oxford and then Johnson & Johnson, did the same.

The protocols, which are each over 100 pages long, reveal details about trial participant selection and monitoring, safety parameters, and the evidence researchers will use to determine efficacy. It is unusual for drugmakers to reveal these trial blueprints or share data before the study has concluded.

Dr. Tal Zaks, chief medical officer for Moderna, told *The New York Times* that Moderna had consulted an outside ethics expert who advised the company that the only way to win trust was to be “transparent to the point of discomfort,” prompting the company to be the first to release the trial protocols.

Thou doth advocate too much

Dr. Alejandro Cane, who serves as the vice president, North America Medical and Scientific Affairs, Pfizer Global Vaccines at Pfizer agrees that transparency is the path to take when it comes to communicating about vaccines.

“From the beginning, [Pfizer] committed to be as transparent as possible during the vaccine development process and we will continue to do that,” he says.

Like many of the drugmakers developing potential COVID-19 vaccines, Pfizer has made information about its vaccine process and progress, including the recently added clinical trial protocol, prominently available on its consumer website. The company hosts a vaccine-themed podcast that discusses the scientific, cultural and political elements of vaccination. Pfizer has also recently announced plans to launch a direct-to-consumer education campaign as part of its COVID-19 strategy.

“I think companies are thinking long and hard about what they can be doing now to better reassure and inform the public about the strict safety and efficacy standards for new vaccines,” says Landmon, clarifying that a pharma company can’t make evidentiary claims about a vaccine if the data doesn’t yet exist.

It’s a fine line for pharma companies to walk when it comes to being vocal and transparent about vaccines in development, without overtly marketing them — especially when the general public perceives much of pharma’s actions as profit-driven.

When Moderna released early results from eight volunteers enrolled in the phase 1 clinical trial for its mRNA vaccine in mid-May, the drugmaker’s stock valuation soared. But scientists said the readout lacked meaningful data and critics came down hard on Moderna, accusing the company overhyping the findings just to boost shareholder value.

“It’s interesting because I don’t know what companies can do. There’s such a hunger for information. So if a company releases information in order to help with the national dialogue about whether or not a vaccine is plausible, how do

EUAs issued for COVID-19 drug and biological products

On Feb. 4, 2020, the HHS secretary determined that there is a public health emergency that involves the virus that causes COVID-19. On the basis of this determination, the secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic effective March 27, 2020.

COVID-19 convalescent plasma

Issue date: Aug. 23, 2020

Requested by: The Office of the Assistant Secretary for Preparedness and Response (ASPR)

Regiocit

(a citrate-based replacement solution designed for use in continuous renal replacement therapy)

Issue date: Aug. 13, 2020

Requested by: Baxter Healthcare Corporation

Fresenius Propoven 2% Emulsion

(to maintain sedation via continuous infusion in patients)

Issue date: May 8, 2020

Requested by: Fresenius Kabi

Remdesivir

(antiviral drug that inhibits viral RNA synthesis)

Issue date: May 2, 2020 (revised Oct. 1, 2020)

Requested by: Gilead Sciences

MultiFiltrate PRO System and multiBic/multiPlus Solutions

(to provide continuous renal replacement therapy)

Issue date: April 30, 2020

Requested by: Fresenius Medical Care

Hydroxychloroquine sulfate and chloroquine phosphate

Issue date: March 28, 2020 (Revoked June 15, 2020)

Requested by: Biomedical Advanced Research and Development Authority (BARDA)

they do that in a way that doesn't cause people to accuse them of being opportunistic?" says Arthur.

"If you're a pharma company and you make too heavy of a push, you risk all the credibility you've earned," says LaMattina.

Drugmakers have taken a more neutral approach by collaborating with industry peers and government agencies to share information about vaccines.

"Public education is critical, and [Pfizer] aims to increase awareness of the importance of vaccinations in collaboration with patient organizations, medical and public health institutions," says Cane.

It was Pfizer's Bourla who issued a five-point plan early in the pandemic, calling on the biopharma industry to join Pfizer in committing to "unprecedented collaboration to combat COVID-19." The plan called for all members of the "innovation ecosystem" including pharma companies, government agencies and academic institutions to commit to working together in addressing the pandemic. Bourla has been particularly vocal about Pfizer's vaccine journey, speaking out directly against the politicization of vaccines, as well as addressing vaccine safety and vaccine skepticism candidly in numerous media appearances.

But now, with many projecting Pfizer will "win" the vaccine race — or at least, be the first company to submit its vaccine data package to the FDA for review — the drugmaker that has been most outspoken may find itself in the hottest seat in the house.

Uncertainties remain

On Sept. 10, Commissioner Hahn tweeted the FDA's plans to issue expanded guidance on EUA for vaccines to prevent COVID-19. This was seen as an effort to shore up public confidence in vaccine safety and the agency itself.

Even before the guidance was made public, the agency indicated that the EUA criteria would be more rigorous than outlined in the previous guidance. On the same day Hahn announced that new guidance was forthcoming, Marks said that the standards for a vaccine EUA will look more like those of a full biologics licensure.

"If we are going to issue an EUA, it's going to be like an EUA plus," Marks said during a virtual Duke-Margolis Center for Health Policy meeting.

One of the more notable new provisions — reported through anonymous sources before the FDA released the guidance on Oct. 6 — is that vaccine manufacturers seeking an EUA must follow trial subjects for a median of at least 60 days after the subjects receive the final dose (which in most cases is the second dose) of the vaccine.

This has landed critics and enthusiasts alike on the doorstep of Pfizer — the drugmaker who has been the most optimistic about a vaccine timetable — with Bourla repeatedly saying that a conclusive readout from Pfizer's phase 3 mRNA vaccine trial is possible by the end of October.

The debate over the feasibility of an October vaccine from Pfizer has played out intensely in the media. Some argue that if the new EUA guidance were to be implemented, the math doesn't add up to an October EUA for Pfizer — because Pfizer's vaccine trial, which requires a second dose 21 days after the first dose, had not enrolled

subjects early enough to allow for two months of follow-up by October.

But Bourla has doubled and tripled down on his timeline, despite the potential ramifications of releasing a vaccine during the most politically charged time of the year, calling Election Day "an artificial day" and vowing to produce the data when it's ready.

Some public health experts aren't satisfied. More than 60 researchers and bioethicists sent a letter to Bourla and the Pfizer board of directors, urging the drugmaker to wait until late November before filing an application for an EUA, in order to make sure that all trial participants have been monitored for a minimum of two months following administration of the second dose.

"There is too much at stake," the letter concludes. "Submission of an application for an EUA before this standard is met would severely erode public trust and set back efforts to achieve widespread vaccination. In short, a premature application would prolong the pandemic, with disastrous consequences. The reputation of Pfizer and the pharmaceutical industry would be severely damaged."

President Trump has called the new EUA guidance a "political move" and initially said the White House "may or may not approve it." At present, it appears as though the FDA intends on following its guidelines even without the White House's blessing. But no matter how the plotline unfolds, the result is mounting uncertainty and skepticism about vaccine safety.

With infectious disease experts warning of a likely cold-weather surge of coronavirus infections and deaths, the need for a safe and effective vaccine — and public acceptance of this vaccine — is at the forefront of public health.

Pharma's role in producing vaccines is clear, but the industry's role in building trust surrounding vaccines is more complicated to define. Above all, science and safety must prevail. In a situation where trust is dangling precariously by a thread, there is little margin for error.

"If we blow this — if we approve a vaccine too soon, and things go south, we will kill any hope of people accepting a COVID-19 vaccine. And that vaccine is our one real hope of getting beyond all this," says LaMattina. "We've got to get it right."

Meagan Parrish
Senior Editor

Focus on: South Africa

Africa's high-tech hub of pharma manufacturing

Nearly two decades ago, a dark cloud lifted over South Africa's relationship with the global pharma industry.

The drama started in 1998 when 39 pharma companies waged a legal battle with the South African government over a new law that would allow the country to import generic versions of branded antiretrovirals (ARVs) — the drug cocktails responsible for prolonging the lives of patients with HIV. The drugmakers argued that the law infringed on patent rights, and according to *The New York Times*, closed factories, canceled investments in South Africa, and sued the country's government.

But three years later, after a global public outcry and accusations that the industry was keeping South Africans from gaining affordable access to the HIV medications, the coalition of pharma companies agreed to drop the suit. When the news broke, government supporters uncorked champagne bottles and danced through the courtroom.

The decision was a turning point — not just for South Africa's patients, but also for its pharma and health care industries. Although South Africa remains at the epicenter of the global HIV pandemic, its ongoing struggles with the virus and its push to treat the millions of patients living within its borders have also helped pave the way to the country becoming a high-tech hub of pharmaceutical distribution and manufacturing.

Embracing innovation

Six months after the landmark patent dispute with the drug industry was resolved, South Africa's home-grown generic drugmaker, Aspen Pharmacare, was permitted to begin producing ARVs from patents licensed from GlaxoSmith-Kline, the world's most dominate producer of anti-AIDS medications at the time. Aspen was already the region's largest generic drugmaker, but thanks to the deals to produce ARVs, the company expanded its reach.

In 2018, Aspen's billionaire CEO, Stephen Saad, told *CNNMoney* that the company delivers daily ARV treatments to 1 million patients and that its efforts to provide ARVs in South Africa is probably Aspen's "greatest achievement."

Today, Aspen boasts a broad portfolio of branded and generic drugs that it produces at 23 manufacturing facilities, and according to Saad, is the No. 1 producer of anaesthetics outside of the U.S. Aspen is among the world's top 20 generic drug producers and is widely heralded as one of South Africa's greatest business success stories.

All told, the pharmaceuticals industry in South Africa comprises more than 200 pharma companies, and is valued at about $3 billion, according to Keeran Ramnarian, a partner/director at PwC.

South Africa's pharma industry has yet to make much of a splash on the global market and the majority of drugs exported from larger South African pharma companies, such as Aspen, stay within the African continent. Instead,

much of South Africa's pharma products are sold to the government who distributes them through the country's local health care plan.

"Government contracts control the manufacturing landscape," Ramnarian says.

Although many multinational companies distribute medicines in South Africa's pharma market, the local production scene is dominated by generics and mostly focused on the country's more prominent killers: HIV/AIDS, tuberculosis (TB), and hepatitis A and B, as well as common medications for influenza, pain and other everyday ailments.

Because there are only two facilities that can produce active pharmaceutical ingredients (APIs), according to McKinsey & Company, local manufacturers rely heavily on API imports to produce finished formulations. All together, about 80-90 percent of the pharmaceuticals on the market are imported, Ramnarian says.

But while this all might sound like the makings of a low-margin, low-tech industry, Ramnarian says that South Africa's pharma facilities look a lot more like those in advanced regions than the plants you might expect to find in the developing world.

On the cutting edge

"Most of the South African pharma companies operate high-tech manufacturing facilities," Ramnarian says. "Many of these facilities are comparable to modernized facilities in more developed countries with advanced IT platforms, procurement, quality control and communication platforms between service providers."

In fact, writers at *Chemistry World* opined last year that because the Southern African Development Community, a regional economic

The impact of ARVs on HIV in South Africa

South Africa has the largest ARV program in the world, which has had a dramatic impact on the quality of life for patients living with HIV

People living with HIV in South Africa

7.7
MILLION

Population infected with HIV
(aged 15-49)

19
PERCENT

Government funding invested in HIV programs

$1.54
BILLION
in 2017

Portion of HIV patients taking ARVs

62
PERCENT

Life expectancy in 2010

56
YEARS

Life expectancy in 2018

63
YEARS

—Avert

community comprised of 16 member states, has identified flow chemistry as a critical development area, the country could become the next hub for high-tech continuous processing — provided that pharma manufacturers in South Africa continue to cross the digital divide.

Innovative pharma-based solutions have found their way into patient care settings as well. A *PBS NewsHour* report from 2016 showed how these advancements were on display inside a Johannesburg clinic called Right to Care. Facing a workload of 15,000 patients a month, the clinic invested in becoming "the most efficient clinic in South Africa," according to its CEO. Inside, a robotically controlled pharmacy was set up to dispense medications, while ATM-like machines were created to help HIV patients access needed drugs wherever they are in the country.

"We embrace technology as a nation," Ramnarian says.

At pharma plants, Ramnarian says that the emphasis on modern technologies has also helped many improve their regulatory standing.

"There are several facilities here that are FDA-approved and that meet GMP standards for the World Health Organization," he says.

In 2016, Deloitte also reported that 90 percent of the Africa's roughly 500 internationally accredited laboratories were located in South Africa, which demonstrates the country's robust and advanced life sciences R&D infrastructure.

Despite these strengths, the country's pharma industry is being confronted with many challenges.

COVID-19 vax studies

Several drug developers are now conducting coronavirus vaccine studies in South Africa including:

- Novavax
- Johnson & Johnson
- University of Oxford

> We embrace technology as a nation.
> —Keeran Ramnarian

Bolstering regulations

About two years ago, South Africa swapped out its old drug regulatory agency with a new and improved version called the South African Health Product Regulatory Authority (SAHPRA). Like the U.S. Food and Drug Administration, the mission of SAHPRA involves three pillars of oversight: safety, efficacy and quality. But one of the prime goals with SAHPRA was to create a more streamlined entity that could tackle the country's enormous backlog of drug applications.

According SAHPRA, the agency inherited a whopping 16,000 drug applications still waiting for approval from the country's previous regulator. While some of the applications date back to 1992, about half of them were submitted in the last five years. They also run the gamut of critical, high-priority drugs including treatments for HIV, cancer and TB.

Naturally, there's a large impetus to get these drugs through regulatory channels and into the hands of the waiting public, and the pharma industry has been putting pressure on South Africa's government to deliver these treatments to patients more quickly.

To meet this challenge, SAHPRA has reportedly set two concrete goals: reduce the regulatory decision timeframe from its average of 1,422 calendar days in 2017 to 275 working days; and clear its backlog within two years.

Part of SAHPRA's strategy involves eliminating applications that are no longer relevant and/or have no commercial interest to its applicants — and in May 2019, the agency reported that it had removed about 3,000 applications that fit that criteria. SAHPRA has also improved its collaboration with other regulatory bodies to leverage their data and evaluations on certain drugs to create an "abridged review" model that streamlines applications.

Yet, a major roadblock is hovering over SAHPRA's ability to hit these targets.

The human factor

In 2018, SAHPRA reported that it had 178 full-time employees — not enough to speed its regulatory review process. Since 2019, the agency has been on a major hiring drive, seeking to increase its staff to over 450 full-time employees over the next five years. Rather than relying on external reviewers as South Africa's previous drug regulator had, SAHPRA is hoping to build its internal staff capacity to create more efficient capabilities. In October 2019, SAHPRA reported that its "Backlog Clearance

Team" had been onboarded and trained, and that the agency is meeting key milestones on its quest to catch up with drug application reviews.

But the agency has also admitted that it is facing challenges with attracting and recruiting new internal evaluators. Ramnarian says that the skills-shortage situation is a problem being faced by South Africa's pharma industry as a whole.

"This is something that is being continuously addressed," Ramnarian says. "A lot of pharma companies here are investing in training to upscale resources. And there are initiatives at universities offering pharmaceutical degrees. So, there are a lot of public/private initiatives happening to make sure we keep these skills in the country."

So far, one of the only multinational companies with a significant manufacturing presence in South Africa is Sanofi, which Ramnarian says has facilities that are just as technologically advanced as other leading-edge plants around the world. And as the country works to improve its pharma expertise and regulatory framework, Ramnarian says that South Africa could become a more sought-after destination for other Big Pharma companies looking to establish manufacturing operations.

"Companies are attracted to South Africa because we do have a strong infrastructure and a sound regulatory environment," he says.

Changes ahead

Given the importance of health care in South Africa, the market potential for pharma is high. Last year, *Chemistry World* reported that South Africa has the world's fifth-highest per capita expenditure on pharma — and growth has been steady, especially in the generics segment.

"In the last few years, growth in pharma has been between 5-10 percent — higher than normal inflationary growth," Ramnarian says. "This is especially true in generics. And as more products are registered, the market will grow even further."

Beyond generics, South Africa's pharma market is also seeing potential growth in emerging therapeutic areas such as heart disease and diabetes.

With the country's legacy of apartheid, which set deep divisions in the societal standing of its citizens, the South African government under president Cyril Ramaphosa is also in the process of creating health care policies that will guarantee more equal access to drugs. Ramnarian says that the goal is to implement these health care initiatives within the next five to 10 years, and that the government is already becoming an increasingly larger purchaser of pharma products.

"Pharma companies support this initiative because it will boost their sales," Ramnarian says.

Overall, the country has moved far beyond its troubled past with the pharma industry and sees the vital part drugmakers play in improving their way of life.

"The pharma industry is very key to the economy as a whole," Ramnarian says. "There is a lot that needs to be done in terms of improving health care and getting drugs to the masses. Pharma plays a big role in that."

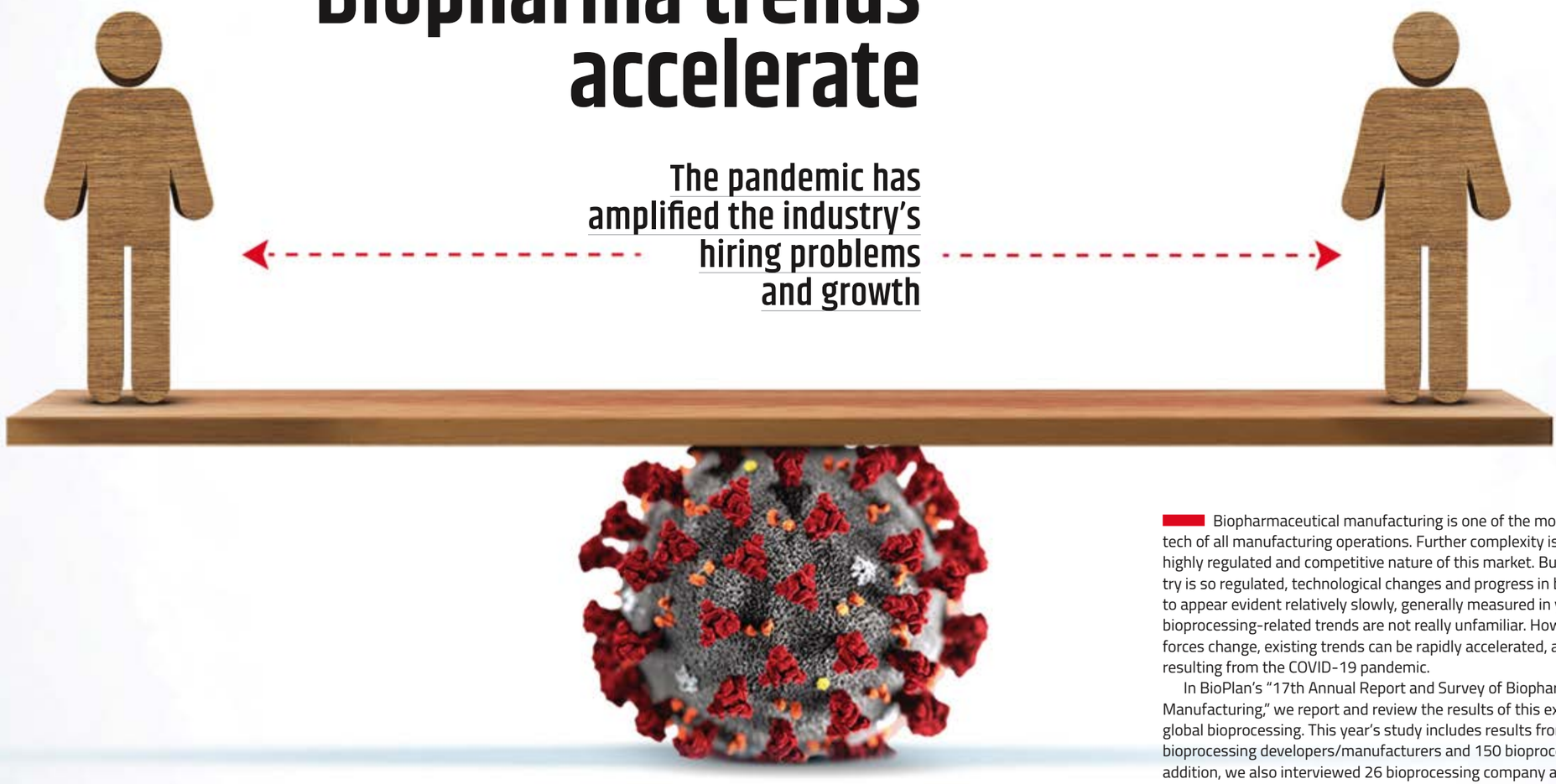
One of South Africa's biggest pharma wins

In 2012, scientists at the University of Cape Town's Drug Discovery and Development Centre reported that they found a new compound to combat malaria. A deal with Merck to co-develop an R&D platform aimed at identifying malaria treatments followed three years later. Then in 2016, the university reported that it had struck gold again, this time finding a compound that it said could be an even more potent malaria treatment with the potential to "block transmission of the parasite from person to person."

Ronald A. Rader
Senior Director, Technical Research, BioPlan Associates

Biopharma trends accelerate

The pandemic has amplified the industry's hiring problems and growth



Biopharmaceutical manufacturing is one of the most complex and high-tech of all manufacturing operations. Further complexity is added due to the highly regulated and competitive nature of this market. But because the industry is so regulated, technological changes and progress in bioprocessing tend to appear evident relatively slowly, generally measured in years. Thus, many bioprocessing-related trends are not really unfamiliar. However, when external forces change, existing trends can be rapidly accelerated, as we are now seeing resulting from the COVID-19 pandemic.

In BioPlan's "17th Annual Report and Survey of Biopharmaceutical Manufacturing," we report and review the results of this extensive survey of global bioprocessing. This year's study includes results from surveying 130 bioprocessing developers/manufacturers and 150 bioprocessing vendors. In addition, we also interviewed 26 bioprocessing company and vendor executives regarding the long-term changes and trends expected at industry responds to the pandemic. Here, we review some of the top-level ongoing trends affecting bioprocessing, including hiring and staffing difficulties, which could have long-term negative impacts on the industry.

Growth continues

Before the pandemic most major bioprocessing-related trends were related to the decades-long consistent growth of the biopharmaceutical industry, which continues at a rather steady rate of approximately 12–14 percent annual growth in revenue.

To this mix we are now seeing the impact of COVID-19 on the industry, including acceleration of many ongoing trends. This includes an upcoming wave of new facility expansions coming online for COVID-19 and other pandemic and biodefense products development and manufacturing. Already, about 1 million liters or more bioreactor capacity can be seen as being devoted to pandemic vaccines and therapeutics manufacturing. Much of this is proceeding at full scale production "at risk," even before trials results are available. For example, Roche and Regeneron recently agreed to "set aside" a total of 140,000-liter capacity for manufacture of a candidate vaccine. Other companies are also diverting existing capacity to pandemic products. Considerable new capacity is being added, beyond the usual sizable amount continually added. For example, Samsung recently announced building a new $2 billion,

>250,000-liter, "super-plant" in South Korea; and WuXi Biologics is building the largest single-use facility (48,000-liter batch; 6,000-liter perfusion) in Ireland. Although many of these projects were in-process prior to the pandemic, COVID-19 has accelerated the need.

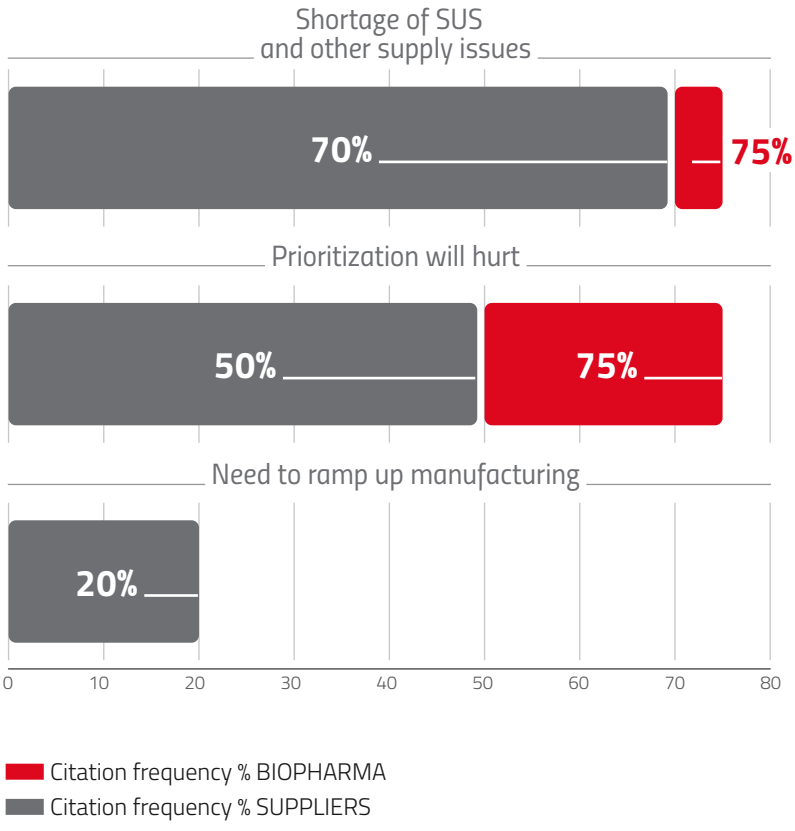
Adapting and addressing the pandemic

The bioprocessing sector and biopharmaceutical industry have effectively adapted to the ongoing pandemic, including continuing manufacturing and R&D, implementing needed staff and operational changes, and paying greater attention to assuring robust supply chains. Key activities, including R&D and manufacturing, are often being increased to address the pandemic. The most commonly cited fears are shown in Exhibit 1.

The top fear noted was the concern about difficulties and delays in obtaining needed single-use supplies in a timely manner. With many facilities ramping-up pandemic-related R&D and manufacturing and others purchasing more supplies to have more in storage, the preexisting shortages of many single-use system (SUS) supplies are worsening. The second most common fear cited was "prioritization will hurt," which refers to the new fact-of-life that nearly all suppliers and many developers are now prioritizing their orders and activities, pushing pandemic/biodefense-related purchases to the front of the line. Prioritization combined with expected worsening of ongoing shortages, including high-purity polymers, will result in more facilities having longer wait time for suppliers to fill orders, particularly single-use supplies. "Need to ramp up manufacturing" relates to many facilities now rapidly building new and expanding manufacturing capacity, often at world-class scales and speculatively, even before trial results are in.

EXHIBIT 1

Pandemic-incited fears



Hiring/staffing: A "perfect storm" of trends

Despite strong trends involving an increase in automation, a major confluence or "perfect storm" of complementary trends is and will result in increased problems hiring and retaining bioprocessing staff. The biopharma industry can and will manage, well enough, capacity-wise by shifting around manufacturing. New facilities and expansions can be brought online relatively quickly, generally within a few years. However, even before the pandemic, bioprocessing staff were chronically in short supply (e.g., ~40 percent of the industry is experiencing problems hiring staff in process development).

And the situation is only getting worse with COVID-19. It takes a long time to train staff, starting with undergraduate life sciences, often graduate training, and most critically, months of on-the-job training. Thus, staff expertise takes many years to develop. There will continue to be a major human capital, talent, knowledgeable staff "crunch" or shortages in the next few years.

Complementary trends that are colliding to form a worst case situation for bioprocessing hiring and staffing issues include:

- **Continued rapid industry growth:** Driven by consistent ~12 percent annual growth in biopharmaceutical revenue, bioprocessing activity and expenditures.
- **Pandemic response:** Related R&D and manufacturing is being rapidly ramped-up at dozens of facilities, with over 100 COVID-19 vaccines added to the industry's

development pipeline. Staff with virus- and vaccine-related expertise are already in short supply.

- **Cellular and gene therapies coming online:** These fields are seeing very rapid growth. This includes BioPlan estimating a current 500 percent shortage of bioprocessing capacity, with 5x current capacity needed (would be used if available). Hiring and staffing in these sectors is already very tight with shortages growing, with the situation made even worse by cellular therapy being particularly labor intensive.
- **Biosimilars/biogenerics**: The industry has recently and will continue to place emphasis on biosimilars directed to highly developed markets and biogenerics directed to lesser- and non-regulated international commerce. This includes >1,100 biosimilars/biogenerics either in development or marketed worldwide, bringing many new countries and hundreds of companies into bioprocessing. U.S./EU CMOs have generally reported seeing a 15 percent annual increase in projects in recent years attributed to biosimilars/biogenerics.
- **Continuous processing:** Some bioprocessing sectors are planning for adoption of continuous upstream perfusion and downstream continuous chromatography. Facilities report they are currently evaluating options or implementing continuous processing adoption. Staff with relevant experience are already in short supply.
- **Experienced staff are leaving:** Baby boomers, post-WWII-born staff, those with the most experience and senior positions, are reaching retirement age.
- **Insufficient new staffing candidates:** There are not enough undergraduate and graduate degreed individuals available and these candidates typically have no relevant experience, with it generally taking ≥6 months to train for any bioprocessing-related position. More will likely be entering these fields in response to the more

When external forces change, existing biopharma trends can be rapidly accelerated, as we are now seeing resulting from the COVID-19 pandemic.

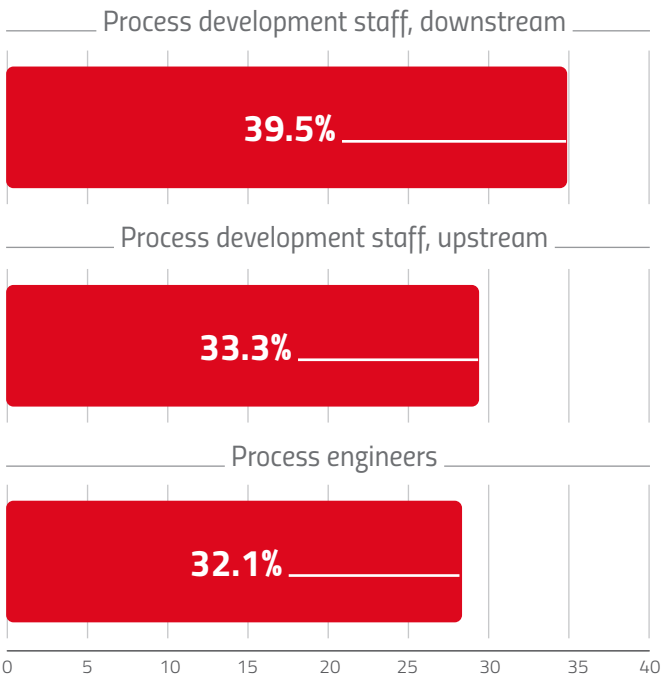
Ongoing trends

Major ongoing trends evident before the pandemic included the likelihood of more:

- **Biological products,** often each with smaller markets, including more orphan and individualized products
- **Bioprocessing companies and facilities worldwide,** especially in major markets and Asia, with significant worldwide expansion of bioprocessing capacity, with worldwide capacity (total bioreactor volume) now approaching 17 million liters.
- **Regionalization of facilities,** with commercial manufacturing facilities placed in more regions and countries
- **Cellular and gene therapies facilities,** with a large number of products coming online
- **Hiring difficulties,** which arelikely to worsen and create significant bottlenecks
- **Modular-constructed facilities,** including cleanrooms and suites
- **Developing-region bioprocessing,** including cloning or construction of GMP facilities in developing countries.
- **Flexible manufacturing facilities,** including use for manufacture of multiple products
- **Adoption of single-use systems,** including at commercial scales often involving scaling-out with multiple 1,000-2,000 bioreactors.
- **Adoption of continuous processing,** including upstream perfusion and continuous chromatography, as these become more mainstream.
- **Efficiency, productivity and downsizing in bioprocessing,** as titers and yields continue to incrementally increase, size of facilities will shrink.
- **Diverse and novel products in development and marketed,** e.g., cellular and gene therapies; novel antibody frameworks; antibody-drug conjugates; live microbe therapeutics, etc.
- **Process automation,** to achieve needed efficiency, expect more monitoring, control and data recording/processing, PAT, etc.
- **Use of bioprocess modeling,** expect more data mining, PAT, QbD, etc., with down-scale modeling increasingly important
- **Use of improved expression systems,** CRISPR and other genetic engineering advances
- **Complex regulations,** as more complex molecules and platforms advance, and as developing countries seek to sell into mature markets, regulations will drive many specific needs and trends.

EXHIBIT 2

Which job positions are difficult to fill?



positive image the biopharma industry is now seeing related to its pandemic responses.

- **Growth in Asian bioprocessing:** Bioprocessing activity and capacity are rapidly increasing in China, South Korea, India and other Asian countries.

Future hiring demands

As the industry expands on many fronts, hiring will present more severe problems, especially where rapid growth is involved, such as in cell and gene therapy and pandemic vaccines. We asked respondents which job positions are currently difficult to fill (Exhibit 2). Of the 25 areas covered, downstream process development staff was again this year cited as the most difficult to fill by 39.5 percent of respondents. This was followed by upstream process development staff and process engineers.

The steady growth in bioprocessing and smooth operation of the biopharma industry could be constrained by the need for qualified staff. The needs for specifically trained staff with hands-on bioprocessing experience have remained stubbornly in place, year after year.

Shortages of experienced staff will likely worsen as experienced baby boomer staff retire, and pandemic vaccine and therapeutics bioprocessing, as well as growth in developing regions such as China, add to demand worldwide.

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Steve Zarichniak
Technical Solutions Consultant

Kari Christensen
Channel Business Manager

The parallel path

Pre-designed automation systems can enable manufacturers to quickly go from approval to production

Recent events have shown that unexpected medical needs can result in stock sector volatility, instability in multiple areas of the economy from large to small businesses, strict border controls and limits on free movement. These conditions pose challenges to the pharmaceutical sector, highlighting the need to rethink medical device, testing and drug supply chains as well as the speed at which solutions are delivered to society.

Pharma manufacturers leading the development of drug and vaccine products realize that new technologies are the strategic drivers of innovation, safety and speed. As clinical trials are finalized, the ability to rapidly pivot to produce new products and ramp-up to meet production demand severely tests technology infrastructures.

The ability to simulate, visualize and qualify manufacturing strategies — even in advance of the typical commercial readiness timelines — are the levers needed to speed execution. The availability of real-time manufacturing data, with enhanced visibility and the power of predictive insights, will enable agile response to demand fluctuations.

A fast-track solution

Some believe the solution to most efficiently ramp up production of potential clinical therapies is to facilitate development of full commercial scale manufacturing earlier, while treatments and preventions are still in clinical trials.

A pre-structured process automation solution can be available for use in development applications in months and enable pharma companies to immediately scale up to full production once regulatory approval is granted. Parallel path development of an engineered solution can

start with minimum formulation details on a final therapy.

The manufacturer can even start to apply digital transformation to the manual steps during clinical trials to better consolidate and analyze data and prepare electronic submittals for regulatory review. The project can start with a supervisory control and data acquisition (SCADA) system overlaying the manual data collection. Then, data can be used to prepare for the final production automation design. The best SCADA solution to use is one that can be easily transformed into a full-blown distributed control system (DCS) solution when needed, as production becomes more complex.

Fast-track automation includes process automation elements that can be rapidly configured virtually and remotely once a therapy is approved and ready to be produced for commercial distribution. A treatment or vaccine can go from approval to production in as little as four weeks depending on process requirements (Exhibit 1).

Deliverables and implementation

A delivered fast track automation solution may include an automation system, SCADA or DCS depending on process requirements, detailed engineering of the system design and applications, project execution and validation, and process equipment skids specified and procured by an authorized solution partner.

The complete system is scalable to meet the needs of varying process requirements and integration is already pre-planned. Automation can be planned for processing several potential therapies until final trial results and approvals are complete. That way, a pre-prepared manufacturing system is ready to go for whichever therapy is approved.

A project delivery "ecosystem" can be positioned to enable rapid delivery of both appropriate expertise and necessary equipment. Global centers of excellence, engineering teams, internal project execution and authorized solution providers can form a team to provide expert installation. This project ecosystem can serve the needs of pharma at an expedited pace.

Implementation starts with development of the automation system on a virtual engineering platform in a private cloud. The design and engineering may include application configuration and qualification services provided by a selected authorized channel solution provider. If a manufacturer wants to repurpose existing process equipment, the integrator will work with the facility to integrate the identified equipment into the final design.

Hardware is then assembled and shipped to the data center, where the facility's servers, virtual hosts and switches are set up; and to the site, where the process equipment,

EXHIBIT 1

Example comparison timeline showing time saved using a parallel path approach

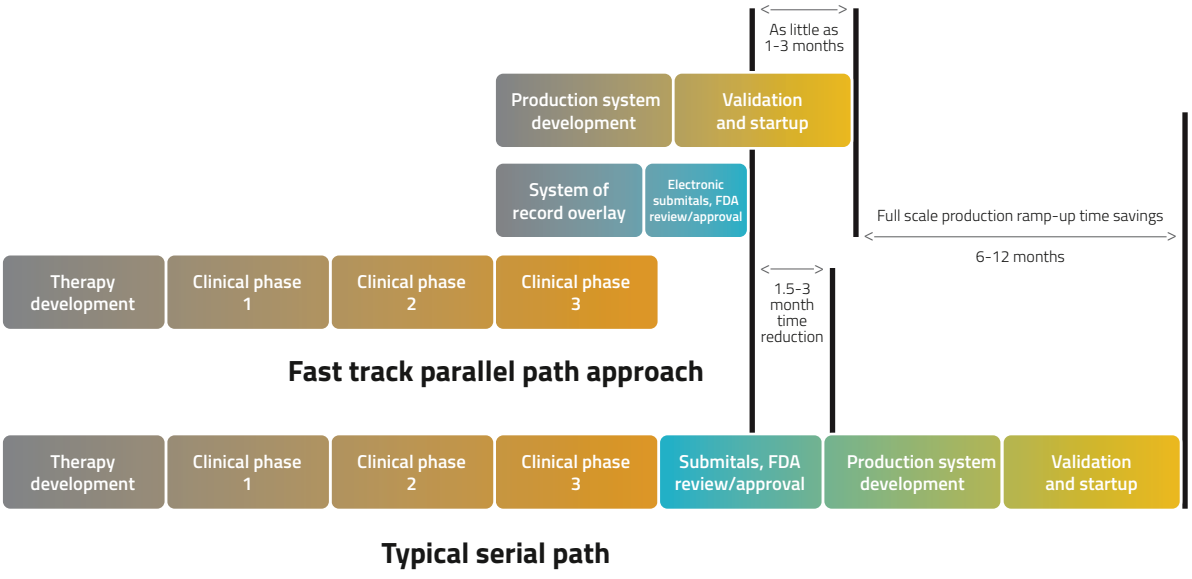
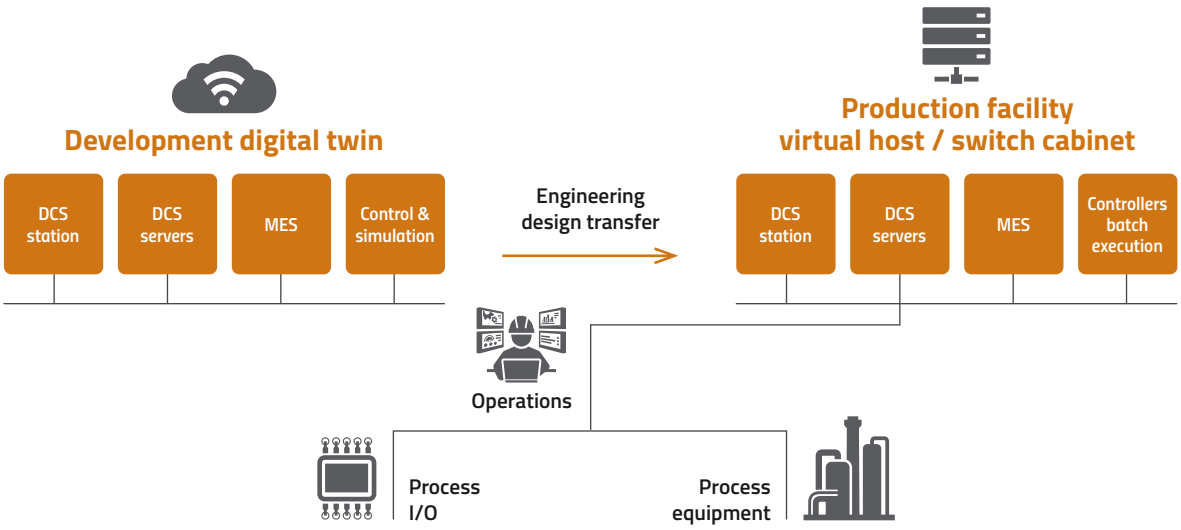


EXHIBIT 2

Fast-track automation system developed in a virtualized environment, then transferred to the production environment



skids and controllers are installed. Finally, the engineering design is transferred from the virtual host to the production system.

Technologies enabling faster startup

A manufacturer should choose an automation vendor that has continued to evolve and innovate, generating significant advances in automation technology. Integrated, yet "open" technology promotes the ability to integrate seamlessly with most modern equipment from any manufacturer and should leverage a breadth of complete virtual and cloud solutions. Some examples of automation advances include:

Lean automation project execution: A lean execution solution enhances project implementation services with standardized equipment cabinets, virtualization, cloud engineering and auto-device commissioning for the greatest efficiency and flexibility. Lean implementation enables engineering to be done from anywhere in the world. The advantage of lean project implementation comes from the use of standardized builds, parallel path development and automated engineering transfer, so that configuration is automatic, remote and there is no waiting on last-minute design changes. Employing lean automation project execution alone can enable a large capital project to potentially realize substantial capital savings in automation infrastructure and decrease in time to startup.

Reduced validation effort: An easy transition from recipe testing to execution reduces qualification efforts. Configurations tested in a virtualized development environment (as a development "digital twin") can be downloaded to the production environment without change, moving control strategies to production effortlessly, without modification or reassignment (Exhibit 2).

Batch in the controller: Batch executed in the process controller reduces the engineering effort to design, modify and configure a batch system without shutting down, and reduces recipe maintenance through equipment independent master recipes. It helps manufacturers produce an increasing number of different products cost-effectively and rapidly. The solution should be aligned with international batch standards and include the full ISA S88 batch standard model in the controller.

Remote control from a data center: Using the power of the Industrial Internet of Things (IIoT), an

EXHIBIT 3

Shared compute enables automated load balancing and "smart assignment" to automatically allocate controls to any available control compute

automation vendor can consolidate data and move control to a centralized local or remote data center in a private cloud. The resulting "digital twin" of the control process allows for testing of new recipes and qualification of changes to the automation system offline. The enabler is batch execution located in the controller.

Flexible input/output: By decoupling the data input/output units (I/O) from a specified controller using a highly integrated virtualized environment, the I/O for each piece of process equipment can be connected to virtual data center controllers. This allows personnel to remotely change the production process online. The control system can assign controller power to any I/O as needed (Exhibit 3). This reduces the number of I/O units needed and makes the system simpler, more efficient and flexible.

This smart assignment of control compute can be used in addition to the convenience of universal I/O modules, which can be changed to any digital or analog configuration remotely and instantly without changing out or adding additional equipment when changing automation strategy. This allows late binding of automation strategy at the I/O and equipment level.

Modern benefits

Modern technology components and project execution come together to provide the flexibility necessary for faster advancement from clinical trials to full-scale production of new treatments.

Working together with modular facility construction, manufacturers can quickly go from trial and approval to production. There is no waiting on design and engineering. A pre-designed automation process enables parallel work to start immediately, so manufacturers are ready to go once a therapy is approved.

Pharma manufacturers are finding it easier to move their digital transformation into the future with technologies enabling flexible control, virtual engineering and simulation and real-time data and operational visualization. These enablers provide the agility and speed-to-market for better delivery of medical solutions to those in need.

Thermo Fisher Scientific

Dr. Moussa Saleh
Senior Project Manager

Dr. Christian Mueller
Director Service and Support for EMEA

Connecting labs to power digitalization

Developing a holistic data strategy will enable pharma to create a fully integrated ecosystem

A fully integrated network of laboratories can deliver significant benefits to the pharmaceutical industry. By facilitating improved connectivity and collaboration between their network of laboratories and manufacturing plants, pharma companies can become more productive, strengthen their resilience to disruption and offer greater job satisfaction for their scientists. To this end, digital transformation programs are underway in pharmaceutical companies worldwide.

Well-integrated data systems are a critical component of the connected laboratory, providing a single source of truth accessible across the organization. At present, however, data silos and unconnected systems represent a significant hurdle for many pharma manufacturers, limiting their transformation efforts.

Improving data integration is a challenging process. Attempts to address single gaps between instruments, systems or laboratories won't necessarily deliver data harmonization — and could even hinder future transformation efforts.

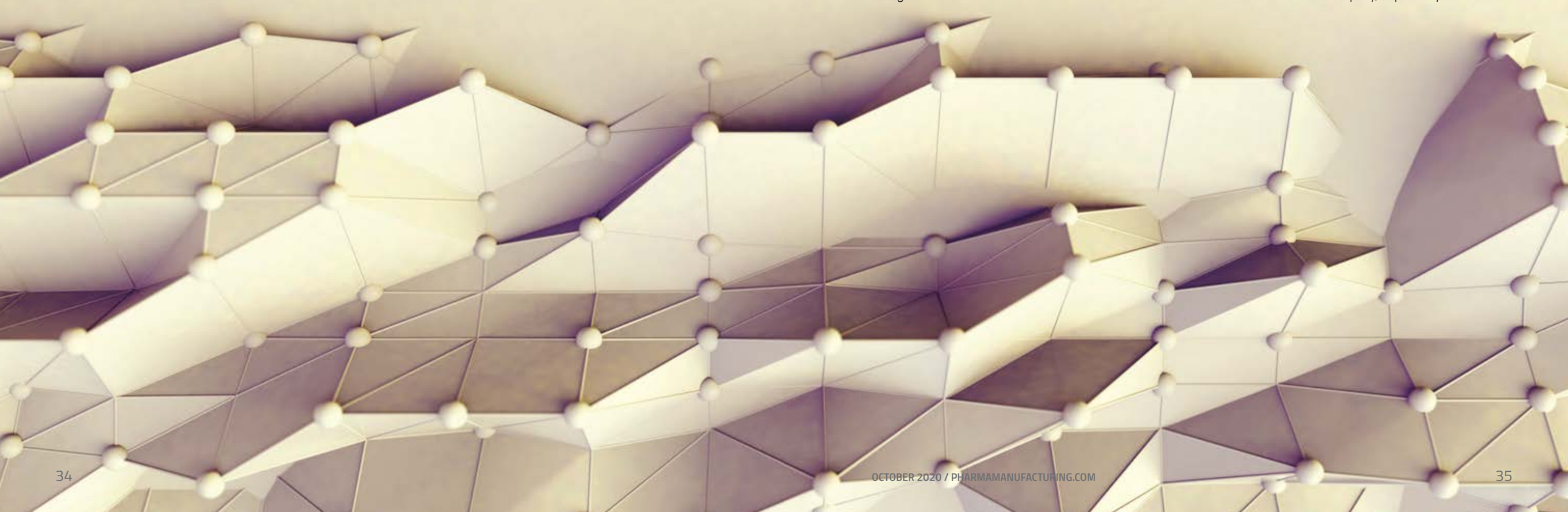
By creating a holistic data strategy and implementing advanced data solutions to connect their laboratories to each other, as well as integrating quality data from the manufacturing plant, pharma organizations can overcome data silos in manufacturing and continue their digital transformation journey.

The drive to address data silos

Data management is critical in pharma manufacturing, for both compliance and timely workflow decisions. High volumes of data both from QA/QC laboratories as well as from Enterprise Resource Planning (ERP) systems must be safely and appropriately stored, so that information can be accessed by the right people at the right time.

However, pharma manufacturers often face data silos. A combination of the disparate data formats of lab instruments, isolated software systems, unintegrated workflows and past acquisitions mean that many organizations have a fractured information landscape. Data may be isolated on one system or available to just one group, limiting communication between individual labs, sites, regions and even external collaborators. Information that could be critical to plant managers waiting to release product, or when collated with other details might provide a crucial answer to a manufacturing issue, is often left adrift.

These data silos also pose significant challenges for the manufacturing process by creating gaps in data integrity. This could compromise the completeness or consistency of datasets, and the accuracy of the insights discerned as a result. Equally, disparate systems



require the manual transfer and input of data, which can represent a sizeable drain on efficiency, particularly where data needs to be transferred between international sites. The productivity of scientists is therefore reduced by needing to spend time on these highly repetitive and error-prone tasks.

Without an integrated, standardized system to share information between the laboratories and plants, pharma manufacturers may not be able to realize improvements to manufacturing processes and workflows. Meanwhile, at a strategic level, decision-makers may lack a holistic view of the business to inform the choices that will guide the future of the organization.

Accelerating integration

The drive to create fully integrated data systems and strengthen data integrity has accelerated over recent years and even months. Establishing a single data repository improves data tracking, storage and reporting; that in turn enhances efficiency, facilitates scalability and flexibility across the organization, and improves decision-making. There has also been clear support from a regulatory perspective, with the U.S. Food and Drug Administration establishing the ALCOA+ principles for data integrity in pharmaceutical manufacturing, stating that data must be attributable, legible, contemporaneously recorded, original or a true copy, and accurate.

Pharma manufacturers are now more aware of the potential of cloud-based storage and applications to support the delivery of data integration. The cloud helps facilitate a single source of truth for data and enables easier data sharing across teams and global sites. Importantly, pharma manufacturers have growing confidence in data security in the cloud.

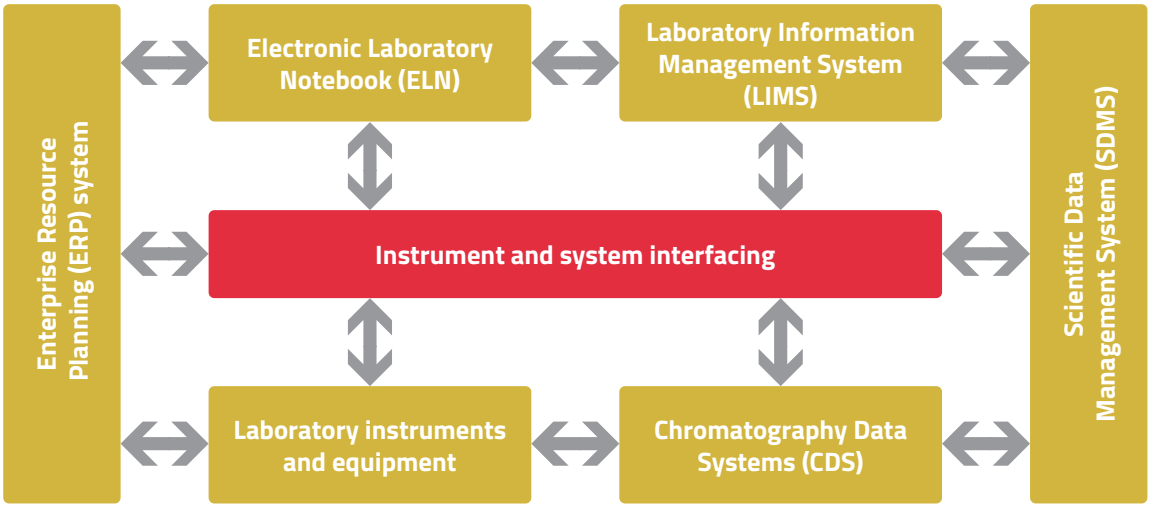
More recently, COVID-19 has underlined the need for data management improvements to support resilience in the face of disruption. Laboratories that are heavily dependent on manual data input have seen their operations particularly disrupted by social distancing requirements. This has in turn made it more difficult to provide plant managers with the timely QA/QC data required. Integrated digital processes, together with data automation, can keep labs operational with fewer scientists on site, and maintain a seamless flow of data to manufacturing plants.

It's also true now more than ever that pharma manufacturers need to be well positioned to provide the fastest and most efficient operation to deliver high quality drug products. This can only be possible if all opportunities are taken to automate and streamline processes, and to ensure information is made available to those who need to make critical operational decisions. Collating QA/QC data from labs with manufacturing data from ERP systems provides a more holistic view of operations throughout the organization, enabling continual improvements to maximize production efficiency.

In addition to significant short-term operational benefits, single data repositories will enable pharma manufacturers to conduct more sophisticated analyses of their laboratory and plant data to identify longer term patterns and opportunities. With a standardized, central

EXHIBIT 1

A harmonized system connecting laboratory and manufacturing data



data set, pharma manufacturers have the opportunity to benefit from utilizing data analytics, including machine learning, to spot trends over time. These insights enable continual performance improvements, enabling organizations to realize the full value of their data.

The opportunities to maximize the value of data for both operational optimization and longer-term transformation are clear. However, the level of complexity in labs combined with other operational requirements can make delivering integrated data systems a significant challenge.

Establishing a holistic data strategy

The most effective way for pharma manufacturers to establish a fully integrated data system is to develop a holistic data strategy encompassing the whole organization.

In the past, many labs have attempted to address gaps in their data processes individually, with single upgrades or patches that might cover a single integration or section of the organization. However, this approach will leave gaps at the end of the process, and may render it more difficult to integrate new instruments, software or technologies in the future.

By contrast, taking the time to develop a holistic data strategy enables the organization to create a fully connected ecosystem, with a single source of truth from the lab to the boardroom. Manufacturers can map their existing systems, determining where gaps lie and what information needs to be captured and connected to deliver value for the business.

Technology specialists can support this process by providing strategic guidance and identifying the data solutions that will most effectively integrate instruments and software systems, while enabling the adoption of new technologies further down the line.

Integration in action

A data integration program was recently undertaken by a large pharma company. The Chemical and Pharmaceutical Development (CPD) department was using six disconnected systems and over 1,000 disconnected instruments. Importantly, there were large differences between sites and departments, with heterogeneous IT landscapes and inconsistent LIMS usage, which meant the project required significant conceptualization to create one strategy incorporating every system.

The pharma company worked with a technology partner to improve data harmonization. Laboratory Information Management System (LIMS) software was chosen to manage lab data and procedural workflows, and connect with other enterprise systems, instruments and equipment. The built-in integration solution was used to build cross-connectivity between the LIMS, ELN, CDS and SDMS, as well as the instruments and equipment used in the lab. (Exhibit 1)

The higher degree of integration achieved has increased efficiency by 20 percent, with additional improvements to both data quality and integrity. Fewer mistakes are likely through transcription errors, while the labs benefit from the security of a full audit trail, including a risk-based audit system. Information isn't simply captured as "paper on glass," but intelligently linked to improve searchability. Despite the different modules and capabilities, the user experience across the labs is nearly seamless — and scientists now have more time for what they are most passionate about: Science.

This project also highlights the importance of cultural change to a successful data strategy. Scientists are often required to focus on operational tasks, so don't have the time needed to make the transition to new technologies or develop new digital skills. By establishing a holistic strategy that incorporates the people who use the systems, pharma manufacturers can ensure their data integration programs are more effective.

Beyond individual transformation programs, technology vendors have a key role to play in the establishment of a universal data format that will facilitate future integration. Organizations like the Allotrope Foundation and Pistoia Alliance are working to establish standards for common data formats, which will benefit end users going forward.

A platform for transformation

Pharma manufacturers can achieve significant operational advantages by addressing their data silos. An integrated system that connects labs and manufacturing plant quality data across the organization can provide greater efficiency and scalability, facilitate flexibility, and improve decision-making. But importantly, establishing an integrated data system will be a key major step forward for enabling improvements both in the lab and across manufacturing operations to support future transformation. Considering the current need for pharma to be ready to rapidly deliver a large supply of vaccines and treatments, there has never been a more significant time to advance on this digital transformation journey.

With truly connected labs, pharma manufacturers can establish greater collaboration across the business, identify continual organizational improvements and, perhaps most importantly, enable scientists to spend more time on productive, valuable and rewarding tasks. By establishing a holistic data strategy, with the support of a strategic and collaborative technology partner, pharma manufacturers can improve workflows today and be prepared to quickly make adaptations for their needs of the future.

product focus

Meagan Parrish
Senior Editor

The digital leap

Innovations aiding digital transformation

The pharma industry was already in the midst of a slow but steady adoption of digital technologies as a way of beefing up operational capabilities. Once COVID-19 hit, and the industry was asked to suddenly quicken its pace in every way, the need for digital tools increased even more.

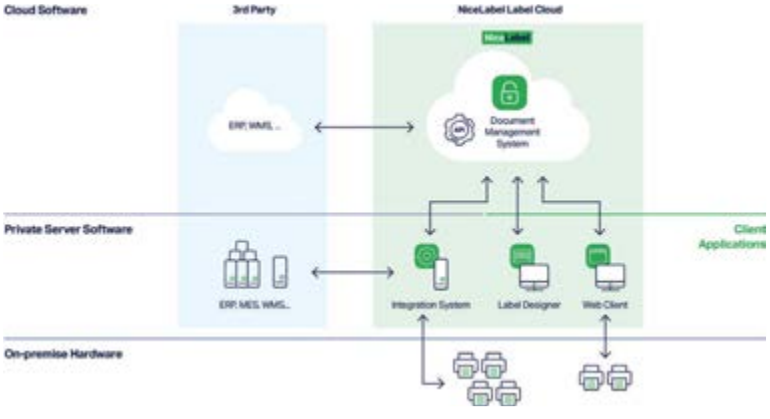
"Pharma supply chains are digitizing across the world, involving many smart advancements like big data analytics, AI and large-scale automation that break down silos and improve efficiency," says Lee Patty, vice president and general manager at NiceLabel Americas. "And with the current pandemic, this trend has only accelerated."

Whether it's through increasing connectivity throughout all areas of operations, providing new tools for analyzing data or helping pharma overcome barriers to advanced technologies, vendors are innovating IIoT-based solutions that make the digital transformation more seamless than ever before.

Centralized labeling

Small mistakes in labeling can lead to major disruptions in manufacturing.

"[Labeling problems] not only can lead to dangerous errors and recalls, but they can also halt digital transformations, reduce traceability, hinder processes like serialization and aggregation and even stall speed-to-market of essential goods," Patty explains.



NiceLabel's Label Cloud automates quality assurance to eliminate manual quality control processes.

Despite the industry's focus on adopting digital tools, Patty says that companies often overlook the value of a central labeling solution — but this is where NiceLabel's Label Cloud comes in.

Label Cloud was developed to allow businesses of all sizes and industries to digitally transform their factory and warehouse labeling processes at a rapid pace. NiceLabel says that the solution integrates easily with other business systems such as ERP and MES, does not require additional IT investment to adopt and is particularly suited for pharma, where regulations change frequently, regional standards differ widely, and consumer safety is of the utmost importance.

"It can be deployed in hours, and with it, users can centrally manage label design, product data and quality control from the cloud and print their own labels locally, from any printer type or alongside any business system," Patty says.

Streamlined analytics

With the push to get medicines to market quickly, increased digitization gives companies the flexibility they need to address this issue by handling specialized products and shorter production runs.

"As pharma companies drive toward implementing these changes, establishing unparalleled operational efficiency and agility is critical," Lisa J.

Through AI algorithms based on machine-learning processes, Antares' AVionics is designed to further enhance system accuracy and reliability over time.

Graham, the vice president of Analytics Engineering, Seeq Corporation, explains. According to Graham, Seeq's advanced analytics software can underpin the "new processes, workflows and culture shifts required for success."

To help streamline connectivity throughout all phases of drug development, Seeq recently launched a beta version of Data Lab, which works alongside two other Seeq applications — Workbench and Organizer. Data Lab was developed to help data scientists expand their Seeq analytics efforts to the rich ecosystem of Python libraries and for direct participation in process data analytics.

"Data Lab also enables data scientists to find insights using machine learning algorithms and libraries, system integrators to create custom analytics for their clients, and asset vendors to enrich their remote monitoring and predictive analytics services for their customers," the company says.

The three applications connect to a Seeq server to facilitate collaboration, access connected data sources, and enable administrative control.

Overcoming implementation barriers

Despite the promise of digital solutions such as AI, pharma companies are often still reluctant to make the switch.

"AI holds a strategic, transformative business value," says Massimo Bonardi, managing and technical director for Antares Vision. "However, limited availability of high-quality data, a lack of processes for collection of knowledge, insufficient understanding of risks associated with the adoption of AI, company legacy culture and regulation can all act as barriers to widespread adoption."

According to Bonardi, Antares' AVionics solution can help users overcome these challenges.

Originally developed for OEE performance tracking, Antares says the AVionics software solutions "can now be utilized to track overall manufacturing efficiencies, ensure process quality, predict equipment maintenance and detail sustainability parameters."

While tracking various key performance indicators (KPIs), AVionics streamlines data into a dashboard that gives operators information from production and packaging lines that can then be used to improve business processes at all levels — from line-level manufacturing through overarching, enterprise-level metrics development.

"Powered by AI, the data collected by AVionics can be used to solve specific problems like anomaly detection, to predict potential production issues, and to enable a fully managed AI governance," Bonardi says.

Data transparency

Although industrial monitoring devices are now widespread throughout manufacturing, solutions that provide real-time status updates are just now hitting the scene. According to Bethany Silva, industry manager for Life Sciences, Endress+Hauser USA, the ability to have real-time data and transparency is enabling a higher level of predictability in pharma.

"Pharmaceutical manufacturers are seeking ways to integrate data throughout their entire ecosystem in a manner fully transparent to all the players involved, from the suppliers of raw materials, components, and parts, to the transporters of those supplies," Silva says.

To that end, Endress+Hauser recently launched its Micropilot FWR30, the company's first cloud-connected radar level instrument, which provides full transparency in the storage and transport of liquids. As the world's first 80 GHz wireless IIoT instrument, it continuously records measurement data that can be accessed at any time thanks to the device's cloud connection.

The Micropilot FWR30 can be installed in less than three minutes and can then be used for level measurement, tracking and inventory management of mobile and stationary plastic tanks.

"Connected devices, such as the Micropilot FWR30, can easily track the availability of materials in real-time, allowing for better and more efficient inventory control and reduced costs," Silva says.

Charlie Johnsrud, AIA, LEED AP
Principal, Bergmann

Reconciling the design process

Meeting the challenge of competing stakeholder priorities requires continuous assessment

The design process for a pharmaceutical manufacturing facility is dynamic, frequently disjointed, and often cyclical. Differing stakeholder perspectives can be a challenge to reconcile. A number of different priorities can all struggle for dominance. From regulatory considerations to building material characteristics, corporate leadership, quality assurance, production and facility management, opposing concerns can lead to a divergent design process, despite guidance from project managers.

Since the stage gate process has been the "way of the world" for over 25-years, few remember when it was the norm for the A/E team to be responsible for estimating to ensure the design was on budget. Significant value engineering efforts, or course correction, were not originally intended to be part of the design process and while they can be used effectively and with good results, they tend to be disruptive and cause inefficiencies for the project team.

With so many unique circumstances in pharma facilities, it can be useful to reflect on the challenges associated with competing priorities and the fundamental approach to reconciling them.

Define success

The table of goals with carefully considered and weighed priorities done at the outset of a project is familiar and a good start, but it should be considered a living document.

The design process naturally reveals opportunities and consequences that may not have been understood, appreciated or even known at the beginning of a project. Knowing all the stakeholders as well as their motivations helps to anticipate what outcomes they will advocate for and which they may cede. Keeping the goals for "success" simple is relatively easily done for cost and schedule but quality can be defined by a wide range of characteristics. Therefore, agreement by all stakeholders on what the specific goals are, as opposed to how to achieve those goals at the start of a project, will keep evaluations simple and allow the team to approach the dynamic process with guidance and not constraints.

Control the "wish list"

Almost every project is seen as an opportunity to secure enhancements cut from the last project, address ongoing operational or maintenance issues, or introduce upgrades. The "wish list" should identify every possible function, capacity, feature, improvement, or "fix" that each stakeholder might desire. The list should be developed in a brainstorming session with all participants and no limitations. While many items may not be within the project charter, identifying and discussing them will set the ground rules to control them.

By agreeing on which wish list items are to be included in the project and which are not, a line in the sand is established with all parties as the starting point. Things will change as a function of design development — as management priorities, budget allocations, and alternate solutions for the original business driver develop. The process is dynamic and the line in the sand will shift after thoughtful assessment of project goals. New ideas will emerge and priorities will shift over the course of a project and being flexible in the approach and methodology to accommodate those shifts will help ensure all stakeholders' highest priorities are achieved.

Put the project's priorities in order

To deliver on the highest priorities of the team, employ methods to assess each component of the facility for operational benefits, estimated first versus life-cycle costs, reliability within the overall operations, and other factors. This assessment should facilitate agreement among all stakeholders on priorities ranked in terms of their impact on the shared definition of success for the project. Each stakeholder should realize that not all of their priorities will be accommodated but a process that allows for thoughtful consideration will deliver a successful operation — the highest priority of the project team.

These activities are familiar to everyone who has participated in a project to design and build a pharma manufacturing facility. Continuously assessing the priorities as part of the dynamic process allows the team to make better informed decisions about the resulting facility and operation. While every project will be operational at some point, the ones that align and address all stakeholders' priorities will deliver true success for the manufacturer.

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John McShane
Managing Partner, Validant

Stealing pharma's sunshine

How sunscreen is driving a resource and capacity shortage

The passage of the Sunscreen Innovation Act (SIA) in 2014 has increased oversight of the safety of sunscreens. Last year, the U.S. FDA issued a proposed rule that, if put into effect, will tighten regulatory requirements for most sunscreen products in the U.S.

But what does sunscreen have to do with the pharmaceutical industry? Sunscreens in the U.S. are considered over-the-counter drugs, rather than cosmetic products, like they are in many other countries. Since they prevent sunburn and skin cancer, sunscreens sold in the U.S. are subject to regulation as drugs.

Products being shipped to the U.S. from Europe and Asia, where many sunscreens are manufactured, have to meet the same 21 CFR 211 criteria. But how are cosmetics manufacturers in Europe expected to understand how to deal with the U.S. FDA, a regulatory agency now increasingly found at their doorstep?

Meeting FDA criteria and GMP compliance for overseas sunscreen has the cosmetics industry looking to the pharma industry for guidance in an unprecedented way. But pharma's resources, including CMOs, consultants and engineering companies, are already wearing thin, stretched to the breaking point by the COVID-19 pandemic.

The need to satisfy the FDA's requests for GMP compliance among OTC products is stretching the CMO supply chain in a manner that is troubling.

A case in point

A leading cosmetics manufacturer in France was producing and marketing a line of cosmetics, including foundations that claimed UV protection with sunscreen. They had an FDA inspection in 2018. Due to a lack of understanding around OTC/GMP regulations, the cosmetics manufacturer's initial 483 response was not well formulated and they received a warning letter.

The cosmetic manufacturer assumed that a simple dedication of fill lines was enough to become GMP compliant, but as pharma is aware, the solution is often much more complex, involving complete fill line segregation to prevent cross contamination, with cleaning and process validation and the equipment qualification steps set up, and then kept in a full-time qualified state. Record keeping levels and personnel, plus costs, go up significantly, with shifts, batch records and cleaning records all needing to be taught, trained and kept up as regular practice.

In most of Europe and Asia, sunscreens are not regulated, so the local manufacturers are not familiar with FDA's OTC requirements. Faced with FDA actions and timelines, many overseas cosmetics manufacturers look to U.S. consultants and engineering companies to help navigate the FDA landscape.

The hunt for a CMO

The fastest route to become compliant for an overseas manufacturer shipping their beauty lines to the U.S. is to use a well-respected U.S. contract manufacturer.

Yet, the CMO industry in the U.S. is already at capacity. To obtain campaign time at one of the larger CMOs, a prospective client can wait over a year. Additionally, sunscreen products may have specific manufacturing process requirements that further limit options. The need to satisfy the FDA's requests for GMP compliance among OTC products is stretching the CMO supply chain in a manner that is troubling.

With the widespread use of sunscreen today and the increased regulatory investigations happening, OTC sunscreens will only receive increased scrutiny, much like drugs receive, in the years to come.

CMOs, pharma engineering and consultancy firms all may become even more resource stretched in the next few years, with overseas cosmetics manufacturers reaching out for help. Sunscreens imported into the U.S. are still big business but they also cannot continue to label them as sun protective without meeting FDA standards.

Overseas cosmetic manufacturers will either work towards bringing sunscreen facilities to U.S. FDA standards or continue to look to outsource to CMOs that understand the requirements — which means pharma manufacturers may increasingly find themselves having to share their partners.

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