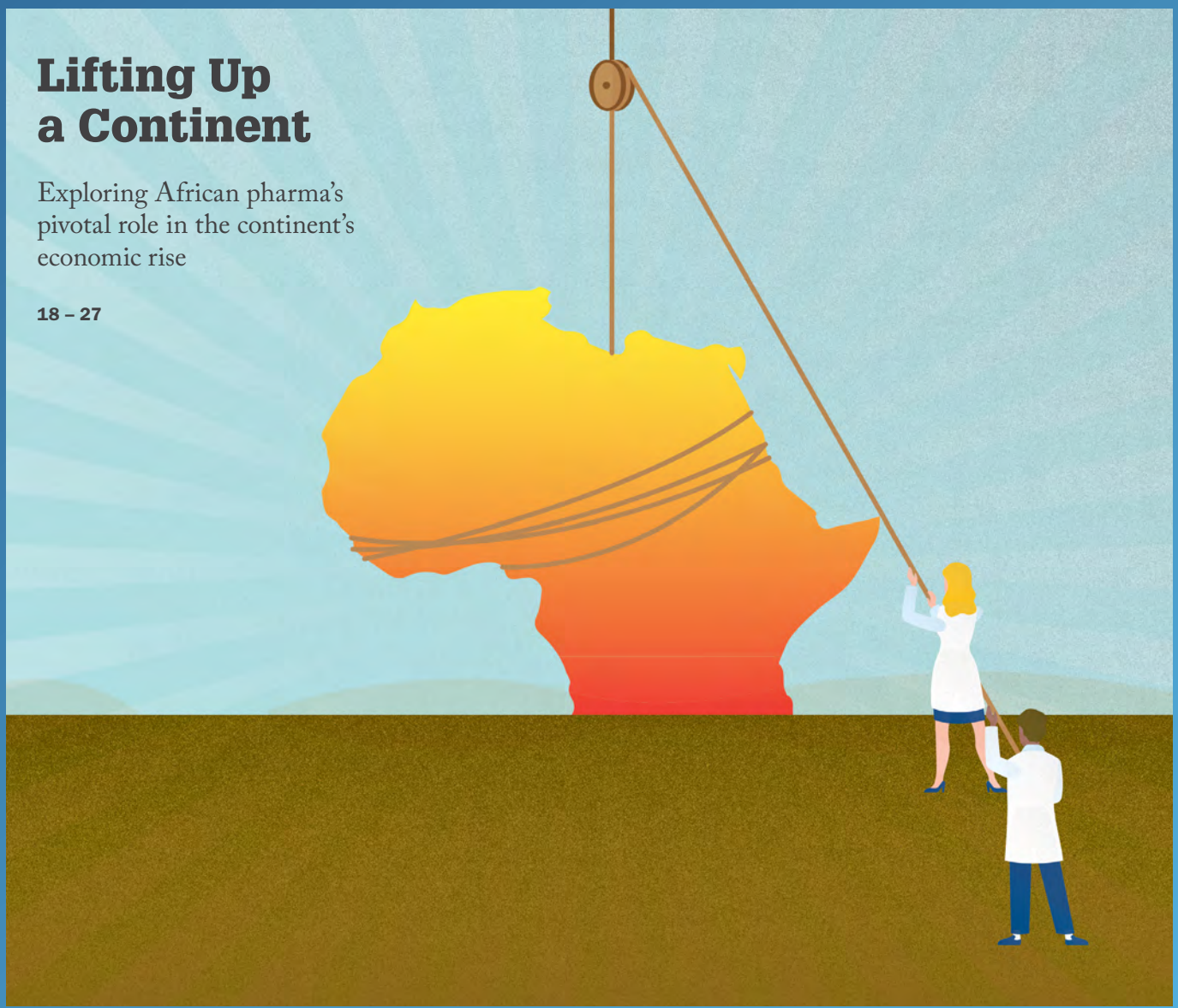
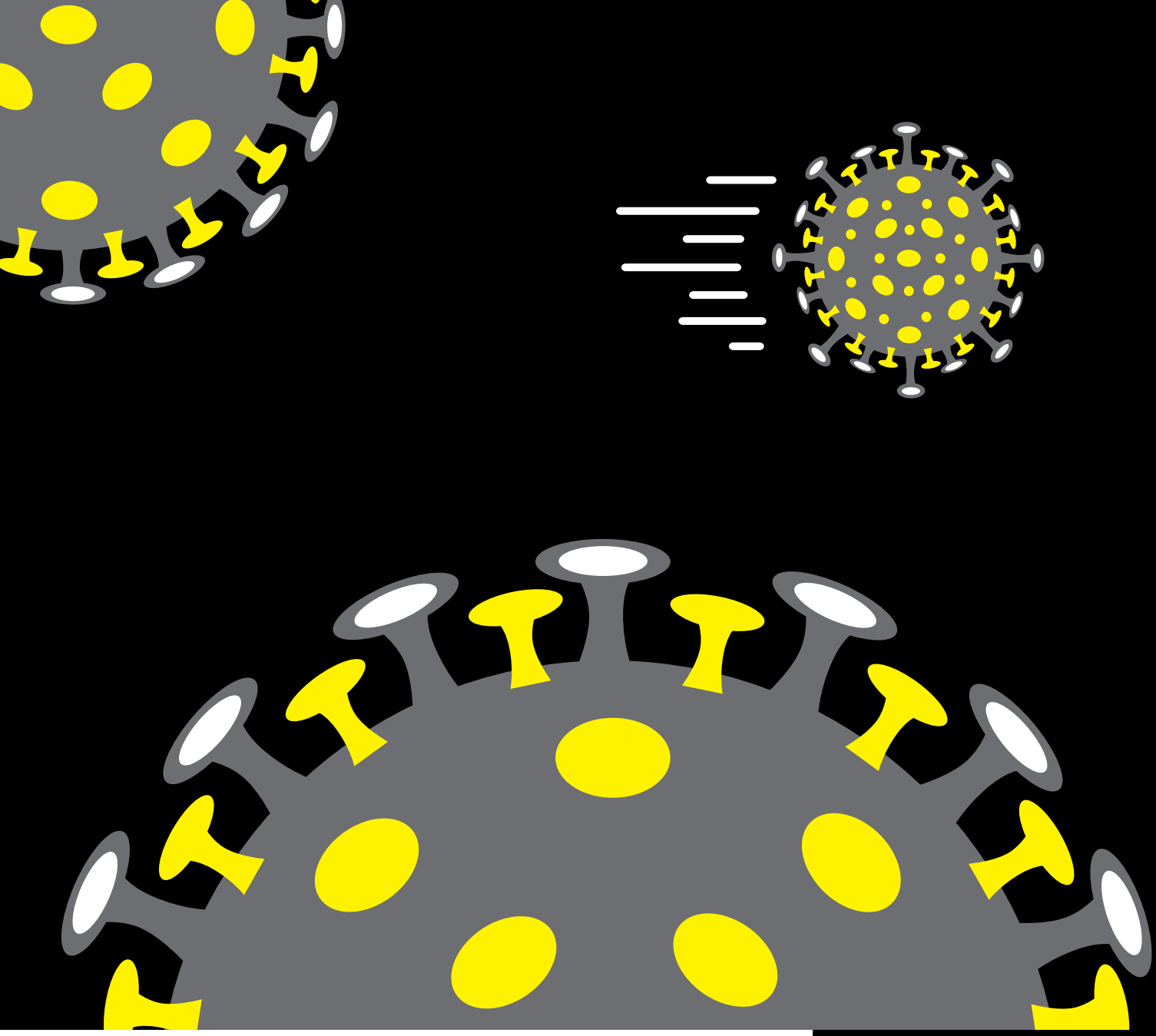
OCTOBER 2020 # 69

the Medicine Maker®



Lifting Up a Continent

Exploring African pharma's pivotal role in the continent's economic rise



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SARTORIUS

Should We Fear the Virus?

The criticality of careful science communication in the age of COVID-19

Apparently feeling better – "GREAT," in fact – after being hospitalized with COVID-19, President Trump told Americans: "Don't be afraid of Covid. Don't let it dominate your life." The comments were (typically) controversial – especially considering the death toll and the harsh reality that the average US citizen will not receive the same standard of care as the President… But what about downplaying the risk of COVID-19 (Trump's preferred approach from the outset) – does it result in fewer people taking measures needed to slow the spread of infection? The reasonable assumption here is that a degree of public fear is a necessary motivator. Is there an ethical case for exaggerating risk to achieve public health outcomes?

Research from Cornell University suggests not; threats about dire outcomes can certainly mobilize more people to take precautions in the short term. But when catastrophic predictions fail to acknowledge the uncertainty of the models used to guide pandemic policy, the longer-term impact can be an erosion of public trust – not only in the models but in science more broadly (1). The Cornell researchers emphasized the importance of "careful and effective science communication for maintaining public support for science-based policies as the scientific consensus shifts over time."

I've previously discussed the problems associated with sensationalization in the other direction – when exaggerated claims and omitted caveats feed a propaganda machine (2). In the case of cell therapies, unproven clinics and do-it-yourself gene editing companies tap into the hype generated to exploit a patient's hope of a cure. A number of these clinics are now claiming to treat COVID-19 (3), and we've also seen groups working to develop and self-administer unproven interventions that they describe as vaccines for COVID-19 (4).

Science communication involves a degree of storytelling. And stories inevitably tap into human emotions (fear and hope in the cases above) – I don't think there's a problem with that. But issues arise when the communicators see their audience as a means to an end. Should we fear the virus? Does Company X's developmental therapy give us hope? The key to careful science communication is – while offering full transparency of all known caveats – allowing the audience to make up their own minds.

James Strachan
Deputy Editor

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1. *SE Kreps and DL Kriner, "Model uncertainty, political contestation, and public trust in science: Evidence from the COVID-19 pandemic" (2020). Available at: https://bit.ly/3lioh2d*
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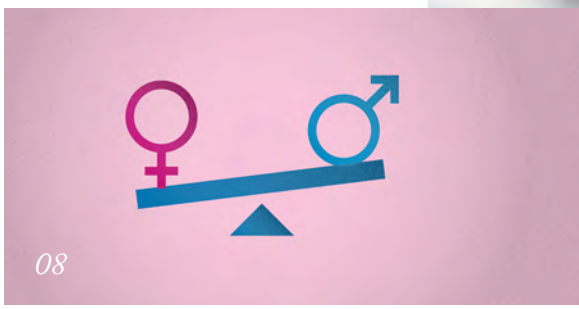

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Upfront

Research
Trends
Innovation

Animal Alternatives

Developing in vitro methods that help vaccine developers reduce animal testing

Though animal testing is an essential part of vaccine R&D, Gideon Kersten, Chief Scientific Officer at Intravacc, believes its role in quality control is debatable. "Not only have our analytical capabilities improved spectacularly, but production processes are now better controlled," he says. "It should be possible to reduce our animal use if in vitro tests can prove a vaccine is produced in a consistent manner."

Intravacc, in collaboration with researchers from Leiden University, the Netherlands, has developed a technique that relies on the enzyme cathepsin S to establish the quality of vaccines (1). Cathepsin S can be used to measure how consistent purified native pathogens in vaccines are inactivated. "The inactivation step in the development of some vaccine types is critical and relies often on formaldehyde," says Kersten. "Using mass spectrometry, we quantified how quickly the enzyme breaks down proteins in vaccine products. The rate of degradation was used as an indicator of how well formaldehyde inactivated the vaccines we tested."

Though the process initially seemed straightforward, the team soon realized that it would be difficult to execute. "Using formaldehyde is really messy! The protein fragments we studied were not only inactivated, but extensively modified by the compound, and we ended up with a heterogeneous mixture," Kersten says. "Though we mapped these modifications in great detail, we then turned our focus to quantifying the breakdown of peptides that were not modifiable because identification of unmodified peptides by mass spectrometry is easier."

The change in direction allowed the team to accurately determine the effect of cathepsin S on degradation. "We now have a method that allows us to establish vaccine quality without animal testing," Kersten says.

The team is now working towards validating their approach before seeking regulatory approval.

Reference

1. *TJM Michiels et al., Sci Rep, 10, 11535 (2020).*

INFOGRAPHIC

COVID-19 Disruption

Tracelink's survey reveals the extent of supply chain disruption caused by the pandemic

Pre-pandemic, 74% of companies reported average, on-time delivery performance from direct material suppliers of 98%

98%

Now? On-time delivery performance is down to

28%

61%

cite persistent supply problems resulting in drug shortages

Sources: TraceLink, "The Only Comprehensive Analysis of the Pharmaceutical Supply Chain During the Pandemic." Webinar; September 24, 2020.

BUSINESS IN BRIEF

Eliminating fossil fuel emissions, embracing supercomputers, and centers of excellence… what's new in business for pharma?

- Biogen is investing US$250 million into a 20-year "Healthy Climate, Healthy Lives" initiative to eliminate fossil fuel emissions across its operations. The company plans to rely entirely on renewable energy by 2040 and will be encouraging and supporting its suppliers to reduce reliance on fossil fuels. The initiative also includes plans to advance the science around how fossil fuels impact human health via harmful air pollutants.
- NVIDIA claims to be building the UK's most powerful supercomputer – expected to come online by the end of the year – to support healthcare research. GlaxoSmithKline, AstraZeneca, Guy's and St Thomas' NHS Foundation Trust, King's College London, and Oxford Nanopore Technologies all plan to take advantage of the system's capabilities.
- After purchasing a new biologics manufacturing facility in Bloomington, Indiana, Catalent says it will create a North American center of excellence for early-phase clinical biologics formulation development and drug product fill/finish services. The facility is expected to begin supporting customer programs in January 2021. The site will integrate with the company's main Bloomington facility located nearby, which recently received a $50 million investment to install additional high-speed vial filling capabilities.
- The FDA is launching a Digital Health Center of Excellence to help ensure that cutting-edge digital health technologies – including mobile health devices, software as a medical device, and wearables – are rapidly developed and reviewed in the US. Bakul Patel, who has been leading regulatory and scientific efforts in digital health devices at the FDA since 2010, is to be appointed as the center's first director.

Top Tier Innovation

Nominate the top pharmaceutical technologies in our 2020 Innovation Awards

Despite a year marked by unprecedented challenges, pharmaceutical equipment companies have continued to develop new technologies that facilitate better and more efficient pharmaceutical development and manufacturing. Continuing The Medicine Maker's annual celebration of innovation, we invite you to nominate the latest technologies that you think are making a real difference to the pharmaceutical industry in our 2020 Innovation Awards.

The Awards – to be published in our December 2020 issue – will celebrate the highest impact pharmaceutical development and manufacturing technologies released in 2020. The innovation can be a piece of equipment, software, formulation technology, drug delivery method, or any other advance that you think could fit the bill. But remember: the innovation must have been released (or planned for release) in 2020.

Nominations close on November 3; have your say before it's too late!

Register your nomination at https://tmm.txp.to/innovation2020

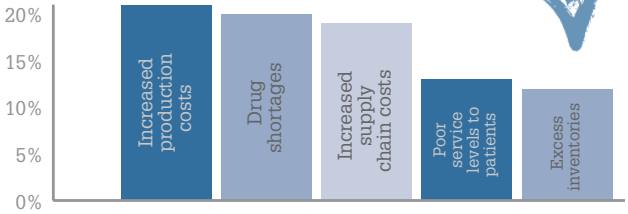
75%

say the pandemic has/will increase problems with diversion, theft and counterfeiting – particularly for test kits, vaccines and anti-viral medicines

64%

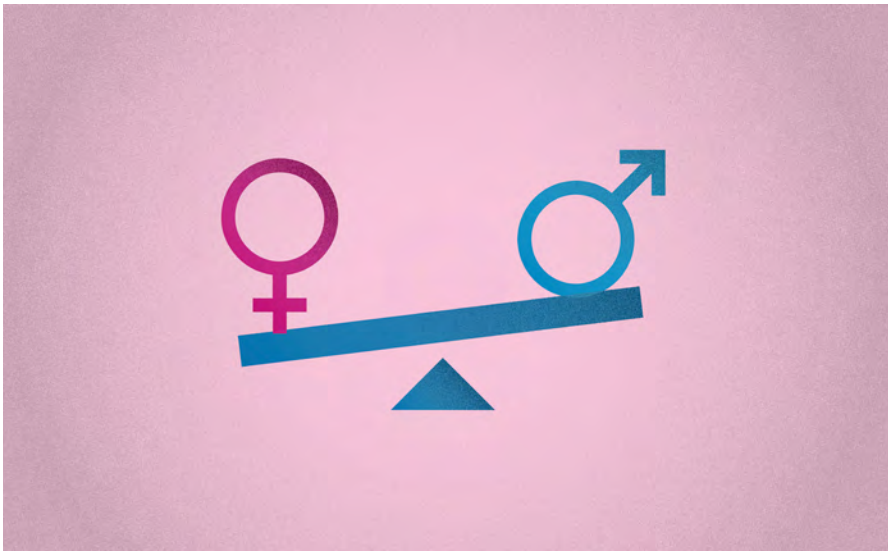
have lost faith in their demand forecasts and ability to plan supply

Primary COVID-19 challenges



The Drug Dose Gender Gap

Does equal always mean fair?



Across industries, women and their allies have fought to close the gender gap. For pharma, the problem is not only a professional one – it affects the health of female patients worldwide. And now, using data from over 2,000 journal articles, researchers from the University of California, Berkeley and the University of Chicago have found that 86 FDA-approved drugs are affected by a drug dosing gender gap (1).

"The common practice of prescribing equal drug doses to women and men neglects sex differences in pharmacokinetics, dimorphisms in body weight, and risks overmedication of women," says Irving Zucker, the study's lead author. "We discovered that 76 of the 86 drugs we investigated had negative effects in female patients."

The Berkeley and Chicago researchers' analysis showed that, when given the same dose as men, women were more likely to experience higher concentrations of a drug in their blood and take longer to eliminate it from their bodies. This pharmacokinetic data, Zucker and Prendergast explain, are strongly linked to adverse drug reactions. "Not only are women at risk of experiencing elevated blood concentrations, but they are also more likely to face worse drug reactions," Zucker says. "In 96 percent of the studies evaluated, women experienced adverse reactions twice as often as men. These were often severe – causing symptoms like depression and hallucination."

But how can we achieve gender parity? Zucker and Prendergast believe there is more work to be done. "Though the US National Institutes of Health has mandated the inclusion of women in clinical trials, credible evidence of sex differences in pharmacokinetics and adverse drug reactions should be made available in drug labels." The authors added that, to attain long-term change, it is crucial to increase awareness of sex bias, its sources, and the countermeasures that can diminish gender disparities in medicine.

Reference

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Don't Exclude the Aged

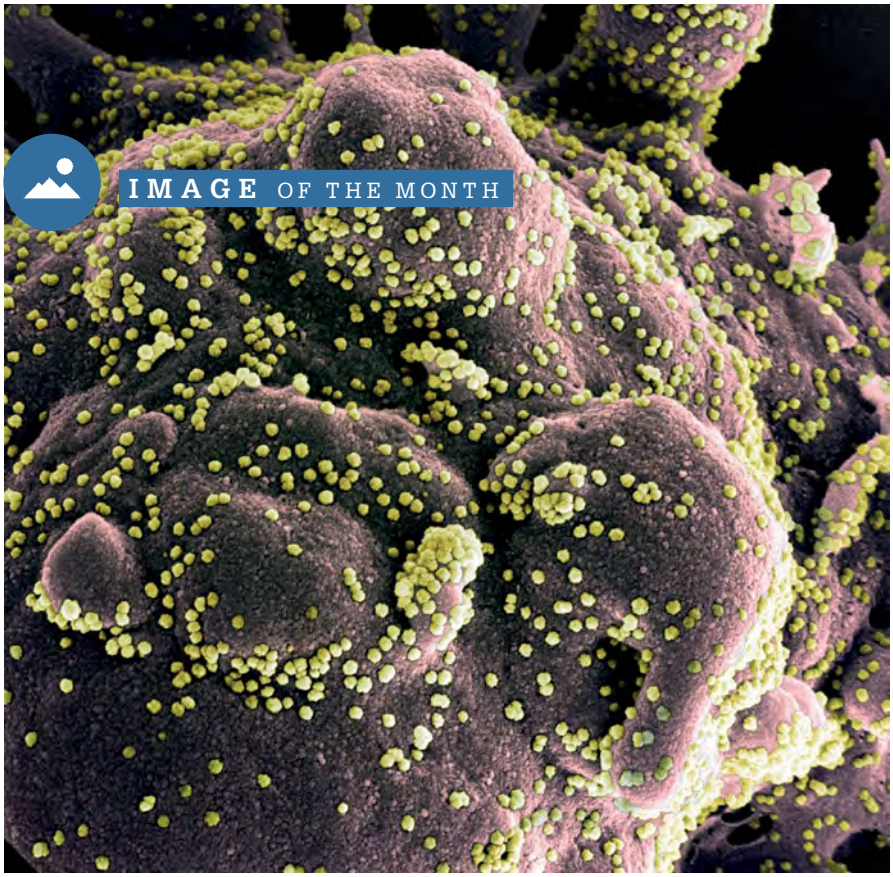
Most clinical trials against COVID-19 exclude the very patients most at risk from the disease

Despite being at higher risk of severe COVID-19, older adults are in danger of being excluded from more than 50 percent of COVID-19 clinical trials and 100 percent of vaccine trials, according to a review of COVID-19 trials on clinicaltrials.gov (1). The authors evaluated trials based on their risk of excluding adults over 65 years old and found that most trials featured either age cutoffs or broad, unspecified exclusions.

Although they acknowledge that some exclusion will always be necessary, the authors argue that enrollment of greater numbers of older adults in clinical trials is possible with advance preparation, staff training, and aging expertise. Senior author Sharon Inouye, Director of the Aging Brain Center in the Hinda and Arthur Marcus Institute for Aging Research at Hebrew SeniorLife, believes that many of the exclusion criteria are "not well-justified, and appear to be more for expediency or convenience of the trialists."

Reference

1. *BKI Helfand et al., JAMA Intern Med, [Epub ahead of print] (2020). DOI: 10.1001/jamainternmed.2020.5084*



Know Thy Enemy

Colorized scanning electron micrograph showing SARS-CoV-2 virus particles (yellow) isolated from a patient.
Credit: NIAD

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QUOTE of the month

"No research team is exempt from the pressures and speed at which COVID-19 research is occurring. And this can increase the risk of honest error as well as misconduct. To date, 33 papers have been identified as unsuitable for public use and either retracted, withdrawn, or noted with concern."

Katrina A. Bramstedt writing on substandard research during the pandemic in the Journal of Medical Ethics: https://bit.ly/30BAKGp

Importation Action

FDA to allow drugs to be imported from Canada

Following on from Trump's Executive Order in July 2020 to increase drug importation, the FDA has issued a "final rule" that will allow certain prescription drugs to be imported from Canada – under specific conditions. The agency has also released Guidance for Industry, which details procedures drug manufacturers should follow "to facilitate importation of prescription drugs, including biological products, that are FDA-approved, manufactured abroad, authorized for sale in any foreign country, and originally intended for sale in that foreign country." The imported drugs would have to be relabeled to US standards, and tested for authenticity, degradation, and established specifications and standards.

In a statement, FDA Commissioner Stephen M. Hahn explained that the agency's Safe Importation Action Plan should help increase competition in the market and lower the prices of prescription medicines.

Reference

1. *FDA, "FDA Takes Actions to Help Lower U.S. Prescription Drug Prices," (2020). Available at https://bit.ly/30gPZo5.*

In My View

Experts from across the world share a single strongly held opinion or key idea.

Harnessing Dark Data

The pharma industry creates significant amounts of data – so why is most of it hoarded and never made accessible?

By Graeme Dennis, Commercial Director, Preclinical Pharma, IDBS

Data is generally recognized as an organization's top asset after talent – but it is rarely treated as such. Although the amount of data produced every day is massive, it has been estimated that 60–73 percent goes unused for analytics, instead relegated to storage (1). This is known as "dark data."

Local storage, an explosion in the number of users at all levels of computer literacy, and well-intended (and justified) data security have all contributed to the volume of dark data that companies retain, whether or not they plan to use it. How can the biopharma and healthcare industries treat this data as a free-standing and central asset by making it accessible in the long term?

Like the unexpressed parts of the human genome, some dark data can be expected to have great meaning and significance – but not all. A key reason this data continues to accumulate is that there is no suitable system to house it. For instance, many in vivo preclinical study results generated by contract research organizations are in portable document formats unsuited to analyzing or in email, an unshared environment by design. This choice is dictated by convenience, but it makes the data not only unshareable, but also invisible to the organization. Even if exposed, many scientists would not even consider using or reinterpreting the data without significant context as to how, when, by whom, and under what precise conditions it was gathered. They may instead opt to rerun the study, depleting time, money, and resources.

The antidote to the dark data morass should go beyond just exposing it. Most companies are guilty of data hoarding, where data is retained regardless of quality or significance. Our goal should not be only to find (and find value in) what is stored, but also to store less dark data. Storage may be cheap, but it's not always best to keep everything.

Instead, the focus should be on retaining contextually rich data. Legacy methods of recording and collating data are prone to errors, but they also fail to provide the full context in which the data was captured. Sometimes called data provenance, these conditions frequently dictate the reusability or applicability of data for interpretation. Instrumentation, lab location, conditions, and materials used are just some of the many factors that should be considered throughout the drug development lifecycle. Sample origin, transport conditions, and custody are also essential. Capturing this information relies on advanced informatics infrastructure and significant forethought in system design.

IDBS has a longstanding presence in the data space and I have observed a proliferation of standalone systems across siloed specialties and disciplines. When it comes to realizing the benefits of data, I have three central pieces of advice: recognize data maturity, explore integration approaches, and embrace a "data first" cultural shift.

First, classifying data according to its level of maturity is wise because it enables assignment of resources, effort,

"Legacy methods of recording and collating data are prone to errors, but they also fail to provide the full context in which the data was captured."

and priority to align with broader company goals. For instance, data may be considered fully dark or sequestered, shared (perhaps on a shared drive or SharePoint), structured (stored in a database), and ultimately standardized (both structured and harmonized with internal or industry standards). Stratifying data this way and then functionally – perhaps according to the most active project, candidate, or biological relevance – can make the process manageable.

Second, it is important to explore integration approaches. The nearer data is captured to the moment of acquisition, the less likely it is to become sequestered. Vendor assessments must raise integration capabilities early and often in the evaluation of candidates. Data pipelining tools, database replication, or scripting can close these gaps, but the best solutions eliminate the gap via integration.

Finally, a "data first" strategy acknowledges the importance of data, socializes it, and provides the tools that enable success. The F.A.I.R. (findable, accessible, interoperable, reusable) data principles provide broadly accepted guidelines for when such a program may be implemented. This type of program will succeed when it is visibly endorsed by leadership and prioritized at the bench. And you should absolutely invite not only champions, but also skeptics to participate – they will provide some of your most valuable input!

Big pharma is increasingly turning to third-party R&D firms to accelerate the early stages of drug development. Today, the most effective of these firms are technology-focused, with a cultural mindset that recognizes the power of data. Method execution and sample management – approaches with origins in manufacturing and QC – have extended into drug development.

By revealing dark data, optimal conditions and processes can be replicated, workload reduced, and efficiency increased. Error detection, for example, becomes much easier when one can pinpoint when and where a certain context changed. By rolling back to this point, it is possible to resume development, rather than starting the entire process again. In essence, dark data can shine a light on the best way forward.

Reference

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A Model Experiment

Harnessing the potential of microphysiological systems to advance drug discovery

By Audrey Dubourg, Product Manager at CN Bio Innovations Ltd., Cambridge, UK

With just one in 10 preclinical candidates in phase I trials likely to gain market approval, the pharmaceutical industry must find ways to develop effective therapeutics faster and more cost-effectively. Pipelines include a mix of drug discovery, redevelopment, repurposing, combination therapeutics, and new modalities, such as gene therapies or regenerative medicines. When it comes to success, however, the translatability of preclinical data into clinical efficacy is only as good as the predictivity of the test models…

Drug discovery traditionally involves two-dimensional monolayer cell culture experiments followed by testing in animals to ensure results translate in vivo. Unfortunately, these models suffer from well-documented inefficiencies and inaccuracies, including oversimplification, insufficient representation of the underlying pathophysiology, and interspecies differences – all of which can lead to poor translatability into the clinic.

Microphysiological systems (MPS) are a relatively new approach that combines bioengineering and cell biology to provide more physiologically relevant data in early R&D stages. MPS build on the concepts of traditional two-dimensional assays, but improve physiological relevance by mimicking aspects of organ function. Systems such as 3D spheroids, organoids, organ-on-a-chip, multi-organs on chips, static micropatterned technologies, and physiome-on-a-chip models combine living cells and microfluidic technologies with drug delivery, stimulation, or sensing tools to gain a clearer picture of how such tools will function in a living organism. The technology's broad applications extend into modelling healthy or diseased organs, studying multi-organ interactions, investigating ADME and toxicity, and screening, identifying, and ranking drug candidates. Single- and multi-organ MPS technologies are designed to mimic specific aspects of organ function or crosstalk; for instance, an MPS that incorporates liver tissue with another organ offers the opportunity to concurrently study efficacy and susceptibility to toxicity. For highly prevalent diseases with well-established impacts on public health, they can also enable investigations into host genetics, treatment responses, novel therapeutic targets, and additional biomarkers. Such investigations are increasingly important for conditions such as non-alcoholic steatohepatitis (NASH), for which there are currently no therapies on the market. Microtissue models of human NASH demonstrate key hallmarks of the disease, giving researchers the opportunity to mimic the stages of disease and elucidate its pathophysiological mechanisms on a cellular level.

By improving risk predictivity over standard research tools, or by providing a more comprehensive model that is not otherwise available, MPS could bridge the gap between traditional cell culture and human studies. But, to maximize their potential, insights gathered from these models should be considered alongside in vivo data – both to provide confidence in the data derived from MPS models and to offer insight into the mechanisms underlying differences and adverse events in animal models. Ultimately, single- and multi-organ MPS could yield efficiency gains, reduce costs, and potentially reduce animal usage.

As MPS technology continues to evolve, advances in the field are extending the lifespan of models, enabling a greater window for long-term experiments, compound dosing, and observations of disease progression – and edging us ever closer to a true simulation of human biological conditions.

Standardize for Success

We're making progress on standardizing single-use systems – and it could mean a more cost-effective supply chain

By Jerry Branscomb, Senior Product Manager of Single-Use Technology for Standardization and Harmonization at Thermo Fisher Scientific

Recent years have seen considerable growth in the adoption of single-use technologies in the biopharmaceutical industry. By eliminating the long,

resource-intensive decontamination and sterilization steps associated with multi-use equipment, single-use has proven that it can help biopharmaceutical organizations boost operational efficiency, improve product quality and consistency, and reduce costs. However, increased demand for single-use is straining supply chains and delivery timelines – an issue I believe standardization can alleviate.

Standardization has historically proven challenging because biopharmaceutical organizations typically require highly specialized (often custom) single-use designs to meet their workflow needs. And if standardization practices are not properly executed and managed, it can be difficult to control configurations that have been functionally optimized and qualified for use in multiple applications. If the same design is being used across different workflows and facilities, for example, we must employ appropriate processes to ensure that any subsequent revisions will not impact the various applications.

Today, there is increasing focus on combining the attributes of several custom designs into one system for use as standard across different bioprocessing workflows. This helps to establish shorter lead times for single-use and simplify purchasing and inventory efforts, making these technologies more readily and sustainably available. Importantly, standardization also removes the risk of variation in the manufacturing process by enabling biopharmaceutical companies to implement more efficient, repeatable, and consistent processes that are quick to deploy and maintain – thereby boosting productivity. Ultimately, standardization can help biopharmaceutical organizations eliminate production bottlenecks and accelerate the release of new therapeutics to market.

Various industry groups have advocated for greater standardization in single-use and guidelines have emerged. The BioPhorum Operations Group (BPOG) standard methods, for example, are designed to enforce industry-wide leachable and extractable testing protocols for components used in the manufacture of single-use systems. Typically, manufacturers of single-use go to great length and investment to perform leachable and extractable testing of their products, a burden that standardizing on specific components could reduce. Following the BPOG standards has also made it easier for biopharmaceutical organizations to directly compare different components using the relevant test data to verify suitability for use in their operations. Ultimately, reliance on BPOG standards simplifies and accelerates the adoption of single-use technologies in the safest and most effective way.

The progress that has been made so far in standardizing single-use technologies has unlocked significant productivity gains for the biopharmaceutical industry – and I believe there is more innovation to come! Developers of single-use systems are constantly devising new technologies and optimized designs that offer the highest standards of performance, consistency, reliability, and safety. And, as we look to the future, single-use standardization will play a vital role in building a stronger and more cost-effective biopharma supply chain.

Zero Defects

Biopharma companies must minimize defects and contamination

By Massimo Mainetti, Global Head of Marketing and Product Management, Datwyler

As the COVID-19 pandemic continues to unfold, the industry is working tirelessly to identify effective treatments and vaccines. There is intense pressure to produce a vaccine in a short time frame, which demands efficiency on all fronts. Naturally, large molecules are being considered as treatments, but manufacturers face the challenge of ensuring that such drugs have zero defects and do not contain silicone contamination from packaging and delivery. Although silicone contamination has been an issue for decades, it can be commonly found in the plungers and stoppers of syringes, cartridges and vials. Because of its ubiquity, the default tendency among pharma manufacturers is to "work around" the possibility of silicone contamination in drug formulation, rather than address the issue head-on. Such contamination challenges are surmountable; indeed, solutions in this space can save time, money and stress, while delivering a better product to the patients.

When producing parenteral packaging for vulnerable or sensitive products, medicine manufacturers should always aim for zero defects. The zero-defect approach better preserves the drug, protects the patient, and upholds the reputation of the drug manufacturer. Injectable biologics have emerged as chief drivers of sales growth in the pharmaceutical industry, but are costly to manufacture and often highly sensitive to extraneous contamination, such as silicone, cellulose, or other particles. If the drug includes unsatisfactory levels of any of these contaminants, the whole batch must be disposed of, representing a significant monetary loss and, as we are reminded amid today's pandemic, precious time wasted in moments of potential crisis. Despite all the industry-standard quality audits and third-party oversight, contamination of large molecule drugs is still commonplace.

What best practices reduce incidence of drug contamination? In the case of silicone in parenteral drug packaging, it can start with complete coverage of any plunger or stopper with a no-silicone fluoropolymer coating. Creating a robust barrier between the drug and rubber minimizes the impact posed by extractables and leachables. Additionally, drug and device manufacturers can seek ready-to-use components in rapid transfer port (RTP) bags, so that drug manufacturers do not have to sterilize their own components. Pushing the washing and sterilization of components further upstream to component manufacturers reduces the manufacturing footprint in a biologics facility, and also keeps the focus on the core competency of manufacturing and filling the drug product rather than on component processing – which itself requires meticulous attention to detail.

Another best practice is to establish clear, transparent channels of communication between key parties – the drug company, the packaging manufacturer, and other essential suppliers. By working more closely, specifiers can easily identify and troubleshoot potential sources of contaminants and eliminate common defects throughout the supply chain; a crucial endeavour when you consider that visible particles accounted for 22 percent of all injectable drug recalls between 2008 and 2012, and that recall events due to visible particulates have been steadily increasing since 2009. Component manufacturers should consider redesigning production facilities for packaging and delivery systems used in large molecule drug applications to eliminate the presence of identified contaminants.

Perhaps the most common contaminants in pharmaceuticals are cellulose (cotton and paper) fibers, synthetic fibers, silicone, plastics, rubber, metal particles and corrosion products, glass particles and vial delamination flakes, skin flakes, and char particles. Eliminating cellulose from the vicinity of production is particularly difficult. Cellulose can be introduced via wood pallets, paper and bags present near production environments. Eliminating paper from the production floor – and, if possible, in the surrounding offices and other areas – by transitioning a facility to all electronic records and communications, can go a long way to reducing cellulose particles that can circulate. Substituting wood pallets with non-contaminating versions made of plastic substrate is also recommended.

Finally, it's necessary to improve product inspection. Camera inspection adds a layer of security the naked eye cannot achieve alone. Cameras do not get tired and do not miss even the smallest anomaly. For regulators, the trend is toward increased stringency. Recently, the FDA set the bar even higher for injectable drug manufacturing by calling for implementation of improved specifications, increased inspection, and improvement in analytical and inspection techniques.

Meanwhile, the creators and end users of large molecule drugs are relying on parenteral drug packaging companies to get as close to zero defects as possible. Anytime there is a market recall, it is not just a financial liability, but a huge risk to the reputation of pharmaceutical company partners and to the health of waiting patients.

The harsh reality? Contamination will always be an issue, and so "zero defects" represents a truly aspirational or idealistic goal; we in the industry must tackle this engineering challenge head on so that we can at least get as close as possible.

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Focus on Quality – and the Rest Will Follow

Amgen developed the Multi-Attribute Method (MAM) to obtain high-fidelity understanding of the quality of its own biologics – which is raising the bar across the biopharmaceutical industry

Da Ren is Scientific Director, Jette Wypych is Executive Director, Attribute Sciences, and Ting Song is Senior Scientist, all at Amgen, Thousand Oaks, California, USA.

Amgen has always had one overriding goal: to serve patients. With an emphasis on diversity, collaboration and, above all, quality, the company aims for continuous improvement in every sector of the business (see "Building a Culture of Innovation."). "In fact, quality was the foremost driver behind the development of multi-attribute method (MAM)," says Amgen's Scientific Director, Da Ren. "We wanted to develop a holistic control tool applicable along the entire bioprocess, including release and stability testing."

Using a whole set of conventional characterization and control methods, which often assess each attribute with a different assay, did not fit the bill. Enter high-resolution accurate-mass (HRAM) mass spectrometry (MS) and its potential to directly identify and quantify relevant attributes in a single assay.

"The old view was that 'the process is the product' – but we turned that on its head by defining the product by its critical quality attributes (CQAs) and their associated desired levels, which is the "blueprint" for designing the processes to manufacture the most safe and efficacious product. In other words, we start with the final desired product in mind, and the process design follows," says Jette Wypych, Executive Director of Attribute Sciences. MAM is an ideal analytical tool to enable this approach, as MAM has the capability of measuring a large number of post translational modifications in the product at the molecular level.

Challenges and rewards

The original concept of MAM was conceived by Izydor Apostol at Amgen in 2010. Richard S. Rogers (then member of the Amgen MAM team) and other colleagues went on to demonstrate the potential of MAM and published Amgen's work in a scientific paper in 2015 (1). Though MAM showed clear scientific and technical promise, the challenge of driving the project from concept to an accepted QC release tool in a GMP setting still lay ahead; channeling the significant power of HRAM-MS into a method capable of robustly, accurately, and routinely measuring CQAs relevant to safety and efficacy in a cGMP environment. This process was no small task. "The transition required and improved implementation and robustness analysis," says Ren. Other constraints included the need to control costs (without resorting to inadequate instruments) and minimize footprint (so that multiple instruments could fit in a single QC lab).

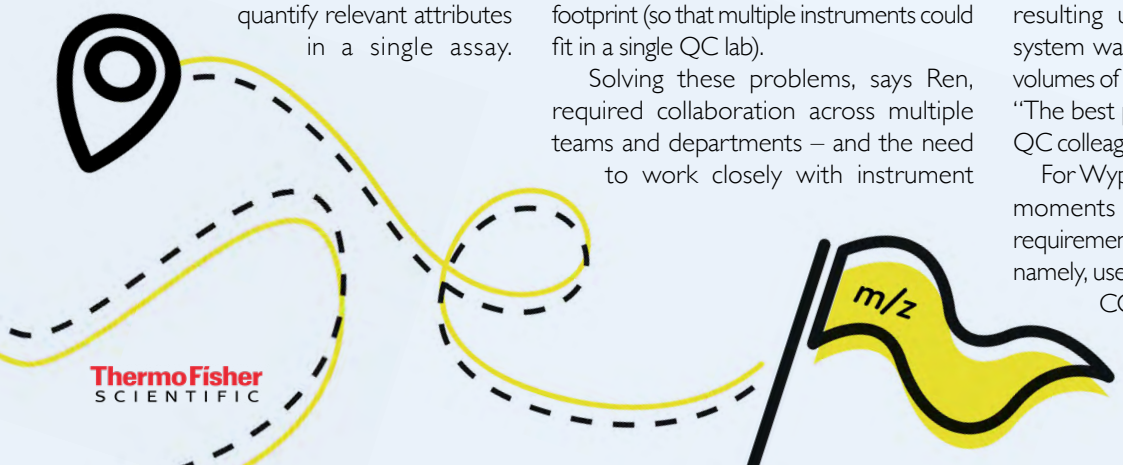
Solving these problems, says Ren, required collaboration across multiple teams and departments – and the need to work closely with instrument manufacturers. But the results have been extraordinarily gratifying. "In addition to quantitation of predefined CQAs, MAM's new peak detection capability is outstanding," says Ren. "It is capable of detecting any new peak (a potential impurity that is not predefined) in the sample against a reference standard. The high resolution and accurate mass features allow it to detect co-eluting peaks with very small mass shifts, such as those associated with deamidation, which conventional methods and low-resolution instruments simply cannot identify."

Another issue faced by the team involved data processing and presentation – the volume of information generated by MAM was incompatible with a visual output. Again, the cross-functional, team-based approach triumphed: today's MAM uses a bespoke computational algorithm that evaluates observed masses frame by frame, assigns them to the previously identified attributes, and alerts users to above-threshold new peaks.

However, the team was well aware that intelligent solutions are of little use if operators cannot apply them in a high-throughput environment. "The technology had to be used by QC specialists, not mass spec specialists," says Wypych. "And that meant robust methods and user-friendly software were essential."

It often takes a lot of effort to make something feel easy, comments Ting Song, Senior Scientist at Amgen, but the team was committed and motivated. The resulting user-friendly and automated system was able to rapidly process large volumes of data into actionable information. "The best part," says Song, "is hearing my QC colleagues saying how easy it is to use!"

For Wypych, one of the most rewarding moments was seeing MAM fulfil the requirements for a release and stability tool; namely, user-friendly, accurate, quantifiable CQA monitoring and new peak



detection. "At that point, I knew we had a scientifically defensible method that we could apply and implement in release and stability testing and share with regulators."

Perfect timing, perfect fit

MAM is becoming increasingly accepted as a better testing strategy within the industry; several biopharmaceutical companies have been evaluating it in QC, and others are planning to do so. The trend is reflected in the growth of the MAM Consortium (www.mamconsortium.org), a network co-led by Rogers and Ren. The Consortium – which has over 300 members, including pharmaceutical companies, regulatory agencies, CDMOs, and instrument/software vendors – meets monthly to discuss MAM and related mass spectrometry technologies.

"At first, many people in the industry questioned the utility of MAM for the QC environment," says Ren. "But now people don't ask why they should use MAM; instead, they ask how to implement the technology."

The credibility of MAM has been further enhanced, says Wypych, by technical publications from regulatory agencies (2), who have acknowledged the importance of MAM's ability to detect new peaks – and thus unexpected product degradants or impurities.

MAM also fits perfectly with ICH Quality by Design (QbD) guidelines. "The ability to characterize and quantitatively measure CQAs and guide process development to obtain target levels of CQAs is essential for QbD in biologics," says Wypych. An added benefit for sponsors and regulators alike was MAM's flexibility. If it becomes necessary to monitor additional CQAs for a given product, MAM can easily accommodate the change. Companies that rely on conventional methods, by contrast, would need to add a new assay to the release specifications. "Industry and many regulatory bodies now accept that MAM can measure an almost unlimited number of specific CQAs related to post-translational modifications at the molecular level, which are deemed relevant to safety and efficacy," says Wypych.

By exploiting the known advantages of HRAM-MS, Amgen has changed the QC testing toolkit forever. "Now, we can monitor CQAs in an end-to-end approach," says Ren. "We identify CQAs during characterization and then – following QbD principles – monitor and control them from development to release." And this – just as Amgen always intended – is bringing about the desired improvements to product quality.

Building a Culture of Innovation

How is it that some companies always seem to be at the leading edge of technology development? Amgen attributes its success to a consistent, sustained approach: employ talented individuals, place them in a supportive corporate culture, and encourage them to focus on quality. The evolution of MAM from concept to QC tool is a testament to what this philosophy can achieve.

Ren notes that employee diversity also plays a key role. "People of different backgrounds approach the same problem in different ways – and this inspires innovation." Wypych agrees and notes how Amgen's culture gives anyone – from any background – the opportunity to grow and blossom.

A second ingredient in the Amgen recipe for success is teamwork. This, says Ren, was fundamental in solving the complex challenges involved in MAM development. "We have a lot of highly talented people – but they are also team players and adept at cross-functional collaboration." The open, supportive culture contributes to the collaborative environment within Amgen, says Ren. "Everybody helps each other and, in the end, the best ideas prevail!"

Ren also pays tribute to external collaborators. "When combining different components in a brand-new system, vendor support is critical." Working closely was essential to ensure acceptable and usable technology outcomes, says Wypych. "We had to develop technical QC solutions that would also be acceptable to regulators. Putting MAM into the cGMP environment raised issues regarding robustness, functionality, consumables and software requirements – addressing them required close collaboration with the vendor. And that's why choosing a vendor with a long-term view is important – biomanufacturers want to avoid the need to change instrumentation every few years."

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To find out more, visit https://themedicinemaker.com/amgenmam

AFRICAN PHARMA *on the* RISE

By Maryam Mahdi

A shared continental vision is driving change in Africa. Over the next four decades, members of the African Union hope to achieve the goals outlined in Agenda 2063 – the blueprint for transforming Africa into a global powerhouse. But the road to economic success and the continent's growth is littered with hurdles that can only be cleared if companies across industries play their part. What does this mean for the pharmaceutical industry? Here, experts give their take on pharma's role in Africa's future and discuss how companies can overcome both historic and new challenges.

STEMMING *the* BRAIN DRAIN

Can African professionals be persuaded to pursue opportunities at home?

By Kelly Chibale

Africa is suffering from a skills exodus. Reports estimate that one in three skilled professionals from Africa now live and work in the developed world (1). This loss of talent has serious ramifications, not only for the continent's economy but also for the growth of its innovative R&D pharmaceutical industry. Africa imports many of the drugs it consumes and has yet to cement itself as a center for R&D. With such heavy reliance on foreign products, how will the continent move toward a more independent future?

The answer lies in dismantling the negative perceptions that hold Africa in a vicious cycle of dependence. For the most part, Africa is viewed through the lens of poverty – and its high disease burden makes it appear like foreign medical innovation is the best option that African governments have to offer patients. Though there is some truth to this notion, it, unfortunately, adds fuel to the fires of afro-pessimistic sentiment. Many pharmaceutical stakeholders both within and outside the continent have yet to see African innovation and the benefits it can bring to patients. And without evidence of innovative pharmaceutical prowess, Africa cannot attract the expert workforce needed to build its pharmaceutical infrastructure.

But even if there were examples of African innovation – and there are – the idea that foreign goods are somehow superior seems hardwired. For example, if asked to choose between a pair of leather shoes made in Italy and a pair made in Zambia, how many people would opt for shoes made by an African craftsman – even if the quality was better? Shoes may seem a trivial example, but they highlight a more serious issue. Even if African companies were developing more high-quality medicines, would patients at home and abroad feel confident in using them?

Though it is impossible to say with certainty how people will respond to Africa's future innovative pharmaceutical offerings, stakeholders from across the continent have the opportunity to confront the perceptions that plague the industry. It will require a multifaceted approach – but, from my own experience, I've realized that we all have a role to play in creating a positive perception of the industry.

A journey home

As an African academic, I have faced the challenging decision of leaving home to pursue educational opportunities. Like many others, the attraction of advanced facilities and thorough training pushed me to pursue international education. My doctoral studies at the University of Cambridge were invaluable – not only was I able to pursue my research interests in a way that would not have been possible in Africa, but I also had the chance to build my network and work alongside individuals at the cutting edge of science. Though I had every intention of returning to my native Zambia once my studies were completed, I found that, without the appropriate infrastructure for research and development, my options would be limited.

The frustration I felt wasn't unique – many other African students and postgraduates have found themselves in similar situations. I chose to return to help support the academic careers of young professionals and launch a drug development center, H3D, at the University of Cape Town. The center focuses on the discovery of potential medicines for disease indications that predominantly affect Africans and developing technology platforms that allow customization of medicines to African patients' needs. Though my decision has brought much value to my life, those who choose different paths cannot be blamed for making the decisions most appropriate for their professional goals.

Nonetheless, we found it difficult to fill positions in the center's early days. We were embedded into the University of Cape Town's ecosystem and our expert team had a wealth of industry experience – but the local professionals we wanted to hire simply weren't there. Advertisements for postgraduate positions, for example, were answered by international applicants. Though it would have been wonderful to have greater South African representation, we found that the people who did apply were attracted to the center because we had managed to create an R&D environment like those found in Europe and the USA.

As the center matured, we were able to showcase our capabilities as a biopharmaceutical operation. This, in turn, attracted a more diverse pool of candidates, and we now have many talented individuals of African heritage working with us. Ultimately, having the right infrastructure in place helps build influence. And that helps drive change not only at the local level but also on a regional and international scale.

Advising government

The inability to retain talent across the continent has caused some to point the finger at governments. "Are our ruling bodies doing enough to prevent the mass departure of skilled professionals?" It's a question

Far right: Kelly Chibale

that arises often. But such a complex issue has no simple answer. I believe that the responsibility for preventing the brain drain does not lie solely with our political institutions. Governments across Africa are investing in the training of their citizens, often sending people abroad to study. But if those who benefit from this funding choose not to come back, there is no return on investment. This, again, feeds into the cycle of dependence that prevents us from reaching our full potential. People rightly have the choice not to return – but if Africa is to develop a drug discovery and manufacturing ecosystem that rivals those elsewhere, it needs a critical mass of talent.

The lack of innovative pharmaceutical manpower also means that African governments haven't seen many scientists and entrepreneurs setting up their own organizations. And despite investing in young talent, they often fail to see the importance of allocating resources to new R&D ventures. Will governments get on board when we can prove the benefits of these operations to society? I believe they will. At H3D, our research on malaria, tuberculosis, and antimicrobial resistance has seen us develop clinical candidates, create jobs, and work with leading figures from big pharma – and it has made the South African government one of our greatest supporters.

Though it is risky, I advise others to take the chance and launch their own R&D facilities. Doing so will force our leaders' attitudes to change and could help build a robust innovative pharmaceutical ecosystem across the continent. We have the power to influence change, but we must take opportunities to do so as they arise. We owe it to future generations of scientists.

For a better tomorrow

African pharma has a promising future. More than ever, companies who take risks are establishing themselves as serious partners for international organizations. H3D recently partnered with the African Academy of Sciences, Bill and Melinda Gates Foundation, and the Medicines for Malaria Venture on "Grand Challenges Africa," a scheme that encourages innovation to address the continent's health and development needs. The project aims to expand the drug discovery community across Africa by, amongst other things, linking African academic institutions with partners from big pharma – crucially important for the future of our industry. The more R&D centers we have with advanced capabilities and robust infrastructure, the greater our impact. It won't be easy to achieve, but it is within our reach.

I am also excited by the possibilities that regulatory harmonization will bring to the community. At the regional level, regulatory bodies are improving access to much-needed medicines. In southern Africa, for example, ZAZIBONA brings together regulators from Botswana, Namibia, Zambia, and Zimbabwe. The benefit of this transnational collaboration is that, once a drug has been approved in one country, it is deemed fit for the rest. This ensures uniformity of dosing and pricing and ultimately helps improve the perception of our pharmaceutical industry among patients and external stakeholders.

At the moment, a continent-wide regulatory authority is not a reality. But, as an industry, we are getting closer to the point where we can speak with a unified voice. Though we still face challenges, we are proving ourselves willing and capable of managing them. I can only hope that these positive steps forward will give some of Africa's best and brightest pause for thought when making decisions about their professional futures.

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the HOUR HAS ARRIVED

Can the African Medicines Agency mobilize quickly enough to respond to growing healthcare issues?

By Sarah Adam and Cyntia Genolet

With SARS-CoV-2 infections on the rise, health systems across Africa are facing increasing pressure. Though researchers are working around the clock to unlock the science to help treat the disease, regulators must play a key role in ensuring the rapid – yet safe - development of treatments and vaccines. But Africa faces a significant stumbling block in its ability to address the pandemic: varying regulatory systems across the continent make it difficult to mount appropriate responses. Efforts for regulatory harmonization have been underway for the past decade, and this work has never been more important. Parliaments are now calling for approval to establish the African Medicines Agency (AMA) (1) – a proposed regulatory authority that would oversee the harmonization and convergence of medical and pharmaceutical regulation for African Union (AU) member states. Recently, Margaret Agama-Anyetei, Head of Health, Nutrition, and Population at the African Union Commission, urged the AU to ratify the treaty for the formation of the AMA before its next assembly in February 2021. The benefit, she explained, was that "instead of talking to eight regional economic communities or 55 countries, there would be one organization speaking on behalf of the continent (2)."

The AMA is expected to be essential in enabling patients to access safe, effective, high-quality, and affordable drugs, treatments, and vaccines. The main purpose of the agency will be to coordinate ongoing regulatory systems, provide guidance, and to foster reliance and regulatory harmonization across the continent. These aims are crucial to responding to public health threats, such as COVID-19. They will also help thwart the dangerously large and thriving market for falsified medicines. The unregulated sale of fake drugs is responsible for tens of thousands of premature and unnecessary deaths among African patients who unwittingly fall prey to counterfeiters. The WHO stated that the continent accounted for 42 percent of all counterfeit drug reports between 2013 and 2017 (3).

With the need to manage such significant issues, most people are in agreement that a continent-wide body will coordinate the work already being done by national regulatory authorities (NRAs) and allow the pharmaceutical industry to make good on its promise to leave no-one behind. But with the disruption caused by the pandemic, how near are African governments to realizing their goal?

Initiatives now

The pandemic has slowed down the process of ratifying the AMA in some countries because it has become the sole major issue confronting and preoccupying national authorities. However, "We are making good progress," said Margareth Ndomondo-Sigonda, AUDA-NEPAD's Head of Health Programmes. She explained that the results already achieved by the African Medicines Regulation Harmonization initiative (AMRH) have proven "key in building robust regulatory systems in Africa, including the establishment of the AMA (4)."

Africa's national regulatory authorities (NRAs) have already faced many challenges that come with infectious diseases – the HIV-AIDs crisis, Ebola and malaria have all tested capabilities. However, with COVID-19, NRAs can now benefit from virtual working methods that the pandemic has, in a matter of months, made the new norm for many. Using modern digital infrastructure, we hope to accelerate the implementation of good and efficient regulatory policies and practices and make the AMA one of the most efficient and modern regulatory systems in the world.

Africa still has some ground to cover in closing the regulatory gap. With this being said, the AMA should be empowered to foster unprecedented coordination, partnership, and sharing that we've all witnessed during this pandemic, and enjoy the benefits of shared regulatory experience. There is scope for expanding the current expedited processes to facilitate regulatory applications for new drugs, variations, and clinical trials used for COVID-19 treatments and vaccines – without, of course, cutting any corners. We're talking about priority and fast-track reviews, as well as temporary authorizations.

Similarly, the pandemic has underlined the vital need to ensure the continuous supply of existing medicines that patients urgently require. There are a range of ways that regulators like AMA can facilitate the process, including expediting procurement, helping with the security of the supply chain, and fighting falsified medicines.

Elsewhere, the pandemic has, fortunately, prompted a growing awareness of the need for coordinated regulation; 17 countries out of the 55 have now signed the AMA treaty, demonstrating that they see the agency's work as vital. Ghana and the Seychelles ratified the AMA last month; just after three other countries – Burkina Faso, Mali, and Rwanda – did the same.

Today, there are various coordinated national efforts to combat and mitigate the effects of COVID-19 led by the Africa Centres for Disease Control and Prevention (Africa CDC) Africa Task Force for Novel Coronavirus (AFCOR) and WHO Afro, in

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collaboration in particular with the African Vaccine Regulatory Forum (AVAREF) and the Africa Medical Devices Forum (AMDF). In addition, the AU launched a new multi-stakeholder initiative via the Africa CDC: The Consortium for COVID-19 Vaccine Clinical Trial (CONVACT). It aims to get more than 10 late-stage vaccine clinical trials up and running as early as possible on the continent by bringing together global vaccine developers and funders, as well as African organizations that can facilitate clinical trials.

So far, so...

Though the AMA is not yet a reality, other pharmaceutical bodies are working to address current health threats. AVAREF and other stakeholders have been successfully working together, often sharing data and collaborating on new initiatives – examples of this are the clinical trial authorizations (CTAs) for hydroxychloroquine and ritonavir involving 14 countries in an unprecedented joint review. If expedited, CTA could be delivered in just over 30 days and, in an emergency, 10-15 days compared with the conventional 6-12 months if national regulators go it alone. But this approach is just one piece in the complex jigsaw to remove potential inefficiencies and delays resulting from repeated steps and duplication of work.

Thankfully, progress in information sharing and implementation is being made. Our industry's commitment to "define the best science-based regulatory strategies for ensuring the availability of COVID-19 medicines and vaccines" is being realized and whether or not the AMA is approved before the AU Assembly meets again, pharma is dedicated to supporting those most in need. Leaning on decades of innovation and experience, the international community will be able to contain and find real solutions to the COVID-19 pandemic together.

Cyntia Genolet is Head of Health Systems and Africa Policy

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CRISIS POINT

How are African countries handling the COVID-19 outbreak?

Over the last 9 months, COVID-19 has claimed hundreds of thousands of lives – and thrust the pharmaceutical industry into the spotlight. The sector is now under pressure to deliver safe and effective solutions to an unprecedented problem. And though the world's eyes may be on the West when it comes to the development of new therapeutic options, pharmaceutical industries in other parts of the world must also evolve to manage the fallout from the disease.

African countries have not experienced the huge death tolls of some of the world's most developed economies, but concerns about their ability to manage the long-term effects of the pandemic remain. Here, Paul Tanui, Senior Programme Officer – Technical Support at the African Union Development Agency - NEPAD, and Arthur Minsat, Head of the OECD Development Centre's Europe, Middle East, and Africa unit, outline how the pandemic is affecting the continent's pharmaceutical industry and consider opportunities for change.

What is the current state of African pharma?

Paul Tanui: Some estimates indicate that over 70 percent of Africa's pharmaceutical needs are met through importation. A number of African countries rely entirely on imports for their pharmaceutical supply – but many are working to change this. In 2007, for example, the African Union Conference of Health Ministers mandated the development of the Pharmaceutical Manufacturing Plan for Africa (PMPA) – a roadmap to improved pharmaceutical capacity. As a direct result, the African Medicines Regulatory Harmonization (AMRH) initiative was established. Since its inception in 2009, it has helped build a regulatory environment for the development of a more robust pharmaceutical sector.

Today, there are regional pharmaceutical associations in Southern, Eastern, and Western Africa, as well as a continental organization for regulatory issues: the Federation of African Pharmaceutical Manufacturers Associations (FAPMA). In alignment with AMRH, these industry associations and FAPMA provide a voice to promote Africa's pharmaceutical industry. They interact as a common front with governments, multilateral institutions, and international procurement agencies to help push African pharma forward.

Arthur Minsat: The local pharmaceutical sector is burgeoning in Africa and, as Paul stated, most pharmaceutical goods are imported. Local manufacturers produce about 25-30 percent of pharmaceuticals and less than 10 percent of medical supplies that are on the African market. Over the 2016-18 period, only South Africa, Egypt, Kenya, and Morocco (in order of magnitude) exported more than $100 million, while importing about $5.8 billion in medicinal and pharmaceutical products. More than half (57 percent) of Africa's official exports in pharmaceutical products are directed to neighboring African countries. Producing pharmaceuticals locally on the continent is key to better fight local diseases, increase resilience, and advance the African Union's Agenda on productive transformation. Too few multinational pharmaceutical enterprises invest locally in Africa. Policies can continue to improve the incentives for better investment, and working together regionally is paramount. Here, the implementation of the African Continental Free Trade Area (AfCFTA) offers larger economies of scale by tackling the issue of fragmented markets for the local production of generic medicines, or by pooling the procurement of medicines.

How is COVID-19 affecting Africa?

Minsat: The crisis is affecting African economies through many interdependent channels. The African continent is very dependent on the international economy: commodities earnings slumped, trade in goods and services became disrupted, and external financial inflows fell drastically, in particular remittances from Europe, foreign direct and portfolio investment. Many economies suffered from massive capital outflows. COVID-19 led to postponing the implementation of the Continental Free Trade Area, thus limiting the expansion of internal trade. Countries have to run fiscal deficits, by spending more to mitigate the economy, health, and social impacts, while revenues slumped in many countries. The risk of a debt crisis becomes more acute in some countries. As a result, Africa is facing its first recession in 25 years, with various GDP forecasts ranging from -2.1 percent to -4.9 percent.

Africa's pharmaceutical value chain is disrupted through three main channels. First, it suffers from lower access to medicine supplies owing to the shutdown of manufacturing facilities globally. African countries import much of their pharmaceuticals and protective equipment from Europe (51.5 percent of total imports), India (19.3 percent) and to a lesser extent Switzerland (7.7 percent), China (5.2 percent), the United States (4.3 percent) and the United Kingdom (3.3 percent). Second, heightened competition to access basic goods (e.g. masks) made them less available and more expensive for many African countries. Globally, about 40 countries implemented bans on the export of certain drugs, pharmaceutical ingredients, or medical equipment (so as to be able to tackle domestic demand), leading to shortages in import-dependent countries. Third, macro-economic channels (in particular currency devaluation and capital outflow) have also impacted the sector.

Arthur Minsat, Head of the OECD Development Centre's Europe, Middle East, and Africa unit

Paul Tanui, Senior Programme Officer – Technical Support at the African Union Development Agency - NEPAD

On the bright side, the COVID-19 crisis also gave unprecedented impetus for developing health and pharmaceutical services online and locally. Public and private pan-African cooperation based on new technologies allowed countries to negotiate better prices for medical supplies with certified global suppliers. The Africa Centres for Disease Control and Prevention – in collaboration with Janngo (a pan-African tech startup), Afreximbank, and 20 international partners and foundations – has launched a pooled digital purchasing platform – the Africa Medical Supplies Platform – to support African governments ordering diagnostics and medical equipment on the global market. Afreximbank will facilitate payments, and logistics partners (including African national carriers and global freight forwarders) will expedite delivery. In the longer term, supporting the digital transformation of African economies could foster innovative solutions in the health and other sectors, and accelerate the economic recovery.

How well is Africa coping with the pandemic?

Tanui: In my opinion, though there have been difficulties, the National Regulatory Authorities (NRAs) across Africa have responded quickly to the pandemic. NRAs have a key role in ensuring that approved products meet quality, safety, and efficacy standards. Throughout this period, they have ensured appropriate access to diagnostic tests and treatment. They've also found support from technical committees, like the African Medical Devices Forum and the African Vaccine Regulatory Forum, who have provided guidance on clinical trials.

What about access to essential medicines?

Tanui: In addition to responding to COVID-19, NRAs are continuing with their regular activities – ensuring faster approval of products used in other diseases and contributing to the optimal functioning of Africa's healthcare systems.

Minsat: The informal workforce is the most vulnerable. About 82 percent of African people live without social protection, and the majority pays out-of-pocket healthcare. Data collected from more than 45,800 respondents across 34 African countries over 2016-18 highlighted that more than half (53 percent) of Africans went without needed medicines or medical treatment at least once during the 12 months preceding the survey. This demonstrates the

AFRICA IN NUMBERS

$26 billion is the value African pharma is expected to reach in 2022

2% of the worldwide pharmaceutical market is accounted for by African countries

375 drug makers across the continent

The countries with the strongest growth between **2011** and **2016** included:
Morocco **6%**
South Africa **8%**
Algeria **9%**
Botswana **12%**
Nigeria **13%**
Egypt **14%**
Kenya **17%**

COVID-19 IN AFRICA

At the time of writing **47** countries are affected

1,175,267 cumulative cases

25,825 deaths

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urgency to expand health and social protection coverage through the development of national social protection action plans to achieve universal protection and improve its quality.

What lessons can be learned from other regions' management of the crisis?

Minsat: Africa's epidemiology curve is at an earlier stage than many other parts of the world, which means African policy-makers have been able to learn many lessons to handle the pandemic better. Most African governments reacted more quickly to prevent the pandemic from spreading. Many governments also provided rapid support to the local economy, in the form of macro-economic and monetary interventions, lockdowns, e-schooling, support to enterprises, entrepreneurs, and cash transfers. However, we also saw the limits of lockdown and other policies in Africa, notably due to the size of the informal sector. Since late April, the necessity to keep the economy afloat led countries like Cameroon, Mauritius, Niger, Rwanda, and South Africa, to ease containment measures gradually, even though the infection curve had not yet reached its peak. The scope of the pandemic remains uncertain as cases are likely underreported and data collection varies across countries. By September 2020, the number of confirmed COVID-19 cases in Africa had risen to a million with over 50 percent in South Africa, and caused about 30,000 deaths.

It's crucial to recognize the importance of international cooperation in mounting an appropriate response.

- In the immediate term, the international community should provide adequate support to the healthcare sector, its workers, and social infrastructure. Major producers of medical products should refrain from export bans and other trade policies that fragment production and increase the costs of essential supplies for import-dependent countries. Debt cancellation or even restructuring may also become imperative to enable countries to respond and continue to conduct counter-cyclical fiscal policies.
- In the medium-term, large domestic and international resource mobilization should be prioritized and co-ordinated at the continental level to support health systems. Most African Union countries are still far from meeting the 2001 Abuja declaration target to allocate at least 15 percent of their annual national budgets on health. By 2011, only Tanzania had hit the target while 11 countries had cut their health expenditures. If African nations can develop mechanisms for early, synchronize economic policy with social and healthcare policy, and develop the capacity to monitor and evaluate these policies, it should lead to a quicker response to the virus.

What can be done to support the continued growth of the African pharmaceutical industry?

Minsat: The pandemic is exposing Africa's reliance on external suppliers in meeting its internal demand for medicines. However, African pharmaceutical and manufacturing companies are stepping up to produce critical supplies amid global shortages, disrupted supply chains, and export bans. African leaders can now decide which production capabilities are essential for the continent's health security going forward and provide those industries with the support they need to survive and develop.

- Countries should use this opportunity to accelerate the implementation of the Pharmaceutical Manufacturing Plan for Africa (PMPA) and establishment of the African Medicine Agency (AMA) by prioritizing investment for regulatory capacity development; pursuing convergence and harmonization of medical products regulation in regional economic commissions; and allocating adequate resources for AMA.
- Accelerating progress towards the next phases of the AfCFTA, particularly the agreements on investment, competition policy, and e-commerce, will create an environment conducive to establishing regional value chains in pharmaceuticals and will be critical to position the region as an attractive investment destination as the regional and global economy starts torecover.
  I am confident in the bright future of the African pharmaceutical industry, given the high demand, the renewed political momentum, and the ingenious spirit of African entrepreneurs.

Tanui: The PMPA business plan has identified several incentives that will support the growth of the pharmaceutical industry. These include:

- supporting affordable finance
- strengthening regulatory systems and harmonization
- enhancing the quality and efficiency of production
- promoting technology transfer initiatives
- developing enabling policy and skilled human resources

Young scientists should also be encouraged to pursue careers in NRAs and the pharmaceutical industry. As they become experts in QC, GMP, and industry, we will have a wealth of talent to help guide our future trajectory. But seasoned professionals also have a role to play; their mentorship of upcoming regulatory professionals will be vital for developing skills and knowledge.

I can only express my optimism for the future of our industry.

Understanding the Oligonucleotide Landscape

Though attracting growing interest in drug development circles, oligonucleotide-based therapeutics present manufacturers with specific processing and characterization challenges

Oligonucleotide-based therapeutics represent the changing face of drug discovery and development. Designed to prevent or modulate the translation of a specific gene, these therapies have the potential to tackle previously undruggable targets and could set the tone for the future of personalized medicine. As of January 2020, the FDA has approved 10 oligonucleotide drugs, but the number of therapeutics moving into and through the development pipeline is blossoming with six of these oligonucleotide drugs approved between 2016 and 2019 (1). Here, Genentech associate scientist Alexandre Goyon outlines the pros and cons of currently available techniques for characterization of oligonucleotides – and considers what the technologies of tomorrow might look like.

What are the main types of oligonucleotides?

When it comes to pharmaceutical clinical development, there are two main categories of oligonucleotides:

- Antisense oligonucleotides (ASOs) – single-stranded, typically 10 to 30 nucleotide units
- Small interfering RNAs (siRNAs) – double-stranded, each strand containing typically 19 to 23 nucleotides.

Each class of oligonucleotide comes with its own advantages and limitations. For example, siRNAs can be more potent than ASOs for some targets as they involve different enzymes for the RNA cleavage mechanism of action, i.e. RNase H1 for ASOs and Ago2 for siRNAs, but siRNAs can lack stability and effective strategies must be employed to ensure their delivery to target sites. Lipid nanoparticles can be used as carriers to transport siRNAs to the target cell's cytoplasm and improve siRNA stability against ribonucleases. siRNAs can also be conjugated to a ligand called GalNAC for transportation to the liver.

What's the regulatory view on oligonucleotides?

Oligonucleotides are considered small molecules since they are manufactured by solid phase synthesis. However, as mentioned by Mohan Sapru of the FDA, there is no ICH and FDA regulations that specifically address the quality expectations of the diverse oligonucleotide products (2). Discussions about legislation are ongoing!

Some of the challenges are addressed in two industry-led white papers produced by a collaborative team from Ionis Pharmaceuticals, AstraZeneca, GlaxoSmithKline, Sanofi-Aventis, Janssen Pharmaceutical, F. Hoffmann-La Roche, Biogen and Novartis in 2017 and 2020 (3,4). In the papers, the authors issue advice on myriad chemistry challenges affecting oligonucleotides and encourage information sharing and chemistry, manufacturing, and control (CMC) harmonization strategies between research groups to reduce the risks that these therapies can potentially pose to human health. They have sparked much discussion about the next steps regulators could take.

What analytical technologies are used for the characterization of oligonucleotides?

There are several, including (5):

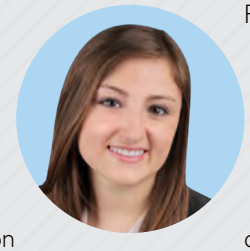
- Ion pairing reversed-phase (IPRP) chromatography – the most common method for the analysis of oligonucleotide impurities. It can separate shortmers, longmers, and phosphodiester (PO) impurities, among others. It can be coupled to mass spectrometry in particular when combining the alkylamine ion-pairing agent with hexafluoroisopropanol (HFIP).
- Anion exchange chromatography – this can also be used to separate impurities, but the large amounts of non-volatile salts involved prevents its direct coupling to mass spectrometry, which is one reason why IPRP is more widely used.
- Hydrophilic interaction chromatography (HILIC) – there have been surprisingly few published reports about the use of HILIC for oligonucleotides. HILIC has the advantage of allowing direct coupling to mass spectrometry without using ion-pairing agents. There is a great diversity of stationary phases, which could provide orthogonal separation to IPRP and thus be complementary.
- Size exclusion chromatography – this method is used with double-stranded oligonucleotides such as siRNAs in order to determine the number of single strands in the double-stranded product using non-denaturing conditions.

How would you like to see analytical technology in this area improve?

The first oligonucleotides were investigated about 30 years ago and it is only in recent years that the industry's interest in them has been renewed in part due to the advances in oligonucleotide chemistry engineering and delivery systems. In my

Oligonucleotides: Perfecting Purification

By Manuela Sevilla, technical expert at Tosoh Bioscience



For the companies pursuing oligonucleotide-based therapies, the relative complexity of their synthesis can pose purification challenges. Oligonucleotides are short DNA or RNA molecules that are "grown" via the addition of nucleotide groups in a series of solid-phase synthesis cycles – a failure in this process can allow impurities to emerge. Some chemical modifications are necessary to improve their pharmacokinetics and stability. These could result in another source of impurities.

Irregularities in the manufacturing process can lead to the formation of the following common impurities:

- Shortmers – oligonucleotides missing one or more nucleotides, or N-1
- Longmers – oligonucleotides that include more than the intended number of nucleotides, or N+1
- Lack of protecting groups (derivatives of existing functional groups that decrease reactivity and increase stability)
- Phosphodiester impurities (PO) in phosphorothioate oligonucleotides

A helping hand

Fortunately, when it comes to removing impurities that occur during oligonucleotide manufacturing, a range of chromatographic techniques ensure that the highest levels of purification can be achieved.

Anion exchange (AIEX) chromatography is the optimal solution for addressing variation in strand lengths – shortmers and longmers. AIEX separates oligonucleotides by the negative charge of the backbone. Because siRNAs are highly polar by nature, Tosoh's high-performance anion-exchange medium, TSKgel SuperQ-5PW (20), can easily separate unwanted synthetic strands from the desired product. Consisting of highly cross-linked hydroxylated methacrylic polymer beads and with a particle size of 20 µm, this resin offers both high resolution and high loading capacity – essential from a productivity point of view. And this resin is available as SkillPak pre-packed columns for faster method development!

Analytically minded

Characterization and quality control of oligonucleotides essentially apply the same modes of chromatography as purification. In AIEX chromatography, TSKgel (U)HPLC columns based on non-porous particles are available with the same surface and ligand chemistries as the TOYOPEARL and TSKgel purification media. TSKgel DNA-STAT or DNA-NPR columns offer fast kinetics and high-resolution separation.

Size exclusion chromatography (SEC) can also be applied in combination with light scattering detection. The TSKgel UP-SW2000 UHPLC column can separate oligonucleotides differing by one base in length. And when coupled with our new LenS3 multi-angle light scattering (MALS) detector, a detailed picture of the oligonucleotide purity can be achieved.

Options aplenty

At Tosoh Bioscience, we've amassed a wealth of experience in the development of chromatographic methods for downstream processes and characterization – and we are happy to help in any process optimization. From small-scale academic environments to big pharma, we can support all your growing needs; we pride ourselves in continually advancing our product offering in line with industry advances.

Oligonucleotides are the next frontier in biopharma – and we are there for you in your pursuit of a healthier future.

opinion, there are three main areas for improvement in the field of analytical chemistry. Firstly, it's important that we limit oligonucleotides' non-specific interactions with metal surfaces and, therefore, the use of truly biocompatible instruments and columns will become crucial. Secondly, the use of superficially porous particles may improve the separation of the larger oligonucleotides being developed today. Thirdly, the use of volatile mobile phase in cation exchange chromatography is an important trend for antibodies. Hopefully, a similar strategy could be applied for the anion exchange analysis of oligonucleotides, but column development would have to focus on reducing the amount of salt needed to elute oligonucleotides.

Developments in the oligonucleotide space are happening at a rapid pace, and it's truly exciting to be a part of this field! Regulators are paying increasing attention to these products and the approval of new therapies will certainly help us push the boundaries of their potential.

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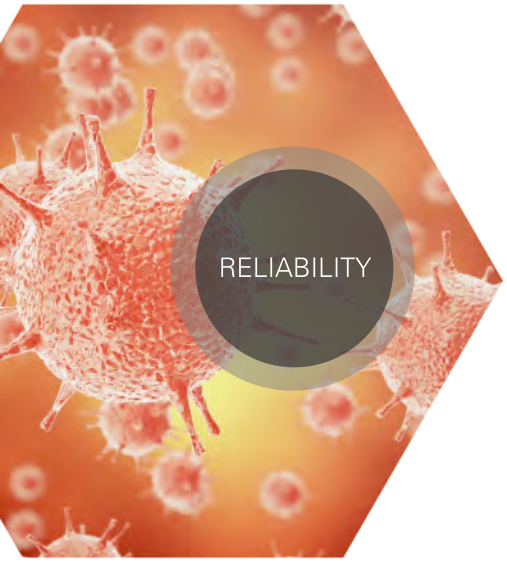

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A Living Elixir?

Live biotherapeutics are microorganisms isolated from the human gut with the potential to treat diseases such as Crohn's, cancer and even Alzheimer's. Duncan Peyton, Chief Executive Officer at 4D pharma, walks us through its pipeline, including oncology, and why the inherent safety profile of this new class of medicines makes them so exciting for developers – and patients.

By James Strachan

What led you to the live biotherapeutic field?

My background is in genetics. Interestingly, I started off in microbial genetics at a small biotech in the early 1990s. In addition to a passion for the science, I was also interested in the business side of things, so I decided to go back to university to study law. There, I learned more about corporate finance and started working for a private equity and venture capital firm. They wanted to get into healthcare and biotech, so I was able to become an investment manager.

And that led me to set up my own fund with my business partner, Alex Stevenson, mainly focusing on small biotech businesses. We had a lot of success, but we always felt under pressure from investors to deliver quickly – which can be difficult in a field with a high rate of clinical failure – so we started looking for something reliable that could succeed over the longer term. Once we heard about the microbiome, we felt we had our answer.

How did you find out about the microbiome?

In 2011, our fund was looking at around 300 early stage research projects a year to invest in. One of those companies was a shark antibody business, based out of Aberdeen University, which Pfizer inherited from Wyeth. We travelled up to have a look at the technology and while we were there asked if we could take a look at some of the other stuff they had too.

There was a group that had identified two bacteria that could dampen down the immune system. They were actually planning on using the bacteria in pig feeds to prevent disease in piglets when they're being weaned. But we looked at the data – which included mechanistic details – and thought "there's a therapeutic here." We decided to invest in a research project within that group and after realizing that there are many other bacteria with different mechanisms of action – all of which should be inherently safe and free from side effects – we began to appreciate the potential of the microbiome as an untapped resource for pharmaceutical development. With this in mind, we founded 4D pharma.

Why are live biotherapeutics inherently safe and what does that mean for drug development?

Microbes already exist inside the human body, which makes them inherently tolerable and unlikely to produce side effects. This is huge from a drug development perspective. Pharma companies lose around 30 percent of products at each clinical stage. Why? More often than not due to safety and toxicology. Often you'll see this cited as a reason for high drug prices too – companies have to charge high prices for their successful drugs to recuperate the funds they lost for the unsuccessful ones. What if clinical trials were tests of efficacy alone because the products are inherently safe and tolerable? The huge development risk would be slashed.

And from the patient perspective, I'm sure everyone reading this has been touched by cancer in some way, and many will have seen how ill people feel when they're taking some of the commonly prescribed chemotherapies. It's not uncommon for someone to opt against an effective treatment because of the potential side effects. Another example is Crohn's disease, which can severely impact a patient's life – even in terms of

growth and puberty. Patients (or their parents) often have to decide whether or not to take an immunosuppressant with some very serious side effects. With live biotherapeutics, you can develop a treatment that is likely to be safe and easily delivered by an oral capsule – as opposed to expensive, immunosuppressive injections.

Which projects are you most excited about?

I'm most excited about our oncology program and our prime candidate MRx0518. We are currently working on a clinical trial with Merck & Co. and their checkpoint inhibitor, Keytruda. Keytruda is, of course, a successful drug that is generating close to $4 billion in sales in a single quarter. But there are some major limitations. Firstly, it only works in three-out-of-ten patients; secondly, some patients, such as those with non-small cell lung cancer carrying certain mutations, don't respond. Naturally, Merck is interested in finding ways to expand the number of patients that Keytruda can treat.

Our preclinical research showed that MRx0518 can reduce tumor volumes and

"When we launched the company in 2011, the FDA hadn't even defined a live biotherapeutic."

tumor size as a monotherapy. And when you dose MRx0518 with a checkpoint inhibitor, you see a synergistic effect. So we're trying to find out whether MRx0518 is effective in checkpoint inhibitor refractory patient populations – patients who have stopped responding to drugs like Keytruda. The question is: can we re-stimulate the immune system?

Usually when you re-treat a patient who has already stopped responding to a checkpoint inhibitor you would expect something like a five percent response rate – so we set the bar in our combination trial at 10 percent. In our initial population of 12 patients with growing tumors, some of whom had received seven or eight different prior treatments, five had durable responses to MRx0518 in combination with Keytruda. That was a fantastic result and we're excited to conduct later stage trials, with an approval next year potentially on the cards.

Do you understand the mechanism behind the effect?

To successfully develop a live biotherapeutic, we believe it's vital to distill down the essential components of the microorganism and understand how it works at the molecular level – we try to treat these products like any other pharmaceutical. Taking this approach, we've discovered that a specific region on MRx0518's flagellum acts as an agonist for TLR5 on the cell surface, which triggers a signaling cascade leading to immune stimulation. We've carried out studies with flagellin knockout MRx0518 and found little to no TLR5 activation or immunostimulatory effects.

Are there many manufacturing challenges associated with live biotherapeutics?

For live biotherapeutics broadly, there is a potential for change to occur between batches and over time if not properly controlled because of the complexity of the product. This problem is multiplied exponentially if the product contains multiple organisms. We're only dealing with single-strains, which allows us to more easily control the identity, purity, potency, and stability of our products.

Another challenge is that there aren't many CDMOs out there with the experience of manufacturing live biotherapeutics, so we decided to manufacture in house. The main challenge for us was ensuring that our bacteria are not exposed to oxygen during the process (they are anaerobic). To do this, we had to develop some novel manufacturing techniques. For example, we use a "Quality by Design" approach to efficiently and effectively optimize fermentation and lyophilization conditions, as well as developing in-house some of our own hardware used in the production process.

So there are challenges, but they aren't insurmountable. We have an cGMP-certified live biotherapeutic manufacturing facility in Spain and we've put nine programs through our manufacturing process – with some products having a stable shelf life of two years and counting.

Interestingly, we've also found that scaling up into larger tanks has actually improved titers – our production engineer tells me it has to do with fluid dynamics favorably altering the flow of nutrients in the bigger vessels.

Given the novelty of the field, what are the regulatory hurdles?

When we launched the company in 2011, the FDA hadn't even defined a live biotherapeutic. The first definition came in 2012. That said, we've found the regulators to be very easy to work with. Their main concern is, of course, safety. But they are also scientists. If you can present a logical argument – supported by a solid dataset – they tend to be receptive. In fact, Alex was asked, on behalf of the MHRA, to work on the European Pharmacopeia chapters on quality standards for live biotherapeutics, so we've had a role in setting the regulations for live biotherapeutics. And, as I've said, live biotherapeutics are microorganisms that exist in the human body, which makes them inherently safe – and that really helps allay the concerns of the regulators.

How would you summarize the potential of the field?

In more recent years, the microbiome has garnered a lot of attention. But back in 2011, if you were to tell someone that your plan was to isolate bacteria from someone's fecal sample, put it in a capsule, and feed it to a patient to cure Crohn's disease, they would have thought you were mad. Fast forward to 2020 and it's looking like we might be able to address neurological conditions, such as Alzheimer's and Parkinson's with the microbiome – two of the biggest problems we face as an aging society. If you'd have told me this three years ago, I might have thought you were mad! But that's where we are today.

From our perspective, we're closing in on bringing a live biotherapeutic drug to market. But we're talking about a single strain of a single microorganism. The human microbiota consists of something like 1000 different species of microorganisms, so it's fair to say we haven't even begun to scratch the surface of what might be possible in terms of pharmaceutical development. We're talking about an entirely new class of medicines with the potential to transform how we treat many diseases.

Serving a Rising Power

The gene and cell therapy market is growing, but does it have the CDMO support needed to maintain its upward trajectory?

Gene and cell therapies (GCTs) are capturing the attention of players from across the pharmaceutical industry. And with rapid growth comes the need for support from specialized CDMOs. Here, Brian Min, CEO of GenScript ProBio, explains how the company is gearing up to help the global GCT community deliver on the promise of these exciting therapies.

How did GenScript ProBio get started in the GCT sector?

We live in a world where 4 million people are diagnosed with cancer each year; ultimately, our goal is to see as many successful GCT products reach patients as possible. It's an area with an upward trajectory. Though GCTs were first developed in the USA, there is a massive opportunity for companies around the world to get involved with the progression of the field. China, for example, was quick to adopt the concept and now runs nearly as many CAR T trials as the USA. The problem the market now faces is that, despite the huge network of talented companies, the number of CDMOs that are able to help in GCT product development are few and far between. We can help companies achieve their goals through our expedited services. GenScript has supplied R&D grade plasmids to GCT companies since 2004, and continues to serve these companies with process development and GMP manufacturing.

How does GenScript ProBio serve its GCT customers?

We are a one-stop-shop provider for plasmid and viral vectors, with products ranging from R&D to GMP grade. Our total GCT solutions cover chemistry, manufacturing and control of plasmid and virus for IND filings, as well as clinical and commercial manufacturing. We also ensure phase appropriate compliance, data integrity, and traceability with robust quality management systems.

We currently offer R&D to GMP grade plasmid and viral vectors to support pre-clinical and clinical studies, and in 2022–2023 our GMP commercial center will begin supporting commercial-scale productions for our increasing pool of customers and projects. These facilities will help us meet customer needs, and signpost our commitment to shortening development timelines – significantly lowering R&D costs and building a healthier future.

Could you speak to the importance of plasmids and viral vectors supply?

Viral vectors are crucial for introducing genetic material into cells – there are over 2,600 ongoing gene therapy clinical trials that rely on them. Developers need a steady supply of lentiviruses and adeno-associated viruses (AAVs), and other viral vectors such as vaccinia, retro, adeno and herpes can be produced with protocol transfer from customer. Stable supply might not be a problem in early clinical trials, but it can become an issue when mass production is needed to address larger trial cohorts. And I believe this could be the biggest bottleneck for the field.

Another challenge companies face is that, though lentiviruses and AAVs are showing promise in the clinic, there are concerns around the potential for side effects. Companies simply must select vectors with ensured safety and purity for their GCT products.

Innovation through collaboration

What's your best advice for accelerating GCT development?

The manufacture of viral vectors is likely to be one of the biggest constraints that developers will face as they shift from clinical trials to commercialization. Avoiding this particular bottleneck is directly linked to accelerated development. Many CDMOs have longer wait and lead times to conduct the GCT product development and manufacturing, and we are able to substantially shorten these time frames. Though some companies may have in-house facilities, choosing an experienced CDMO partner is also important for ensuring regulatory and clinical success while minimizing the burdens of capital investment and running costs.

How is COVID-19 affecting the GCT community?

In the first half of 2020, the number of companies working on regenerative medicine therapies globally passed the 1,000 mark for the first time, with 415 companies entering clinical development. Of these, 515 are developing gene therapies and 632 are developing cell therapies. But the pandemic has affected the progress of many clinical trials, causing delays to regulatory applications and approvals. Even with these challenges, the market is expected to pick up in the second half of the year. At GenScript ProBio, our customers benefit from reliable and uninterrupted GCT manufacturing thanks to our manufacturing capacity located across the globe including the US and China, and we will be there to support our customers through it all.

For more information, contact cdmo@genscript.com

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The Battle for the Future of American Healthcare

Did the forecasted drug pricing storm come to pass following the 2016 US election? And what might the 2020 elections mean for pharma and the Affordable Healthcare Act?

By James Strachan

Four years ago, The Medicine Maker made a bold prediction: regardless of who ended up in the White House, the pharma industry would have to weather change – with particular regard to drug pricing (1). Hillary Clinton had a long history of opposing rising drug prices, but Donald Trump was also making noises in favor of Medicare price negotiations and "repealing and replacing Obamacare." In fact, one of Trump's campaign promises was to allow American consumers to purchase drugs from abroad. Chris Dale, Director of Public Relations and Communications for Turchette, said that Medicare price negotiations and drug importation would become immediately politically untenable after a Clinton victory (due to the balance of power in the House of Representatives), and would only be possible if Trump won. Thus, we envisaged a strange situation whereby the USA would only see some of Clinton's pharma-related policies if Trump became president. In the words of then Novartis CEO, Joe Jimenez, "We believe that, no matter which candidate wins, we will see a more difficult pricing environment in the US." So did we?

Trump seemed anything but the "business as usual" candidate – an image he's deliberately cultivated in interviews and on social media via more than 17,000 Tweets since he officially declared his presidential candidacy in July 2015 (see our sidebar: Talking the Talk). But, as far as pharma and drug pricing goes, we haven't yet seen radical changes. "This is something I was clearly wrong about," says Dean Baker, co-founder of the Center for Economic Policy and Research. "I expected Clinton to win, but even if she didn't, I thought Trump would feel some pressure to rein in the drug companies. As it turned out, spending on drugs rose more rapidly under Trump than during the Obama years."

According to Baker, spending on prescription drugs rose by 6.3 percent annually under Trump compared to a 5.5 percent rate under Obama-Biden. "The general direction in the Trump years has

been upward, with a peak of 9.7 percent in the first quarter of 2020, then a drop to 4.4 percent in the second quarter," said Baker in a recent blog post (2). "This falloff is a direct result of the pandemic, as many people put off doctors' visits, which meant that they would be prescribed fewer drugs. So, before the pandemic, drug spending was rising at a rapid and accelerating pace."

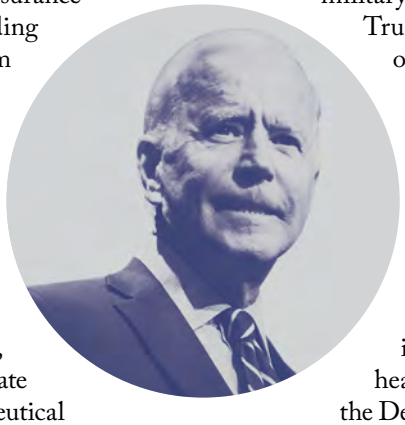
In March 2018, Trump promised, "You'll be seeing drug prices falling very substantially in the not-too-distant future, and it's going to be beautiful." Then in May, 2019, he said "Drug prices are coming down; first time in 51 years because of my administration." But, according to the consumer price index, prescription drug prices in the USA rose during the Trump presidency by 5.9 percent from December 2016 to December 2019. Though this represents a moderate reduction in the rate of the increase, it is in line with the upward trend seen in the USA over the past couple of decades (3).

Why haven't we seen the kind of radical shift in drug prices? President Trump decided in early 2017 – apparently following a meeting with pharmaceutical industry lobbyists and executives – that he would not seek to allow Medicare to negotiate directly with pharmaceutical companies. Since then, the President launched a number of policies aimed at reducing drug prices (see our sidebar: Trump's Pricing Policies on page 42).). But according to Monique Dabbous and her colleagues at Aix-Marseille Université, France, Trump's primary focus has been on repealing the Affordable Care Act (ACA) (4).

On his first day in office, President Trump signed an executive order instructing administration officials "to waive, defer, grant exemptions from, or delay" implementing parts of the ACA. But, a few months down the line, Trump's plan to repeal and replace "Obamacare" failed – largely due to the late Republican senator, John McCain, voting against the new plan. And though President Trump has been unable to repeal the ACA, he has been able to weaken it, mainly by dissolving the "individual mandate" penalty, which anyone without coverage had to pay. However, the result was a 32 percent increase in average premiums, according to the Kaiser Family Foundation (5) (although most received subsidies to offset those premium hikes) – likely because, without the financial penalty incentivising people

to take out healthcare insurance, insurance firms anticipated lost revenues.

Further reforms made to the ACA include: i) allowing states to add "work requirements" to Medicaid, ii) ending payments made from the federal government to insurers to motivate them to stay in the ACA insurance exchanges, iii) expanding access to short-term "skinny" plans (allowing them to last for up to one year and be renewable for three years), and iv) slashing funds to facilitate HealthCare.gov sign-ups (5). Taken together, George Sillup, Associate Professor of Pharmaceutical & Healthcare Marketing at Saint Joseph's University, USA, says that Trump's efforts to dismantle the ACA has made it "more challenging for those who are underinsured (no drug coverage) to get affordable coverage".



A change of priorities?

In 2016, the affordability of prescription drugs was one of the most important issues in American politics. According to a poll conducted the week following the last US election, healthcare was rated as the third most important factor in peoples' vote for president – above foreign policy, terrorism, immigration and either candidate's personal characteristics (6). And when thinking about healthcare priorities, dealing with the high price of prescription drugs topped the public's list (7).

Today, in the midst of an international pandemic, and following protests and riots against racism and police violence, drug pricing may be lower on the public's priority list this time round. Fiona M. Scott Morton, Theodore Nierenberg Professor of Economics at the Yale University School of Management, agrees: "We have such important issues of democracy, corruption, and racial injustice to worry about."

Baker thinks the Democrats are focusing on the pandemic and Trump's lack of respect for norms – most recently his alleged disrespect for people in the military. On the other hand, Trump is focusing more on painting a picture of the Democrats as dangerous radicals. "In neither case is there much room for talking about healthcare," he says. "That may change, and my expectation is that a shift to healthcare would benefit the Democrats more than the Republicans (coverage has fallen and costs have risen sharply under Trump), but I know better than to try to predict the course of this campaign..."

Sillup also hasn't seen healthcare discussed much in the media, but that might be about to change. "A recent ad by Biden addressed the issue and I anticipate that will increase as we ramp up for the presidential election," he says.

In fact, the COVID-19 pandemic may have led to an improvement in the reputation of pharma companies. Researchers from The Harris Poll found that 81 percent of Americans polled recalled seeing or hearing something about the industry during the pandemic, with 40 percent believing that pharma's reputation had improved since the beginning of the COVID-19 outbreak. Rob Jekielek, managing director at Harris, said the industry was at its highest ever point in terms of its reputation and relevance (8).

Interestingly, before the last election Baker advocated expanding the role of public open research as a means of reducing drug prices. This has, in a way, taken place during the development of drugs and vaccines related to the coronavirus. But the government has not taken ownership of the research – potentially feeding into the good press surrounding the pharma industry at present. "Moderna, which is generally thought to be the leading US contender to develop a vaccine, had pretty much all its research costs paid by the government," says Baker. "Nonetheless, it will get a patent monopoly on the vaccine and will be able to charge what it wants."

"Instead of procuring drugs in a cost-effective and rational manner, we will be forcing our bad system on to others."

In any case, Baker believes that this could provide an example of where direct funding to develop a vaccine leads to a useful outcome. "It should be possible to point to this example as a reason to have more direct funding in the future, but with the patents going into the public domain so that a new drug/vaccine can be produced as a generic from the day it is approved," he says.

The new landscape

What then, given the new landscape, should pharma companies expect following the outcome of the 2020 US presidential elections? In July, President Trump announced four executive orders to reduce drug prices (see Trump's Pricing Policies on page 42).

So far, only the policy to ensure the USA pays the lowest price for Medicare Part B drugs compared with other economically

similar countries has been officially signed as an executive order – and actually goes further by also including Part D drugs. The move represents a deviation from the International Pricing Index model and instead anchors to the lowest price for a product sold across OECD member countries, with a comparable per-capita GDP, after adjusting for volume and differences in GDP.

Pharma wasn't best pleased with the proposal. "This reckless scheme will eliminate hope for vulnerable seniors and other patients waiting for new treatments by drastically reducing investment in cutting-edge scientific research and development," said Michelle McMurry-Heath, CEO of the Biotechnology Innovation Organization (9). "That is why we will use every tool available – including legal action if necessary – to fight this risky foreign price control scheme."

PhRMA CEO Stephen Ubl agreed, arguing that the administration "has doubled down on a reckless attack on the very companies working around the clock to beat COVID-19," and that the order is an "irresponsible and unworkable policy that will give foreign governments a say in how America provides access to treatments and cures for seniors and people struggling with devastating diseases" (10).

Scott Morton argues that the result of the policy would be high US prices exported to its allies. "This is particularly egregious and poorly thought out," she says. "Instead of procuring drugs in a cost-effective and rational manner, we will be forcing our bad system on to others."

Scott Morton would rather see the next president tackle barriers to entry: "Getting generics into the market by eliminating pay for delay, REMS abuse, restriction of samples, and price fixing to name a few," she says. "Also, biosimilars must have the same scientific name as the innovator, not face undue approval hurdles at the FDA or loyalty rebates and other contracts that act as a barrier to entry. Finally, government purchasing (Medicare, Medicaid, and so on) should incentivize a physician (in Part B, or on the medical side of commercial plans) to buy a lower cost drug."

Sue Peschin, President and CEO of the Alliance for Aging Research, concurred in an article for Stat News. She pointed out that an Avalere study found that fewer than one percent of older adults in Medicare Part B would see a reduction in out-of-pocket costs as a result of the international pricing index model (11) – though it is not clear how the inclusion of Part D might affect the analysis. She also criticized the policy for endorsing the cost-effectiveness standards often used by other governments, such as the UK, which she described as "discriminatory."

According to a more recent Avalere analysis, any potential savings will depend on how the system identifies the range of per-capita GDPs considered "comparable," what drugs volumes are used for adjustment, and what pricing sources are used for calculating MFN (12).

Either way, as Rachel Sachs, a law professor at Washington University in St. Louis and an expert on drug policy, pointed out on Twitter (13), it seems unlikely that the Trump administration would be able to finalize the necessary regulations before the November election. "In the best case scenario, it would still take quite some time to implement the model," she says.

Interestingly, the Democratic-controlled House also passed a bill in December of 2019 that would have allowed the US Department of Health and Human Services to negotiate prescription drug prices using other countries' prices in a similar way to Trump's proposal (Republicans opposed the bill and Trump threatened to veto it). We may, therefore, see some sort of proposal implemented regardless of which candidate wins the election – though we've made similar predictions before...

Trump's Pricing Policies

May, 2018
Trump's American Patients First blueprint to lower drug prices and reduce out-of-pocket costs by focusing reforms on the opaque world of pharma rebates and discounts.

June, 2018
President Trump jawboned pharmaceutical CEOs to limit and/or delay their company price increases, with Pfizer reporting pricing pressures from many sources, including those from the administration.

July 2018
The Biosimilar Action Plan was rolled out to lower drug prices by promoting greater competition through increased availability of biosimilars in the US.

October 2018
President Trump signed two bills that passed virtually unanimously by Congress to ban "gag orders" in contracts between pharmacies and insurance companies/pharmacy benefit managers (PBMs) to tell consumers that they could get drugs at a cheaper price by paying cash rather than the negotiated contract price on their drug plan.

President Trump also announced a five-year experiment to lower Medicare Part B drug prices. Administered by the Centers for Medicare & Medicaid Services (CMS), US prices will be linked to what countries with similar economic conditions pay for drugs by creating an International Price Index (IPI) Model (10).

July 2020
President Trump announced four executive orders to reduce drug prices: passing discounts obtained by health centers from drug companies on epinephrine and insulin to people with low incomes, allowing for safe importation of certain drugs by states, prohibiting deals between pharmacy benefit managers and drug manufacturers, and ensuring the US pays the lowest price for Medicare Part B drugs compared with other developed nations.

September 2020
President Trump signed an executive order to expand the drugs covered by the proposed "most favored nations" pricing scheme to include both Medicare parts B and D so that Medicare would refuse to pay more for drugs than the lower prices paid by other developed nations.

For sources and further elaboration, see: https://themedicinemaker.com/business-regulation/pharma-in-the-firing-line

Obamacare in the balance

Thus far, we've paid very little attention to the man who is, at the time of writing, leading the national presidential polls: former Vice President Joe Biden. He too has promised to put a stop to "runaway drug prices" and the "profiteering of the drug industry." In fact, Biden advocates two policies that Trump touted four years ago: allowing people to buy prescription drugs from other countries and repealing laws that prevent Medicare from negotiating lower drug prices with drug companies. "These are both good measures to lower prices," says Baker. "If he gets in, the extent to which he follows through will depend on the political pressure from both sides."

The major differences between the two candidates may, therefore, be found not in their approach to reducing the cost of prescription drugs, but rather in their views on healthcare – specifically the Affordable Care Act. "If Biden wins, the ACA will be the foundational building block of an improved healthcare delivery system – one that retains cover for pre-existing conditions," says Sillup. "If it's Trump, then he'll try to dismantle it. But, as with his first term, he'll need an alternative before he does that."

Baker agrees: "The Trump administration has done everything it could to sabotage the ACA. That would surely continue if he were re-elected." Baker points to Biden's promise to make the subsidies more generous, which he expects him to follow through with. But he's most excited about his proposal to

"The major differences between the two candidates may, therefore, be found not in their approach to reducing the cost of prescription drugs, but rather in their views on healthcare."

lower the Medicare age to 60. "That would be huge, as the older pre-Medicare age population has the greatest need for health care," he says. "I don't know if he will be able to do five years at once, but even one or two years would be a huge foot in the door towards a universal Medicare program."

The Affordable Care Act also faces another existential threat. Following the recent death of Supreme Court Judge Ruth Bader Ginsburg, President Trump may appoint (with the approval of the Republican-controlled senate) a conservative justice before the election takes place. This might give the Supreme Court enough conservative votes to declare the Affordable Care Act unconstitutional – causing 20 million Americans to immediately lose health coverage. Nicholas Bagley, a law professor at the University of Michigan who specializes in health issues, tweeted, "Among other things, the Affordable Care Act now dangles from a thread" (14).

Lawyers have argued that the Republican-backed tax-cut law of December 2017 rendered the ACA unconstitutional by reducing the ACA's penalty for not having insurance to zero. This means if Biden were to win the election, he – along with a Democratic Congress – could in theory make the entire issue go away by reinstating the penalty for failure to have insurance (15).

For now, all we can say is that both candidates are advocating policies that would create a new pricing environment for pharma companies. And with regards to healthcare, the outcome of the election may be a crucial turning point: will America build upon the foundations of the ACA? And if not, then what?

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Pacesetting Leadership

Lessons Learned with Kiran Mazumdar-Shaw

As the founder of India's largest biopharma company, Biocon, Kiran Mazumdar-Shaw's influence is far-reaching – but her professional life has taken a few surprising turns. From launching a biotech company with two retired tractor mechanics as her first employees to creating a global brand, serendipitous events and an entrepreneurial spirit have guided her along an unusual career path. Here, she shares the experiences that have shaped her 40-year career – and the lessons she has learned along the way.

Career setbacks can fuel future success

I never intended to pursue a career in biopharma. As a trained brewmaster, I wanted to earn my stripes in my chosen industry, but the professional culture at the time held me back. Women weren't particularly visible in the sector and actively choosing to pursue a career in it was unusual. Though I had the credentials to make it, no one was willing to give me the chance to prove it.

Despite my disappointment, I sought out new opportunities. When a biochemical company in Ireland hired me as a trainee manager, I jumped at the chance to develop my knowledge in a new industry – and the experience inspired me to set up my own company at home in India. Using enzyme technology, I planned to develop products needed for alcohol production. My colleagues in Ireland supported the idea and we became business partners. But trying to create a brand-new service, product, or experience is an inherently risky process. I realized this when I first began looking for funding. Bankers would stare at me with blank expressions as I tried to explain the potential of enzyme technologies for the brewing sector. Unconvinced, they turned me away empty-handed. My lack of business experience and scant personal savings didn't help either…

The rejection was difficult to handle, but it didn't dent my determination. Without a loan, I had to scrape together the little money I had to set up my first office (which was conveniently located in my garage.) I also rented a shed to house the machinery I'd purchased, and Biocon was born. Now, I needed employees… But who would want to work for a 25-year-old with nothing but an idea to her name?

The only people brave enough to take on the challenge were two retired tractor mechanics who operated the machinery and helped get the ball rolling. To be viewed as a reputable business, though, I needed scientists and engineers who could take our operations to the next level. I made connections with academic institutions and found like-minded individuals who, excited by the prospect of this unconventional business, took the bold step to join us.

We quickly matured and began the daunting journey from lab to market. My partners in Ireland were willing to manufacture everything we developed in India so, within five years, we had developed a credible homegrown technology. Brewing companies were now approaching us to learn about our products. Knowing that my company was of value to the industry gave me a sense of satisfaction – even after my initial rejection, brewing was still an integral part of my professional life.

When we were ready to scale up our operations, I returned to the banks, hoping that Biocon's years of effort would inspire their generosity – but their skepticism remained. "We don't invest in homegrown technologies," they said. "If you want to license a technology, we can make the funds available, but loaning you money for your own technology is out of the question." This second round of rejections hit me hard. At the time, I hadn't considered any alternative forms of funding, and we couldn't reach our full potential without money.

But serendipity answered. Shortly after these disappointing encounters, I met a banker who had just started a venture fund. Our technology and ethos appealed to him and he became our first-ever investor. At the same time, Unilever acquired our Irish partners' business and went on to teach me a lot about intellectual property and what it takes to be a player on the global stage. With this newfound support, I started thinking strategically about where I wanted Biocon to go next. It occurred to me that we could expand our horizons – so we spent the next 20 years developing and diversifying our enzyme technologies to serve a range of industries before ultimately ending up in biopharma.

"We spent the next 20 years developing and diversifying our enzyme technologies to serve a range of industries before ultimately ending up in biopharma."

Address the problems that matter

I've always been socially conscious and, as a young entrepreneur, it concerned me that many of the environmental issues affecting our society were being ignored. But I realized that our growing company could be a platform for change. Our portfolio was expanding and many of our clients belonged to industries notorious for their polluting protocols. Some used acid hydrolysis to convert complex carbohydrates down to simple sugars – an efficient process, but one whose long-term consequences received little consideration.

My colleagues and I became strong advocates for enzyme hydrolysis as an alternative. By this stage, Biocon had gained enough credibility to bring difficult conversations to the table, and we were determined to make sustainable practices part of our clients' culture. Some were hesitant – enzymes were much more expensive than the chemicals they were accustomed to – but they were willing to give the idea a chance. The long-term cost savings from using environment-friendly enzyme technology convinced them to make the switch. Over the years, many of these companies have put eco-friendly practices at the heart of their social responsibility strategies. But the work is never finished; we continue to bring attention to ecological issues and explore ways to help. As a company that has worked on cleaner and greener biotechnologies based on enzymes, we have taken a novel approach to revive some of Bangalore's polluted lakes. We have implemented a three-step bioremediation process using technology which is unique and cost effective in comparison to conventional draining and cleaning processes and have succeeded in restoring the ecosystem of the dying 35-acre Hebbagodi Lake, located in the outskirts of Bengaluru. This project has won several awards including a place in the Limca Book of Records for introducing the largest artificial floating wetlands in India. Having successfully revived the dying Hebbagodi lake, we are leveraging the experience to rejuvenate the polluted Yarandahalli lake.

Our move into the biopharmaceutical sector put a new perspective on the problem. India is the diabetes capital of the world and, at the time, most patients

Biocon Today

Biocon may have initially started out in a garage, but today it's a very different story. Biocon employs over 12000 employees and brings in annual revenues over US$870 million. The company's portfolio includes small molecules, novel biologics, and biosimilars. Biocon was the first Indian company to have a biosimilar approved in the USA and in Japan, and is one of the largest producers in the world of statin and immunosuppressant APIs. It is considered to have the largest biomanufacturing capacity in all of India.

Biocon has repurposed its "first-in-class," humanized IgG1 monoclonal antibody Itolizumab that selectively targets CD6 cells, to help treat acute respiratory distress syndrome (ARDS) in COVID-19 patients. The Indian health regulator has approved this novel biologic therapy for restricted emergency use in India to treat moderate to severe ARDS patients hospitalized with COVID-19.

Over the years, the company has won numerous awards. Achievements in 2019 included:

- Biocon was ranked 6th on the prestigious Global Biotech Employers rankings 2019 by US-based Science Careers magazine
- Best Biotech Patents Award 2018-19 from the Indian Drug Manufacturing Association's 58th Annual Day celebration
- Awards in four categories, Women L&D Programs, Diversity Policies, Large Enterprise and Diversity Programs, for the Bowin HR team
- State Level Award in Implementation of Best Safety Practices from the Department of Factories, Government of Karnataka
- Annual Greentech Environment Award for Outstanding Achievements in Environment Management in the Pharmaceutical Sector for the Hyderabad API facility

Kiran Mazumdar-Shaw has also received many personal awards and honors. She recently won the EY World Entrepreneur of the Year Award 2020. She was conferred with the Order of Australia, Australia's highest civilian honor in 2020 and recognized with the Knight of the National Order of the French Legion of Honour, France's highest civilian honor, in 2016. For her outstanding contributions to the progress of science and technology, she got the AWSM Award for Excellence in 2017, the Othmer Gold Medal in 2014 and the Global Economy Prize for Business the same year. She has been conferred with the Honorary Doctorate by Deakin University, a leading Global University based in Victoria, Australia, and was elected as a member of the US National Academy of Engineering for her contributions in the development of affordable biopharmaceuticals and India's biotechnology industry. She is also a full-term member of the MIT Corporation, the board of trustees of the MIT. The Indian government has recognized her achievements through two of its top civilian awards, the Padma Shri and the Padma Bhushan.

used disposable pens to administer insulin. Though convenient, their daily use generated significant amounts of medical waste. We decided to introduce reusable pen technology to the Indian market – not only addressing the environmental problem, but also giving patients across the country access to affordable recombinant human insulin.

Prior to our transition into biopharma, many diabetic patients relied on highly immunogenic animal-derived insulin because they couldn't afford alternatives. I've always believed in the importance of medical access, particularly in the developing world. Biocon has become synonymous with the development of treatments for these areas of unmet need because of our desire to level the playing field. Although widespread poverty is a reality, it shouldn't dictate a person's quality of healthcare. As long as income-based inequality exists, my colleagues and I will fight for change.

Be ready to find inspiration in unexpected places

By the early 1990s, India's pharmaceutical sector was booming. Where previously only a handful of homegrown companies had existed, many had now cemented themselves in the pharmaceutical landscape. It was encouraging to witness pharma's rapid growth, but I found inspiration elsewhere...

The world's eyes were on India in the 1990s because of its IT capabilities. The efficiency of the country's software services attracted an international client base. And that pushed me to investigate their development model and create a platform specifically for pharma. My many years in the industry had taught me the need to accelerate early-stage research and I believed that a research support service would help. I launched Syngene in 1993 and, since then, it has grown from strength to strength, supporting many R&D programs from start to fruition.

Biocon commenced its pharma journey in 1999 by leveraging its capabilities in fermentation technologies derived from its long experience in manufacturing enzymes; this was unlike other companies in India which were largely focused on generics made by chemical synthesis. Furthermore, we were amongst the early movers in developing a portfolio of fermentation-derived statins which gave us a leadership position in this segment. We simultaneously chose to expand our strategic options from small molecules like statins to recombinant proteins like insulin to address the growing healthcare challenges associated with diabetes.

Our product portfolio was not limited to generics or biosimilars; we sought opportunities to address unmet needs in these therapeutic segments through novel biologics and novel targets. These were marked by high entry barriers wherein we were required to make significant investments in a full range of

"My many years in the industry had taught me the need to accelerate early-stage research and I believed that a research support service would help."

R&D capabilities, spanning process and analytical development to pre-clinical and clinical research.

These investments have helped Biocon in its journey of building the science, scale and expertise needed to enhance access to essential drugs for patients on the lowest rung of the economic ladder. Through its "Mission 10 cents," Biocon is today offering recombinant human Insulin at less than 10 US cents/day for direct procurement by governments in low- and middle-income countries, where millions of people cannot access insulin as it is unaffordable.

Biocon today has one of the largest global biosimilars portfolios spanning insulins, monoclonal antibodies and other recombinant proteins for diabetes, cancer, immunology and other therapeutic areas and is well positioned to offer lower costs and increased access to this highly innovative class of drugs.

Master the art of accepting advice

My late father was one of the most influential figures in my life. He believed that good leadership was built on giving people the freedom to discover their own capabilities. His thoughts on the subject have always resonated with me, and I've tried my best to apply them to my own companies – giving my employees the space to tackle issues using their own initiative. Though I was always there to guide them, I wanted my team to feel confident in their own decision-making skills. I'm as passionate about their continued growth, as I am about my own, and it's a privilege to watch them build the strength of character to make hard decisions when necessary.

Another important lesson my father taught me was to always give back. He always said, "Money is not a currency to buy favors, but a means to make a difference." As my companies grew, I became able to extend a hand where there is a need. From the arts to healthcare organizations to R&D, both at home and abroad, I seek out opportunities to help. One example that I'm proud to be involved with is the grassroots effort expanding access to primary care across India. Over the years, I have helped develop new healthcare centers nationwide and we now have an army of health workers ready to treat and support patients across the country.

But charity is not about the size of the donation given or personal gain; it's about the sincerity of the action and the attention that can be brought to a meaningful cause. I'm glad that my father instilled this idea in me because it has brought, and still brings, much purpose to my life.

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A Wealth of Experience

Sitting Down With… Richard M. Johnson,
President, and Chief Executive Officer,
Parenteral Drug Association

How has international experience shaped your career?

I've always been interested in travel. And throughout my career, I've had opportunities to pursue foreign assignments and learn from people with different cultural backgrounds. Their unique perspectives have helped enrich my own. In a previous role, I was lucky enough to be based in Switzerland for 18 months, where I worked on the development of an API site – a difficult task! In the early years of my career, the European Union didn't exist, so regulation across Europe was varied. The differences between the US regulatory environment and that of our Swiss partners meant that we had to explain our ideas on manufacturing to them without dictating what they should do. The experience forced me to develop better communication skills. I couldn't just regurgitate regulatory directives; I had to find ways of thoughtfully explaining the aspects that mattered.

In the years since, regulation across Europe has harmonized and there are very few notable differences between US and European pharmaceutical guidelines. However, in other regions of the world, there's still work to be done – and, through the Parenteral Drug Association (PDA), my colleagues and I are helping manufacturers understand the benefits of regulatory convergence, as well as the ways cGMP practices can improve their manufacturing capabilities. I've certainly found a great deal of satisfaction in these projects and they continue to affect my professional life.

What are the biggest changes you've witnessed?

When I went on my first international assignment, emails didn't exist. Neither did cell phones. To communicate with my colleagues abroad, I had to wait for their telexes to be sent through to the hotel where I was staying. Now, things are very different, and the world is connected in ways I never would have anticipated back then. This interconnectedness is mirrored in the way manufacturing has progressed over time. During my first working trip to Europe, companies had many manufacturing plants spread across different countries. Today, many companies have consolidated their production processes – often, though not always, through outsourcing.

Another major change is the rise of biologics. They dominate the pharmaceutical market today, whereas a decade ago, most blockbusters were small molecule solid dosage forms. This shift has had an impact on delivery systems, too. Autoinjectors, for example, have become commonplace. And I suspect that the current pandemic will spark new changes that will shake up the industry yet again.

What are the goals of PDA?

PDA is a not-for-profit organization. We are made up of individual members rather than companies. Though we all have different backgrounds, we are united by a common goal: the advancement of pharmaceutical and biopharmaceutical manufacturing. We, for example, started working on biologics in the 1980s – well before they became prevalent in wider pharmaceutical circles.

Our tagline is "Connecting People, Science, and Regulation." It is certainly a great descriptor of what we do – and one that predates even my membership! Our organization holds a variety of volunteer-led activities and develops consensus statements on manufacturing topics. Training our members is also important to us. We own a facility – a miniature manufacturing plant – where we host more than 150 classes each year, allowing our members and other industry professionals to gain hands-on experience. And, of course, we are heavily engaged in interaction with regulatory bodies around the world – and many of our members are, in fact, regulators. Importantly, everyone at PDA has an equal role to play. Our members are also consultants and critical suppliers to the industry. All voices help inform the way the organization operates.

What do you predict for pharma's future?

Cell and gene therapies are fast becoming an integral part of the pharmaceutical landscape. They aren't just treatments; they're cures! PDA holds several meetings each year where we invite people whose lives are directly affected by these products to share their stories. It's amazing to see first-hand how a lifetime of ill health can be transformed using a cell or gene therapy.

Although these advanced medicines are exciting, we must not forget the importance of other types of treatment. Take COVID-19 as an example; there is a pressing need for a vaccine for us all – but, for patients affected by the virus, other types of medicine are also necessary. Striking a balance between old and new treatments is crucial to the future success of the industry and its ability to manage emerging healthcare needs.

What advice would you give someone just starting out in the industry?

First, don't be afraid to try new things. It's easy to get stuck in a rut, but being open to new opportunities can remedy that. Some of the most exciting and memorable moments of my career have been shaped by unexpected offers to participate in experiences outside my comfort zone. Second, recognize that mistakes are ultimately learning opportunities. Missteps in the drug manufacturing process are obviously out of the question – but anyone with experience will tell you that those times when things don't go your way can be some of your best. Don't wallow in self-pity; pick yourself up and do better next time.

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