NOVEMBER 2021 # 81

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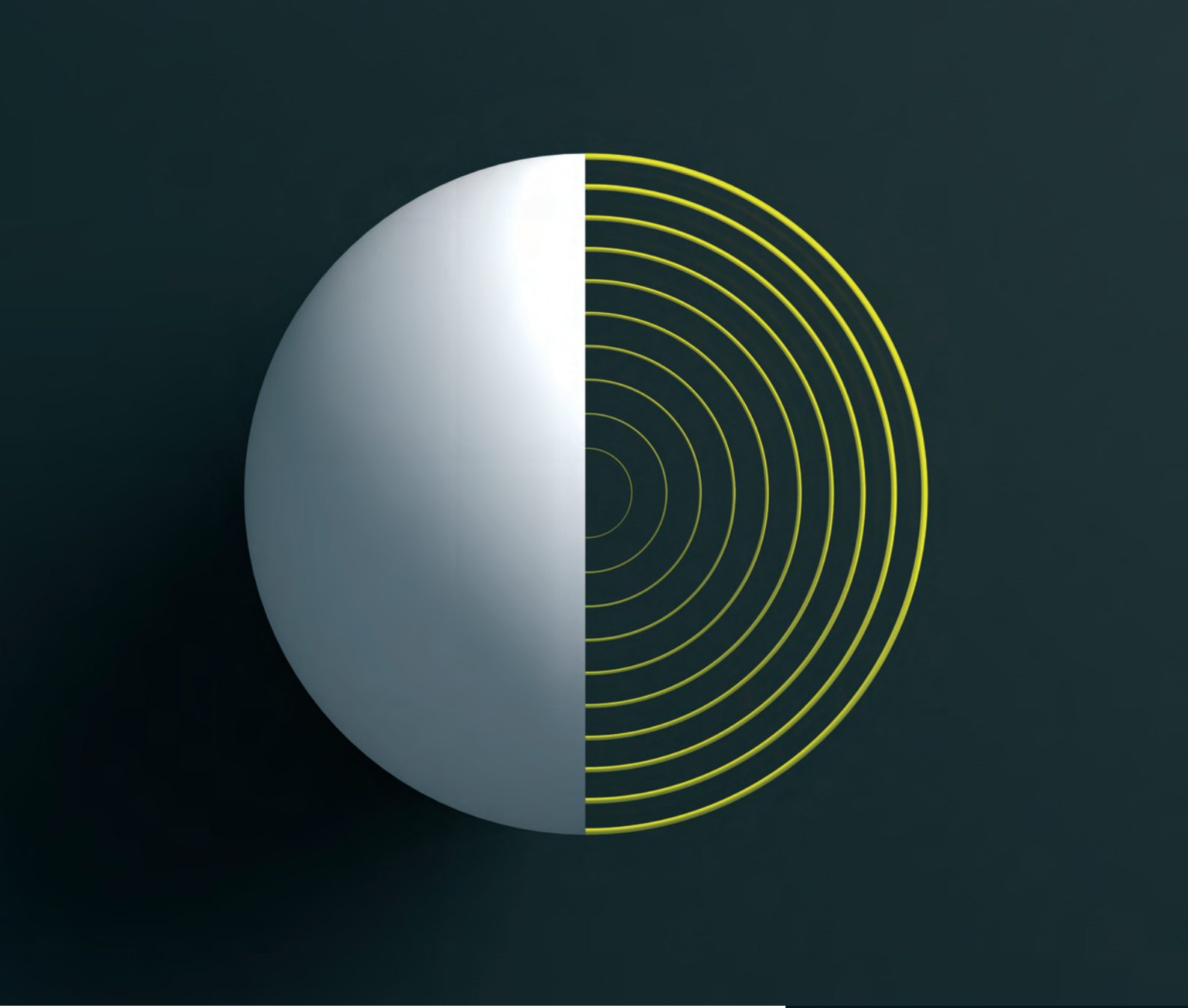

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A Warm Welcome to Biosimilars

The FDA has approved just three biosimilars in 2021 – but the approvals could shake up the field as discussions around interchangeability intensify

It's been a rocky road for biosimilars. The FDA approved its first biosimilar in March 2015. Six years on, only 30 other biosimilars have been approved. The FDA only approved three biosimilars in 2020, and 2021 looks to be another slow year with only three approvals at the time of writing – at least on the surface...

In reality, it could represent a big turning point. Two of the three biosimilars approved so far are "interchangeable" with their reference products, which could allow for automatic substitution at pharmacies.

In June, the FDA approved Mylan's Semglee (insulin glargine-yfgn) as the first interchangeable biosimilar insulin for Lantus (1). In a statement released at the time, Janet Woodcock from the FDA said, "Today's approval of the first interchangeable biosimilar product furthers FDA's longstanding commitment to support a competitive marketplace for biological products and ultimately empowers patients by helping to increase access to safe, effective, and high-quality medications at potentially lower cost."

In October, the FDA approved an interchangeable biosimilar to Humira (adalimumab): Boehringer Ingelheim's Cyltezo (2).

Other biosimilars to Humira have already been approved by the FDA, but the interchangeable designation will put Cyltezo in a strong market position. Notably, none of these Humira biosimilars will likely reach the market until 2023, as Humira is protected by patents until then.

The introduction of interchangeable biosimilars will certainly change the market in the US, but many hurdles are likely to lie ahead. Each US state has its own laws around interchangeable biosimilars, with many requiring the patient to be notified before any substitution occurs; it's possible that there could be pushback from patients but that will depend a great deal on the positioning.

Given that biosimilars can deliver significant cost savings to patients, every new one successfully approved deserves fanfare. The third biosimilar to be approved by the FDA in 2021 is Samsung Biopepis' Byooviz (ranibizumab-nuna) – a biosimilar to Lucentis (3). Welcome to the market, Byooviz and Semglee! And a (pending) welcome for Cyltezo and other Humira biosimilars for 2023.

Stephanie Sutton
Editor

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On The Cover

Is the (social) media the medicine? Pharma's channels in the chaotic 2020s.

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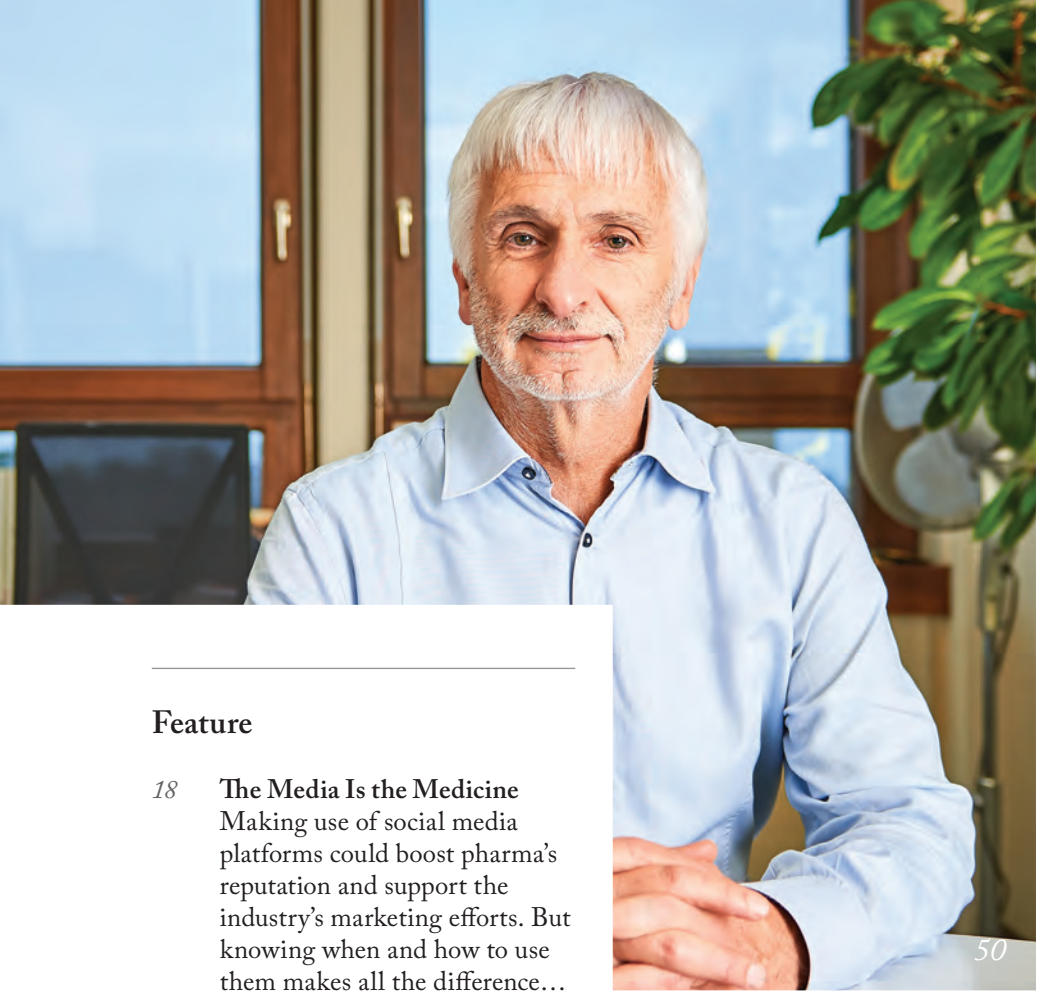
Upfront

In My View



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Painted Cells and Scrambled Jigsaws

A drug screening project reveals a welcome surprise: potential insight into the action of several agents interfering with SARS-CoV-2 assays

A team at the Max Planck Institute of Molecular Physiology, Dortmund, Germany, have found that many well-characterized active ingredients could affect cholesterol homeostasis – a feature that may prevent SARS-CoV-2 from infecting host cells (1) and explain the activity of those compounds.

Led by Herbert Waldmann, head of the department of Chemical Biology, and Slava Ziegler, a project leader at the institute, the researchers screened over 15,000 molecules and used an assay technique – cell painting – to profile and compare the molecules' activity in cells to that of previously identified active substances.

"In cell painting, upon treatment with small molecules, cells are simultaneously stained with six different dyes to detect their various compartments," Ziegler says. "The use of multiple dyes enables greater coverage of cellular phenotypes and activities within a single experiment and without necessitating genetic modification."

Following this assay, the team found that some molecules influenced the cholesterol balance within cells – changing patterns of cholesterol biosynthesis. "We realized that a huge number of characterized compounds with diverse targets had extremely similar morphological profiles," says Ziegler. "We simply could not leave those compounds alone and therefore set out to figure out what they had in common." The scientists now believe that this mechanism may explain why these types of compounds have been detected as hits in anti-SARS-CoV-2 screens of repurposing drug libraries.

Data increasingly suggest that SARS-CoV-2 relies on membrane cholesterol for entry into host cells, Ziegler explains. "The activity elicited by the active compounds we identified affects cells' ability to export cholesterol from lysosomes. The lower cholesterol levels, therefore, trigger the expression of cholesterol biosynthesis genes. These cellular changes influence a variety of processes that rely on proper lysosomal function or membrane cholesterol, such as autophagy and viral infection. Therefore, caution should be taken when drawing conclusions regarding these compounds, since their cellular activity may be related to their physicochemical properties rather than to a given target."

At present, the team in Dortmund is analyzing further bioactivity clusters containing compounds with highly diverse bioactivity annotations. Their work in this area is far from over, but Ziegler remains excited. "This means that we have more riddles to solve and more puzzle pieces to put together – and I am looking forward to this detective work!"

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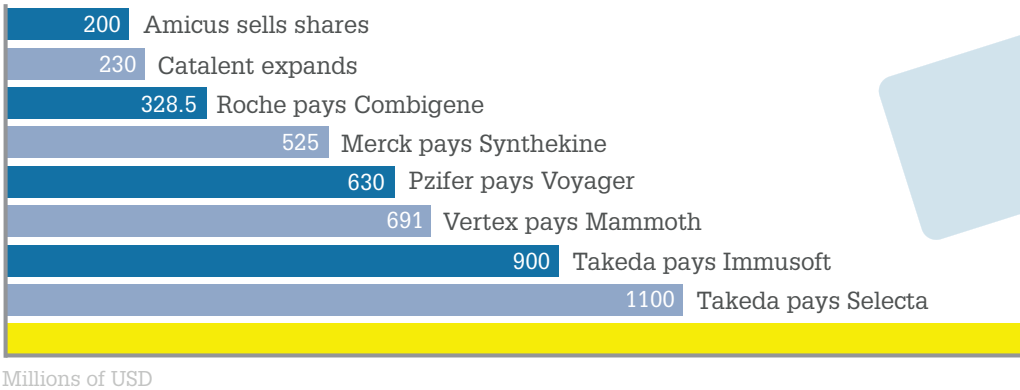
INFOGRAPHIC

Show Me the Money

Every month, a new wave of deals, acquisitions, and expansions washes over the advanced medicine field. Some figures are sizable, others… gargantuan




Credit: Chris Sampson /flickr.com

BUSINESS-IN-BRIEF

This month, we zoom in on what's going on in the world of advanced medicine

- With plans to target rare diseases by optimizing gene therapy, the Bespoke Gene Therapy Consortium launched this month. Consisting of 10 pharma companies, five nonprofits, the NIH, and the FDA, it aims to improve understanding of adeno-associated virus gene delivery vectors.
- Scientists from the Texas A&M University have created light-switchable "LiCAR-T" cells that, coupled with imaging-guided and surgically removable nanoplates, can be spatially and temporally controlled. Though there are precedents for blue light-operated CAR T cells, the team shifted the activation window towards the red end of the spectrum, substantially mitigating side effects, including cytokine release syndrome, in solid tumor and hematological cancers in mice.
- A study at the University of Southern California has demonstrated that it is possible to use gene editing to help geckos regenerate perfect copies of lost tails. Normally when a lizard loses its tail, it regrows a cartilage tube structure, which lacks the spinal column and nerves of a normal tail. Researchers were able to replace the lizards' adult neural stem cells with embryonic stem cells and improve regeneration of the lost appendage.
- A method to unravel the pathways involved in DNA repair during editing has been used to enhance the efficiency and accuracy of prime editing. Repair-seq, developed at Princeton University, allows researchers to generate mechanistic models of DNA repair – based on the contribution of various repair pathways – which can be used to optimize the system. The team plans to use repair-seq to improve additional editing technologies.
- Researchers from Purdue University and Jinan University have used gene therapy to turn glial cells into neurons, restoring visual function after stroke in a mouse model. Though visual responses were drastically reduced after the stroke, mice recovered following the NeuroD1 delivery to the visual cortex.

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Astra-Amplifiers

An industry partnership will put self-amplifying RNA to the test

AstraZeneca has struck a deal with VaxEquity to use the Imperial College London spinout biotech's self-amplifying RNA (saRNA) platform. The agreement marks AstraZeneca's first major RNA deal and will allow the company to work on the development of advanced therapies with greater potency levels than current mRNA therapeutics (1).

saRNA is known to support longer-lasting protein expression than conventional RNA. It also offers the opportunity for lower dosing and cost savings across a wide range of applications – significant advantages for both patients and companies.

As part of the agreement, AstraZeneca will develop up to 26 drug targets using the platform, and VaxEquity will receive up to US$195 million in milestone payments. "This collaboration adds a promising new platform to our drug discovery toolbox. Once optimized, the platform will allow us to target novel pathways not amenable to traditional drug discovery across our therapy areas of interest," said Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, at AstraZeneca.

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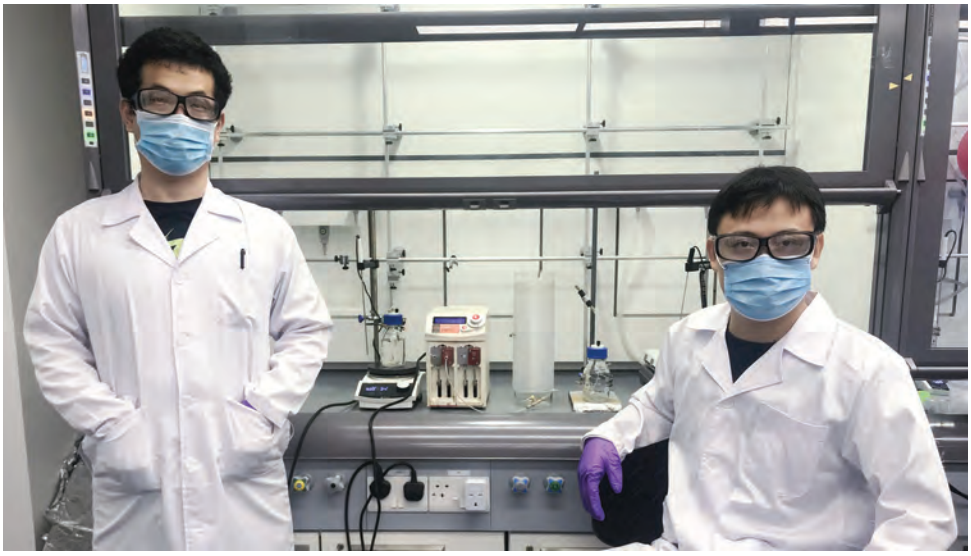

Continuous Synthesis

Solid-phase synthesis: an auto-magic medicine for the ills of continuous-flow processing?

Batch manufacturing is a far-from-perfect process and Associate Professor Wu Jie of the Department of Chemistry at the National University of Singapore knows it. Proving the power of continuous synthesis, he and his team have automated the production of pharmaceutical compounds, beginning with a demonstration of the production of prexersatib, a molecule used in cancer treatment. Their fix lies in merging solid-phase synthesis (SPS) and flow operation (1).

"In batch manufacturing, intermediates need to be isolated and purified before subsequent processing," he says. "This is inevitably accompanied by loss of products, waste generation, as well as cumbersome manual work." But SPS, he explains, allows for increased flexibility. It condenses several synthetic steps into a single uninterrupted process, avoids the purification and isolation of intermediates, and benefits from a range of processing advantages including mass/heat transfer, better reproducibility, and enhanced safety.

Wu says, "By applying the SPS-flow system into the auto-assembly of drug molecules, the target molecule grows on a solid support while all reagents and catalysts stay in the mobile phase. At the last step, the product is detached from the resin, followed by a single purification to afford the pure product. This strategy avoids the problem of reagent/solvent/byproduct incompatibility between synthetic steps and enables automation with longer synthetic steps and a much wider range of reaction conditions and reaction types."

But continuous flow isn't perfect either. Wu says that "fully end-to-end continuous-flow syntheses rarely exceed two steps before offline purification. To realize a fully multistep continuous-flow synthesis is challenging, mainly due to issues originating from solvent and reagent incompatibility, the accumulation of side-products, risk of clogging, and mismatch of time scales between steps in a consecutive processing chain."

Wu and his team remain optimistic. They are well aware that automated SPS-flow synthesis could have the potential to produce many important pharmaceutical molecules and have already begun tests aiming to scale up their platform.

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Backwards Vax Moves Forward

Can we use reverse vaccination to manage autoimmune diseases?

Researchers at the University of Buffalo, New York, have developed an unconventional vaccination approach to help manage the symptoms of chronic and autoimmune conditions (1). The technique, known as reverse vaccination, trains the immune system to ignore foreign substances rather than attack them.

Where traditional vaccination teaches the immune system to react to foreign invaders, the team's antidrug antibody approach builds immune tolerance in patients by pairing enzymes and essential proteins with Lyso-PS, a fatty acid that increases the immune system's tolerance of foreign substances. The researchers claim that this method can be used to train the body not to attack. The treatment shows promise in both intravenous and oral formats, which the team believes could boost patient compliance.

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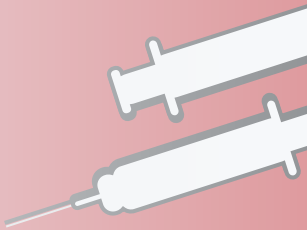
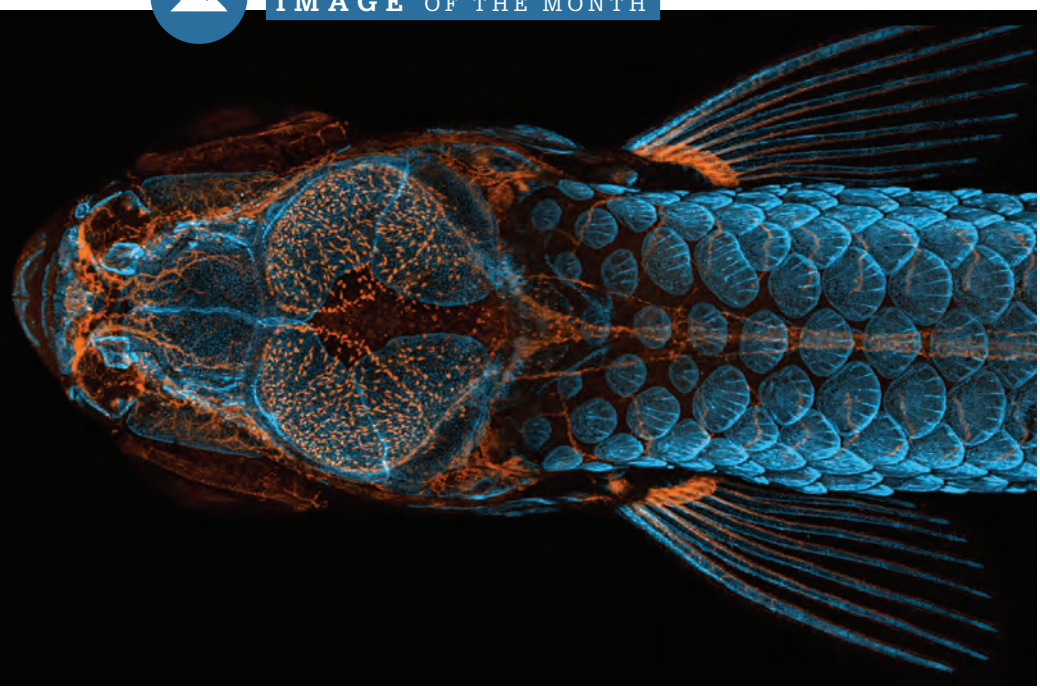


IMAGE OF THE MONTH



A to Zebrafish

An award-winning shot of one of pharma's favorite creatures, the zebrafish. Photographer and NIH researcher Daniel Castranova stitched this incredible piece together from 350 individual images captured through confocal microscopy. The species owes its special place in drug discovery to numerous valuable properties, including high fecundity, ease of drug administration, and structural similarity to mammals.

Credit: Daniel Castranova, NICHD/NIH/flickr.com

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QUOTE of the month

"It is unacceptable that access to the lifesaving HPV vaccine can be shaped by your race, ethnicity or where you happen to be born."

Nothemba (Nono) Simelela, Assistant Director-General for Strategic Priorities and Special Advisor to the Director General, speaking on the contemporary relevance of the story of Henrietta Lacks. https://bit.ly/HL-WHO

Paranoid or Prepared?

Wanting to win any battle, anywhere, the US military has commissioned a vaccine against the plague

Californian firm Dynavax has signed a US$22 million agreement with the US Department of Defence (DoD) to develop a plague vaccine (1). Dynavax will combine its CpG 1018 adjuvant with the DoD's rF1V vaccine in a Phase II trial that will begin in 2022.

A US military spokesperson emphasized the role of this planned vaccine in defending forces abroad rather than civilians at home, speaking of a "vision to deliver a full, layered medical countermeasure capability to enable a protected and unencumbered Joint Force to fight and win in any global CBRN (chemical, biological, radiological, and nuclear) battlespace."

Although no statement was issued regarding the source of such a challenge, it is true that both the USSR and US had active programs to weaponize plague during the cold war. The world's governments may have good reason not to rule out the possibility of an alternative arms race...

Reference

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In My View

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

The Time Is Now for Digitally Simplified Bioprocessing

Bringing digital tools and data analytics together will improve success rates in bioprocess operations

By John Moore, President, Scientific Bioprocessing, Pittsburgh, US

Real-time patient data and analytics are increasingly available thanks to wireless sensors, wearables, and online apps. For example, patients can now detect atrial fibrillation episodes using a personal mobile device that provides an FDA-cleared six-lead electrocardiogram. Why can't this type of advanced technology also be integrated into the biomanufacturing lifecycle – from lab and animal testing to patient trials – to improve success rates for new product development?

New biopharmaceutical product development success rates are extremely low – only 11.7 percent on average, 3.5 percent as a worst case, and 29.8 percent in the best case, with an estimated total cost of US$780 million for the average scenario (1). These costs balloon up to nearly $2.5 billion for the low success rate scenario – so even a modest increase in success can have a profound financial impact on manufacturers and patients.

Enter digitally simplified bioprocessing. Digital tools such as smart sensors that monitor critical process parameters including pH, dissolved oxygen, glucose, and critical quality attributes (such as impurities) generate large data sets that someone – often an entire team – needs to parse. Digital tools coupled with sophisticated machine learning platforms can trawl through that data, simplify bioprocessing, and provide manufacturers with actionable insights. In my view, digitally simplified bioprocessing is the key we need to unlock the black box of biomanufacturing, identify trends, and tie early culture data to patient outcomes.

Predictive analytics platforms could connect data and therapeutic outcomes across the biomanufacturing spectrum (including early-stage laboratory research, scaleup, animal testing, clinical trials, and post-market surveillance). These algorithms would recognize significant patterns and predict therapeutic safety and effectiveness. Algorithm prediction accuracies don't have to be perfect to move the success rate needle and accuracies would continuously improve as large data sets became available. Ultimately, we'd see higher new product development success rates, shorter times to market, and reduced costs. This is the power of digitally simplified bioprocessing.

Machine learning in bioprocessing is not a novel concept. However, current artificial intelligence applications are highly targeted and compartmentalized.

Successful applications include digital twins of sections of the bioprocess, development of virtual process control strategies, microbial strain engineering, protein engineering, cell imaging, particle monitoring, and early drug formulation, and screening. The adoption and implementation of artificial intelligence and machine learning remains low for several reasons: lack of internal expertise, inadequate data sets, data privacy and integrity, lack of automation, cost, and regulatory hurdles. But there are huge benefits to persevering and overcoming these hurdles. By combining data obtained via smart sensors from early research and development to preclinical results and patient outcomes, these algorithms can offer manufacturers actionable insights for decision-making and even ultimately automate decision-making through deep learning. Though the latter scenario may be further out on the horizon, the former is well within reach with today's technologies…

Biological therapies are here to stay – and manufacturing challenges are not going away. Digital tools coupled with powerful software platforms will empower scientists and engineers to bring better-quality products to patients faster and at lower costs.

Reference

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Eyeballing Advanced Medicine

Despite considerable progress, ocular gene therapy development remains challenging – but an emphasis on more efficient preclinical processes could streamline the route to market for these valuable therapies

By Sergio Lainez Vicente, Senior Manager Business Operations in the Cell & Gene Therapy/Large Molecule area, and Jaleel Shujath, Vice President of Marketing and Content, both at Absorption Systems, a Pharmaron company

Cell and gene therapies (CGTs) are among the most exciting therapeutic modalities pioneered in the last 30 years. They promise to treat a diverse range of intractable clinical indications and, when successful, deliver life-changing results. In 2017, Spark Therapeutics' Luxturna product for Leber congenital amaurosis – a single-use AAV-based therapy that corrects a mutation in the RPE65 gene – became the first gene therapy approved by the FDA. Since then, a growing number of ophthalmic gene therapies have been tested in clinical trials to treat conditions such as age-related macular degeneration, Stargardt disease (an inherited form of macular degeneration), and choroideremia (a rare form of retinal degeneration).

Ophthalmic gene therapies are becoming popular within the CGT area because the eye is an appealing target. It is an immune-privileged organ – thanks to the blood-ocular barrier – and involves compartmentalized anatomy that is easily accessible and can be examined in vivo by high-quality imaging techniques. The eye can be used to test gene delivery to a wide range of tissues, as it contains endothelium (cornea), epithelium (cornea, ciliary body, iris), muscle (ciliary body), and neuronal cells (retina) while the presence of the blood-retinal and blood-aqueous barriers concentrates vectors in the target area, allowing therapies to be delivered with minimal systemic exposure. The use of the contralateral eye as a control is also beneficial. Furthermore, significant progress in understanding the pathogenesis of eye disease has afforded scientists an expansive knowledge of genetic mutations that cause vision loss.

"Ophthalmic gene therapies are becoming popular within the CGT area because the eye is an appealing target."

However, before any ophthalmic gene therapy can receive regulatory approval, it must overcome several challenges. Despite growing interest,

it is predicted that only 30 to 60 gene therapies could be in active clinical use by 2030 (1). To successfully get more gene therapies to patients, it is essential to understand the hurdles so that we can implement solutions during the development process.

In truth, gene therapies are still an emerging therapeutic modality. As such, the gene therapy space lacks a foundation of approved products to leverage when developing new therapies. This means the regulatory framework is rapidly evolving, including the regulatory bodies' guidance on safe market routes for gene therapies. Drug developers must therefore ensure they are familiar with and carefully follow the most current guidelines to avoid unnecessary delays during the preclinical development stage. For regulators, ophthalmic gene therapies also present unique safety considerations because they commonly involve a single dose. Such considerations include not only the accurate determination of the dose injection for first-in-human evaluation but also the extrapolation of in vivo immunogenicity into humans. Another significant challenge arises from the fact that ophthalmic gene therapies typically target rare genetic disorders, with drug developers often facing scarce patient populations and the resultant risk of underpowered clinical trials. With this in mind, developers must demonstrate the effectiveness of candidates for market application early on in preclinical testing.

"The gene therapy space lacks a foundation of approved products to leverage when developing new therapies. This means the regulatory framework is rapidly evolving."

So, in light of the above, what must organizations consider when designing preclinical ophthalmic gene therapy programs? First, because ocular anatomy varies widely between species, choosing models of the right species and at the right developmental stage is critical. On top of this, the selected in vivo model must accurately mimic the pathophysiology of ocular diseases in humans. Here, the identification and development of new models (e.g., to model de novo mutations) can help to better predict the efficacy of candidates in clinical studies. Specialized models, such as genetically modified mice, immunodeficient animals, and disease-induced models can also improve target validation of candidates, and thus should be explored. Pre-screening these models for ophthalmic abnormalities prior to preclinical in vivo studies is essential, as this can help ensure reliable modeling of disease states while reducing experimental variability. Once models are selected and studies have begun, leveraging advanced imaging technologies can allow researchers to precisely identify structural changes in the eye and thus evaluate the efficacy and toxicity associated to the gene therapy product in greater depth.

Developers must also bridge the gap between rodent disease models and human-relevant species (for example, pigs) to predict potential safety concerns for humans more effectively. For ophthalmic therapies in particular, the use of non-human primates may be required, as they have true macula (a section of retina at the back of the eye) and fovea (an area of the retina that allows for visual acuity) and the most similar retinal physiology to humans.

Finally, for product approval, a validated in vitro potency assay needs to be developed – but all too often developers will consider this requirement far too late. To streamline your program, the development of this assay should start as soon as possible during preclinical testing, as not having a GMP-qualified in vitro potency assay during phase III clinical trials will incur significant delays and sizeable costs. With ophthalmic gene therapies, the choice between ocular and non-ocular derived cell lines for in vitro potency assays and analytical release testing should be carefully considered, as non-ocular derived cells (adherent and growing in monolayers) may be easier to go through GMP qualification and validation as compared to retinal-based cell lines growing in suspension.

With more rigorous and optimized preclinical testing comes more robust evidence for clinical utility, avoiding unnecessary delays in (and increasing the likelihood of) regulatory approval by generating comprehensive data packages before Investigational New Drug application. Ultimately, these developments can help bring more life-changing therapies to patients quickly and allow the innovation happening in the ocular gene therapy space to continue at pace.

Reference

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Driving Down Biosimilar COGS

To keep biosimilars costs as low as possible, take a good look at your purification and characterization processes

By Amanda Turner, Senior Product Manager, Custom Antibody Products, and Khaled Mriziq, Senior Global Marketing Manager, Process Chromatography, Protein Purification Group, both at Bio-Rad Laboratories, CA, USA

The expensive, specialist methodologies that underpin the development and manufacture of important biological medicines typically result in associated costs being passed to healthcare providers, insurers, or the patients themselves. Biosimilars, therefore, are welcome players in the market. As originator therapies reach patent expiry, biosimilars aim to deliver on the promise of greater affordability and wider access to biological therapies. However, the world of biosimilars is exceptionally competitive – with many biopharma manufacturers racing to become the first to leverage the opportunity of blockbuster exclusivity loss.

Although biosimilars must only demonstrate equivalence to the originator/reference product to gain regulatory approval, standards remain rigorous, and interchangeability with the reference product needs to be shown regarding molecular structure, biological activity and efficacy, safety, and immunogenicity. Purification and bioanalytical

"In our view, upfront planning and access to the most effective protein purification and bioanalytical tools are vital to reduce the risk of failure."

"Notably, the reliability and reproducibility of the data generated are contingent on the quality of the antibody reagents selected."

characterization processes can comprise more than half of the total development cost for a biosimilar (1). In our view, upfront planning and access to the most effective protein purification and bioanalytical tools are vital to reduce the risk of failure, maximize the chances of timely regulatory approval, and ensure long-term drug quality during large-scale manufacture – and beyond.

Purification and recovery methods must achieve high protein purity and yield – but by cost-effective means, as costs need to be kept as low as possible to compete effectively in the biosimilars market. Removal of impurities, including host cell protein, DNA, viral contaminants, protein aggregates, isoforms, and other species, should use high specificity chromatography technologies that are able to withstand elevated throughput rates and variable pH conditions. The traditionally favored Protein A resins provide excellent specificity but are an expensive option. Alternative high-capacity resins, on the other hand, can offer opportunities to lower expenditure while also optimizing purification processes (2–4); for example, ion exchange resins have demonstrated comparable results to Protein A-based processes regarding the efficient clearing of impurities with good binding capacity and stability – and without the limitations of flow rate or pH conditions (3). Mixed-mode chromatography resins are unique in their ability to combine varying forms of molecular interaction (for example, hydrophobic, ion exchange) via a single-support matrix, and can reduce the number of purification steps required in some cases (4). Integration of such technologies within existing pathways allows efficiencies to be made with minimal disruption to the development plan.

Purification optimized? Check.

Next, let's look at the comparative clinical studies needed to determine pharmacokinetic and immunogenicity profiles of the reference product and biosimilar. You'll need to develop sensitive and selective ligand binding assays using specialized antibody reagents. Notably, the reliability and reproducibility of the data generated are contingent on the quality of the antibody reagents selected, so securing high quality, reproducible antibodies early in the development lifecycle is beneficial.

When the biologic is a monoclonal antibody, anti-idiotypic antibody reagents are critical for bioanalytical assays comparing biosimilar and reference product functionality. In vitro antibody generation methods (for example, antibody phage display) can selectively produce reagents demonstrating high specificity for defined regions of the drug, allowing assays to be designed to detect free drug, total drug, or the drug-target complex. In vitro technology offers the benefit of antibody generation within three months, while traditional animal immunization methodologies can be slow (approximately six to nine months) and may not result in the desired level of specificity. Recombinant antibodies are sequence-defined from the outset and well characterized, permitting an indefinite supply of reproducible capture and detection reagents. Through antibody engineering, technologies can be incorporated that enable site-directed conjugation and fast assembly of antibodies in monovalent or bivalent Fab and full-length immunoglobulin formats (for example, SpyTag-SpyCatcher technology) (5). Such innovations enable tighter control of critical reagents and speed up the assay design and optimization process, resulting in more sensitive and robust assays.

As with all biological products made in cellular systems, small molecular changes may arise between biosimilar batches and alterations are introduced over time as the manufacturing system evolves. Reliable bioanalytical assays are vital in demonstrating that molecular modifications do not deleteriously affect drug efficacy or safety, and in ensuring the success of the drug – long after regulatory approval.

As an increasing number of biopharmaceutical developers seek to maximize the opportunity of biosimilar medicines, robust and accelerated approaches to bioprocessing and bioanalytical data generation are becoming increasingly important for success. In our view, those companies that embrace technologies to enhance the efficiency and quality of their methodologies are most likely to avoid regulatory setbacks – and thrive in this hugely competitive marketplace.

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ADCs: Still Room for Improvement!

Antibody drug conjugates are starting to transform cancer treatments, so let's maintain the momentum

By Antoine Attinger, Associate Director, Pharmacology & Screening at Debiopharm, Switzerland

In the early 1900s, German Nobel Prize scientist Paul Ehrlich proposed the concept of the "magic bullet." For me, antibody drug conjugates (ADCs) are about as magic as bullets get. And I believe ADCs have the potential to dramatically change cancer treatment. By combining monoclonal antibodies specific to antigens present on particular tumor cells with highly potent anti-cancer agents, we gain high lethality toward the targeted cancer cells while leaving healthy cells unharmed. Not magic, but scientific knowhow!

The US FDA approved its first anticancer ADC, Mylotarg, for CD33-positive acute myeloid leukaemia (AML) patients aged over 60 in 2000. And though there have only been 10 more approvals since then, more than 80 ADCs are in clinical trials today – ranging from phase I to phase III (1). And I am pleased to say we are in that list with promising phase II results for the treatment of B-cell malignancies. Our ADC specifically targets the CD37 antigen of the surface of B-cells to release a toxic DM1 payload (2). We hope to eventually offer an alternative therapeutic target for the treatment of diffuse large B-cell lymphoma (DLBCL), a type of non-Hodgkin lymphoma, and other B-cell malignancies. In addition to DLBCL, various forms of cancer including leukemia, ovarian, and breast cancer have been impacted by targeted therapy – and hopefully there will be much more to come for patients!

Targeted therapy through ADCs can be also used in conjunction with other therapies, provided side effects are minimal. Improved understanding of the mechanistic basis of ADC activity will enable the possibility of combining therapies with other agents, including immunotherapy, therefore enhancing the ability to undergo simultaneous treatments.

In my view, however, there is still room for improvement – both in terms of ensuring safety of the patient and the effectiveness of the treatment. Right now, intense research is tackling four main challenges ahead of ADC optimization. First, almost by definition, ADCs must be able to specifically identify a target that is highly expressed on tumor cells and minimally expressed on healthy cells and tissues – and that is not an easy task! Second, diffusion into the tumor mass can be difficult because of the inherent size of antibodies; smaller entities, such as antibody fragments, are being developed to improve tumor penetration. Third, the cytotoxin needs to be potent enough to have a sufficient cancer-killing effect when released into cancer cells. Fourth, the chemical linker that connects the antibody to the cytotoxin must be stable enough in the blood circulation to avoid systemic toxicity – while also being able to rapidly release the payload when the ADC is inside the cancer cells. This latter challenge is a particularly vibrant area of research, with new generations of linkers being continuously explored.

"ADCs must be able to specifically identify a target that is highly expressed on tumor cells and minimally expressed on healthy cells and tissues."

The progress we've witnessed so far should motivate further exploration into the potential benefit that ADC technologies can bring to cancer patients worldwide. I firmly believe that ADCs will continue to pave the way to meeting unmet needs in oncology – as long as we remain focused on those four challenges.

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Welcome to the Era of Smart Solid Dosages

On-dose authentication technology can help deter counterfeiters, while also helping patients better engage with their medicines

By Ali Rajabi-Siabhoomi and Gary Pond

Globalization and increased outsourcing activities have led to some very complex supply chains for pharma manufacturers – and that means an increased risk of counterfeiting and diversion, putting both brands and patients at risk. Today, many countries have implemented serialization requirements for secondary packaging to track and trace products throughout the supply chain, and many pharma companies also add additional security features, such as holograms and security inks to their packages to further deter counterfeiting. All these moves have huge benefits. But the industry needs to go even further.

One of the main channels for counterfeiting today is online illegal pharmacies – with hundreds of new outlets appearing online each month. These pharmacies have increased significantly during the COVID-19 pandemic – as today there is even more desire from consumers to shop online, with medicines being no exception. When searching for online pharmacies, it's common to find links to both legal and illegal pharmacies; more worryingly, it can be hard for patients to tell the difference. Random sampling by the FDA of 10,000 online pharmacies, found 97 percent of them to be operating either illegally or not following regulations. The World Health Organization reports the chances of a patient getting a counterfeit drug product online is over 50 percent.

At the same time, counterfeiters are becoming more adept at copying many aspects of a medicine, including the package, label, the foil induction seal, and even the appearance of the tablet itself. Moreover, counterfeit, and diverted medicines can also find their way into legitimate supply chains. In one recent example; Gilead warned of counterfeit versions of two of its top-selling HIV medicines in the USA. These drugs are expensive and considered specialty products; they are only distributed by a small number of authorized wholesalers in the USA, and the FDA requires them to be dispensed in their original packaging. You would expect that it would be highly difficult to counterfeit these medicines, but the counterfeiters used genuine Gilead bottles and added a counterfeit foil induction seal. The package looked genuine, and there wasn't an easy way for patients or people in the supply chain to quickly determine if the actual tablets were real.

Not only can counterfeit medicines potentially contain dangerous ingredients, but they often have no therapeutic effect. HIV is a life-threatening disease and a patient's viral load can quickly go out of control if they stop taking genuine medication. More and more, counterfeiters are targeting valuable medicines like this because of high demand from patients – and the high monetary rewards.

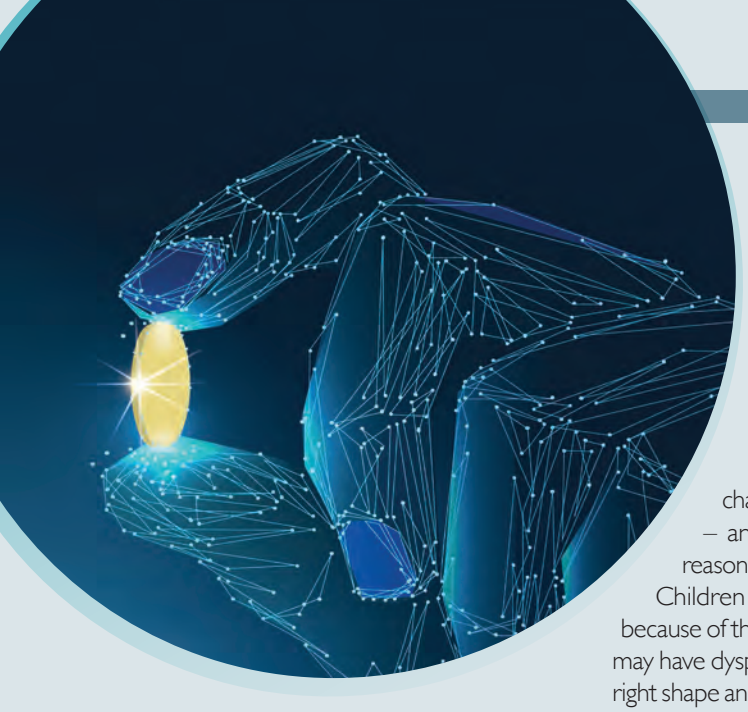
At Colorcon, we've been looking at ways to secure medicines at the individual dose level, so even if the original packaging is taken away, the actual tablet can still be authenticated.

For the patient

At Colorcon, our purpose is "To improve health and wellness through convenience, compliance and safety." We offer a range of pharmaceutical coatings, excipients, and formulation development assistance, including process guidance, for oral solid dosages. We don't work directly with patients, but our customers – the pharma companies – do! We feel it is our responsibility as a leader in solid oral dosage forms and coatings to innovate and bring solutions to the market that help pharma companies to protect patients. When thinking about innovations that can help prevent counterfeiting, we also realized that the same technologies could transform how patients engage with their medicines.

We believe there are opportunities to better secure medicines by targeting protection down to the dosage level. A film coating, such as Colorcon's Opadry® system, already provides many positive benefits including functionality and differentiation. Now, we can also add molecular and microtaggants to the coatings. Our portfolio of on-dose authentication solutions, SoteriaRx®, brings to market the advanced technologies from TruTag and Applied DNA Sciences. The taggants cannot be detected by the human eye, but the tablet can be scanned by an in-field reader to confirm the authenticity of individual tablets. The concealed signature of a taggant can contain information such as product, dosage, and manufacturing site. Think of it as adding an invisible barcode to individual tablets – and, as the technology is so unique, it's almost impossible to reverse engineer or copy.

Colorcon



But this technology doesn't just help deter counterfeiters; it can also be used to better engage with patients. Some pharma customers we are working with want to use the taggants in a very covert way (so only a small number of people within the company would know about the presence of the microtaggants), but others are interested in a more overt approach, including consumer participation, given that an increased number of people are buying medicines online. We're now working on options that allow companies to engage with their patients and confirm the authenticity of medicines using a smartphone. When a patient scans a tablet to check authenticity, companies can also provide access to support materials, such as the product leaflet, information that explains the benefits of the medicine, the importance of adherence, what to do if there are side effects, and even the ability to opt into reminders to take the medicine at the right time. In other words, such "smart" medicine not only brings authentication closer to the patient but also helps them feel more comfortable with how they take the medicine.

Non-adherence is a huge challenge for healthcare systems – and patients may have many reasons for not taking their medicine. Children often dislike the medicine because of the taste, while elderly patients may have dysphagia. Carefully selecting the right shape and size tablet is very important to ensure that as many patients as possible can take the medicine comfortably. For many adults, however, a significant cause of non-adherence is simply the patient mindset; if a patient has a negative experience or believes that the medicine will not work for them or may harm them, it becomes a very powerful motivator for non-adherence. Patients can also be influenced by news of counterfeit medicines, which can make them lose trust in the manufacturer, or even the pharmaceutical industry. The industry is very concerned about how counterfeits may impact brand integrity and corporate reputation – further harming more patients who may fail to take their medicine as a result.

Simply put, counterfeiting and product diversion have the potential to harm patients and brands everywhere.

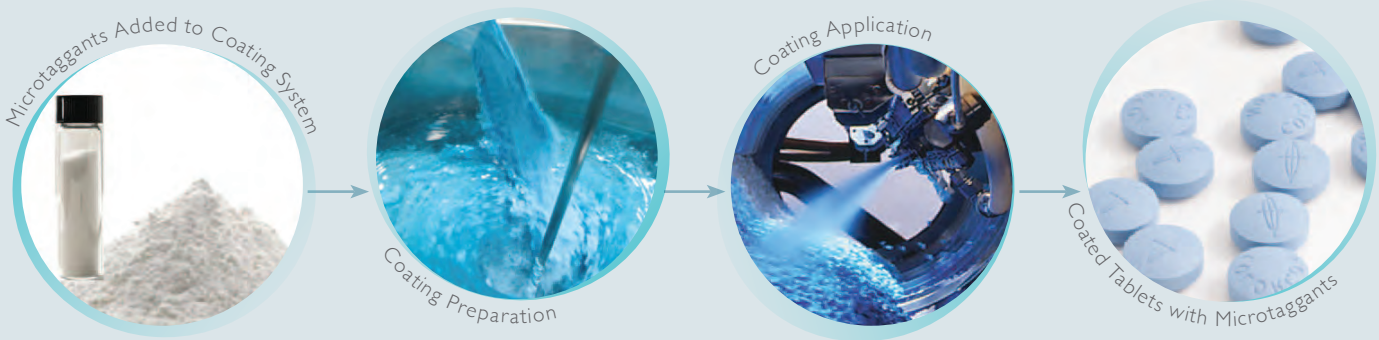
A smarter future

Smart medicine is an increasingly important topic for the pharma industry as companies look for ways to engage more with patients and encourage them to take their medicines as prescribed. Many factors contribute to making a medicine smart, including what goes into the packaging, what goes into the dosage form itself, and how the patient may engage with their medicine. All patients can benefit from greater information and support that ultimately improves safety and adherence. Wouldn't it be fantastic if they could get this directly from the tablet through an integrated smartphone?

We're very positive about the future of SoteriaRx®. Especially following the FDA's issuance of guidance on the use of physical-chemical identifiers (PCIDs) in solid oral dosage forms; in brief, PCIDs can be incorporated into already approved drugs as a Level I post-approval change. We've aligned our portfolio of authentication approaches with this guidance. We've also sought to ensure the transition to smart medicines is as smooth as possible for customers by demonstrating proof-of-concept with our coatings – and the manufacturing process is the same as for any film-coated tablet.

If you want to explore what smart medicine can do for you, then we're happy to discuss your requirements and provide implementation support.

Ali Rajabi-Siahboomi is Chief Innovation Officer and Gary Pond is Global Product Authentication Lead, both at Colorcon




the Media is the Medicine
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WE ARE NOW LIVING IN THE VIRAL WORLD SOCIAL MEDIA CREATED. WILL PHARMA BECOME FULLY ENGAGED OR DELETE ITS APPS?

By Angus Stewart

Take a guess at when the following words were penned:

"In the past, the effects of media were experienced more gradually, allowing the individual and society to absorb and cushion their impact to some degree. Today, in the electronic age of instantaneous communication, I believe that our survival, and at the very least our comfort and happiness, is predicated on understanding the nature of our new environment."

The answer: 1969 (1).

The author, Marshall McLuhan, also coined a phrase you've likely heard before (2):

"The medium is the message"

We could split hairs until 2069 on the exact meaning and implications of this aphorism, but instead let's take another of McLuhan's points seriously: we make the tools, then the tools make us (3). The strange and confusing world we live in today is to a great extent the product of the newest and most dominant form of communication: social media.

Pharma and social media are not new acquaintances. And in 2014, The Medicine Maker ran a feature on this same topic, looking at regulations, data mining, and the entry of an often-reluctant industry into the social media mire (4).

Since then, the world has turned on its head and new questions need to be asked. We've borne witness to the rise of fake news, and – in many countries – ever-widening socio-political polarization. How have these ruptures shifted pharma's relationship with (dis/mis)information? And how did our anxious digital existences under lockdown affect media marketing strategies to command our attention in the "Eyeball Economy?"

In the wake of a global crisis with an unforgettably online dimension, we now return to the topic of pharma and social media. Has pharma become more comfortable with social media? Which companies are merely "getting it right," and which are breaking new ground? Which medium carries pharma's message best – 240 character tweets and micro-clips, or marathon Youtube uploads and podcast episodes?

In this feature, we can't claim to have found all the answers. But we can present more than a few insights (and highly quotable hot takes) from media sages working in the industry today. You may not agree with every single word, but it's 2021 – who wants to be stuck in an echo chamber?

Read on and make the ghost of Marshall McLuhan proud!

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HYPERREALITY CHECK

Mike Rea of IDEA Pharma speaks frankly on the mud fights, echo chambers, and risks at play in the virtual forums of social media in 2021

"A point of view can be a dangerous luxury when substituted for insight and understanding." - *Marshall McLuhan*

Mike Rea is more than just the CEO of a leading positioning consultancy. He's the podcaster (and YouTuber) behind the show IDEA Collider, a critical thinker unafraid of speaking his mind (you'll see), and a Tweeter-par-excellence under the handle @ideapharma. Oh, and he runs a record label: Medical Records!

As Mike tells us in this excellent exchange, sometimes being right isn't enough. Sometimes you have to know what you don't know.

Do you think social media can help improve pharma's reputation amongst the general public?

Yes, but with a caveat.

If we wish to improve our reputation via social media, then we should do real, concrete things that improve our reputation. Goodwill on social media will then follow. Too often, I think we see the challenge as a species of ad campaign. We believe our reputation is undeserved, and that education will "fix" it. In fact, we might have exactly the reputation we deserve…

I'd love to see pharma genuinely see social media as a way to listen, as well as to talk – to engage beyond the traditional. If we see diversity and inclusion as issues to be addressed, it's reasonable to see social media as a place to do that. However, if pharma lazily resorts to investor-targeted communication, to bland campaigns dreamed up in NYC, or mimicry of entertainment brands, we risk missing the mark. If pharma doesn't engage, there are all kinds of other groups who will do it on our "behalf." Journalists, patients, and others will be talking about our companies and our products, and we won't be in control of it.

Why do some companies fail to embrace social media?

If your company is motivated to seal shut all openings for error, you'll have legal constraints to communication – there is no "perfect" in that kind of world because there is no good and "safe" communication.

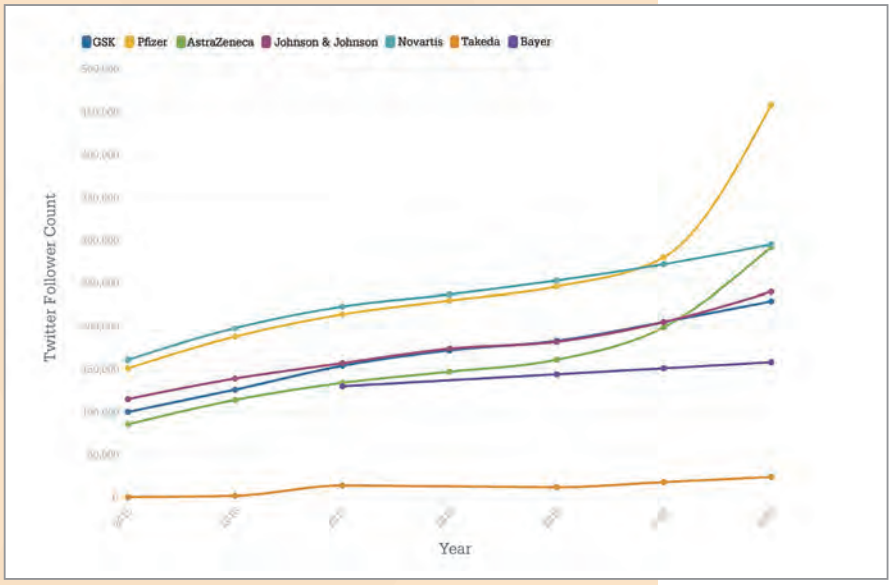
Good, authentic communication needs some vulnerability. It's always safer to say nothing, but that's not a great approach. Those who want to stand for something need to develop a more agile communications policy – to recognize that the world is not the one the senior executives grew up in, and that it is both an opportunity and a risk. If you treat communication solely as a risk, you'll mitigate that risk to the point of disengagement.

Vaccine misinformation is rife on social media. What do you make of what you have seen?

Lots of people get things wrong. But let's be clear – "lots of people" includes almost all of the "experts" who have wanted to seem "expert" throughout. In such a rapidly unfolding situation, it would have been more honest to accept the limits of our certainty. Going over that line has led to figures being proven wrong in a timeframe of mere weeks. Some of these people did admit their errors, but others doubled down.

It is alright to be skeptical, but skepticism exists on a spectrum that hinges on many factors, including your educational background, personal circumstances, and more. We see too much communication that assumes particular motives or lack of education, ignoring the reasons behind individuals'

"Communication is about being heard and understood, not just talking at people – and that's something pharma still needs to learn."



The Numbers Game

Since 2014, marketing has seen a shift in priorities for engagement on social media; quality is the watchword now, and quantity is less of a concern. Why pay Facebook for ad space, only to be scrolled past or "liked" with no further interactions? With this in mind, the numbers do still speak for themselves. Here's a cross-section of how some of pharma's biggest players have fared across time (in terms of follower-count) perched on the mighty bird's nest of Twitter. Pfizer and AstraZeneca saw a sharp increase in followers in 2020, for obvious reasons!

decisions. There are always gaps that exist between the truth and what people will believe, and into those gaps can flood misinformation or disinformation. Some people genuinely want to push falsehoods as truth, and those people often use the same tools and approach as the real experts: credentials, scientific-sounding language, a mass audience…

If we want to counter misinformation and disinformation, it would be helpful to recognize our own role. I'd actually suggest that some of our politicians are the worst offenders, when it comes to dangerous claims, for example, regarding the lack of efficacy of the AstraZeneca vaccine. Public figures who ought to be trustworthy but are too busy pursuing short-term politics have created huge hesitancy that we still see affecting uptake of a truly excellent vaccine. Would it be reasonable to say that Macron did more damage than all of the hydroxychloroquine advocates or 5G/microchip crazies? I think so…

The correct response is to stick to the fundamentals: the discipline of science, and the discipline of the communication of science. As soon as we get into arguments from authority or credentialism, we have lost. As soon as we get into mud fights, we have lost.

We need to stop using "the science" as our validation, because there is no such thing – it is messy and it is never "true." This is something any discipline recognizes.

We also need to accept the limits of our role. Our job is not to tell or to prescribe – politicians and physicians and people have agency. We need to respect their agency and work with it. We have delivered remarkable tools, but we ought not to overstep our role in responding. That classic xkcd web-cartoon "someone is wrong on the Internet" persists as a trope because this is a never-ending challenge. Let's stick to the method we've evolved for proving the value of our medicines, and accept the methods we have evolved for dealing with arguments against them.

How do you think the industry should capitalize on the increased attention around vaccines right now?

I think we need to be cautious. Though we've done something remarkable, only one of the companies has done it without profit. Imagine telling the story differently: "A company who had a vaccine become one of its biggest revenue generators in 2019 saw an opportunity to launch the biggest drug the industry has ever seen, and since then it has increased its prices within a year while also market-shaping towards annualized boosters."

If we try to overcook our own heroism in this tale, there are a lot of things that could take us down a peg or two. Instead we could look to be telling the stories of slow, steady innovation: "mRNA platforms built over a decade, whose value became clear in a crisis. Manufacturing and distribution platforms that were unsung heroes until now. The story of how the UK re-established itself as an ecosystem for learning…"

What lesson would you like readers to walk away with?

The simplest lesson: as soon as you think your corner of the Internet is "right" and that everyone else needs to be taught something, there is a risk. Communication is about being heard and understood, not just talking at people – and that's something pharma still needs to learn.

CAN SOCIAL MEDIA IMPROVE PHARMA'S REPUTATION?

Charlie Badham (Senior Manager, Corporate Development, 4D Pharma): "I think it absolutely can and should. Social media helps you reach a much broader, almost inherently less specialist audience. That's the real advantage: social media makes the information that we're conveying less exclusive. This should be – and is – reflected in the language we adopt. One of the quirks of social media is that it has a different tone to more formal communications, such as official clinical trials, press releases, scientific publications, or regulatory filings. It's more conversational, but also more accessible."

Lee Unroe (VP Marketing, Ori Biotech): "At Ori, what we are saying online is exactly what we're doing offline. We are focused on developing content that is educational, relevant, and transparent – all of which is key to building trust and reputation. We tie everything we do back to our mission: enabling widespread patient access to cell and gene therapies. It's an approach that we believe works to support trust in both Ori and the wider biopharmaceutical industry."

Neil Hunter (Life Science and Corporate Communications Director, Image Box): "Used in the right way, yes. The old British Telecom ad slogan was 'It's good to talk.' In international relations, bilateral communication is the first route to peace.

"Using social media to engage across the life science sector in a non-confrontational way – listening as well as posting – allows for the expression of challenges, which might not otherwise have been appreciated by different stakeholders. Solutions can be shared, and consortia formed to tackle those challenges."

Gareth Roberts (Campaigns and Marketing Manager, Orientation Marketing): "The bad reputation often comes from the idea of exploiting those suffering or in pain. This perspective comes directly from the consumers themselves. Pharma companies can – and increasingly, do – focus on raising awareness of the medical options available. And that helps those patients willing to research and seek information. Of course, varying global regulations mean that the solution is not quite as simple as I put it, but this mode of transparency is certainly something that B2B pharma organizations can aspire to."

Ahmed Samy Mokhtar (Director of Business Development, eureka!digital): "For sure. The public is not fully aware of the tedious phases of drug development, clinical trials, and protracted, costly research. Even after all this painstaking work, a pharmaceutical company might produce a drug that is effective, but unsafe. Or perhaps safe, but not effective enough! The pipeline is colossal, but most of it is buried underground for the general public. Social media is a great tool to educate people in a simplified, attractive way about this and other aspects of the pharmaceutical industry. Showing what happens behind the scenes – the story behind why a drug is effective and safe – can gain the audience's trust."

A FOUR DIMENSIONAL PERSPECTIVE

On a scale of "mates in the pub" to "SEC regulatory filing," where does your social media style sit? 4D Pharma tells us about their approach to social media.

By Charlie Badham, Senior Manager, Corporate Development, 4D Pharma

At 4D Pharma, we face the same communication challenges as the industry as a whole. The overarching mission here is conveying often complex, and sometimes jargon-heavy information, to less specialist audiences. And that's particularly important in our space – the microbiome field. Complex science underpins everything we do: drug candidates, particular programs, and even specific clinical trial readouts… it's a lot, and we have to convey it all to multiple audiences in accessible forms and appropriate language. Here, social media is an excellent tool for reaching each particular audience.

Balance and transparency are also critical. This is not a consumer goods industry – we are not salespeople. These are drugs for serious diseases. We have to present the good with the bad, even if the news is not ideal or completely favorable. In addition, you cannot oversimplify to the point of being potentially misleading. It's all about finding the right balance for each audience.

Balance also applies to tone, particularly on social media. You need a human element – the benefit of voice and personality that social media offers – but you can't be lax, because ultimately these are serious topics we are dealing with. At 4D Pharma, we try to present the key information without leaving our message buried in the weeds. If the spectrum of tone runs from "chatting to your mates in the pub" as a zero to an "SEC regulatory filing" as a 100, on social media we're sitting at about 45; pretty comfortable middle ground.

The companies that handle social media best are the ones that make use of different avenues and different media – in the right context – according to the needs of the situation. In my view, a balanced media presence is the most effective kind of presence – a 30 minute podcast interview can communicate things that a 240 character tweet cannot (and vice versa).

We try to make sure each channel complements the others. If we feature in a YouTube interview or longer article, we will almost always post it on Twitter, LinkedIn, and our website. Our communication channels work best when they all feed into each other.

The democratization of information enabled by the internet, and social media in particular, is a double-edged sword. On one hand it means that everyone can engage in the conversation, but fundamentally it means nobody is in control of the conversation. What you can do in your role is try and minimize any misleading takeaways or veering turns away from the core information.

The case of vaccine skepticism is a perfect example. Over the last year, we've all seen it burgeon online. If you listen to the experts, the message is quite clear. But now, "experts" come with inverted commas. This is hugely down to social media and the way information flows through it. People get into echo chambers, and they end up more entrenched in whatever their initial position was, rather than participating in the "free exchange of ideas" that everybody thought the Internet was going to usher in.

But these echo chambers have real and serious consequences. This is not a debate over sports teams or consumer goods. This is about people's wellbeing and lives. To overcome that skepticism we have to try really hard to share our message in digestible, understandable, accessible wording. As soon as you start hitting people with statistics and jargon, it can provoke an instinctive defensive reaction, and make your listener shut down in the face of that information. As an industry, we can do much better.

To win over skeptics, we have to break down that trench warfare. On social media, we've all seen that an "I'm right, you're wrong" zero sum game mindset gets us nowhere. If you can give a little bit of ground now, you can win back far more later. By understanding the underlying reasons for skepticism, you can facilitate a real conversation. Of course, that's easier said than done, but as an overall strategy, bringing people in works better than shaming, mocking, and excluding them.

The Channels of the Media Masters

"As technology advances, it reverses the characteristics of every situation again and again. The age of automation is going to be the age of 'do it yourself.'"
– Marshall McLuhan

It doesn't take a corporation to launch a platform on the Internet; many of the biggest pharma and healthcare YouTubers, podcasters, and influencers are a party of one. Here are some pharma channels to consider.

MOLECULE TO MARKET

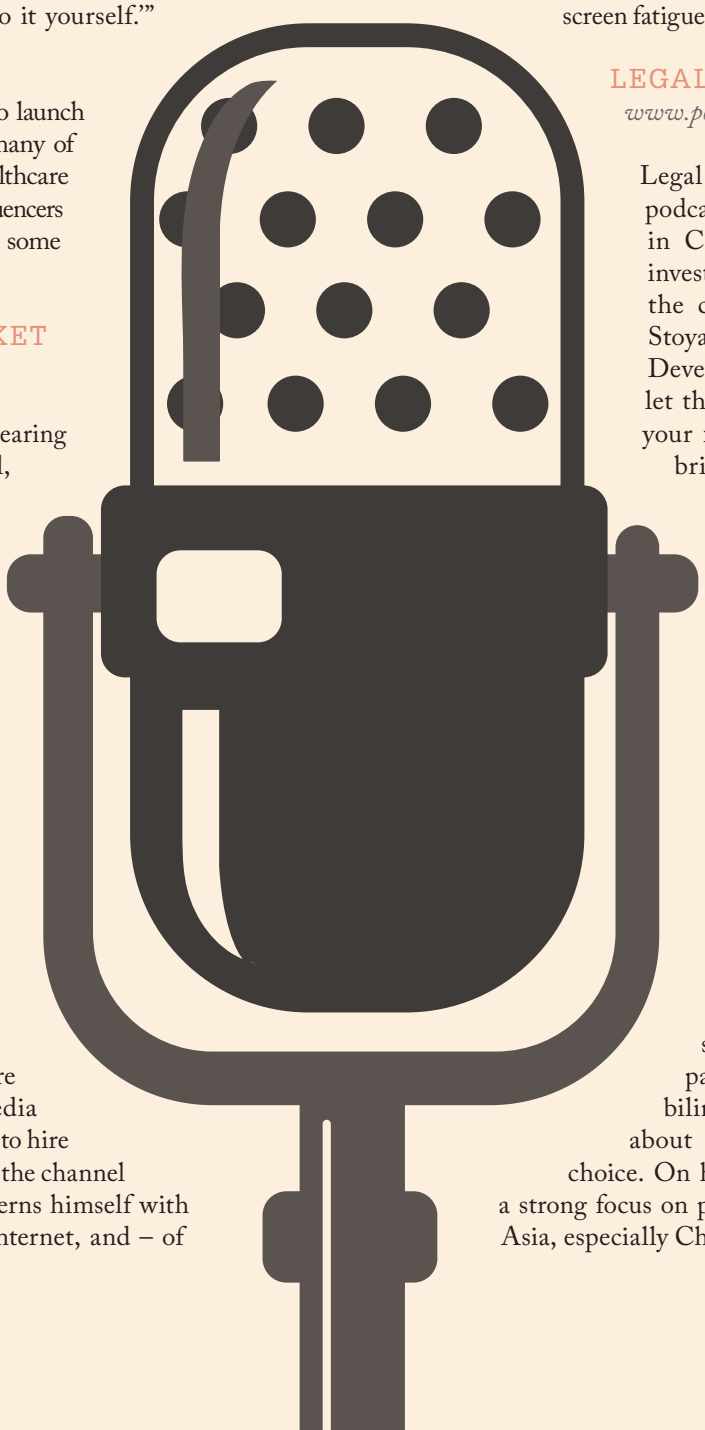
moleculetomarketpod.com

Run by one of the experts appearing in our feature, Raman Sehgal, this podcast focuses on the life science outsourcing space. In each episode, Sehgal chats with a leading professional in the field, covering the issues they face day-to-day as well as the challenges ahead.

THE MEDICAL FUTURIST

www.youtube.com/c/Medicalfuturist

A smoother operator than Bertalan Mesko can scarcely be imagined. On his homepage one is never more than a click away from media channels – and opportunities to hire him as a keynote speaker. As the channel name suggests, Mesko concerns himself with the cutting edge: AI, the Internet, and – of late – vaccines.



IDEA COLLIDER

podcast.ideapharma.com

Another dialogue-based podcast hosted by one of the stars of this feature? Yes and no.

Mike Rea's show doubles as both a podcast and a YouTube show – a great example of a complementary omnichannel approach. If you want to see Mike and his guest talk, go to YouTube. If you only want audio (this is an era of screen fatigue, after all), the podcast is for you.

LEGAL DRUGS

www.podpage.com/legal-drugs-podcast/

Legal Drugs is not, I can confirm, a podcast about bath salts or cannabis in California. Instead, the show investigates and unveils pharma for the consumer, hosted by Angela Stoyanovitch, Director of Business Development at BioAgilytix. Don't let the cheeky podcast name ruffle your feathers – she's not trying to bring down the industry, but she does cover topics such as acceleration, animal testing, and gene editing with neither fear nor favor.

ASIA HEALTHCARE PODCAST

anchor.fm/asiahealthcare

Traditional media has geographic limitations. Broadcasters operate within national boundaries, and low common denominators guarantee regular servings of the familiar. Online, international travel is – in a sense – free. You don't need a passport, hundreds of dollars, or bilingual abilities to learn a little about anything in your country of choice. On his show, Jonathan Chan puts a strong focus on pharma and healthcare in East Asia, especially China.

AD MEN OF THE ROUND TABLE

Four courageous marketer-knights weigh in on what it takes to tilt against the social media windmills of pharma's digital content kingdom

The same wise man who once said "the medium is the message" also said "the content of any medium is always another medium." Inside YouTube there is television and cinema, and inside Twitter is the poem and the telegraph pole. So, dear reader, please remember that inside this article hides a very old medium indeed: a conversation between friends.

Here, Raman Sehgal (Host of the Molecule to Market podcast and the Founder and Global President of ramarketing), Neil Hunter (Life Science and Corporate Communications Director of Image Box), Gareth Roberts and Gareth Pickering (Campaigns and Marketing Manager and Director and Co-Founder at Orientation Marketing, respectively) answer the questions of Angus Stewart.

When it comes to the pharma industry, what marketing specialisms are required?

Sehgal: My experience is from the B2B supply chain side of the pharma sector and, from this perspective, companies need to be where their relevant stakeholders (prospects, clients, potential employees) are looking and spending time. Typically, most companies need a solid digital presence that is also supported by more traditional techniques.

Hunter: Companies need to work out who they want to communicate with, the form of this communication, and then the medium it will use. Most of our biotech clients want to communicate with a wide spectrum of stakeholders from industry, government, and the public. Traditionally, most of these communications have been one-way, but social media provides partial opportunities to engage in two-way conversations with a wider stakeholder group. I say "partial" because some of the pharma industry still needs to wake up to the fact that social media offers the opportunity for dialogue and an interchange of ideas…

The specialism really required is to understand all of the different media available, and to understand and appreciate the best communication format to engage with each group of stakeholders. Corporate and business social media, after taking off, really became over-popular. Many companies and communication agencies moved onto social media entirely and dropped all other media. I consider this a mistake. Social media has proven itself to be a useful weapon in the communicator's arsenal – but it's not the only one.

Pickering: As the post-COVID-19 world moves to more digital initiatives, the pharmaceutical marketer needs to be aware of as many ways as possible of getting the right content in front of the right audience. Some of the traditional digital marketing solutions (webinars, for instance) are experiencing fatigue, as many more companies look to them. It would be wise to consider specific lead generation programs or pay-per-lead initiatives. Exploring the wider options of an account-based marketing approach is also advisable. The companies looking at this will be well ahead of the curve.

Is it true that pharma and social media have a rocky history?

Sehgal: This is certainly less true for the B2B supply chain side of the pharma sector. Adoption of social media channels in this space has been much slower, mainly because most buyers would not have been typically looking for technical services to solve a drug development issue on social media. However, things have changed. Social media usage is common among all age groups, and younger, more digitally savvy buyers are now in charge of sourcing and purchasing decisions. As such, social media channels (especially LinkedIn) play a critical role in raising awareness and generating interest in a company's capabilities. The platforms are also used as social proof. For example, when a buyer is kicking the tyres and looking at various vendors, how a company comes across online can play a vital role. The buyer might be thinking: "I like the look of these guys – I could see us working with them."

Hunter: In the life science industry, big pharma is top of the food chain. As is traditional with those at the top, they end up disassociated from everyone else. Executives surrounded by internal and external "yes" people naturally got used to their bubbles, and were not aware of the reality of how they were actually perceived. There would have been some interesting meetings when social media was first introduced to big pharma. The two-way communication platforms – with the options for anonymity that they enable – would have produced some

significant shocks! Adding in the public, patients, and other stakeholder groups, there is a significant recipe for problems for those who are unaware of how the organization is really perceived. In this situation, execs tend to retreat entirely and refuse to engage. In many organizations, I suspect it would have taken time for the players involved to reach an equilibrium.

Roberts: I guess there has always been a lack of social media activity in pharma, when compared with other industries. Big pharma has always had to tread with caution due to regulations, disclosure, and potential PR nightmares where organizations can lose control of the content and the message. But there is no doubt that social media platforms are used by people that are interested in purchasing products and services, and the two-way conversation that this often produces can be hugely beneficial for those organizations.

Should pharma still be plugging physical or digital media into their social media?

Sehgal: Given I am the host of a podcast called Molecule to Market, I'm probably a little biased!

I absolutely think there is a role for longer, more innovative platforms of content, even in a very technical sector like drug development. People like to know what is going on in their space – to know the latest trends, interesting personalities and so on. The squeeze on travel budgets (not to mention the pandemic) means people need to get their fix of industry insight in other ways. Perusing podcasts, videos, and longer-form content is an effective way to do this.

Although pure posting has a role, it's certainly not king. Every post should have a reason behind it – for example, to educate, inform, or promote.

Hunter: While a picture is worth a thousand words, video and audio input is worth even more. Complex messages can now be explained more clearly with longer-form social media. However, this should be used sparingly. The pandemic has meant that meetings, conferences, roundtables, and almost all business human interactions have been pushed onto screens. All professionals – whatever the industry or sector – are also humans, and we are all suffering from screen fatigue.

As a result, longer-form digital media should be used only where essential. Where messages can be communicated to the market via video, this needs to be done in short and simple bursts, rather than longer explanations.

Pickering: Yes, absolutely. The audience who follow and engage with you are very open to digital media and will watch, listen, read, and absorb anything you have. Keep it short, and be conscious that everyone has time pressures... but remember that in our industry, content really is king... So, yes, absolutely – plug away!

Are there times when it's better to simply not engage on social media?

Sehgal: There are certainly times when you should not engage. Some people use social media (especially Twitter) to vent and just articulate their opinions. When it's unfounded criticism or offensive, it's sometimes best to let sleeping dogs lie. Responding can fuel the fire.

Hunter: Despite all the options that social media offers, there are times when it is not worth engaging. Social media is an anonymous communication media, with minimal repercussions for unidentified transgressors.

Consider that only seven percent of communication is through the words we use; communication by text severs the other 93 percent, so misunderstandings happen on social media all too frequently. And that leads to public arguments that no-one ever wins. Disputes are best solved by taking the conversation away from the public forum and engaging one-on-one, whether it be an investor, partner, patient, or another stakeholder.

Roberts: I don't believe that saying nothing during a crisis is an option. Simply ignoring something and hoping it will go away just isn't viable. Most of the time, the objective should be to open a dialogue serving brand awareness and promoting dialogue with your followers and audience – if there may be a real concern about engaging with a user/post, tread with caution and do so professionally, with empathy. Often – during a crisis for example – saying something may create a degree of negative feedback, but saying nothing at all will likely lead to even more negativity, followed by additional PR problems further down the road.

Do you have thoughts of your own on how pharma can do better online? Perhaps you have a great case study to relay, a gleaming pearl of wisdom, or a hilarious anecdote. Whatever it is, please feel free to send it in via the strangely persistent 20th century medium of email: angus.stewart@texerepublishing.com

COUNTERING THE COUNTERFACTUALS

By Ahmed Samy Mokhtar, Director of Business Development, eureka!digital

A couple of months ago, I received a video on WhatsApp, bundled with the words "forwarded many times." The video's title was "Pfizer CEO refuses to get COVID vaccine." In the video, an anchor asks Pfizer CEO Albert Bourla if he took the vaccine, and Bourla answers that he did not.

A quick search on Google brought me to coverage from the Associated Press that cleared up the matter; Bourla has already received both doses! (1)

As for the video, it was an interview dating back to December 2020 – when there was a limited supply of the vaccine, and when jabs were restricted to high-risk groups. The video stripped the context; Bourla had stated that, as a low-risk patient, he was still in the queue for the vaccine. And that's a good point, not a "negative" one.

How can disinformation like this be combated? First, there should have been an official clarification across all platforms. But that didn't take place; instead, Pfizer responded by email via the Associated Press. We can give Pfizer some credit, though: Bourla did use his own Twitter account to state the truth (2).

Some pharma companies have judged that the cons of engagement with the public outweigh the pros. I take a different view. Imagine there's a rumor afield concerning a medicine or a vaccine and that I'm an ordinary person seeking advice and clarification from the pharmaceutical company. Their social media channel – or even an @ on Twitter – may very well be my first port of call. If you're not on the playground, you lose the battle against whoever is already there – "naughty kids" who may ruin your reputation and disseminate more rumors.

Social media has disrupted traditional means of communication: TV, radio, print, and even websites. In social media, you receive feedback that can serve as key performance indicators, and queries you can respond positively to. But on the other hand, you might find yourself having to deal with challenges from the rumor mill and bad actors in the playground. And that's why pharma companies should be ready for all eventualities, with plans in place for potential crises.

I'll leave you with some handy DOs (and no DON'Ts!), based on my own experience:

DO: Have a strict reporting policy regarding patients' and healthcare practitioner feedback, including product technical complaints and pharmacovigilance.

DO: Analyze well before planning. Understand the online users' behavior, their favorite sources of information, the keywords they usually search, and which key insights might help in communication.

DO: Prepare a robust plan that includes...

- The platforms you will focus on.
- A content plan stating what to say and when, considering relevant main seasons, events, and special days or months, such as World Diabetes Day and Breast Cancer Day.

- Defining metrics and key performance indicators that will be used to measure the overall performance.
- A community management model that lists how to reply to people's comments and private messages. For instance, if someone asks a question, a company should react following a template of pre-agreed answers. If the question is not covered by the template, then protocol directs the query to a defined accountable person.
- A crisis management plan with solid steps including reassurance, investigations, and taking actions.

DO: Have a clear objective before going to social media. Some pharma companies go to social media only for the sake of spending an allocated budget – and that is not an objective!

> "If you're not on the playground, you lose the battle against whoever is already there – 'naughty kids' who may ruin your reputation and disseminate more rumors."

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WINNING CAMPAIGNS

"Once you see the boundaries of your environment, they are no longer the boundaries of your environment."- *Marshall McLuhan*

Sometimes "thinking outside the box" is a meaningless cliche. But in media – and online media especially – walls often prove little more than a mirage. When a pharma organization devotes thought, resources, and a little bandwidth to a problem, it can result in great achievements – and, sometimes, cultural touchstones – as the following examples demonstrate.

ABPI: NEVER SAY NEVER

www.valuingvaccines.org.uk

The COVID-19 pandemic led more than a few of us to try something new. The word "us" here covers housebound working adults, students and teachers, national governments of various levels of competency, and... the Association of the British Pharmaceutical Industry. To help combat vaccine skepticism, the Association launched a campaign named "Valuing Vaccines," which aimed to raise awareness, distribute information, and protect human lives at the local and global level.

ASTRAZENECA: INFANTS GRILL THE EXPERTS

https://bit.ly/3ET478S

"Adorable child asks friendly expert" is by no means a new YouTube video format, but as any thoughtful media theorist or competent biologist will tell you, recombination is mutation's equal as a dynamic force in any ecosystem. Though AstraZeneca's entry into this genre lacks a little spontaneity, the videos have racked up thousands – sometimes ten of thousands – of views, and that's no easy feat.

PFIZER: CATFISH AND TESTIMONY

www.pfizer.com/counterfeiting/counterfeitawarenesscampaign

In recent years, Pfizer has mounted media campaigns against counterfeit medicine in both the UK and the US. The American campaign deployed the hashtag #FakePillsKill in January 2021, paired with a rapid-cut video of three young people sharing testimonials of near-fatal encounters with counterfeit medicine. This followed an October 2019 Pfizer UK campaign that also targeted young people with a riff on hookup app culture underlining the dangers of being "catfished" by counterfeit medicine.

NOVARTIS - CAUSE UPON CAUSE

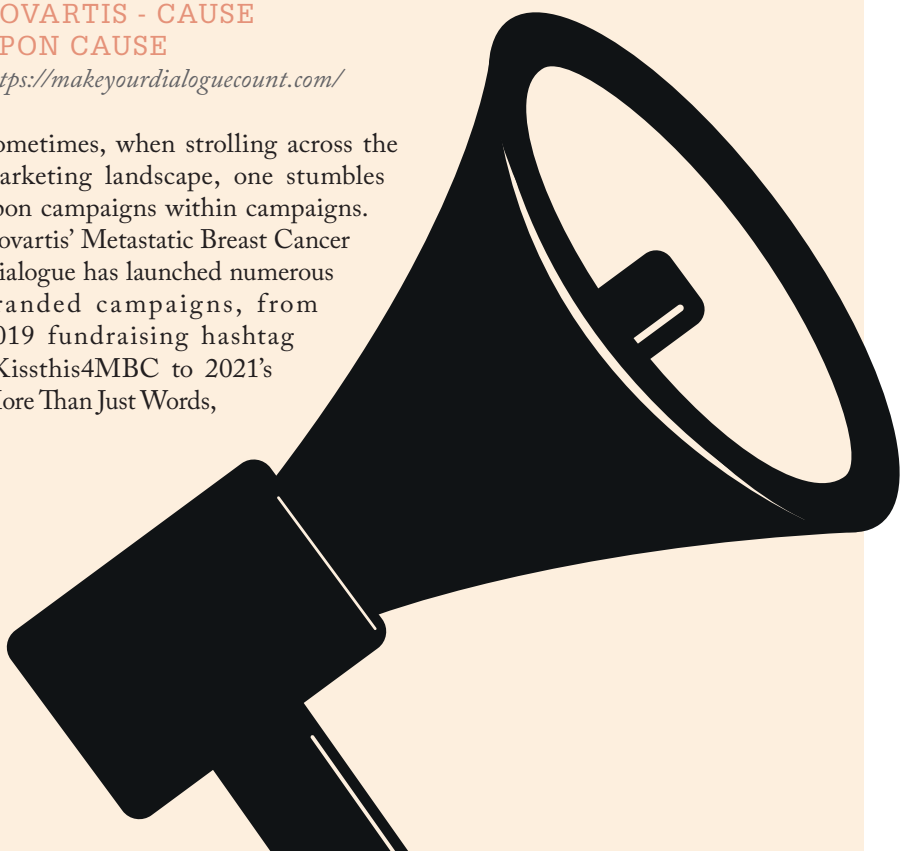
https://makeyourdialoguecount.com/

Sometimes, when strolling across the marketing landscape, one stumbles upon campaigns within campaigns. Novartis' Metastatic Breast Cancer Dialogue has launched numerous branded campaigns, from 2019 fundraising hashtag #Kissthis4MBC to 2021's More Than Just Words, a US-only initiative to improve breast cancer care for black communities. The overarching initiative – now named Make Your Dialogue Count – has a particularly strong Instagram presence, and visually-pleasing aesthetics to match.

SCHOTT – THE RECEPTIONIST WHO LOVES GLASS

https://youtu.be/w6cYgMAzitE

And finally, if you think there is no room for humor in the pharma industry, allow me to introduce The Receptionist. In this short film series by glass manufacturer SCHOTT, we follow our eponymous hero – a smiling but socially awkward mensch who tries and fails heroically at charming the international execs he runs into, throwing out ill-timed sales pitches and gesticulating wildly, with käsebrot clenched firmly in-hand.



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SoteriaRx® provides a level of authenticity, transparency and brand protection not previously available to the Pharma industry.

Protect
company reputation and brand integrity

Secure
product and improve patient safety

Smart
medicines to connect with your patients

Brands and patients at risk

The rise in counterfeit and diverted drugs is a major problem for the pharmaceutical industry. Added to this is the significant growth of illegal online pharmacies, exposing patients to even more counterfeit products.

The solution: Smart Medicines

SoteriaRx on-dose authentication provides the industry with a unique, covert, powerful solution. Medicines are made smart with on-dose taggants that can be authenticated at any stage of the supply chain.

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Responding to Changing Needs

When it comes to delivering biologic medicines to patients in need, choosing the right packaging partner can make all the difference

The pharmaceutical industry is never stagnant; advances happening at all stages of the drug development process mean that packaging suppliers must react quickly and provide high-quality packaging and devices to meet expectations. But what tools and resources are necessary for a rapid response? For PCI, the recently launched Center for Excellence in Biotech Packaging is an essential part of its customer service arsenal. Providing the scale and flexibility to cater to the individual requirements of a diverse array of companies across the industry, it is an example of true manufacturing productivity. Here, The Medicine Maker speaks with Alex Weaver, Director of Engineering at PCI Pharma Services, to discuss how the company is responding to the evolving needs of pharma companies and to dive deeper into the capabilities of its new flagship center.

How have industry trends changed customer requirements?

The pharmaceutical industry is increasingly becoming a biotech-centric sector, with companies developing more biologic products than ever before. With this shift toward biopharmaceuticals, companies are also more closely considering cold chain requirements and the time out of refrigeration when developing new product lines. There is also the trend for patients to administer medicines at home, leading to greater demand for patient-centric drug delivery devices, such as auto-injectors and pre-filled syringes.

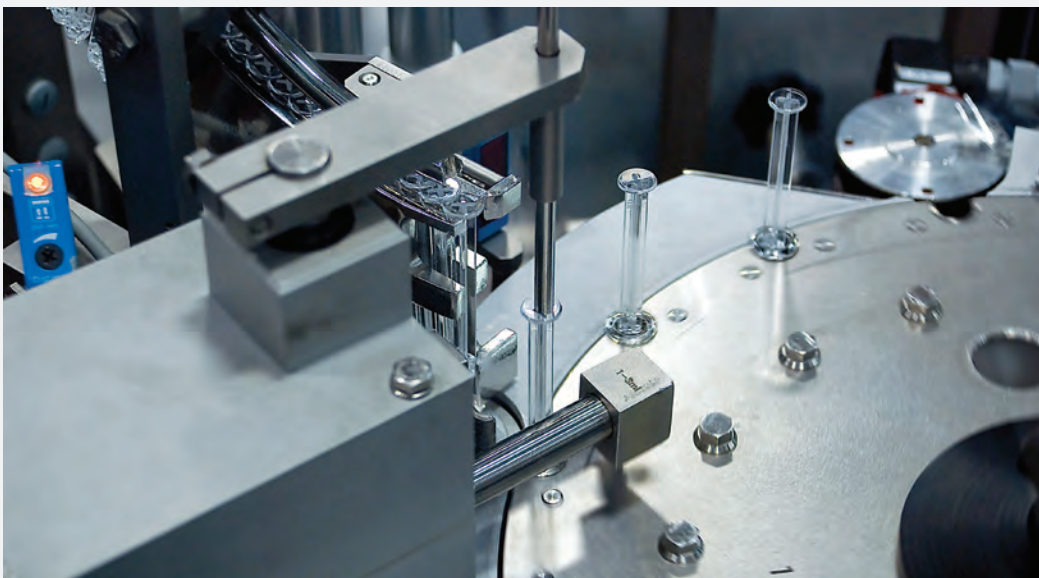
These emerging trends are giving packaging suppliers new avenues to explore and consider – and advances in the biopharmaceutical market mean that they must develop enhanced packaging options to keep pace. In addition, it goes without saying that pharmaceutical manufacturers cannot afford packaging defects or excessive testing that requires drug product to be scrapped or wasted; nevertheless, these are still common issues! Suppliers must find ways of overcoming such problems, but what steps should they take to produce superior packs and devices? Well, in my view, investment in the right equipment helps a supplier to expand their capabilities and ultimately helps ensure that the best medicines reach as many patients as possible.

How has packaging equipment evolved to keep pace with change?

Biologics are complex products and this complexity makes them expensive to develop, manufacture, transport, and store. And it also influences the cost of the delivery devices and packaging required to house the drug. For example, in traditional operations, the average pill bottle could cost as little as US$2 to produce, but a delivery device for a biologic could cost anywhere between $50 and $100 to manufacture. The high cost of these devices can be attributed to device complexity and quality assurance; companies need peace of mind that the systems they choose will be defect-free, safe, and easy to use. And that means the technologies and equipment used in operations today are increasingly designed for fast and efficient quality checks.

What role will the Center of Excellence in Biotech Packaging play in meeting customer needs?

We've invested over $25,000,000 in our Center of Excellence in Biotech Packaging.



The site is home to state-of-the-art equipment, expert personnel, and high quality training materials – all of which help us achieve our goals of providing customers with best-in-class packaging and devices. The growth of the biotech sector shows no signs of slowing, which is why it was so important for us to invest in our capabilities. Our flagship site expands our capabilities across the US region – providing innovative packaging solutions for biologics and injectable products. Importantly, the center mirrors the expertise of our European sites in the UK and Germany, meaning customers worldwide are able to access the same quality of service.

The wealth of resources available means that we are able to support the biopharmaceutical sector as it continues to develop the drugs of tomorrow. We have more machines than ever before for pre-filled syringe assembly and labeling, and we have also acquired auto-injector assembly machines and top load cartoners to ensure that the best quality packs and devices can be produced quickly and cost-efficiently. In addition, this new roster of machinery allows us to quickly switch between production formats – in other words, the same asset can be used repeatedly to produce different product models. So, whether a customer wants low volumes of product or large lot numbers, we can rapidly cater to their needs. Simply put, our machinery can be set up in different configurations to meet the specific assembling, labelling, and packaging needs of different biologic products. Whether a product needs a backstop or specific label, we can accommodate a broad range of requirements.

I am confident that our investment in next-generation equipment will enable us to provide broad-scale support to all of our customers, wherever they might be.

What types of projects have you overseen?

You might guess that the biggest project to date involved COVID-19 vaccine packaging. Biologics are often produced in small lots, but the crisis of the situation we faced required the packaging of an enormous volume of product. We worked closely with our customers to design a carton that could contain multiple vials of vaccine. Having multiple vials in a carton allowed us to maximize the speed on the vial labelling process, which greatly outpaced the rate at which we could assemble single cartons. Using a multiple vial configuration in the carton increased speed and efficiency, allowing us to ship out vaccine more quickly – maximizing the number of doses that we sent to patients in the quickest time possible... We also moved the print locations on cartons and syringes to reduce the number of false rejections, and streamlined processes to reduce the labor required to assemble packs and devices. Ultimately, this helped drive down costs for our customers.

Though we had the capacity to fulfil our customer's expectations, I think the pandemic has really highlighted the importance of collaborating with downstream partners to respond to the crisis. Fortunately, PCI has a long history of working with equipment providers and we were able to call on their expertise to create optimal solutions during a time of great need.

What are your predictions for the future?

As we move forward, the industry will have to look more closely at the ways it can reduce waste. The nature of manufacturing means that there will always be some excess produced, but, if we can minimize it, we can drive down the costs of medicines – allowing therapies to reach more patients worldwide. This latter goal is paramount to PCI – and we're constantly investigating how we can reduce manufacturing waste; the more solutions we develop to help achieve this the better! After all, when you eliminate waste, everyone wins – from the drug developer to the end-user. Through our efforts in these areas, we hope to have a long lasting impact on the biopharmaceutical sector. What is certain is that we will always stay committed to our goal of bridging the gap between pharmaceutical innovation and patient needs.

Best Practice

Technology
Quality
Compliance

Stepping Away from the Flame

With a wealth of sensitive data under its belt, the pharmaceutical industry is ripe for cyberattacks. With the risk of infiltration ever-present (and growing), how can companies protect themselves?

By Maryam Mahdi

When asked to cast his mind back five years, Vishal Salvi, Chief Information Security Officer (CISO) at Infosys, describes a simpler time for the pharmaceutical industry. Though cyberattacks were on the rise in the financial and telecom sectors, they had not yet managed to affect drug manufacturers. Unaware of the severity of these attacks, pharma failed to develop control methods as rigorous or regulated as those of other industries. "Half a decade ago, we lived in the pre-ransomware era. Pharma companies didn't have to worry about cyberthreats," Salvi says. "But the internet is a shared information highway. Though pharma was initially unaffected, its exposure to this vast network meant that it would eventually be burned."

Within a few short years, the flames came closer – and the industry experienced one of its earliest and most significant tastes of cybercrime. The burn came in the form of Merck's 2017 cyberattack. Racking up damages of over US$1 billion, the company fell prey to malware, NotPeyta, allegedly developed by the Russian military hacking group Sandworm. The attack, which pushed the company to decommission 30,000 computers and paralyzed its operations, underscored the seriousness of cybercrime

in pharma and highlighted the need for robust infrastructure to protect against future infiltration. "The stark reality is that the industry is woefully insecure. Though the Merck attack wasn't targeted, it had huge consequences for not only the company, but also the USA's strategic drug stockpile," says Charles Fracchia, founder BioBright and Vice-president of Data at Dotmatics, a scientific data company driving the automation of laboratory workflows.

As Merck pieced its manufacturing capacity back together, it had to rely on the national reserve to supplement its supply of HPV vaccine Gardasil, revealing major points of strain in the country's biomedical infrastructure. The attack sent shockwaves through the industry – a stark reminder of the power of the digital interface for destabilization.

But the looming threat hasn't deterred pharma from pressing ahead with its goals of embracing concepts like Industry 4.0 – which by its nature will introduce more technologies to the pharmaceutical sphere. In fact, since the attack, internal and external pressures have prompted pharma companies worldwide to adopt more digital tools to facilitate drug discovery and development. The COVID-19 pandemic has further motivated companies to consider digital technologies' ability to streamline and optimize practices and manufacturing operations in more recent times. "COVID-19 changed our technology architecture," Salvi says. "As a result, security controls, which were heavily centralized, have become dispersed. If the pandemic had struck 10 to 15 years ago, we wouldn't have had the capacity to introduce such systems. But, in many ways, the industry's evolution over the last few years primed it to transition to using more digital systems at scale."

Pharma's newfound agility was demonstrated by the rapid development of the first generation of COVID-19 vaccines, Fracchia explains. "One of the metrics that emerged from the pandemic (and is of great interest to me) is the fact that, in under 600 days, the Moderna vaccine was approved for emergency authorization use – ready to be administered to hundreds of millions of people worldwide. The vaccine has undeniably improved global health security, but this would not have been possible without strong digital workflows and frameworks."

Though the shift towards digitized practices has benefits in terms of the industry's ability to respond to change, Fracchia argues that it comes with a need to implement further security measures. "We are now seeing companies led by data and that's a transformation all must make to keep pace. But with this comes the need to embed security in companies' operations from day one. Otherwise, they will be building on fragile foundations," he says.

However, for some companies, introducing cybersecurity systems early on may be a challenge. Many have a well-established presence within the industry and may not have considered the impact of cybercrime on their businesses in their initial launches. Though digital solutions will offer opportunities to modernize and create pertinent interventions for patients, do these companies now have the savvy to avoid the risks posed by digital threats?

Old mindsets, new problems

A major hurdle in implementing robust security systems is the use of legacy resources, equipment, and plants. Many of the manufacturing sites used today were developed well before Industry 4.0 became a pervasive concept, explains Salvi. "Though companies are keen to digitize, overhauling existing systems to cater to Industry 4.0 concepts won't be easy. It is very difficult to upgrade old systems to accommodate new security

Vishal Salvi

Charles Fracchia

frameworks. What's more, pharma has not historically been at the forefront of the cybersecurity movement." This, he argues, is the root cause of challenges in deploying and embedding security systems.

"Pharma is getting its wake-up call. Alongside the healthcare industry, it is one of the most targeted sectors by hackers and other bad actors. Though some issues remain, many companies are now looking at how they can invest in cybersecurity that works for their operations," he adds.

But not all industry players are moving quickly to deploy cybersecurity systems. Even with high-profile examples to learn from, some have yet to adopt any at all. According to Fracchia, these companies face consequences as severe as bankruptcy – both financial and reputational. "It can result in a total loss of trust in products and services. This change in opinion can happen virtually overnight. But, beyond individual losses, it has consequences at the macroeconomic level. Today the USA's bioeconomy accounts for up to five percent of our GDP and is growing much faster than other sectors. So cyberattacks could stunt the growth of this flourishing sector."

With risks posed to both profit and reputation, businesses that have been slow to adopt newer systems must quickly develop strategies to mitigate infiltrations and attacks. Salvi believes that this will rely on strong leadership with expert knowledge on cybersecurity-related issues. "Though companies are generally aware of the problem, they can struggle to address it," he says. "But that's understandable. Creating comprehensive strategies against such a rapidly evolving problem isn't easy. It requires more than an investment; companies need active CISOs who can look at the issue holistically and provide operational and tactical action plans for the rest of their businesses to implement." To date, he adds, this has been unheard-of in the pharmaceutical industry. Strategic hiring at the executive level will therefore be key in creating company-wide solutions.

The top-down strategy

Echoing Salvi's sentiments, Fracchia believes the first step any company can take is to educate its board members and C-level executives. "Top-level executives just don't understand the full scope of the issue and this is a limiting factor for the industry," he says. "A great deal of work needs to be done to improve understanding of the field. Though CISOs are undoubtedly an integral part of any security response, they can't be viewed as the cyber-janitor – ready to clean up messes when they occur. The whole team must actively engage with the issue so that real lines of defense can be developed."

But, even with the right education and tools, Salvi questions the willingness of some executives to actively engage with the issue. "How many companies are truly proactive about tackling cybersecurity? And how many are choosing to move slowly because the problem they're facing is out of their comfort zone?" he asks. "To deal with cybersecurity issues effectively, companies must talk about pain points and actively participate in building an industry-wide understanding of the topic."

As the industry's top executives further engage in cybersecurity education, forums for open dialogue will be key in supporting their growth. Salvi outlines that there are many consortia and initiatives – both open-source and monetized – available to help guide companies. He says, "Whether developed by regulators, government or industry, there are many programs that companies can access to build their understanding of the cybersecurity ecosystem." He cites the NIST cybersecurity framework developed by the US Department of Commerce as an example of the guidance companies can explore. "With online learning

"Top-level executives just don't understand the full scope of the issue and this is a limiting factor for the industry."

modules and case studies available, the platform is an important tool for companies' continued development and has been used as a cross-sector resource for some time now," he says.

The recent launch of the Bioeconomy Information Sharing and Analysis Center (BIO-ISAC) is also helping to bring the industry one step closer to improving cybersecurity practices. Working with government, lawmakers, and pharmaceutical stakeholders, the nonprofit organization shares cyberthreat information with its members from industry. "We can only succeed in preventing threats to our bioeconomy if information is dispersed through all industry circles," says Fracchia, who was recently appointed to the organization's Board of Directors. "BIO-ISAC aims to detect potential threats and identify areas of vulnerability for pharma and life science companies. Our goal is to help as many people as possible understand that cybercrime is more than just an IT problem; it affects everyone from bench scientists to management. The more people who are sensitized to the issues it causes, the better."

Future focus

Looking ahead, pressures beyond education will undoubtedly affect pharma's interactions with cybersecurity platforms. According to Salvi, companies will have to closely monitor the growing attack surface – the points within networks that are vulnerable to infiltration. "We are rapidly introducing change to our digital platforms. The pace at which it is introduced means that companies are exposing themselves to more risk than ever before," he says. "The refresh cycle for operating systems, or the rate at which key elements of IT infrastructure are updated, used to be four or five years. Now it is roughly 18 months long. So you can imagine the number of potential risks companies have to manage."

As the attack surface broadens, companies will undoubtedly need specific guidance from regulators as to how the problem can be managed. Though laws like the EU's GDPR and the USA's HIPAA protect patient data, regulators provide less clarity regarding proprietary data owned by pharmaceutical companies. "Globally, there is clearly a lack of concrete regulation on cybersecurity," says Fracchia. "Without clear legislation or guidance, companies are left to navigate the Wild West of vendor solutions – resulting in companies' adopting systems that are inherently deficient for managing threats." To address these areas of uncertainty, BIO-ISAC is working closely with key decision-makers in the regulatory space to introduce a new framework for this type of data. For now, companies will have to wait for clarity.

But, as cybersecurity issues evolve (and the sector continues to grow), hiring and training professionals to deal with regulatory issues among other challenges will be essential. Presently, the talent needed to drive the sectors' progression remains a "rare commodity" – in part, Salvi explains, due to the field's complexity. "It's difficult to train cybersecurity professionals. The huge number of domains and tools makes it challenging to have all-round expertise in all of them and the current 'supply' doesn't meet the industry's future demand," he says. But, like other companies engaged in the cybersecurity sector, Infosys supports the development of future talent. The company has trained over 2,500 graduates in the last three years to help build the professional pipeline. "If we can tap into developing talent, we can help ensure that we have a capable workforce to preempt problems and protect pharma's most valuable assets."

To learn more about BIO-ISAC, visit https://www.isac.bio.

Fueling Precision Medicine

Here's how the next century of bio-innovation could look – from sequence to therapeutics...

By Darlene Solomon, Senior Vice President, Chief Technology Officer, Agilent, California, USA

The 20th century saw an explosion of technological advances that completely reshaped modern life. Transport shot from the earth's surface to the skies, and then into space. Scattered telegraph lines reconfigured to form a global, multimedia internet. Glass-lensed microscopes gave way to a host of sophisticated analytical modalities that reveal the world around us in astonishing detail. More than any other in history, the 20th century was the Century of Technology.

Today, the surge of discoveries and development continues, particularly in biology. And it's very possible that our counterparts in the future may look back on the 21st century as the Century of Biology (1).

The key to planning for – even shaping – the future lies in our ability to identify patterns in social and technological change. Individual trends may come and go, but megatrends – which reflect movement on a global scale – are essential for us to recognize and understand.

The era of DNA sequence

One megatrend of distinct promise is the emergence of enormous volumes of DNA sequence information as a driving force in biological discovery; precision medicine and cellular manufacturing are poised to transform DNA sequence information into a tool of remarkable power.

Precision medicine is the ability to understand and treat disease at a molecular level. It has already begun to effect revolutionary change in oncology, where cancer subtype classification and treatment is transitioning from organ (for example, lung, breast, colon) to biomarker (for example, EGFR, HR+/HER2, BRAF). Cellular manufacturing – the ability to reprogram cells for practical, useful purposes – is also capturing and transforming industrial biotechnology. Many chemicals and materials traditionally produced through petrochemical processes are now harvested as products of engineered biological cells. In addition to sequence information, cellular manufacturing requires deep understanding of cellular metabolism and pathway interdependencies. The expansion of this understanding is being accelerated in turn by the vast amount of metabolomic information now becoming increasingly available through advances in mass spectrometry.

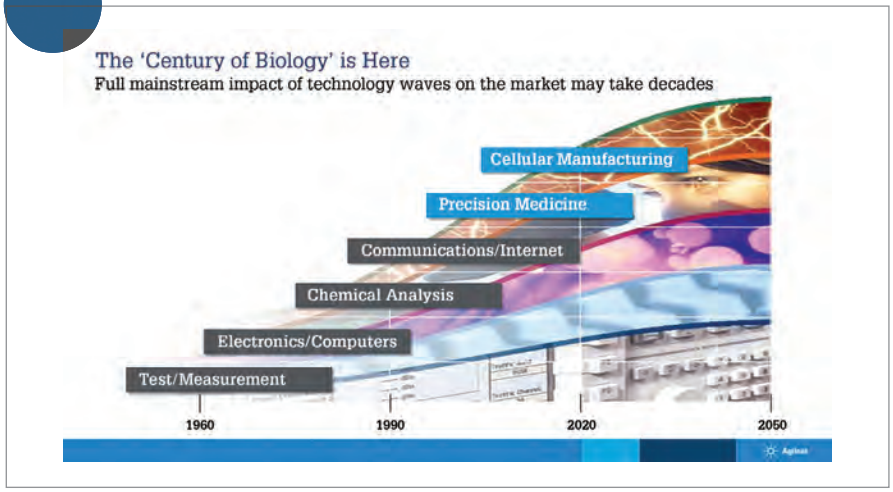
Compared with traditional chemical synthesis, cell-based manufacturing is generally more sustainable and can often produce new, better-performing materials. A leading early example is Dupont's Sorona biopolymer (2), an alternative to nylon partially produced through the reprogramming of *E. coli*. When used in consumer products, such as footwear, not only does Sorona biopolymer produce less greenhouse gas emissions but it also has better stain resistance and is rated as more comfortable than the alternative by customers.

Both of these waves of change share a common driver; the past 20 years have seen a marked shift away from biology as a primarily qualitative science toward a biology that is increasingly quantitative. This shift carries the promise of one day allowing us to understand, model, and predict biology in much the same way that we are now able to do in the physical sciences – an exceptionally complex proposition that lies beyond our current capabilities.

At a fundamental level, as the current rapid growth in our capacity to understand and control biology at the molecular level both deepens our understanding of disease and fuels parallel advances in industrial biotechnology, these life science technology waves reciprocally open new areas of discovery, amounting to a self-accelerating continuum of understanding in the life sciences.

The hidden power of the code

Even beyond the knowledge gained from individual sequence milestones – say, focused analysis of this species



or that disease state – the sheer volume of sequence information available to researchers today is, itself, transformative. Since their relatively recent introduction, sequencing tools have undergone rapid generations of improvement in speed, accuracy, affordability, and accessibility. The cumulative body of sequence knowledge these tools have uncovered has also driven similar improvements in the bioinformatics tools needed to help researchers make sense of it all.

In the process of sifting through this rapidly accumulating mountain of data, certain actionable knowledge has begun to surface. We are now seeing concentrated efforts to develop methods and technologies that take advantage of this knowledge; for example, enabling us to edit and engineer the sequence to further the goals of precision medicine and cellular manufacturing.

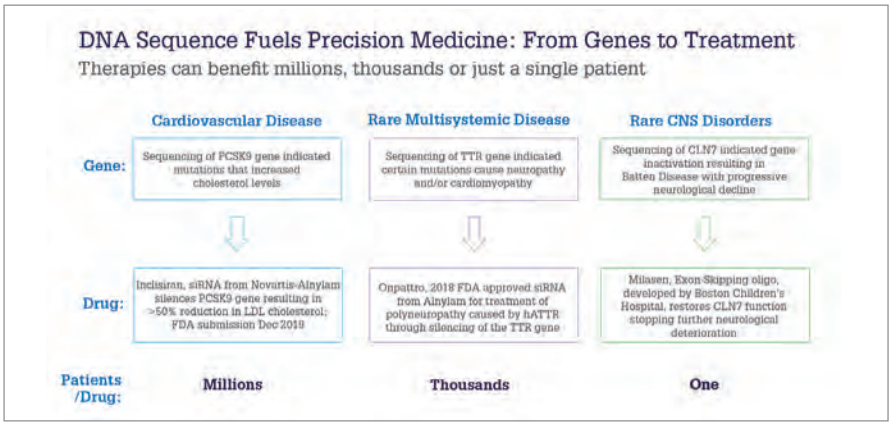
In addition, the abundance of sequence information has opened fields of study such as metagenetics and the microbiome – fields whose enormous complexity had until now rendered them largely inscrutable. We are already beginning to understand the many ways the microbiome contributes to a growing list of complex health conditions – and academic, venture, and industrial resources are now searching for ways to manipulate the microbiome to improve health outcomes relating to digestive disorders, cancer, mental health, immune deficiencies, and more.

Precision medicine aims to improve therapeutic outcomes by adding a previously missing but critical factor to the treatment equation: the unique biology of the patient, as revealed through examination of their relevant molecular information.

Three examples…

Focusing on genetic sequence as a driver of precision medicine, I'd like to offer a few examples of how precision therapies might benefit millions, thousands, or just a single patient. In each case, the new therapeutic is an oligonucleotide – a short sequence (less than 100 base pairs) of RNA or DNA that can interact with its target through a variety of functional mechanisms.

Firstly, inroads are being made in the treatment of cardiovascular disease through sequencing of the PCSK9 gene. It was discovered that various mutations of this gene are associated with high low-density lipoprotein (LDL) cholesterol levels, which are a factor in multiple diseases. The knowledge that this gene played a role (and that high LDL levels weren't simply a matter of poor diet) has contributed to the development of inclisiran (Novartis/Alnylam) – a short interfering RNA (siRNA) therapeutic that acts to silence the PCSK9 gene and effect clinically significant reductions in LDL cholesterol levels. In principle, such sequence-based insight could change the lives of millions of patients. The resulting drug is already approved in Europe, and pending approval in the US. Sequencing remains a critical tool in such treatment scenarios because it is essential to know which patients have mutations in the PCSK9 gene to identify candidates for inclisiran therapy.



Secondly, similar progress has been made in the treatment of a debilitating condition known as hereditary transthyretin-mediated amyloidosis. Sequencing of the transthyretin (TTR) gene revealed mutations that were an essential contributory factor, opening the possibility of a gene-targeted therapeutic strategy. Treatment with Alnylam's Onpattro (patisiran) – the first siRNA drug approved by the FDA – was found to effectively silence this gene, reversing the progression of polyneuropathy in a majority of patients, and improving the quality of life for its thousands of sufferers (3).

Thirdly, and perhaps the most personalized of all precision medicine outcomes, we have the development of milasen – a one-of-a-kind drug created in less than one year by Timothy Yu's team at Boston Children's Hospital to treat a disease caused by a mutation affecting a single patient (4). In 2017, sequence information from the DNA of that desperately ill child, Mila Makovec, revealed a genetic alteration disabling her CLN7 gene, resulting in Batten disease – a very serious and ultimately fatal malady of the nervous system. The customized antisense oligonucleotide therapeutic that was developed for her on the basis of this alteration was given the name milasen. After the FDA gave permission, Mila received the medication just nine months after her one-of-a-kind mutation was identified. The treatment substantially improved Mila's condition, reducing the number and length of her seizures and adding years of improved quality of life prior to her sad passing in 2021.

Milasen is a case study in our ability to achieve positive clinical outcomes based on an intimate understanding of pathogenic mutations. Such "n of 1" therapies, as they have come to be called, truly illustrate the potential of sequence information to enable treatment previously thought impossible for diseases with a genetic component.

The emergence and early success of these precision medicine efforts is triggering significant changes in the way the pharmaceutical industry approaches therapeutic development. One benefit is that clinical trials aimed at smaller and well-defined patient populations can be far more streamline, lowering a key hurdle in bringing a drug to market.

A newly developed drug that works in only 20 percent of the general population may have a much higher efficacy rate – and much greater odds of gaining FDA approval – for a smaller and more narrowly defined target patient population. This "rescue of therapeutics" approach – itself a direct result of deeper molecular insight into the therapeutic approach – offers pharma companies an avenue for monetizing R&D investments that might otherwise have been abandoned.

Century of biology; decades of precision medicine

Looking forward, oligonucleotides will continue to advance precision medicine and the molecular treatment of disease. Beyond antisense and siRNA, several new mechanisms of oligonucleotide therapeutic action are being demonstrated, including small activating RNA, regulatory RNA, and CRISPR genome editing.

CRISPR derives its sequence specificity through the use of application-specific guide RNAs that specify the site-to-be-edited. And it is quickly establishing itself as a superior enabler for both ex vivo gene modified cell therapy and in vivo gene therapy. Cell and gene therapy are the fastest growing segment of biopharma and a potentially transformative frontier for precision medicine, because they not only treat disease – they can cure it. To enable such breakthroughs requires a functional understanding of genetics and an ability to target genetic edits – both of which are greatly enabled by widespread access to sequence information.

DNA sequence is already a keystone of biology, and we look forward to discovering the full impact of this megatrend – not only on precision medicine and cellular manufacturing but also on the technology waves yet to be defined as we continue our journey into the Century of Biology.

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The Bioprocess Curator

What's going on in the biopharma industry? Here's a quick roundup from the last month…

Left to right: Representatives from Alcon , Huma, Novartis Pharmaceuticals Corporation, Global Blood Therapeutics *Credit: PRNewsfoto/The Galien Foundation*

In the biopharma industry, things can change faster than you expect – with dozens of announcements every day, including new collaborations, licensing agreements, mergers, acquisitions, appointments, equipment launches, and, of course, scientific breakthroughs – from new research papers to product approvals.

We have just launched a newsletter: The Bioprocess Curator. We trawl the news coming out of the biopharma industry (and sometimes beyond) each fortnight and curate the top stories into a fuss-free digest that can be read in just five minutes.

Sign up at tmm.txp.to/biop-cutor.

If you're looking for an immediate snapshot of what's going on in biopharma, here's a roundup of some of the most important news of the last month, as featured in The Bioprocess Curator.

The Promise

Early research that could lead to big things in the future

Seek and destroy. Researchers from the UK's University of Cambridge have released a remarkable video showing T cells hunting and killing cancer cells – as well as the moment they reload to kill again. According to the team, the refuelling of a T cell's toxic weapon is regulated by mitochondrial translation. They hope that the work will pave the way to engineering T cells into more effective serial killers of cancer cells.

Winning innovations. The Galien Foundation has announced the winners of the 2021 Prix Galien USA Awards. The awards focus on "innovations that have improved the human condition." Global Blood Therapeutics won Best Biotechnology Product for Oxbryta (voxelotor); Novartis won Best Pharmaceutical Agent for Entresto (sacubitril/valsartan); Alcon won Best Medical Technology for its Acrysof IQ PanOptix trifocal intraocular lens; and Huma took the Best Digital Health Solution category with its remote patient monitoring program.

mRNA on track. VaxEquity is collaborating with AstraZeneca to progress its self-amplifying RNA platform to proof of concept; platform could produce vaccines and other therapeutics.

In a bubble. Work at the Karolinska Institutet has produced extracellular vesicles that can deliver drugs, including protein-based drugs and genetic material, to different tissues.

COVID-19 detection. Bio-Rad launches Bio-Plex Pro Human IgA and IgM SARS-CoV-2 panels for research use to detect IgA and IgM antibodies against four SARS-CoV-2 antigens.

Bountiful development. PhRMA report shows 261 medicines in development for 29 neurodegenerative diseases; all are in clinical trials or awaiting FDA review.

The Process = The Product

News, technologies, and research affecting manufacturing and product control

Stable mates. After conducting an inter-company collaboration exercise, including benchmarking surveys, the Formulation Workstream of the BioPhorum Development Group (BPDG) has published a research paper discussing in-use stability and compatibility studies of biologics with diluents and administration compounds. The paper includes approaches that can help guide the strategy and design of in-use stability and compatibility programs.

Keep it cool. The PDA has released guidance for maintaining the quality of

temperature-sensitive medicinal products during transport. Technical Report No. 39 Revised 2021 (TR 39) Guidance for Temperature-Controlled Medicinal Products - Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment covers the shipping site, product shipment, and storage at the receiving site.

Continuous control. Open-access research paper in the Journal of Chemical Technology and Biotechnology looks at continuous biomanufacturing and the challenges posed by batch definition and the ability to trace raw material through the process. The authors use a process train simulation to compare the conventional batch definition based on a fixed time, to a new batch definition based on the greatest common divisor of the time period of the unit operations; the latter appears to result in better control.

PAT pals. Matica Biotechnology and Sartorius have agreed to collaborate on streamlining and optimizing PAT technologies, automation software, and single-use platforms for large-scale vector production.

On CHO. Researchers discuss how full-length IgG and Fab antibody formats impact production in CHO cells – and identify targets that could increase manufacturing efficiency.

Hybrid approach. GEA launches kytero single-use pharma separator which combines the performance of its larger stainless steel centrifuges with disposable separation tech

Tackling viscosity. Merck releases excipient technology platform that combines amino acid and anionic component platform to reduce viscosity of protein-based drugs.

Biomanufacturing 4.0. Review article discusses move towards integrated biomanufacturing and process intensification – and the potential of digitalization in process monitoring and control.

The Business Bulletin Board

- COVID-19 treatment AT-527 from Atea and Roche fails phase II trial and leads companies to change the design of ongoing phase III trial.
- Thermo Fisher Scientific opens biologics manufacturing site in Lengnau, Switzerland; site includes both single-use and stainless steel, with bioreactor capacity up to 12,500 L.
- Merck and GSK mutually agree to terminate bintrafusp alfa partnership after INTR@PID Lung 037 study did not replicate encouraging data observed in early studies.
- BioNTech announces it will commence work on a manufacturing site for mRNA-based vaccines in the African Union in mid-2022
- Waters and Sartorius combine BioAccord LC-MS system with Ambr bioreactor to accelerate clone selection and process development
- Xencor and Janssen team up on Plamotamab and XmAb CD28 bispecific antibody combinations for B-cell malignancies.
- SGS completes expansion of bioanalytical testing lab in France; lab provides additional capacities, including mass spectrometry, immunoanalysis, and cell-based bioassays.
- Insilico Biotechnology, Ajinomoto, and Ajinomote Genexine sign agreement for smarter development of cell culture processes using digital twin technology
- Merck opens 140,000-square foot gene therapy manufacturing facility in Carlsbad, California; enables suspension production of viral vectors up to 1000 L
- LSNE Contract Manufacturing installs new lyophilizer and doubles sterile drug product lyophilization capacity at Madison, Wisconsin, parenteral manufacturing site.
- Cellumed and ARTES sign development and license agreement for microbial production cell lines, processes, and documentation manufacturing enzymes for mRNA vaccines.
- PTC Therapeutics opens new gene therapy manufacturing facility in Hopewell, New Jersey; includes equipment to handle plasmids and AAV vectors.
- I-Mab completes patient enrollment of the phase III trial of human CD38 antibody felzartamab in combination with lenalidomide for multiple myeloma.

The Patient

From drug pricing to safety and side effects

For the kids. The WHO has recommended GSK's RTS,S vaccine (Mosquirix) for children in sub-Saharan Africa and other regions with moderate to high malaria transmission. The recommendation came after data from pilot studies in child clinics showed that the vaccine, in combination with other approaches, such as insecticide-treated nets, could reduce the incidence of deadly severe malaria by 30 percent.

Paper withdrawn. Scientists retract preprint study that vastly over-estimated the incidence of myocarditis post-vaccination with mRNA-based COVID-19 vaccines.

Myth busters. New Jersey's life sciences trade association releases white paper that corrects common myths about Prescription Drug Affordability Boards and their harmful impact on patients.

New purpose. Pilot project from EMA and Heads of Medicines Agencies launches to support not-for-profits and academics wanting to repurpose existing medicines.

Swimming with the mRNA Current

How RNA is making waves in the industry – and leading to new research projects and increased demand for new manufacturing capacities and facility design

By Bill Jarvis

Long before COVID-19 hit and mRNA vaccines took to the global stage, RNA-based projects were already on the increase in the pharma industry. In fact, CRB has been involved in the related oligonucleotide technology market since the mid-90s, and we have relationships with many principal equipment manufacturers in the space including Cytiva and AK Bio. Since 2010, we've started to see a dramatic ramp up in activity in the area off the back of successes like Spinraza – a small population antisense oligonucleotide therapy for spinal muscular atrophy.

We were also working on mRNA-based projects long before 2020, but it is apparent that the rapid approval of the Pfizer/BioNTech and Moderna COVID-19 vaccines have energized the mRNA product development field. The successes of these vaccines has been hugely exciting for the world, but in the pharma industry they have also demonstrated that drug regulators are open to new approaches; the Pfizer/BioNTech vaccine was the first mRNA-based vaccine to ever receive regulatory approval (full approval was granted by the FDA in August 2021).

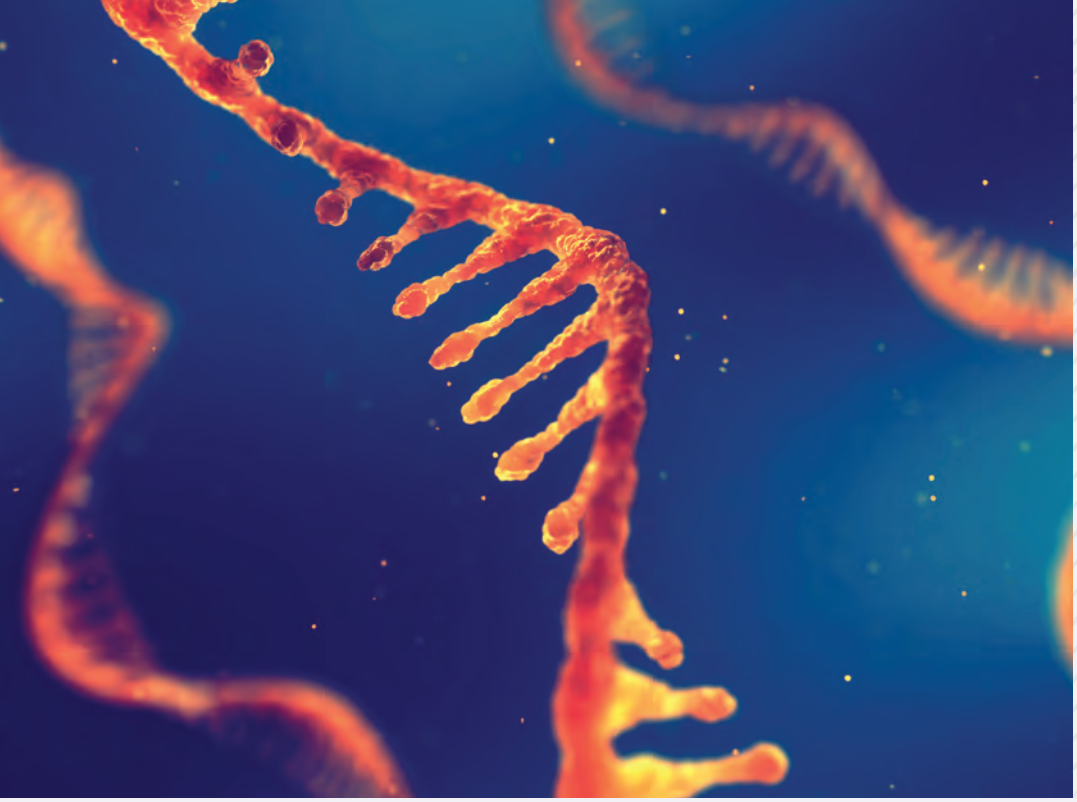
This proof-of-concept of mRNA products has led to a significant increase in activity, with pharma companies worldwide now investing heavily into production facilities that can ramp up their ability to make the necessary materials for mRNA-based products. Companies also see real potential in the fact that mRNA-based products can be produced as a relatively straightforward synthesis reaction, rather than being biologically grown, which allows products to be manufactured under shorter timelines (although downstream purification is still required). mRNA also allows manufacturers to get significant product yield from a relatively small manufacturing scale, which means the capital investment in equipment (and facilities) can be smaller too.

But it's not only the mRNA field that is seeing greater attention; the entire RNA field is now in the spotlight. Though oligonucleotide projects have been on the uptick for years, we're now seeing unprecedented demand for new facilities – both for mRNA and oligonucleotides, particularly in North America, Europe, and China.

RNA challenges

RNA-based therapeutics have unique manufacturing challenges compared with traditional biologics, and this can affect how you design and set up your manufacturing facility. mRNA-based therapeutics, such as the COVID-19 vaccines, are often manufactured using in vitro transcription – an effective and reliable approach for replicating naturally occurring long-chain RNA molecules (usually around 1000 base units, or longer). Here, the main challenge lies in setting up the right RNA template that will be replicated and expanded to production. This isn't necessarily an easy task for researchers, but when it comes to the manufacturing process and facility design, the setup is straightforward; broadly speaking, the process just needs a stir tank and the appropriate starting raw materials and enzymes to kickstart the wonders of biological chemistry. Downstream, the process steps are similar to that of a biological process, such as tangential flow filtration and chromatography steps. Some of these unit steps may use alcohol or other flammable liquid, so it's important to design for the presence of flammable solvents; for example, considering specific electrical classifications and architectural design features to deal with necessary safety regulations and code requirements.

We've also worked with a few clients who use self-replicating RNA. If that is a possible part of the portfolio, it may make sense to opt for a higher degree of biological containment in the facility – just in case. High containment isn't typically required for RNA projects, but the self-replicating nature of some of these polymers can be a cause for regulatory concern. And that's particularly true for CMOs, who want to give the impression of high quality and demonstrate to their customers that they are taking state-of-



A Passion for RNA

With 30 years at the company, I am one of CRB's longest resident process engineers. I've had the opportunity to work with many different technologies and projects, including monoclonal antibodies and vaccines, but my speciality lies in chemical synthesis, including hazardous materials and flammable solvents. In recent years, I've done a lot of work in the synthesis of short chain RNA molecules and formulating RNA into vaccines. The vaccine work has, of course been very active due to COVID-19.

the-art precautions to protect the integrity of their products. Given the increased interest around RNA right now, we're seeing many CMOs looking for additional capacity in this technology niche.

The manufacturing process for oligonucelotides (usually modified short chain RNA segments) is different. Oligonucelotides are chemically synthesized one base unit at a time, with very high yield per coupling, but the yield reduces with each step as errors accumulate. If the molecule of interest is a long-chain RNA molecule, yields can drop off dramatically by the time you reach the end – possibly as low as 30 to 40 percent for a molecule with 100 base units, for example. This is perhaps the most significant manufacturing challenge with oligonucleotides, particularly given the raw material cost of the chemically modified oligonucleotide base unit amidites that are used to synthesize the molecules.

When it comes to setting up a facility for oligonucleotide production, the design of the facility needs to consider a number of aspects; for example, you'll need the right air classifications to protect the integrity of the product. The techniques used to synthesize the molecules are also often dependent on large volumes of flammable liquids for the synthesis process, so the designer needs to ensure your manufacturing space meets safety regulations and code requirements in this regard.

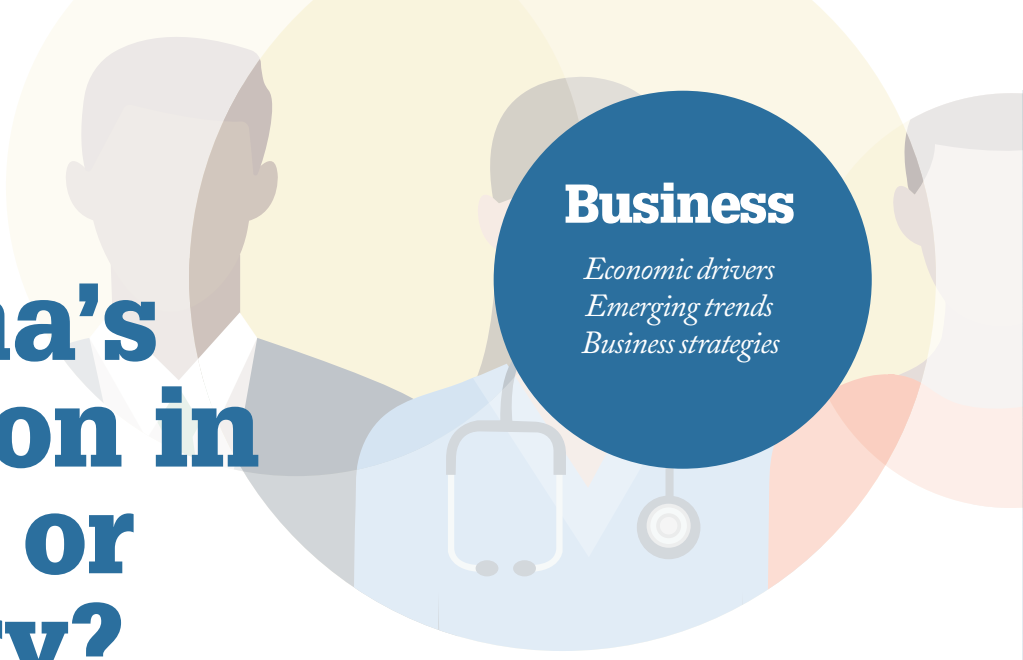
Contamination is another concern. So far, all of these molecules are parenterals – and some are intrathecal injections (injected into the spine). That means downstream purification and formulation steps must protect against environmental contamination, similar to requirements of any injectable vaccine, biologic or other parenteral drug.

Another challenge impacting the entire biopharma industry right now is the supply chain; there can be problems obtaining raw materials and even equipment. However, even outside of pandemic times, there can be supply chain issues. One of the main chemicals used in the synthesis process for oligonucleotides is acetonitrile, which has experienced shortages in the past. It's likely that more shortages, particularly in the specialized genetic base unit raw materials will be seen as activity in the area continues to increase. The good news is that as demand for those raw materials increase and specialized raw material production facilities are brought on line, it is likely the unit cost of those raw materials will decrease.

A facility to be proud of

Those of us at CRB feel like we have grown up with the RNA industry; we've watched this technology space go from niche to one of the hottest areas of biopharma development. Billions of dollars are now being invested into design and construction work on RNA manufacturing facilities – and it's fair to say we're busy! It's really exciting to think about how all of this will affect the therapies of the future. We're certainly putting a great deal of effort into training people internally on these technologies – and specifically how they affect facility design. Over the years, we've been involved in many projects – either designing new capacity or expanding existing capacity, particularly in the oligonucleotide space. And I'm pleased to say we have many repeat clients. Why do they like to involve us in their projects? Mainly because we make their problems go away – especially in terms of equipment set up within those facilities. Our experience in this technology area is unequal; we know what to look for and how to design a safe but efficient facility. But we also know how to design a place that is a pleasure to work in and something for which our clients will be proud.

Bill Jarvis is a Process Engineer with CRB



Is Pharma's Reputation in Paradise or Purgatory?

The Association of the British Pharmaceutical Industry (ABPI) recently published an index that tracks UK pharma's domestic reputation. We spoke with the ABPI's Director of Reputation, Jill Pearcy, to see if it's all sunshine and rainbows – or simply suffering.

By Angus Stewart

What is your role in the industry?

When I joined the ABPI, I was working on developing our new Code of Practice. The updated Code was issued recently, which is really exciting. Now, I'm working on reputational tasks, including promoting our Code principles and helping companies to embed those in their daily activities. I'm also working on the Pharmaceutical Reputation Index, as well as our equality, diversity, and inclusion strategy, and sustainability topics. So my role is broad, but everything I deal with feeds into – and drives – reputation.

Monitoring and benchmarking is very interesting, which is partly why I enjoy working in this corner of the pharmaceutical industry. I get my teeth into a range of intellectual problems, and work with very engaged colleagues who are experts in their own particular fields. So the work is stimulating and the company is good.

What branches of knowledge or expertise did you have to draw from?

My background is in communication, so I've been working on the various aspects of reputation and communications for many years. Before I came to ABPI, I was working on HS2 (the plan for Britain's first high-speed railway) and leading corporate communications there. I'm used to working on the public-private sector borderline where trust is absolutely vital.

What inspired the ABPI's Pharmaceutical Reputation Index?

We started working on this around 18 months ago to understand what our stakeholders think – including what is driving trust; we hoped the resulting information would help our members build better partnerships and collaborations. We also wanted to get a feel for the trends – and how we compare with other sectors. I felt that reputation wasn't being tracked in sufficient detail – it's included in other global reports, but extracting the essential information often felt more like art than science. We'd studied reputational perceptions, but only in discrete areas. In short, there was a gap in our existing knowledge of pharmaceutical reputation, and the Index is our attempt to fill that gap.

How exactly do you define "pharmaceutical reputation?"

We followed the tried and tested model that Ipsos Mori use, which looks at four main drivers: trust, familiarity, favorability, and advocacy. We can frame the model with four key questions.

1. Do you believe the organization will do what they say they're going to do?
2. Are you familiar with what they're doing?
3. Do you like what they're doing?
4. Would you speak highly of them, if prompted?

We use various different markers that help build an overall picture of reputation. It's not a simple case of "do you like someone or not?" It's about how one feels in terms of trust.

How does UK pharma compare with other sectors?

In some places we are ahead – we're viewed more favorably than banks, for example. But a key point to consider is that

Key figures and findings from the Index

- The favorability of UK pharma fell from 50 to 46 percent between July and October 2020, but had bounced back to 55 percent by March 2021
- 60 percent of the UK public say their views on pharma have become more positive over the course of the pandemic
- 98 percent of the British Members of Parliament studied had a positive view of UK pharma's response to the pandemic, and 92 percent believe the sector makes a positive financial contribution to the economy
- 76 percent of healthcare professionals agreed that global pharma companies are "doing all they can" to combat COVID-19; 57 percent felt that UK pharma supported the NHS during the pandemic
- In all cases, 'Neither agree nor disagree' and 'Don't Know' outweighed any negative feelings about UK and global pharma

pharma is not directly consumer facing in the UK, so consumer brands often score more highly on awareness. Nevertheless, in every section of our Index, you can see how we measure against different sectors. For example, the National Health Service (NHS), universities, and health charities are trusted more than pharma, whilst food and drinks companies, internet companies, banks, and automotive companies are trusted less. It's a mixed picture, but we land somewhere in the middle.

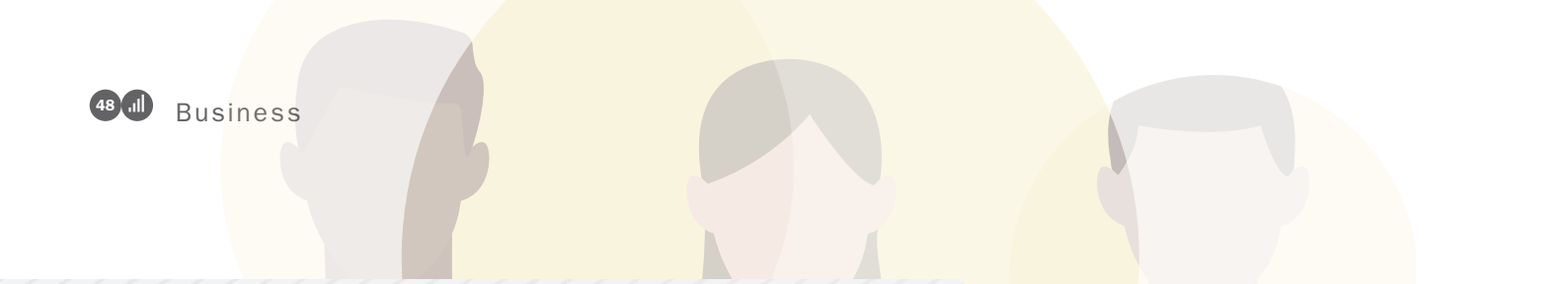
Are any of the key components of reputation especially relevant for pharmaceutical companies?

I think they are all important. Trust only happens when every component interlocks and you feel quite positive towards companies. However, favorability also depends on familiarity. Recently, we've seen pharma make gains in favorability, but no such improvement in familiarity – and that's the area where we hope to do better.

Why is UK pharma's reputation important to the ABPI?

As a trade body, we lead engagement with politicians, patient groups, and charities. We're right at the center of many initiatives crucial to public health; for example, we worked very closely with the government and public sector on Brexit and the pandemic.

We've got to be sure that our stakeholders have confidence in what we're doing. But we also need to know where any potential pain points are – areas where we can improve or where there is a deficit of trust.



Comms Director Elaine Towell on ABPI's recent social media engagement

We've run two conferences in the last four years. The most recent came just before the pandemic. There, we heard some really good case studies showing how our members are using social media to build awareness of the work they do to help patients. We also analyzed the social media habits of all attending members to get a picture of how digital trends are changing in pharma.

Even more recently, we ran a vaccine confidence campaign on social media. The ABPI had never really engaged with the general public in that way before. Following hashtag #valuingvaccines, we worked with the NHS, the Department of Health, MHRA, and various groups within media and society to align our communications and provide the facts and figures that could help address vaccine hesitancy. Some people are misinformed about the work our industry does, but others people have genuine fears about vaccines and trying to allay those fears is what we've been doing for seven or eight months now.

Whose opinions do you seek to build the Index?

There are three main groups. First, we have a nationally representative sample of the general public. Second, we have a mixture of healthcare professionals, ranging from doctors and nurse prescribers to chief and hospital pharmacists. Thirdly, we recruited about one hundred Members of Parliament from the largest political parties.

How did the planning and the significance of the Index change – if at all – because of the pandemic?

We shifted our tactics slightly; we didn't carry out any face-to-face focus groups. And we also pushed our survey of healthcare professionals back to fall 2020, because we felt it wasn't appropriate to approach them in the first waves of the pandemic. Our work with MPs didn't really change, as that line of communication was online to begin with.

Of course, we've had huge amounts of attention from the media. Today, ordinary people are actually using the names of pharmaceutical companies in everyday conversation, which is extremely unusual for us. This huge increase in awareness has made a very big difference. People are seeing the positive impact of the efforts that the industry has made.

Do you think pharma will see long term shifts in opinion because of COVID-19?

I think it's too early to say. We certainly hope that the reputational gains we've made will continue. Companies have perhaps become more used to being visible and being really positive about their role – and that's a good thing. It feels like there is a behavioral shift that we can build on; perhaps we're getting better at telling our story.

And what about changes in perception over longer timescales?

Over the decades, the most salient changes have been within pharma's evolving code of practice. (I won't go into details here, but in the past there were accepted practices that no company would consider now). Society's expectations around behavior have also changed hugely. There are different expectations around transparency too. We studied views on disclosure, and it's clear it is a really important aspect of trust – and it's another aspect that has changed greatly over the years. People rightly expect more of companies today – and companies want to live up to those higher expectations.

Our new Code of Practice – released at the beginning of July 2021 – has four principles: benefiting patients, integrity, trust, and respect. I think these all have a massive impact on reputation.

Based on the results in the Index, what do you think that UK pharma companies or even the ABPI need to do to further enhance the industry's reputation?

We need to build familiarity and embed the gains made during the pandemic. Right now, the proverbial door is ajar. I think it's up to us to make sure that complex topics are shared in an intelligible way. We have to go to people, not expect them to come to us.

One route through the door is via social media. Social media is where many conversations are taking place – but it's very challenging for companies to make sure that the right information goes to the right people. Companies are communicating much more in the virtual space, and that's only going to continue. But it must be in a mindful and responsible way. Key questions to ask yourself: "What conversations are you having?" "What information are you sharing – and with whom?" "Is there a clear distinction between the conversations you are having with health professionals and those with lay people?"

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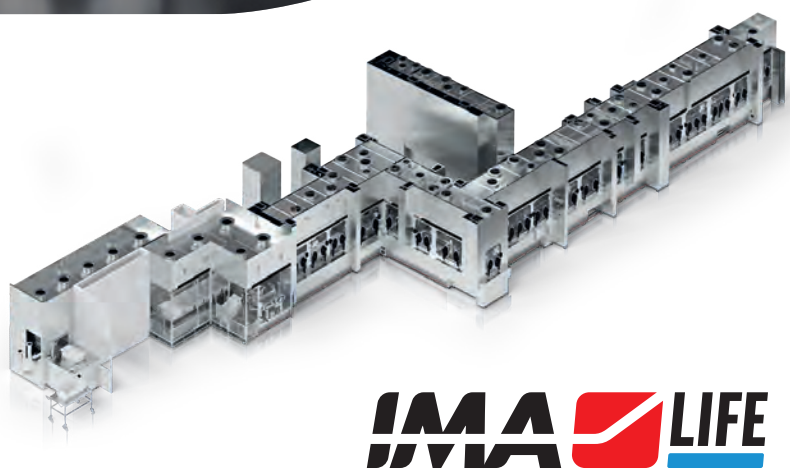

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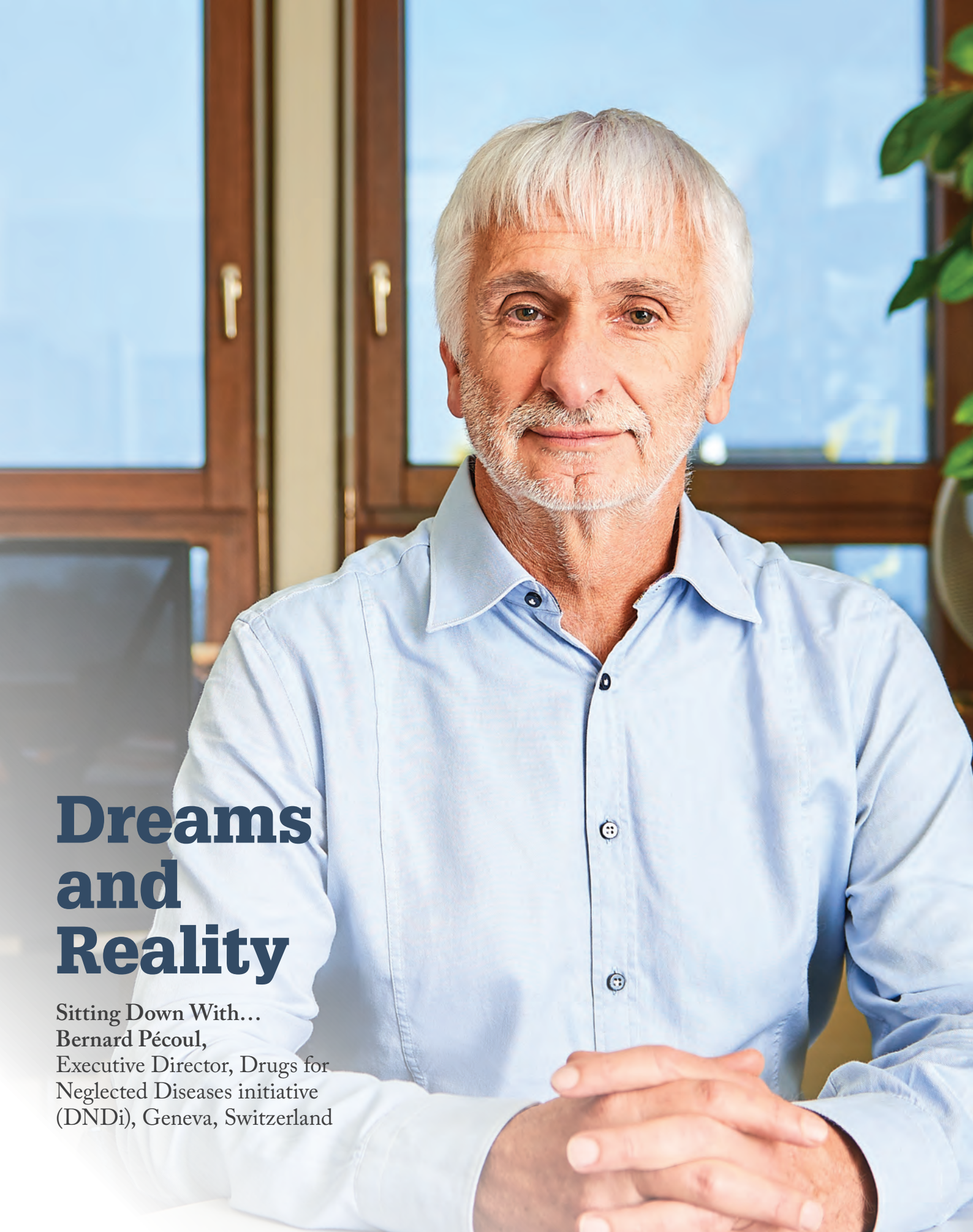

Dreams and Reality

Sitting Down With…
Bernard Pécoul,
Executive Director, Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland

How did your career begin?

Upon completing my training as a doctor, I applied to Médecins Sans Frontières (MSF/ Doctors Without Borders). I intended to join for six months, but I stayed for 20 years, eventually becoming its Executive Director in France! With MSF I worked in dangerous situations across unstable regions such as Rwanda, Somalia, and the borders of Honduras and El Salvador. Often, I saw patients who were affected by infectious diseases and without appropriate treatment. The contrast I witnessed at this stage in my life – between my experience in hospitals in France and what I faced abroad – stayed with me and influenced everything that followed.

What are the origins of DNDi?

At one critical moment with MSF, we were using an arsenic-based treatment called melarsoprol to treat sleeping sickness. The toxicity killed one out of 20 patients, but we had no other option; it was the only drug available. It was absolutely unacceptable and we wanted to come up with a better solution. We evaluated the existing research and development for neglected populations and documented the lack of investment. Following this, we created the Drugs for Neglected Diseases initiative as a body that would at least try to demonstrate that another way was possible.

And we succeeded! We proved the viability of a model that is smaller, more collaborative, costs less, and can prioritize neglected patients' needs.

Is DNDi as concerned with neglected regions as with neglected diseases?

For me, "neglected disease" is an important concept, but so is "neglected people." These are people whose medical needs do not attract investment from the classical model because of a perceived lack of return on investment. Of course, poverty is the central problem. In the last two decades of the 20th century, medical science made great progress – but for whom?

How do you work with the pharma industry?

DNDi began as a dream. In the early 2000s, some said we would never convince a pharmaceutical company to join our project – but, ultimately, the opposite proved true! There is a massive inequity of investment in neglected diseases and regions, and this has given us the credibility to attract the partners we wanted.

To share one example, with a pharma partner, we developed a response to the sleeping sickness crisis by combining two existing drugs developed by companies that are today part of Bayer and Sanofi. Together, we developed a first combination to improve the situation slightly, but the treatment remained very complex. So we continued our research and selected totally new drugs.

The first was fexinidazole, a product developed in the 1980s and abandoned because of lack of profitability. Eventually, we presented a full dossier to regulatory authorities in Europe and Africa. The product is now used as a 10-day oral treatment in Africa. We brought in a pharma company partner, Sanofi, to work together with relevant partners in Africa – particularly in the Democratic Republic of Congo and Kenya – and with several public institutions in different parts of the world to achieve our goal.

We are also completing the development of a new chemical entity called acoziborole, a single-dose oral treatment that can be administered at the point of diagnosis, even in the most remote places. Since humans are the only reservoir of the disease, it will contribute greatly to our efforts to eliminate it. This project is also in partnership with Sanofi, among others.

How do you build relationships?

New technologies and the internet have improved our capacity to work as a "virtual" model but, if you want to build strong partnerships, you need to do it offline. Opening regional offices and networking platforms to be closer to patients and their reality has always been part of our strategy. You cannot perform a clinical study on your screen!

Where would you like the next generation to carry the baton?

We need to stop thinking about innovation as something Europe, North America, and Japan bestows upon the rest of the world. Asian, African, and Latin American groups will increasingly lead – of course, they will still collaborate with partners in the global North, but in a leading role.

In terms of processes, I hope open-source models succeed. At DNDi, we brought eight companies together to share their libraries of molecules for neglected diseases. They've pooled resources on the condition that, if something comes from this bank of chemical compounds, it will be made available for development. I hope the next generation of researchers adopt models just like this.

What role should the state play?

In the private sector, we need to work with various companies. But, for the public sector, we need governments that are engaged in their responsibility to deliver public goods. Without commitment from governments, partnerships with academic institutions will not suffice. Whether the partner is a Ministry of Health or a Ministry of Research, it is a political power in the country and its commitment is crucial for our projects to succeed.

If you had never joined MSF, where would you be today?

Before leaving for that originally planned six months, I had expected to continue my career as a medical doctor. In fact, I had even begun to specialize in nephrology. I always tried to maintain contact with nephrology but, year after year, my involvement in public health replaced it. I even stopped for a year to study for a Masters of Public Health in New Orleans; after that came the next stage of my life, finding new ways to implement the lessons I learned in my youth.

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