DECEMBER 2019 # 60

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From imagination to innovation:
who made this year's list?

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Online this Month

A Year in Review

As the year draws to close, it's good to look back and review the previous months. Here are some popular cover features published in The Medicine Maker throughout 2019.

If there are provocative topics you'd like to read about – or write – in 2020, get in touch with our Editor, stephanie.sutton@texerepublishing.com.

February
Old and Forgotten
Are the needs of elderly people being overlooked when it comes to developing appropriate dosage forms? Academics and industry experts give their views on how pharma can better support older patients.
https://themedicinemaker.com/issues/0219

May
Under Construction: Pharma's Cannabinoid Bid
The cannabis business is booming as century-old legal conventions restricting use begin to unravel. We examine how drugmakers entering the fray should deal with the dosage, delivery and bioavailability challenges.
https://themedicinemaker.com/issues/0519

August
How to Find Your Secret Source
The complexity and scope of tasks within the (bio)pharma industry lend themselves to outsourcing – especially for small companies – but finding the right partner can be daunting. Do you opt for individual suppliers or a one-stop shop?
https://themedicinemaker.com/issues/0819

October
Sustainability and Responsibility – Beyond Buzzwords
Pharma actively works towards improving human wellbeing but we only have one planet on which to enjoy good health. We highlight what some companies are doing to reduce their environmental impact.
https://themedicinemaker.com/issues/1019

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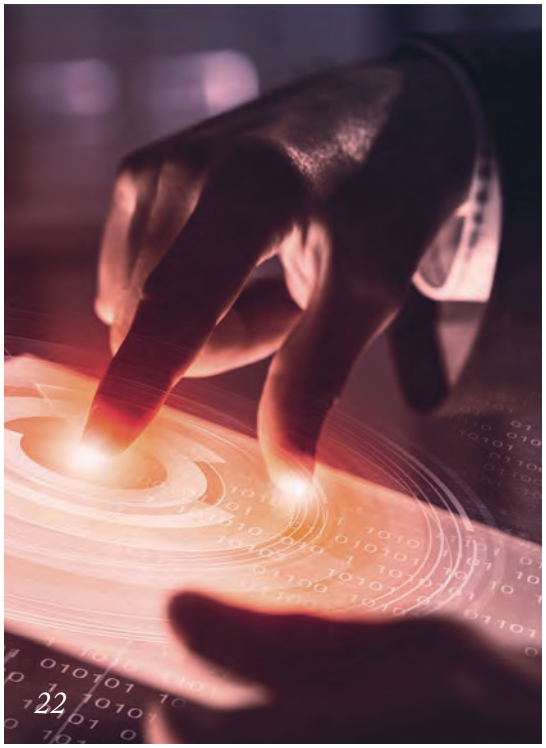

On The Cover

Celebrating the top drug development and manufacturing technologies of 2019.

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In My View

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NextGen

Best Practice

Reports

Sitting Down With

the **Medicine Maker**

ISSUE 60 - DECEMBER 2019

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Joy to the World?

The UK's "sovereignty" debate does not end with an agreed UK–EU relationship. It extends to all trading partners – with potential implications for pharma and patients across the world.

This is the season to be voting (in the UK at least). And though, at the time of writing, it remains to be seen whether the Conservatives will win enough seats to pass the Revised Withdrawal Agreement, I have been thinking about life after the UK leaves the EU – and the implications for pharma.

The Brexit debate can arguably be characterized as a trade-off between "parliamentary sovereignty" and "free trade." In other words, to what extent can parliament minimize trade friction while also being free to set its own rules and regulations? This dichotomy applies to any trading relationship – not just the EU – and will be central to the UK's negotiations with trading partners across the globe, including the US, Australia and Japan.

From a pharmaceutical and healthcare perspective, trade agreements clearly have the potential to impact policy, potentially constraining regulatory sovereignty in these areas in return for market access. For example, a recent analysis identified 10 types of provisions in a data set of trade agreements (1). These included extended periods of exclusivity for patented medicines, investor-state dispute settlement mechanisms, procedural requirements for national pharmaceutical pricing and reimbursement programs, regulation of pharmaceutical marketing, and rules applying to state-owned enterprises and government procurement of pharmaceuticals. According to the authors, many of these provisions have the potential to impact access to affordable medicines, as well as local production and health security.

I'm not trying to be disparaging about trade agreements. In fact, I have detected some optimism in the UK pharma industry when it comes to the prospect of enhancing trade with the US market. For example, during a panel discussion at Pharma Integrates, London, Scott Johnstone, CEO of the Scottish Lifesciences Association, said, "Our companies are focused on the US rather than Europe. And that's where the opportunity is." At the same time, we must be clarify what "enhancing trade" really means, and understand that tipping the "sovereignty scale" too far (in either direction) has the potential to impact the industry – and ultimately patients.

Assuming Brexit goes ahead, leaving the EU is really the first step in the Brexit process. It will be up to industry associations and patient advocacy groups to ensure that their voices are heard as the UK reformulates its relationships with the rest of the world.

James Strachan
Deputy Editor

Reference

1. *D Gleeson et al., "Analyzing the impact of trade and investment agreements on pharmaceutical policy: provisions, pathways and potential impacts" (2019). Available at: https://bit.ly/2r02Lcp.*

Upfront

Reporting on research, personalities, policies and partnerships that are shaping pharmaceutical development and manufacture.

We welcome information on any developments in the industry that have really caught your eye, in a good or bad way. Email: stephanie.sutton@texerepublishing.com

Waste Not…

How can wood be used to produce pharmaceutically relevant compounds?

Working towards a sustainable future is a common goal for responsible pharma companies, but making greener pharmaceuticals requires new approaches to drug development and manufacturing. Researchers at the University of Groningen in the Netherlands have an interesting proposal: using wood chips as the starting material for pharmaceutically relevant compounds. Katalin Barta, Associate Professor at the university, tells us more…

What inspired your novel approach?

Our research took advantage of lignin, a cross-linked phenolic compound known to give wood its strength. Lignin is considered a waste material in the production of paper because it can contribute to its yellowing. Huge amounts of lignin are produced each year.

Though other research groups, including my own, have explored the possibility of turning lignin into polymer building blocks or bulk chemicals, our idea was to harness the potential of the functional groups "built by nature" in lignin to produce pharmaceuticals that are structurally more complex molecules. We found that lignin derivatives share many structural features with modern pharmaceuticals, making them ideal starting materials for the synthesis of drug candidates. Through a series of catalytic methods, we were able to produce a series of medicinally relevant compounds.

What pharmaceutically relevant compounds can be developed from lignin?

Our research focused on the production of benzazepines derivatives, an important class of pharmaceuticals, to which the anti-anxiety drug diazepam belongs. Conventionally, equal amounts of benazepine and waste are produced, but our catalytic method, in combination with the use of non-toxic, recyclable and biodegradable solvents, allowed the compound to be made without unwanted waste.

After testing roughly 40 of our compounds in assays, our research partner, Anna Hirsch at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) in Germany, was able to identify the promising antibacterial and anticancer properties of 19 of the compounds produced through our research.

Why are green practices so important to pharma?

Cost, regulatory issues, intellectual property demands, and rigorous market competition are all drivers for the industry's increased motivation to change its practices. In addition, companies want to respond to the needs of their customers who are often

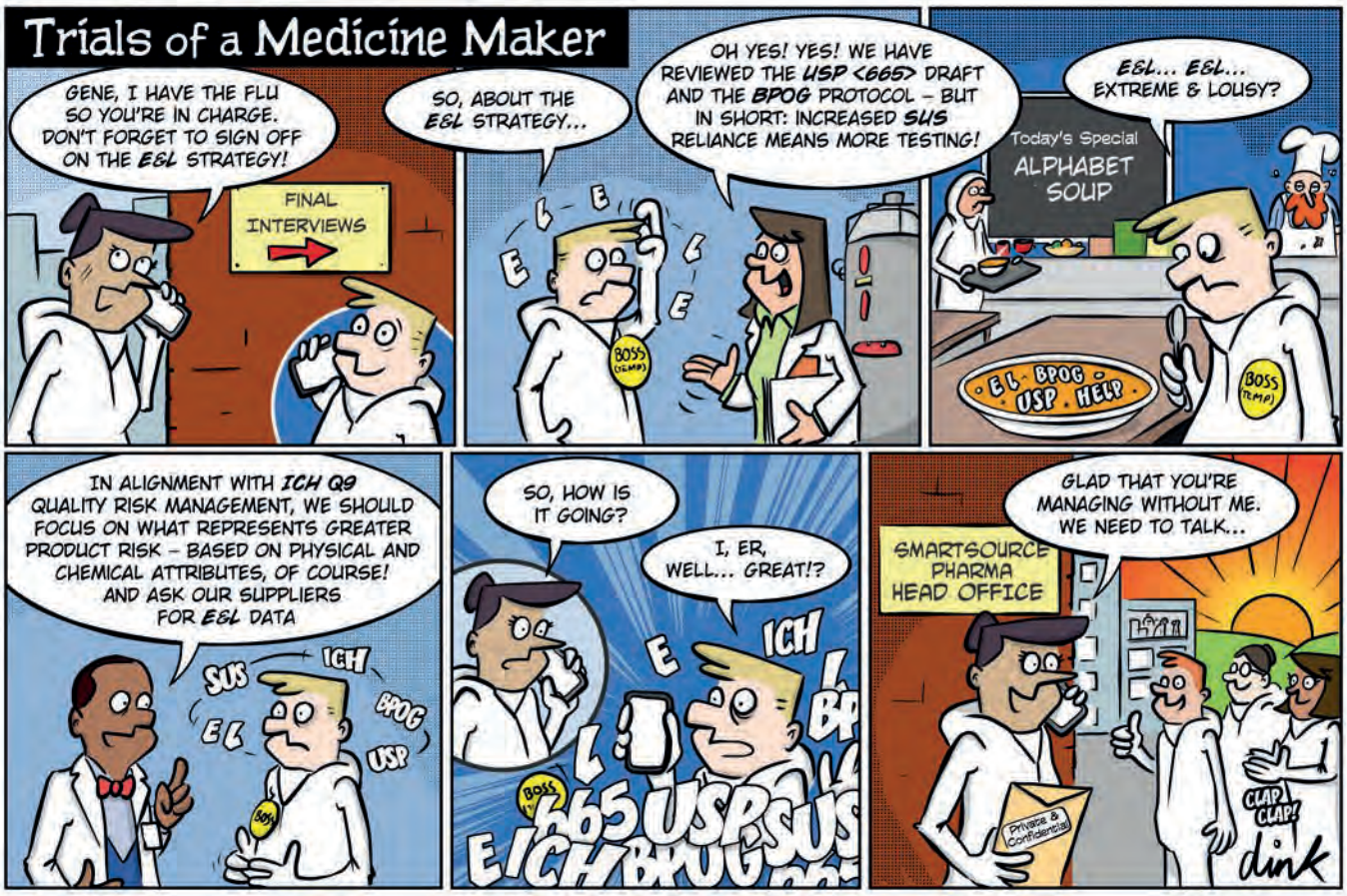
interested in issues related to environmental protection and how renewable the products they purchase are.

Pharma companies have realized that they can no longer rely on purely conventional organic chemistry methods that frequently use multi-step syntheses that typically require tedious separation steps and use copious amounts of solvents. For example, in 2005, the ACS Green Chemistry Institute initiated the ACS GCI Pharmaceutical Roundtable Initiative to encourage the implementation of green chemistry and benign methods in the pharma sector. Almost all major pharmaceutical companies took part, which highlighted the significance of the issue. The industry knows that innovation related to new processes, new chemical routes, and the development of waste-free transformations has to happen at the fundamental scientific level. And that's also why we are so excited about it from the perspective of academic research.

What's next?

I can see two different potential lines of research we can now pursue. One is to identify short and sustainable routes to the production of existing pharmaceuticals and their precursors. The other is to generate new compounds that can elicit biological activity. But either route will help highlight the usefulness of lignins for pharma.

For more adventures featuring Gene and Eva check out our website: themedicinemaker.com/additional-data/cartoons
If you have any ideas you'd like to see in future comic strips about bioprocessing then get in touch with us at info@themedicinemaker.com or look up #TrialsOfAMedicineMaker on Twitter.



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Special Delivery

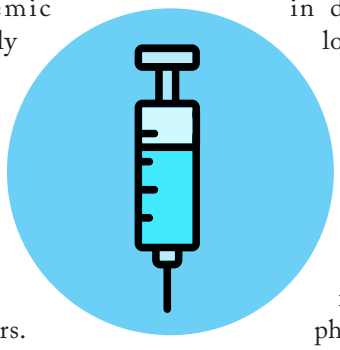
A novel protein-engineered hydrogel offers a less toxic sustained release alternative to synthetic platforms

"Hydrogels are essentially 3D polymer networks," explains Jin Kim Montclare, Professor of Chemical and Biomolecular Engineering at New York University's (NYU's) Tandon School of Engineering. "They have the capacity to encapsulate small molecules, but they can also transition between gel and solution states, which liberates specific compounds into the internal environment in response to stimuli like temperature and acidity."

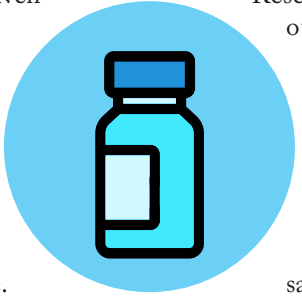
Though academic research has previously demonstrated the ability of synthetically produced hydrogels to be used for drug loading and controlled release, such technologies are often associated with toxic crosslinkers. Montclare says that the protein-engineered gel developed by her team demonstrates the capacity to load and deliver drugs without the risk of harm, as protein hydrogels are more biocompatible than synthetic hydrogels (1).

When exposed to the high temperatures of the internal environment (37 °C), the team's "upper critical solution temperature" (UCST) hydrogel quickly returns to its solution state, allowing for rapid release of any loaded drugs. Ultimately, the aim is to eventually develop protein hydrogels that respond to specific temperatures for different drug delivery applications.

"This is the first thermo-responsive protein hydrogel based on a single coiled-coil protein that transitions from solution to gel at low temperatures through a process of self-assembly, without the need for external agents," says Montclare. "The majority of hydrogels in development have a lower critical solution temperature and, though they are completely miscible at temperatures below a critical value and can be molded into nanoparticles, films and coatings for pharmaceutical use, their solubility decreases as the temperature of a given environment rises."



When the team bound curcumin to their hydrogel, it remained stable at a physiological temperature for two weeks, allowing for sustained drug release. Because the drug leaves the hydrogel mainly through diffusion, the team were limited as to how much control they could exert over release. "The drug release is controlled in the sense that we were able to control the amount of drug product used. However, we'd have to do more studies to see if or how the release is affected at different loading concentrations of curcumin," Montclare adds.



The team now plans to investigate how fluorination of the gel's hydrophobic pore could further improve its thermostability, and will gain more understanding of the effects of pH and ionic strength. "We've also partnered with the Air Force Research Laboratory to further our understanding of the mechanisms behind gelation and are also working in collaboration with other organizations to use our hydrogel as a delivery vehicle to accelerate wound healing in diabetic mice," says Montclare.

Reference

1. *JK Montclare, "Thermoresponsive Protein-Engineered Coiled-Coil Hydrogel for Sustained Small Molecule Release", Biomacromolecules, 3340–3351 (2019).*

In All FAIRness

After joining forces with Roche and Bayer, will the Pistoia Alliance's latest toolkit help companies deal with the data explosion?

Back in 2016, FAIR (Findable, Accessible, Interoperable, Reusable) guiding principles were published in Scientific Data in an attempt to support companies using digital technologies to find, make use of and reuse the data most relevant to them. But new data is produced on a daily basis and many companies have struggled to implement the FAIR measures.

The Pistoia Alliance – an organization seeking to lower the barrier to R&D and innovation – is looking to lend a helping hand. Alongside Roche and Bayer, the Pistoia Alliance has launched its FAIR Implementation project to develop a data management toolkit, which will consist of best practices, training materials, use cases and methodology for change management, to help companies manage the wave of change that digitalization has brought to the pharma industry.

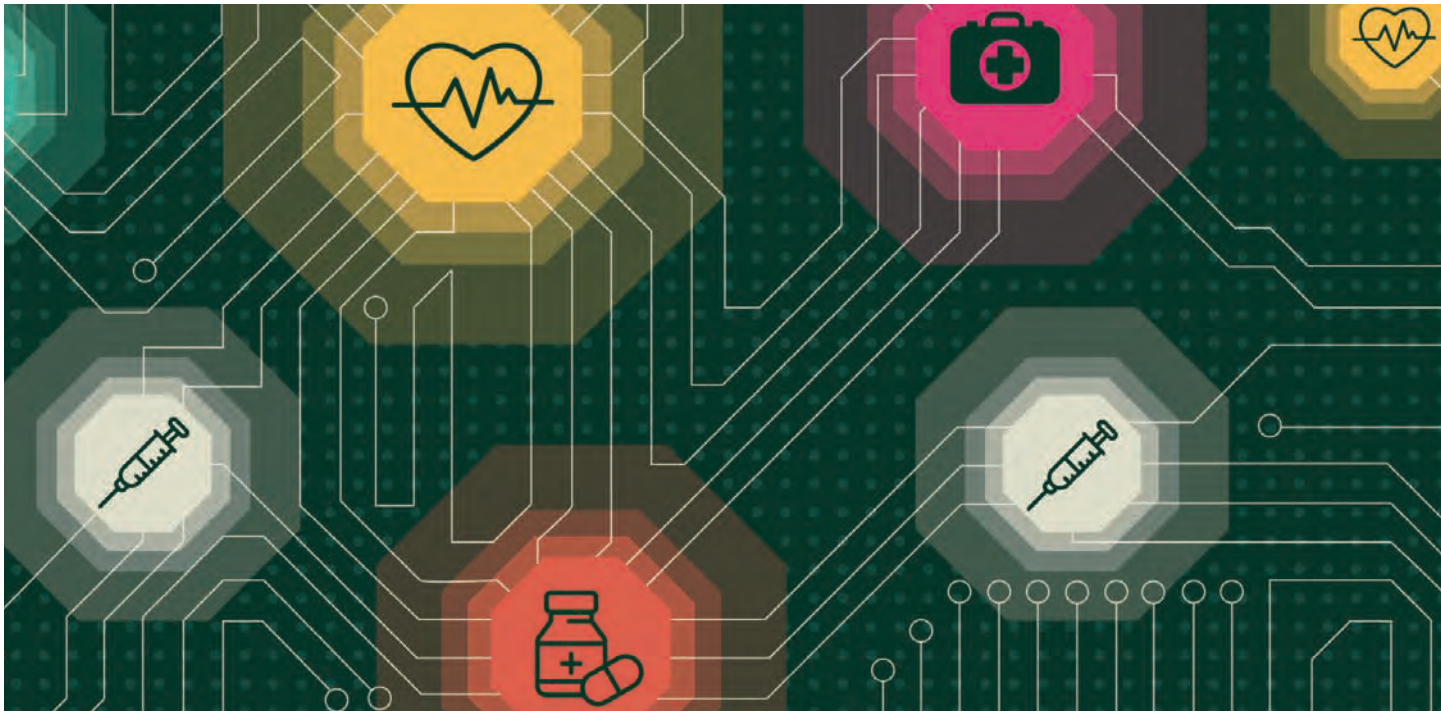
"We created the FAIR project because it is better to work together as industry peers and share our expertise, rather than have each organization attempting to adopt FAIR by itself," explained Ian Harrow, a consultant at the Pistoia Alliance. "As the life sciences industry continues to transform digitally, the sector needs clear and practical guidance on how data and relevant metadata is captured and managed to foster greater collaborative partnerships and more effective application of artificial intelligence and machine learning."

Earlier this year, the Pistoia Alliance hosted several workshops to discuss the toolkit. Harrow explains that it was clear that a number of pharma organizations saw the need for FAIR to make their R&D efforts more productive. "The FAIR Implementation toolkit should help drive crucial change and prevent companies from dealing with the problem of harnessing data in isolation. We hope that the FAIR toolkit being developed by this project will bring together companies to learn from each other and undergo this culture shift together," said Harrow.

Enabling companies to share data should help improve best practices by increasing efficiency and preventing work being repeated unnecessarily. The Pistoia Alliance wants companies to recognize that not all data are proprietary, and non-competitive data could offer great value to an R&D project.

The Pistoia Alliance is also looking for other interested parties and companies to come forward and get involved in the project. To find out more please get in touch with Ian Harrow: ian.harrow@pistoiaalliance.org

When officially launched, the toolkit will be hosted on a user-friendly, open access website.

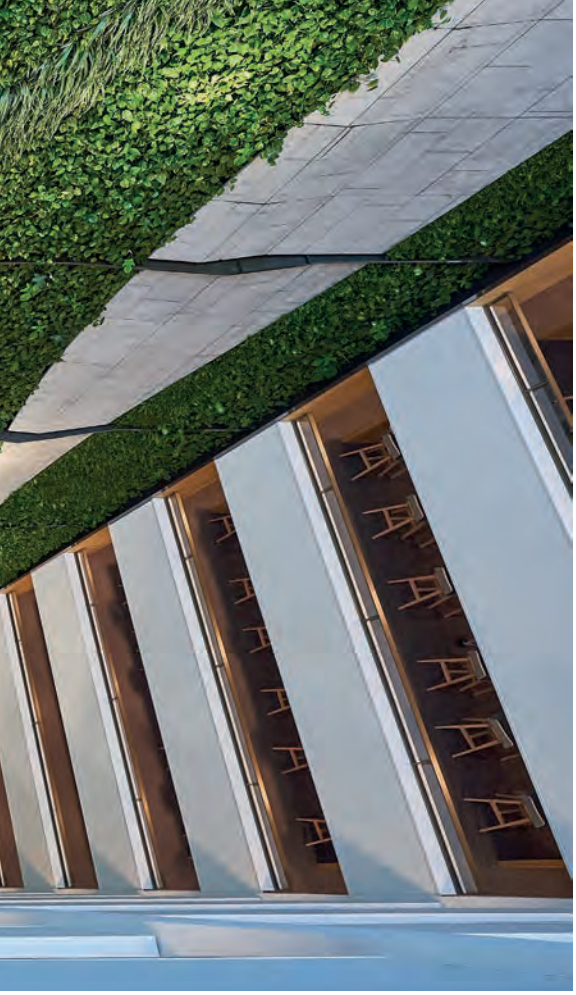


On to Pastures New

Dutch authorities hand over the keys to the EMA's new HQ in the heart of Amsterdam's financial district

The UK's Brexit referendum in 2016 has caused uncertainty for many businesses in the pharma sector. For the EMA, it meant relocation from London to a more secure spot in the European Union. Since March 2019, the EMA has been operating from a temporary site, the Spark building, in Amsterdam Sloterdijk. But now, a purpose-built 19 storey building in Amsterdam's Zuidas area is ready for action. Constructed in under two years, the completion of the new HQ met the EMA's November deadline.

"I actually love the time pressure. It is an amazing challenge to build an office in such a short period of time. Something like this would usually take twice as long," said Frans



Rombouts, Project Director at Heijmans, the construction-services company that took on the build . "On March 8, we started working on the design – a phase that generally takes over eight months; our final design was finished in half a year – an unprecedented achievement in the Netherlands."

Guido Rasi, the EMA's Executive Director, who recently signed the lease, thanked the Dutch authorities for supporting the agency's goal of finishing construction by November, but reflected on the broader challenges of the move in an interview with Agence France Presse (1). "The move was painful. It was painful because it was a choice to move to London, and this came out of the blue. [Our staff] had to find jobs for spouses, schools [for their children, and adapt to] a different way of living."

Though the building doesn't overlook Amsterdam's famous canals, it does boast a 38,000m^2 floor space, a rooftop terrace, and a vertical garden. The building exceeds the "excellent" rating of BREEAM (a sustainability assessment method that is used to masterplan projects, infrastructure and buildings) and has a Bijna EnergieNeutraal Gebouw (BENG – nearly zero-energy building) performance, meaning that at least 50 percent of the energy used in the building comes from sustainable sources.

The 900 staff who will call the new site home should officially begin working there in January 2020, once all technical equipment has been installed. During the transition from the Spark building to the Zuidas site, the EMA says it will limit the number of face-to-face meetings.

Reference

1. *France 24, "Dutch flaunt Brexit booty with EU agency opening". Available at: http://bit.ly/2Lg4EZl.*

The Best of The Best

Don't forget to nominate pharma's most talented individuals for the 2020 Power List!

Whether championing the manufacture of advanced therapies, or working diligently to improve bioprocessing for biopharma drugs, or continuously developing traditional small molecules, the pharmaceutical industry is always striving for the best. For five years, The Medicine Maker has celebrated the people behind the industry's progress through our annual Power List.

Nominations for the 2020 Power List are now open and we want to receive your nominations for the people in the drug development and manufacturing industry that you feel deserve a spot in this prestigious list! Perhaps a hard working colleague, an inspirational mentor, or an industry hero who takes pride in pushing the industry forward.

Nominees will be considered in one of three categories:

- influencers in the small molecule drug industry
- influencers in biopharmaceuticals
- influencers in cell and gene therapy

Nominations from all areas of the industry will be accepted (and you can nominate yourself if you wish!).

Nominate now at http://tmm.txp.to/pl2020-noms

Nominations will close in early January 2020 and the final list will be published in April 2020.

The Digital Age of Formulation and Support

Free "virtual assistant" tools offer a starting point for formulation – and easier access to regulatory documentation and other enabling information

Frank Romanski is a chemical engineer by training, but has spent almost all of his career in the pharma industry. Today, Romanski is part of BASF's Pharma Solutions Business. In recent years, BASF has placed a huge emphasis on digitalization – the company was named Digital Transformer of the Year in 2018 and has also been developing a series of free virtual assistant tools for the pharma industry. We spoke with Romanski to find out more – and to ask why the digital revolution is so important.

What drove the company's digital strategy?

BASF is a relatively old company; we've been around for over 150 years – and it's fair to say we've accumulated a lot of knowledge and data over that time! But you can't simply bring this full wealth of data to market in an analogue way – as there's only so much you can fit into a handbook! Consequently, digitalization is very important for us – and it's also essential for improving the speed and efficiency of the whole drug development process. Pharma development is a very manual process, built within an antiquated system; it is not the fastest or most agile industry because of the regulatory and quality challenges, yet there are certainly ways in which some areas can be easily improved using digital systems. For me, our digitalization strategy was about asking what we could do to make things easier for our customers. How could we make processes faster, more efficient, and save resources? The answer was to provide access to the many support services that BASF Pharma Solutions offers, such as technical, regulatory and quality support, but in a digital, fast, and on-demand way.

How can digital technology benefit formulation?

In the past, we've released handbooks and different guides to assist with formulation – and I'm proud to say that our generic handbook is still widely used, despite being over 20 years old! But with digital technology at our disposal, we can do better.

To start, we have developed ZoomLab, a digital formulation assistant – it is important to note that it is free to use for any formulator. To put it simply, the tool provides a strong starting point for a formulation. The majority of formulators do not start from scratch; they start with an approach or technology that they have used before – the inherent danger being that the formulator may be shoehorning a molecule into an approach that isn't really optimized for it. Often, formulators then follow a trial and error approach, testing several "off the shelf" formulations before finding one that is viable (again, perhaps not optimal). With ZoomLab, you enter some cursory technical information about your API, such as density or particle size, and then target profile, such as tablet size and release profile. Note that none of this information is retained by BASF, and disclosing the detailed chemistry of the molecule is not required to function fully. Next, the formulator selects preferred excipients and/or approaches, and the tool then generates a list of suggested starting formulations – and comprehensive instructions on how to produce them step-by-step.

Most importantly, ZoomLab is not a marketing tool that simply spits out backroom formulations geared at directing the formulator to BASF. It is a tool designed by scientists, for scientists, with the aim of optimizing the final formulation. The recommendations it provides are equivalent to consulting with an industry expert. It is not strictly an artificial intelligence tool, but it uses sophisticated mathematics in terms of how powders and ingredients interact with one another to determine outputs like flowability and tabletability. Finally, it creates a list of potential formulations, together with a 5-star rating system of how they are expected to work. We advise you to go for the

"ZoomLab is not a marketing tool that simply spits out backroom formulations geared at directing the formulator to BASF. It is a tool designed by scientists, for scientists, with the aim of optimizing the final formulation."

approaches with the higher star ratings of course, but the choice is up to the formulator, who may opt for a starting formulation based on additional factors or ingredient limitations.

What other new virtual assistants have you launched?

The second tool is RegXcellence, which is designed to improve interactions around regulatory documents – an area where digital can save a lot of time and stress! Regulatory affairs often involve the consolidation of countless quality and regulatory compliance documents. At BASF, we are constantly sending PDF documents to customers to support regulatory filings. In my former days as an account manager, I would sometimes be emailing over 100 documents per day! It's a tedious and manual process that is limited to person-to-person interactions – and often our salespeople need to speak with BASF regulatory experts to put the right package of documents together.

If a pharma manufacturer receives a question from a regulator about a filing, they may only have a finite amount of time to answer with a supporting document. Here, person-to-person interaction is a hindrance. What if you are dealing with someone in a different time zone? Or if the person you need is on vacation, off sick, or unavailable for other reasons? With RegXcellence, the customer can log in via an online portal, find the ingredients they are using from BASF, and select any, all, or a pre-made package of the documents that they need, all instantly – no longer do they have to wait for someone to send the documents manually.

When we have a new specification or regulatory document, it is usually sent to the customer directly, or upon request. Now, a customer will receive (opt-in) push notifications from the app to explain that a document they downloaded months ago now has an updated form. This way, the customer will be continuously updated. RegXcellence also stores documents a customer has used in the past for easy access.

Our third digital tool is MyProductWorld – a digitized version of all of the brochure-type material that we have, including lists of excipients and APIs, each separated conveniently by application or market segment, such as solutions for solubilization, biologics, or skin delivery applications. It's much easier to navigate as a digital tool; users can locate the chemistry they need for certain areas and order a sample, check compendial status, download supporting documentation through RegXcellence, and start formulating their first lab trials on ZoomLab, all in the same online portal!

All three of these new tools are available from a single digital portal that companies can log into: https://info-mypharma.basf.com.

Why are you personally so passionate about the importance of digitalization in pharma's future?

Digital technology is not a gimmick. I believe our tools – and other digital technology – can really have a big impact on the industry. Pharma companies have emphasized to us that digital tools can really improve their lives, particularly if they can get what they need at the click of a button. However, to be useful, digital tools must also be easy to use, reliable and updated constantly. We've discussed RegXcellence with regulators and they are also really excited about it. To be honest, that was a bit of a surprise, but clearly, the regulatory agencies are quite keen for data transfer to be easier and more transparent. From their perspective, this really helps with compliance.

And I'm delighted to say this is only the start. I can't reveal all that is to come, but ZoomLab was developed with solid oral dosage as a starting point, with newer functionalities such as sustained release and enteric formulations, to come in the near future. Next, we plan to tackle more sophisticated challenges like poor solubility and bioavailability. My core expertise is in solubilization, so I know this is a real headache for the industry. I'd like to think that we can get to the point where tools can point formulators to the right solubilization technology for their molecule, which will save a huge amount of time and energy – and perhaps tools like this can be used to rescue drugs previously killed in the formulation phase because they didn't have adequate bioavailability.

One final note. We discussed here today digital tools that are primarily external, but let's not forget that we can leverage big data and digitalization during synthesis, manufacturing and control, as well as the supply chain. There is huge potential for digitalization to make a real difference to many bottlenecks within the pharma manufacturing world.

In My View

In this opinion section, experts from across the world share a single strongly held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of pharmaceutical development or manufacture. They can be up to 600 words in length and written in the first person.

Contact the editor at: stephanie.sutton @texerepublishing.com

Getting on Target for Alzheimer's

Biogen revitalizes hope for Alzheimer's therapy, but their work highlights why we still need greater selectivity

By Neil Cashman, Chief Scientific Officer at ProMIS Neurosciences; and James Kupiec, Chief Medical Officer at ProMIS Neurosciences

In October 2019, Biogen sent shockwaves through the Alzheimer's community when it reanimated aducanumab, its previously dismissed therapy candidate for Alzheimer's disease. Upon analysis of additional data supporting aducanumab's efficacy in patients with longer term, high-dose exposure, Biogen plans to now submit the drug candidate for FDA approval in early 2020. If approved, aducanumab will be the first disease-modifying therapy for Alzheimer's, which, as a reminder, is currently the only disease on the "top ten" causes of death without treatment.

Biogen's surprising, but welcome, reversal not only puts hope on the horizon for a near-term Alzheimer's treatment, it also – perhaps more importantly – revitalizes work supporting next-generation amyloid beta (Aß)-targeting candidates that can selectively target only its toxic form, beta-amyloid oligomers (AßOs).

Aducanumab gets us only partially there: 35 percent of patients experienced ARIA-E (brain swelling), revealing the critical need for improved AßO-targeting precision to achieve both greater safety and efficacy. At high doses, aducanumab binds more AßOs, supporting its efficacy, but it also binds amyloid plaque, which is off-target and triggers brain swelling. This unwanted binding of an otherwise benign clump of insoluble protein is what leads to this significant dose-limiting side effect of ARIA-E. Regrettably, definitive data demonstrating the neurotoxic role of AßOs were just becoming available when the clinical development program for aducanumab was devised.

By way of background, Aβ is a protein that occurs naturally in the brain and its monomeric form has an important role in cell-to-cell communication.

"Despite clear indications that targeting Aß plaque would not be an effective strategy for disease-modifying AD therapy, therapeutic R&D continued to focus on plaque."

"These largely unprecedented events both revived interest in Aß toxicity and validated decades of research that deepened our understanding of it."

Hundreds of scientific and clinical studies support its role in sporadic AD, which led researchers to propose the so-called amyloid hypothesis in the early 1990s. The hypothesis posited that, in susceptible individuals, high levels of Aβ monomers in the brain lead to the formation of aggregates that eventually combine to form fibrils, and ultimately plaque deposits. At the time, researchers believed that plaque deposits were responsible for the neurotoxicity and atrophy observed in the brains of Alzheimer's patients.

This early hypothesis guided Alzheimer's drug development for several decades while researchers continued to study the role of Aβ in the progression of Alzheimer's disease. Over time, they learned that amyloid plaque was only minimally neurotoxic and, therefore, incapable of causing the massive neuronal cell death found in AD. However, several large studies targeting plaque were already well underway. As these trials continued, researchers continued to amass evidence that sharpened our understanding of the neurotoxic role of AβOs, offering a more precise target for drug development. Between 2000 to 2010, the target was further defined: data showed that soluble, toxic Aβ oligomers propagating in a prion-like manner were in fact the drivers of neurodegeneration and cognitive decline in AD patients, and the causative agent in AD. The Aß hypothesis was revised to reflect this emerging consensus.

What happened next was perplexing. Despite clear indications that targeting Aß plaque would not be an effective strategy for disease-modifying AD therapy, therapeutic R&D continued to focus on plaque. Call it exuberance. Call it desperation. Call it a cabal. Whatever the reason, drug makers didn't end their Aβ plaque trials. Even more dumbfounding, they created new ones, all focused on the wrong form of Aß.

As study failures mounted – somewhat spectacularly in phases II and III – enthusiasm for the amyloid hypothesis disintegrated; along with it, the community's most validated, advanced effort toward long-awaited therapy. Things looked bleak for all involved: big pharma had largely abandoned interest in Alzheimer's disease; small biotechs engaged in next-generation efforts targeting the correct molecular species of Aβ faced dire uncertainty, and; millions of patients and their desperate families were left stranded, literally without a life line.

Then came Biogen's stunning reversal. On October 22, Biogen said re-analyses of data from their late-stage phase III studies show that aducanumab, given at higher doses over a long duration, did indeed reduce the rate of patients' cognitive decline. Biogen brought these data to a seemingly receptive FDA, which invited Biogen's regulatory submission. These largely unprecedented events both revived interest in Aß toxicity and validated decades of research that deepened our understanding of it.

A closer look at Biogen's data reveals a model consistent with one that many proponents of the AßO hypothesis have concluded: a safe, effective disease-modifying therapy for AD must be

highly selective for the toxic form – and only the toxic form – of Aß (i.e, the Aß oligomer). As noted above, despite improvement revealed in Biogen's close examination of its final clinical outcome data, 35 percent of patients still experienced adverse ARIA-E despite attempts to minimize this swelling by titrating aducanumab. Clinical benefit is dependent upon the amount of the therapeutic antibody that reaches the toxic oligomers. However, higher dosing with aducanumab cannot be achieved without an even higher risk of ARIA-E because of its off-target binding to plaque and vascular deposits of beta-amyloid. The bottom line: aducanumab is only weakly selective for the toxic Aβ oligomers. What's needed – and anticipated – is an antibody that selectively targets Aβ oligomers to provide greater clinical benefit and safety.

Biogen has bravely followed its data. Should aducanumab prevail, the AD community owes its researchers a great deal of gratitude, not only for delivering the first therapy for this devastating disease but also for reopening a window of promising possibilities for next-generation candidates targeting soluble toxic Aβ oligomers – not plaque, not monomers and not fibrils. Significantly, recent advances in fluid-based biomarkers will enable earlier "go/no go" decisions as drug candidates move through clinical development. When next-generation therapeutics become available for clinical testing, we will not have to wait until phase 3 to decide whether they provide real value to patients. We daresay, the tide is finally turning.

Why Small Molecules Are Still a Big Deal

Though large molecules and advanced therapies currently dominate headlines, small molecules remain of great significance for the industry – and patients

By Gordon Bates, President, Chemical Division, Lonza Pharma & Biotech

In 2018, major news included Abbvie's Humira, a monoclonal antibody (mAb) approved for the treatment of arthritis and a range of diseases in the inflammation and immunology space, leading the pack of global highest-revenue drugs with sales of around $20 billion. In addition, innovative cell and gene therapies seem ready to revolutionize treatment for diseases from sickle-cell anemia to inherited genetic forms of blindness; the FDA expects to approve 10–20 cell and gene therapy products a year by 2025.

But scratch beneath the surface and you'll see that biologics are not the only big players in the pharma space. Small molecules continue to play a significant role in the development of innovative treatments that benefit the lives of patients around the world. Specialty medicines are increasingly driving global pharma growth, especially in developed markets, with approximately half of specialty sales attributable to small molecule applications.

The continuing role of small molecules is also visible in recent approval trends and the current pipeline. In 2018, the FDA approved 59 new drugs, 71 percent of which were small molecules (29 percent were biologics). Specialty meds – which can be defined as high-cost, high-complexity medicines – are often associated with biologics and are highly visible in today's pipeline, but small molecules represent an estimated 60 percent share versus large molecules. We are also seeing the impact of regulatory incentives with regards to orphan medicines specifically, with orphan designations playing an increasing role in both small and large molecule approvals, and accounting for more than half of US and European approvals in 2018.

"The continuing role of small molecules is also visible in recent approval trends and the current pipeline."

Small molecules continue to play a

role in innovative treatments for the four major indications that account for more than half of global pharma growth: oncology, diabetes, autoimmune, and respiratory diseases. For example, small molecule protein kinase inhibitors, of which the FDA has approved 48, are becoming more important in cancer therapy. Another area of growth entails the use of small and large molecules in combination; antibody drug conjugates (ADC), which couple potent small molecule payloads with the targeting capabilities of monoclonal antibodies, allowing for more precise treatment of cancer (and fewer side effects than standard chemotherapy).

The small molecule landscape is changing in terms of drug product complexity, molecule potency, manufacturing trends, and industry makeup. How the industry responds will shape the next chapter of small molecule drug development. Key trends include:

- Small molecules and their applications are becoming increasingly complex. The majority of today's pipeline consists of poorly soluble molecules that require enabling technology to advance to the clinic and beyond. Target product profiles for new drug products are also becoming more challenging, as therapies become more precise. Failing to reach acceptable bioavailability can be the limiting factor in advancing many new chemical entities.
- Demand for high-potency APIs is on the rise. Over a quarter of drug products in development contain highly potent APIs (HPAPIs), driven by improved targeting in treatments for cancer, diabetes, autoimmune diseases and other indications. For oncology drugs, the proportion with a HPAPI component is closer to three-quarters. These APIs are highly toxic and require specialized manufacturing and handling capabilities, which many smaller innovator firms may not want to build in-house.
- Small companies are driving innovation. The vast majority of small molecule drugs in development are held by small or "emerging" companies with fewer than 100 employees. Our analysis suggests that these companies account for approximately 4,400 candidate compounds – or 70 percent of the small-molecule pipeline. These companies are increasingly bringing successful compounds to commercial production, and typically require access to enabling technologies, development, and manufacturing partners to do so.
- The need for speed. Speed has always been important – but today it is more critical than ever because of the rise in specialty drugs, orphan and breakthrough designations, as well as increasing reliance on the FDA's NDA 505(b)2 pathway. Since smaller companies can be reliant on one or only a few compounds, establishing a clear line of sight to clinical studies and commercialization is imperative. They often need access to phase-appropriate development services, infrastructure, and knowhow to accelerate time to first-in-human studies, through later-phase clinical studies, and for rapid scale-up.
- One size does not fit all. Flexibility is increasingly important when aligning manufacturing services with more specialized and lower-volume drug products. Forecasts are more challenging for specialty products with finite patient populations, and flexible business models and assets are essential. Flexibility further extends across the drug development cycle where integrated development and commercialization can be of value to certain companies and/or drug programs. CDMOs that offer an end-to-end spectrum of flexible development and manufacturing capabilities, as well as complementary service options such as regulatory expertise and counsel, are natural partners for emerging innovator firms or specific innovator programs. For example, ADC programs supported through integrated payload, monoclonal antibody, and conjugation services can bring significant value to customers.

"How the industry responds will shape the next chapter of small molecule drug development."

In short, small molecules are still a big deal – and will be for the foreseeable future. CDMOs with specialized technologies and expertise will continue to help pharma companies advance their compounds. The ability to tailor services to specific customers and drug programs will play an increasingly important role in accelerating patient access to innovative drugs.

The Future of Biopharma – Big Needs and Smart Solutions

In this final article of the series – based on the "Bioprocess Days" event in May 2019 – we interview Günter Jagschies, Senior Director, Strategic Consumer Relations at GE Healthcare, to discuss the evolution of the biopharma industry. The take home: we must never forget unmet needs when developing new medicines.

Why do you find the biopharma industry so inspiring?

One of my personal areas of study and research is the global healthcare situation, particularly the economics and affordability of healthcare. I am passionate about biopharma's role in bringing forward new treatments and solutions for the biggest healthcare problems. The industry has made incredible advances – and this is what motivates me day to day. We work with many different pharma companies, so are involved with a huge percentage of drugs that come to market. I always wanted to be a biochemist and I was very drawn to biopharma. I've never looked elsewhere and I've never worked for any other company either. Today, I have an ambassador role for the business. I do a lot of traveling, giving customer seminars, offering advice, speaking at conferences, and publishing articles. It's really exciting to share knowledge in this way.

What are the biggest advances to come out of the biopharma field?

When I started out in the industry, biopharma was just starting with insulin and the first proteins. For many years, there was only one insulin drug available and then slowly the others started to come through. And now there are many different options for patients! The industry has also diversified from smaller proteins made in bacteria to incredibly large, complex constructs and viruses. And the revenue coming into the industry is now huge.

Manufacturing technologies have also come a long way. There is now increasing use of single-use systems and hybrid technologies, but I think that it is the increases in the productivity of bioreactors that have had the biggest impact. In the last five years, we have gone from titers of around 5 g to 50 g per liter. Five years ago, no one would have thought such high titers would be achievable. Now, it is possible to get the amount of product required from one bioreactor, which opens the door to smaller facilities with a lower CapEx.

What is your vision for the future of biopharma facilities?

My vision for the future is smart and small – with increased flexibility and productivity. Digital tools will play an important role in the factory of the future, integrating all aspects of process monitoring and allowing manufacturers to make rapid decisions or corrections in real time. Biopharma facilities will also be small, working either with just one product in a large quantity or with multiple products, and most likely using connected processing.

Where do the main opportunities lie in the field?

Unmet medical needs should be the focus. There are still many diseases that have no treatments at all, so there are plenty of opportunities for companies to develop new drugs to treat the symptoms of certain diseases, or even cure the disease completely. Today, with the advent of cell and gene therapies, there are so many more options when it comes to developing treatments. We also shouldn't forget new vaccines – prevention is always better than cure!

The biggest opportunities lie in some of the most difficult areas: cancer, Alzheimer's, Parkinson's and even diabetes – which is

Patients Need Better Biosimilars

When it comes to meeting unmet needs, biosimilars have a huge role to play, as they introduce competition to the market that can help to bring down the cost of expensive biopharmaceuticals. However, there is also an argument that biosimilars are not enough – why not update and improve on existing biologics with biobetters? Another speaker at the "Bioprocess Days" event was Soon Jae Park, CEO of Alteogen, who gave insight into the challenges of establishing a biosimilars business in South Korea.

Have you always worked with biosimilars?

After studying for my post-doc in the US, I joined LG Life Science, which was, at the time, known as LG Chemical. The company was the first in Korea dedicated to biological drugs – both new biological entities and biosimilars. I was one of the early members of the company and, during my time there, I worked on many biosimilar programs. We were one of the first biosimilar companies in the world and we obtained European approval for a human growth hormone biosimilar in 2006.

I started Alteogen in 2008 with Hye-Shin Chung – and she is our Chief Scientific Officer today. Our focus is on next-generation biobetters with improved efficacy.

What main challenges have you faced?

A few years ago, Korean biotech companies could not get enough funding because there was a perceived lack of value in the country's biotech. This also impacted us – the slow supply of funding made it very difficult to accelerate our program! Fortunately, the situation is quite different today and there is a lot more venture capital funding available for biotech – in fact, it's one of the top sectors for investment and is also attracting investment from overseas.

How can biosimilars be made better?

We focus on three areas: long-acting biobetters, proprietary antibody-drug conjugates, and antibody biosimilars with complexity. We have developed some special technologies to help us. Our NexP Fusion Technology, for example, increases the half-life of any biologic using DNA recombination and human A1AT, and means that the drug needs to be administered less frequently. We also use our NexMab ADC Technology and Hybrozyme Technology.

What do you enjoy most about the sector?

A friend of mine develops smartphones but, after six months, a smartphone is out of date. Things can change very quickly and it can be challenging to continually innovate in such a competitive landscape. Pharma and biotech have much longer timelines but it means that even if there are setbacks in the middle of the pathway, there can still be room to recover. Of course, sometimes it takes too long to develop something in the biotech world but the important part is that there is an end goal in sight. Eventually, we will arrive at that goal. And if you enjoy the journey then it's a very good sector to work in!

still not fully understood. The industry should not give up on these challenging fields because there will be huge rewards for the companies that make an impact on any of these diseases.

Which challenges will require the most focus?

The greatest challenge now is the affordability of the new medicines developed. In the press and media, there are new stories every week about how expensive some of these drugs are. On one hand it may cost $1000 per year for insulin treatments, on the other hand there are therapies costing over $500,000 per patient, per year. It's obvious that few people (or governments) can afford that. We need to find a way to bring the price down. Some of this may come from new advances in manufacturing, but it may also be that the industry's business models need to change – perhaps being paid for success. And that's not easy because it goes against corporate dogma. But some companies are willing to embrace new ideas; Novartis, for example, demonstrated its openness for new payment models with Kymriah and has been exploring an outcomes-based payment model for the therapy in some countries. I don't think it is quite clear yet exactly how payment models like this will work in broader patient populations, but it's a step in the right direction. It should also be noted in this context that the pharma industry is not the only driver of healthcare costs – there are many other factors that impact the situation, such as hospital systems, insurance and general complexity in terms of how healthcare is delivered.

Ultimately, many medicines are only available to a very small percentage of the global population. We need to aspire to treat every patient in the world – and that means we need some good solutions to the affordability challenge.

THE INNOVATION AWARDS **2019**

the **Medicine Maker**

THE SHAPE OF THINGS TO COME

After a vibrant year of advances in pharmaceutical development and manufacturing technologies, we present The Medicine Maker 2019 Innovation Awards. From single-use bioreactors, to formulation prediction tools, to Industry 4.0 technologies, we celebrate the solutions that help manufacturers make better medicines.

WHAT ARE THE INNOVATION AWARDS?

The Medicine Maker Innovation Awards, published every December, highlight the most groundbreaking drug development and manufacturing technologies that have been released onto the market over the course of the year. Nominations were collected via an online form available at *www.themedicinemaker.com* during 2019.

The Innovation Awards will be back in 2020! Nominations will open in late Spring 2020.

ACGCAPS H+

Capsules with no gelling agent suitable for hygroscopic and moisture-sensitive formulations

Produced by ACG

Suitable for hygroscopic and moisture-sensitive formulations, the ACGcaps H+ capsule is pH-independent and non-ionic, and so complies with the requirements of dissolution performance across all biological pH ranges. The capsules are suitable for granules, powders and pellets for both prescription and non-prescription pharmaceutical ingredients.

Potential impact:
The capsules contain no gelatin, wheat, gluten, animal by-products or starch, allowing them to support the increasing consumer demand for clean label and vegetarian capsule options. In addition, the capsules overcome potential cross-linking issues (a problem with gelatin-based capsules) that can hamper dissolution performance.

AVIONICS

A data monitoring system for real-time tracking of line-equipment efficiency

Produced by Antares Vision

Data are clearly important, but how can they be used to boost pharmaceutical efficiencies? Avionics is a software tool for monitoring equipment performance and efficiency throughout the production process. Among other important metrics, Avionics monitors production status, instant and accumulated speed, overall equipment efficiency and camera performances. The software can be installed as an add-on, drop-in module on lines without impacting previously implemented validation procedures or the performance of existing systems. It complies with regulations, including serialization and aggregation mandates.

Potential impact:
Avionics was designed to help pharma companies to leverage data – initially generated to comply with serialization mandates. Aggregation of performance data can give an overall picture of production processes, helping companies to make data-driven decisions that can improve efficiencies.

BIOCONTINUUM BUFFER DELIVERY PLATFORM

An integrated solution for buffer preparation and management

Produced by Merck

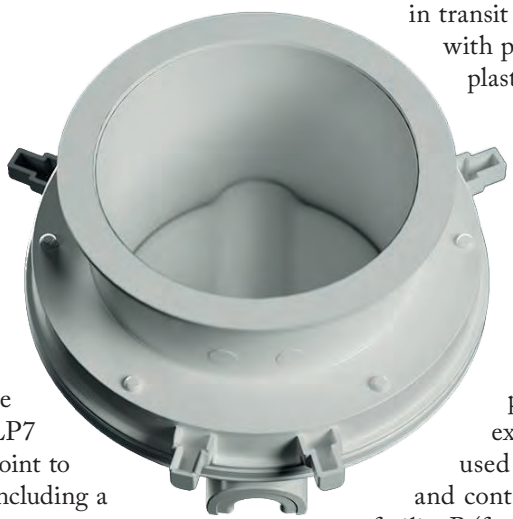
The BioContinuum Buffer Delivery Platform is a configurable offering of buffer concentrates, buffer dilution system, single-use assemblies, and services tailored to provide a high accuracy in buffer preparation and management. The buffer dilution system design and pumps allow for dilution of buffers up to 50:1, including buffers with low conductivity. According to Merck, in a 2000 L bioreactor facility, by using buffer concentrates, the platform delivers an 18 percent reduction in cleanroom area compared with traditional buffer preparation methods.

Potential impact:
Biomanufacturing requires large volumes of buffers for downstream processing, which can often be a bottleneck. As processes evolve and intensify, the focus has shifted to reducing bottlenecks, footprint and capital expenditures while delivering the right buffers at the right time and specifications. Merck's new platform can supply process buffers from the point of manufacturing to the point of use at a "fraction of the resources and facility space."

CHARGEPOINT MULTI-SITE SOLUTION

A disposable solution for transferring high potency and sterile material

Produced by ChargePoint Technology



The ChargePoint Multi-Site solution combines the new ChargePoint Single-Use Passive (SUP), a disposable version of the company's passive mating half of the established ChargePoint Split Butterfly Valve, with the new ChargeBag PE-S single-use packaging. The result allows manufacturers to easily transfer sterile pharmaceutical powders – either between process steps or between facilities. The ChargeBag Pe-S is made from HiPure ULP7 film, a proprietary film made by ChargePoint to meet the demands of aseptic processing, including a high level of integrity, purity and robustness.

Potential impact:
Today, more pharmaceutical companies than ever before have multiple manufacturing locations, resulting in more drug products being moved between facilities. Assuring the integrity of expensive, sensitive powders whilst in transit is a challenge that is currently met with packaging solutions, such as fiber or plastic drums with flexible liners housing the powder form drug product. Though these options meet transportation needs, it often gives facilities a headache when it comes to filling, sealing, handling and emptying the packages safely without compromising the product. ChargePoint's new off-the-shelf solution offers a method of contained powder transfer within facility A (for example, drug supply) and can also be used as a product's primary packaging and container closure for transportation to facility B (for example, drug product formulation).

EVERIC

Modular vials suitable for high potency drugs

Produced by SCHOTT AG, Pharmaceutical Systems

Schott describes Everic as "ultra-pure type-I glass vials" that are suitable for high potency drugs and biologics, and meet the drug stability needs of low-fill drugs (dosages under 1 mL). The vials are offered as a modular concept; pharma manufacturers can choose different elements based on their drug requirements, the administration process and the patient group. For example, Everic Pure vials have a chemically homogeneous inner surface to ensure drug stability; Everic Strong features an improved geometry for improved shock and pressure resistance during the filling process or transport; and Everic Smooth has an outer coating that helps the vials pass more smoothly through production processes. In addition, the particle formation that can occur when pharmaceutical vials rub against each other on filling lines is significantly reduced.

Potential impact:
Primary packaging must be designed to reduce the potential for interaction between the drug and container as much as possible. At the same time, high development costs put pressure on manufacturers to be as efficient as possible during manufacturing operations. With its modular approach, EVERIC helps manufacturers to balance both aspects with stable storage and efficient filling.

F10i

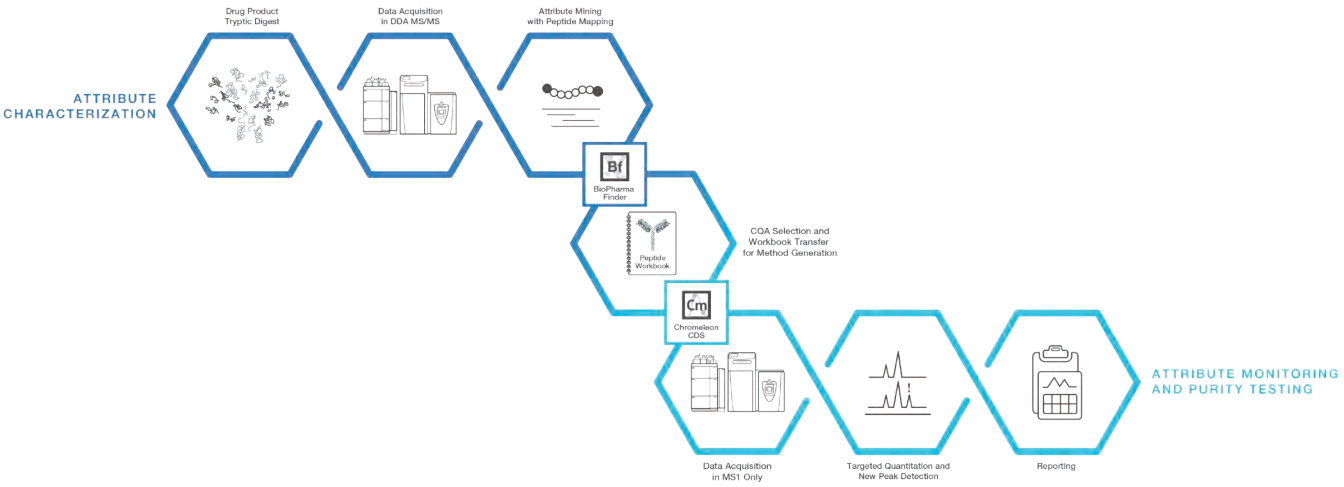
A digital-ready tablet press

Produced by Fette Compacting

The F10i is the first machine of the next generation of Fette Compacting's I Series and is a single rotary press ideally suited for small batches – and optionally also for highly active substances. The system also includes a handling arm to support the operator when changing the turrets, and a mechanical manual turret clamping system. Reflecting the pharma industry's growing interest in Industry 4.0, the press has also been designed with connectivity in mind, with open interfaces for connections to the Internet of Things and manufacturing execution systems.

Potential impact:

The increased use of potent pharmaceuticals means that containment has become a key issue in production; is possible that "dust-proof" could eventually become the minimum standard for pharmaceutical machinery. The new i-Series has a dust-proof design in its most basic version, while window flaps with double-safety barrier systems help to further ensure operator protection when using active substances.



HR MULTI-ATTRIBUTE METHOD FOR BIOPHARMA ANALYSIS

A high-resolution mass spectrometry-based workflow for biopharma characterization and quality control

Produced by Thermo Fisher Scientific

Biotherapeutics are complex to manufacture and confidently characterize, requiring numerous conventional methods to assess individual critical quality attributes. The HR Multi-Attribute Method is an automated, instrument-based approach that can assess multiple CQAs, as well as monitor the manufacturing process. It can potentially replace several conventional methods with one workflow. The system can be used for early development through to quality control and lot release environments.

Potential impact:

The goal of biopharma development and manufacturing is to deliver the highest quality product at the lowest cost and in the shortest possible time frame. Full characterization with the most specific level of information can make a significant difference to achieving these goals. This workflow solution provides standardization and can deliver consistent results across multiple instruments and sites.

HYPERFORMA DYNADRIVE

A single-use bioreactor with improved design, performance, and scalability to larger sizes

Produced by Thermo Fisher Scientific

Thermo Fisher Scientific has updated its range of HyPerforma DynaDrive single-use bioreactors to suit scales of 50 L up to 5000 L. The hardware, flexible drive train with multiple impellers and sparging approach were all designed to optimize mixing dynamics, scale and performance. The turn-down ratio is 10:1 for 50 L and 20:1 for larger sizes. The high power input per volume and volumetric mass transfer performance (measured by kLa) should allow for viable cell densities of around 100 million cells/mL.

Potential impact:
The benefits of single use are well known in the industry, including the reduced risk of contamination and faster turn-around times through the elimination of CIP and SIP. This bioreactor range has been designed to accommodate modern cell line processes across multiple sizes, to maximize facility footprint and to reduce steps in the seed train processes. According to the company, this is the first single-use bioreactor available in 5000 L size to meet production needs and maximize facility footprint.

AND THE WINNER IS...

From traditional small molecules to biotherapeutics to ingenious cell and gene therapies, there is a huge variety in the types of medicines that pharmaceutical companies can produce, with each requiring specific advances in processes and equipment. The solutions highlighted in the Innovation Awards demonstrate serious dedication to all areas of drug development.

But which technology is truly the most innovative? Go to tmm.txp.to/vote-innovation19 to vote for your favorite technology showcased here.
We will publish the development story behind the most popular technology in a 2020 issue of The Medicine Maker. Voting will close on March 11, 2020.

INFINITYLAB LC/MSD IQ

A mass selective detector that delivers confidence in UV analysis results

Produced by Agilent Technologies

The InfinityLab LC/MSD iQ is a mass selective detector suitable for small molecule analysis in pharmaceutical drug discovery, development, quality assurance and quality control, as well as academia and other labs that require mass spectral data for making data-driven decisions. It is designed for users who are looking for more certainty in their LC-based results, and uses Agilent's OpenLab CDS software for data collection, analysis, and reporting.

The InfinityLab LC/MSD iQ resides beneath the Agilent's InfinityLab HPLC stack, to help save on lab space, while the InfinityLab Flex Bench MS, enables mobility, modular mounting of all system components, with integrated waste management, system noise reduction and easy access to all system areas.

Potential impact:

The system was designed with overall lab productivity in mind – the early maintenance feedback features, for example, aim to help lab managers plan routine maintenance around their schedules. The system also incorporates intelligent instrument health tracking to ensure reliable and routine operation. Before sample analysis, an overall assessment of the whole liquid chromatography-mass spectrometry system is performed with a system suitability check.

KUBIO BOX FOR VIRAL VECTORS

A modular platform for the manufacture of viral vectors

Produced by GE Healthcare

Unlike traditional facility repurposing or retro-fitting projects that typically require significant engineering and design resources, as well as the need to appropriately select and procure manufacturing process equipment, the KUBio box for viral vectors is a turn-key product. It is a modular platform that provides fast access to viral vector manufacturing capacity. It is designed to fit within a simple facility shell space, accommodating end-users that are re-purposing or retro-fitting existing spaces.

Potential impact:
There are estimated to be over 700 active clinical trials involving cell and gene therapy – and the vast majority of these make use of viral vectors. This rapid growth has led to viral vector supply issues with a shortage in readily available manufacturing capacity. New manufacturing platforms are needed to address the long wait times at contract manufacturing organizations and lengthy facility build timelines. KUBio box for viral vectors can provide quick access to modular viral vector manufacturing capacity.

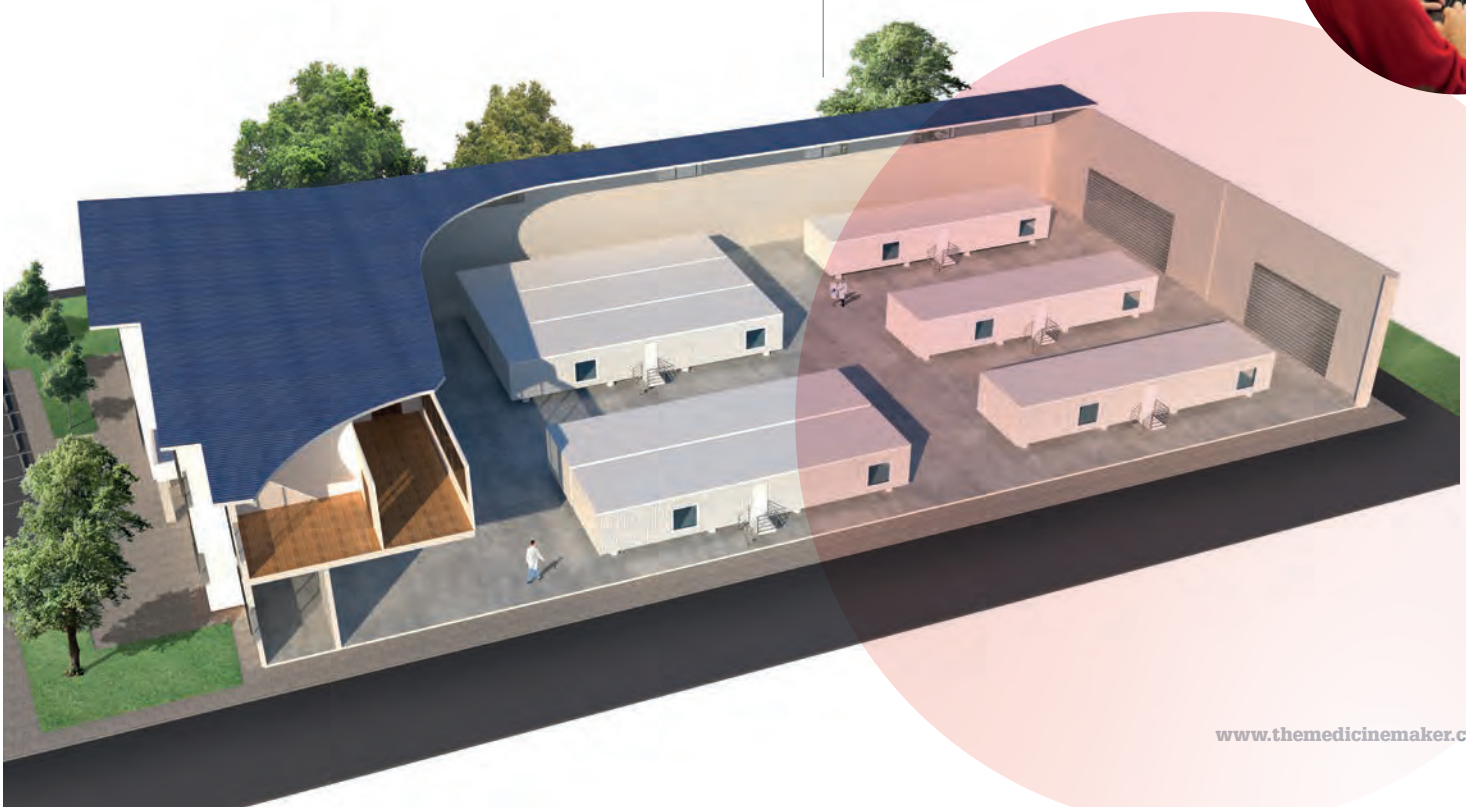
PRIME

A tool to enable faster, leaner API process development

Produced by Hovione Pharmascience

PRIME is a data- and knowledge-based assessment tool to enable development by design. Process development is normally guided by the knowledge of different chemists and is not always focused on a set target. The PRIME tool helps to guide chemists to the points that need to be addressed first to improve process robustness. It also allows statistics from the process to be compared with industry averages. Hovione can use the tool to generate reports for clients.

Potential impact:
Pharma manufacturers face significant pressure to make processes more efficient to bring down the time and cost associated with drug development. PRIME aims to allow manufacturers to develop robust processes in a leaner manner by allowing efficiency to be quantified numerically. Data generated by the tool are useful indicators of what process parameters need to change for improvement.



SCALE-X

Fixed-bed bioreactors that provide a chained and intensified approach to viral vector production

Produced by Univercells

The portfolio of scale-X fixed-bed bioreactors are designed to lower the costs of viral production for both vaccines and gene therapies. Multiple bioprocessing steps are "chained" into one, reducing the footprint of the bioprocess while improving the reliability of production. The fixed-bed design enables scalability from benchtop production to commercial-scale and the bioreactor can also be chained with subsequent downstream processing through integration with the company's NevoLine biomanufacturing platform for complete bioproduction.

Potential impact:
Univercells claims that many existing technologies for producing viral vectors are expensive, difficult to operate, difficult to scale to match commercial demand, or lack the robustness required to successfully and reproducibly ensure high-quality production. The scale-X bioreactor design results in the ability to integrate very high production capacities within a small facility footprint. For gene therapy, this contributes to reducing the development and production costs which are currently still very high, thereby contributing to improved accessibility of novel therapies.

STA-PURE FLEXIBLE FREEZE CONTAINER

Containers for protecting bulk drug substance during cold chain handling

Produced by W. L. Gore & Associates, Gore PharmBIO Products

GORE STA-PURE Flexible Freeze Containers are constructed of a high-purity, biocompatible fluoropolymer composite film – selected for its durability and low extractables profile. GORE has also used a patented bag design that is engineered to maximize container strength. Whereas some companies supply bags based on performance data from film-only durability testing, Gore says it has developed performance testing in alignment with how the product will actually be used. For example, in impact testing, bags were filled with solution, frozen to -86 °C (-123 F) and then dropped from a height of 3 feet. The containers remained strong and did not crack or break, even through five successive freeze/thaw cycles.

Potential impact:
Pharmaceutical manufacturers need durable, high purity materials for storage. Traditional polymer-based containers can become brittle at low temperatures, causing them to break or leak. Manufacturers need solutions that help minimize the risk of container failure and enable them to securely transport frozen bulk drug material.

STARTAB, DIRECTLY COMPRESSIBLE STARCH

Starch-based excipient designed for direct compression

Produced by Colorcon

The size and shape of StarTab particles have been specifically designed to provide excellent flow and compressibility, even on high-speed compression machines. The excipient also provides good tablet hardness and a low disintegration time, allowing formulators to reduce the number of excipients needed in a formulation; for example, superdisintegrants are not required. StarTab also helps enhance the stability of moisture-sensitive active pharmaceutical ingredients.

Potential impact:
StarTab is designed to help formulation scientists simplify formulation. StarTab enables formulations to be made into tablets using direct compression instead of the more complicated wet granulation, shortening development time and reducing the total costs.

PREVIOUS WINNER

The grand winner of the 2018 Innovation Awards was Catalent's Zydis Ultra, an orally disintegrating tablet (ODT) made using resonant acoustic mixing and lyophilization. Zydis Ultra broadens the applicability of the original Zydis technology to a wider range of drug molecules. Oral drug delivery is well recognized as a convenient, economical and safe route of administration. ODTs offer the convenience of "medicine on the go," as they disintegrate quickly in the mouth, usually without the need for water. Catalent believes that Zydis ODT technology can be particularly valuable for boosting patient compliance. Patients suffering from psychiatric conditions, for example, can be prone to refusing medicine (patients may attempt to regurgitate medicine or conceal tablets in their mouths); ODTs disperse too rapidly for such tactics.

The use of resonant acoustic mixing in Zydis Ultra allows the API to be coated for excellent taste masking, and drug loading that is three to four times higher than with a conventional Zydis ODT. Resonant acoustic mixing can coat particles less than 100 µm with minimum impact on final particle size, whereas conventional coating typically results in significantly larger particles that can lead to a grittier mouthfeel in ODTs. Researchers at Catalent have been able to formulate both ibuprofen and acetaminophen (paracetamol) using the technology.

Catalent announced a $27 million investment in March 2019 to help commercialize Zydis Ultra technology. The Zydis development and manufacturing operation is located at the company's 250,000 square foot site in Swindon, UK.

Read the full story behind the development of Zydis Ultra at: https://themedicinemaker.com/manufacture/its-a-kind-of-formulation-magic

XCELERATE

A service for optimizing the design and implementation of active packaging

Produced by Aptar CSP Technologies

Combining Aptar CSP Technologies' active packaging with FreeThink Technologies' expertise in accelerated shelf-life determination, the Xcelerate service aims to help optimize the design of active packaging solutions. The service was launched in response to the increasing complexity of matching moisture- and oxygen-sensitive medicines with their ideal packaging solutions. The Xcelerate process determines a drug product's moisture and oxygen sensitivity using stability studies open to specified environmental conditions, and then uses modeling to create theoretical package designs.

Potential impact:
As drug companies produce more potent APIs, larger molecules and modified release profiles, there is increased risk for stability issues associated with moisture, oxygen and volatile reactives. More modern dosage forms, such as chewable and disintegrating tablets, can also encounter significant shelf life challenges with respect to humidity sensitivity. A customized approach to these challenges can help avoid repetitive design processes and reformulations caused by stability test failures.

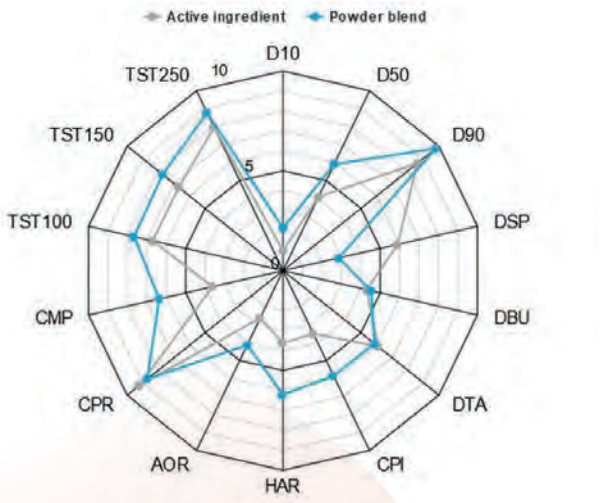
ZOOMLAB

A formulation prediction tool for small molecule pharmaceuticals

Produced by BASF

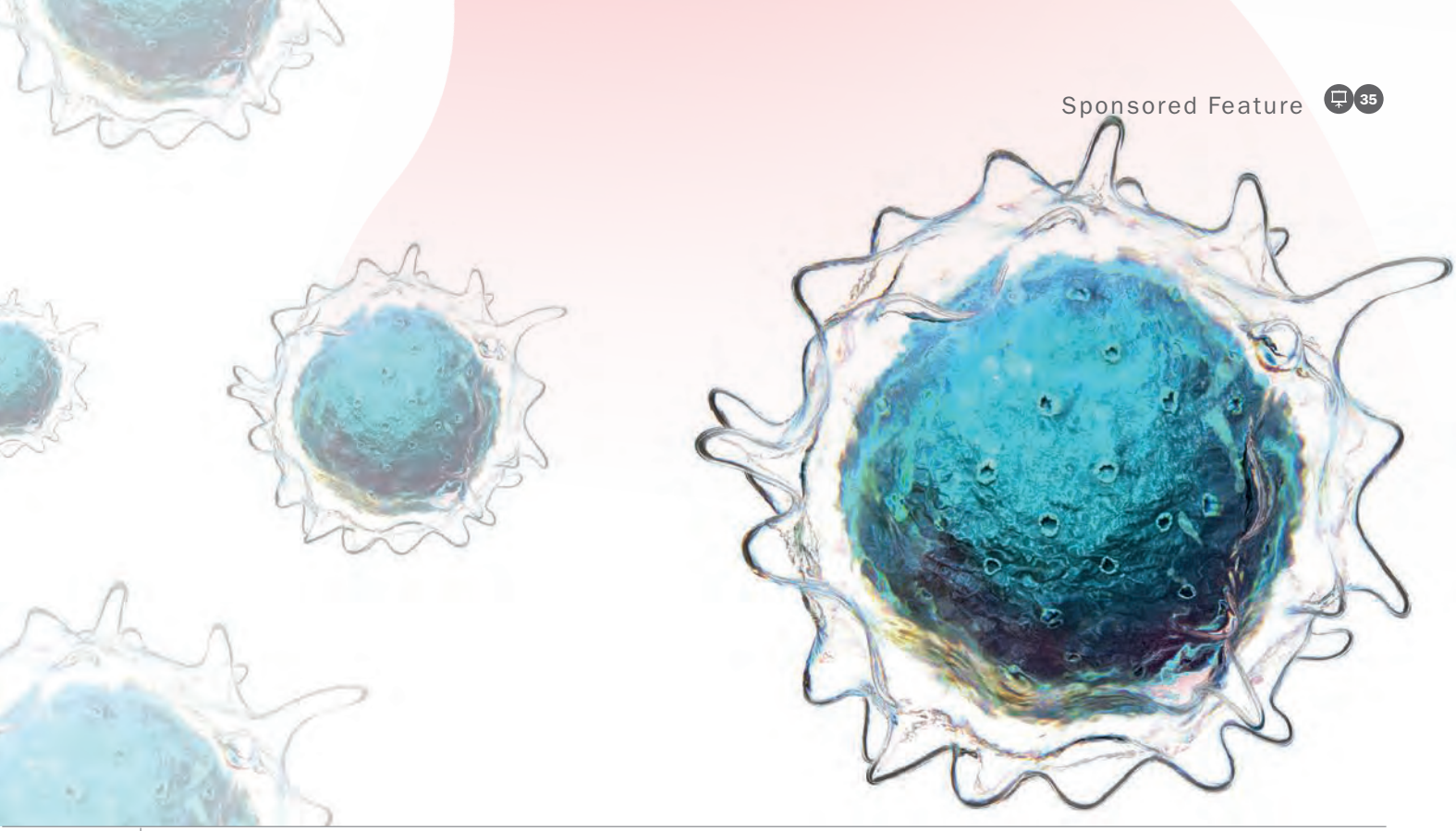
Available online, ZoomLab allows pharma companies to predict and optimize oral drug formulations. After the user inputs certain properties of their small molecule API and defines their target drug profile, ZoomLab uses a proprietary algorithm to instantly predict the optimal excipients to use, and the recommended weight fraction of each ingredient. It also provides recommendations in the formulation for functional excipients such as binders, disintegrants, and more, and the final recommendation will include detailed instructions on how to manufacture the formulation in the user's own lab. Users can also tweak the suggested formulation in silico and see how different excipients can affect their formulation's tabletability, dissolution profile, processability, and more.

Potential impact:
ZoomLab is not a replacement for a formulator; rather, it is intended as a virtual formulation assistant to provide both new and experienced formulators with the opportunity to speed up their formulation process and eliminate costly trial and error. New formulators are able to avoid missteps and can gain valuable formulation experience faster, while experienced formulators can brainstorm and experiment in silico with excipients and ingredient blends they typically don't start with or otherwise would not have thought to use.



THE INNOVATORS

Whether better ensuring patient safety, improving process efficiency, or just making life in the lab or facility easier – meet the companies advancing pharmaceutical development and manufacture.



ACCELERATE EFFECTIVE CELL THERAPIES BY IDENTIFYING T CELLS THAT MATTER

Directly link phenotype and function to gene expression

T cell-based therapies are showing great promise, but have also been associated with significant side effects. Improving efficacy and reducing toxicity has proven challenging because T cell-mediated tumor death relies on complicated cell-cell interactions that traditional analytical tools have not allowed us to fully understand. The complexity of these drugs has driven the adoption of single-cell methods, but these advanced technologies still require us to draw correlative, rather than causative, conclusions based on data collected on different T cell populations.

Berkeley Lights' award-winning Lightning™ optofluidic platform and T Cell Analysis Suite change this by truly enabling longitudinal studies of individual T cells and cell-cell interactions. Single T cells can be selectively placed into thousands of nanoliter-sized chambers on a microfluidic chip based on cell surface phenotype and co-cultured with target cells. Time-lapse imaging is then used to directly assess T cell function (cytokine secretion) and killing (target cell death); then, individual T cells of interest can be exported alive for downstream analysis such as TCR sequencing or RNA-Seq.

This enables recovery of TCR sequences that are directly associated with desired killing behavior, characterization of differences in antigen-specific killing kinetics, and discrimination between multiplexed and serial killing. Importantly, these experiments are performed on thousands of individual T cells in parallel in a single day and on a single platform, enabling fast, actionable, causative conclusions. Such rapid, deep characterization has the potential to not only provide novel insights, but also to accelerate the development of more efficacious cell therapies.

Visit: berkeleylights.com/CellAnalysisSuite to see TCR and CAR-T use cases.

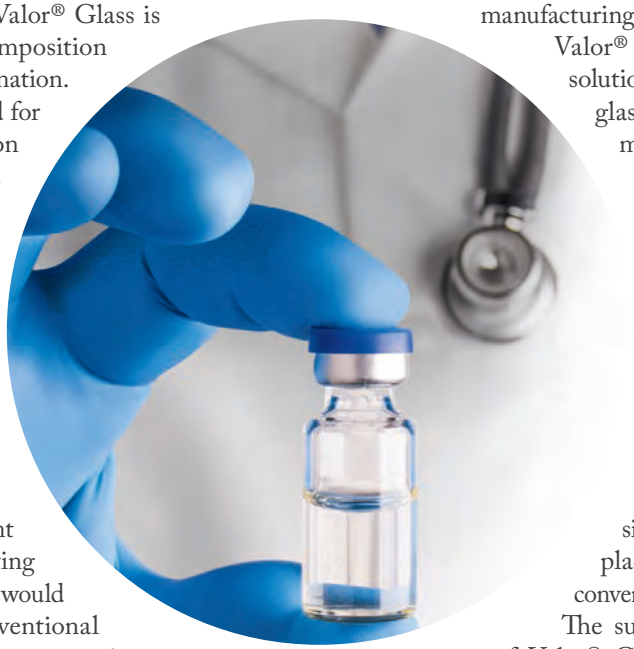
UNSHACKLING PHARMACEUTICAL MANUFACTURING WITH NEXT-GENERATION GLASS PACKAGING

The future of glass packaging is here

Glass is the gold standard material for parenteral packaging applications given its chemical durability, optical clarity, and thermal and mechanical performance. However, conventional glass packaging is not without limitations. All glass containers possess surface flaws that may substantially reduce strength and increase the likelihood of breakage on the filling line. The number and severity of these flaws increase as packaging is transported along the line, particularly from damage created by glass-to-glass and glass-to-metal contact. The performance of fill-finish operations is continually affected by these limitations in direct ways that reduce efficiency and throughput. There are also indirect consequences – the quality of product-filled

containers leaving a facility can be compromised by glass particle contamination or cracks that compromise sterility if they are not detected by routine inspection processes. The pharmaceutical industry has come to accept these limitations as a standard cost of doing business, but innovations in glass are enabling a step change improvement in performance that shatters these old assumptions.

Corning Valor® Glass is a revolutionary pharmaceutical packaging technology that helps protect patients and improve pharmaceutical manufacturing. Valor® Glass is a boron-free, aluminosilicate composition that will not exhibit glass delamination. The composition is also optimized for chemical strengthening by an ion exchange process, resulting in a container that is approximately 10 times stronger than conventional borosilicate glass packaging and capable of withstanding many of the mechanical stresses encountered in fill-finish operations (e.g., glass-to-glass impacts, transitions in container flow, etc.). The exterior surface of Valor® Glass containers is strengthened with a low coefficient of friction (COF) coating. The coating acts as a barrier against damage that would typically be experienced by conventional borosilicate containers, thereby preserving strength and reducing the incidence of cosmetic glass defects. As a result of this damage resistance, Valor® Glass reduces the generation of particles on the line by at least 96 percent improving product quality and helping to protect patient safety. The machinability of Valor® Glass containers is also exceptional – the low COF coating enables glass containers to flow smoothly on the line with fewer micro-stops and jams.



Corning is working closely with customers to demonstrate the value of Valor® technology in pharmaceutical manufacturing. More than 50 line trials have been conducted to date, and the results are clear. Valor® Glass provides substantial improvements across multiple performance metrics when compared to conventional borosilicate glass packaging. Effective line speeds are routinely increased by >20 percent by reducing glass-related downtime events such as vial breakage that requires operator interventions. Overall yields are also increased because of fewer cosmetic and particle rejects while providing a 30-fold reduction in the possibility of forming stable cracks that can compromise sterility. The takeaway message is that Valor® Glass gives pharmaceutical companies and contract manufacturing partners the ability to produce higher quality drugs at a faster rate, thereby improving throughput, increasing incremental unit sales, and delaying decisions to expand their capital-intensive manufacturing footprint.

Valor® Glass technology is a drop-in solution. As with the adoption of any glass package from a new supplier, minor equipment adjustments may be necessary when transferring to Valor® technology, but these adjustments are within normal process windows. The performance of Valor® Glass can be realized with standard equipment and processes, including washing, depyrogenation, sterilization, and lyophilization. Finally, Valor® Glass has the potential to significantly reduce the constraints placed on today's filling lines by conventional borosilicate glass packaging. The superior mechanical performance of Valor® Glass has been demonstrated by lines operating in excess of 600 vials per minute. The additional operational efficiencies provided by these speeds would dramatically change the economics of manufacturing. "Our customers are excited about the benefits offered by Valor® Glass. The potential of running their manufacturing lines at 600+ vpm is a true game changer, and Valor® Glass is the key to unlocking that potential," said Matthew Hall, manager of the applications engineering group for Corning Pharmaceutical Technologies.

Corning recently announced that a leading pharmaceutical manufacturer has received FDA approval to use Valor® Glass as a primary package for a marketed drug product. This marks the first time that the FDA has approved a new glass composition specifically designed for pharmaceutical packaging since the development of borosilicate glasses more than 100 years ago.

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A Natural Combination

A three-in-one approach to drug delivery combines different actives in a hydrogel-based delivery method

By Stephanie Sutton

Polypharmacy – the concurrent use of more than one medication – is common in the elderly patient population, but complicated by strict instructions for use, which increases the risk of non-compliance. Oliver Lieleg, a professor of biomechanics at the Technical University of Munich, Germany, has been investigating how different APIs can be combined in a single delivery system that allows each drug to be released at different times. By combining hydrogels, artificial DNA and nanoparticles, he has shown that three APIs can be combined in an effective drug delivery system. Hydrogels are typically used in ointments, but Lieleg says that the concept could be applied to tablets. We spoke with him to find out more about the work.

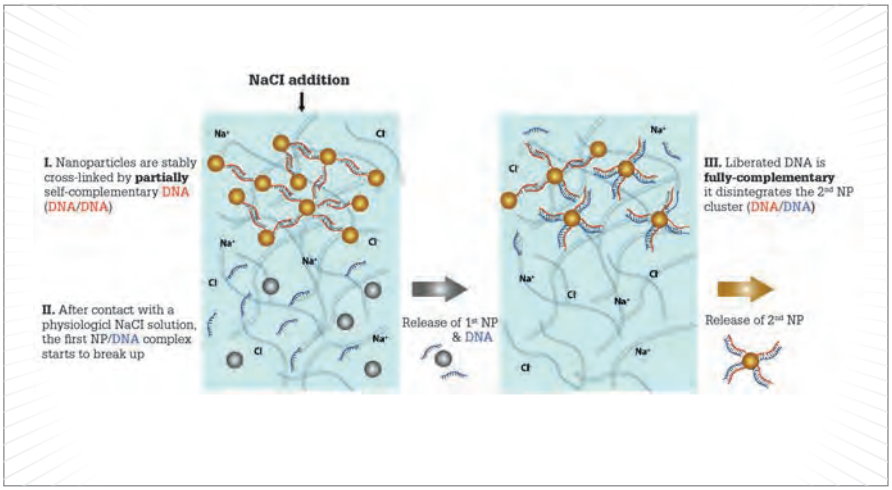

Figure 1. A release cascade of drug nanoparticles using a DNA-based approach.

What inspired your work?

Part of my inspiration for this project comes from an amazing publication from 2009; the researchers had developed a DNA-based nanobox that could be locked and opened again using single stranded DNA. Since then, I always wondered if DNA could be used as a tool in drug delivery. DNA base pairing is very specific and precise, and harnessing different levels of hybridization efficiency to allow for a controlled replacement of DNA strands by other DNA sequences seemed to me like a great way of engineering a sequential cascade of release events… And indeed it was!

I am quite amazed that, despite the progress we've made in the field of biomedical engineering and all the fascinating state-of-the art fabrication technologies available today, such as 3D printing, it still seems easier to make use of what nature offers and to find a different application for biological and naturally occurring materials rather than coming up with a fully synthetic system. Though it's fair to say that nature has had much more time to optimize the materials it uses for controlling complex processes than humankind!

What are the main challenges in combining APIs and ensuring correctly timed release?

To my knowledge, releasing several pharmaceuticals from the same carrier is possible; however, most existing strategies try to retard the release process of a subset of those drugs (which basically entails different release kinetics) – but all release processes start at similar time points. Thus, small concentrations of all drugs will be made available at the same time, even if some APIs are not needed. Installing a logical control sequence into a drug reservoir, which only allows for the release of drug B once drug A has successfully released, is difficult. Nevertheless, that is the challenge we tackled and – at least for nanoparticles (which we use to model different drug carrier particles) – we were successful.

How does your DNA-based approach work?

We embed different clusters of nanoparticles into a hydrogel. In this aggregated form, the nanoparticles are trapped in the gel and cannot escape. However, if the clusters are broken up, individual nanoparticles can leave the gel by diffusion. We use DNA for two purposes: first, to create the nanoparticle clusters and, second, to break them up in a controlled, sequential fashion. By designing synthetic DNA strands such that they act as cross-linking, stabilizing agents on one cluster type, but induce disagreggation of another cluster type, we can obtain a controlled particle release sequence. In short, the break-up of the first cluster type sets free DNA strands which, in turn, trigger the disassembly of the second

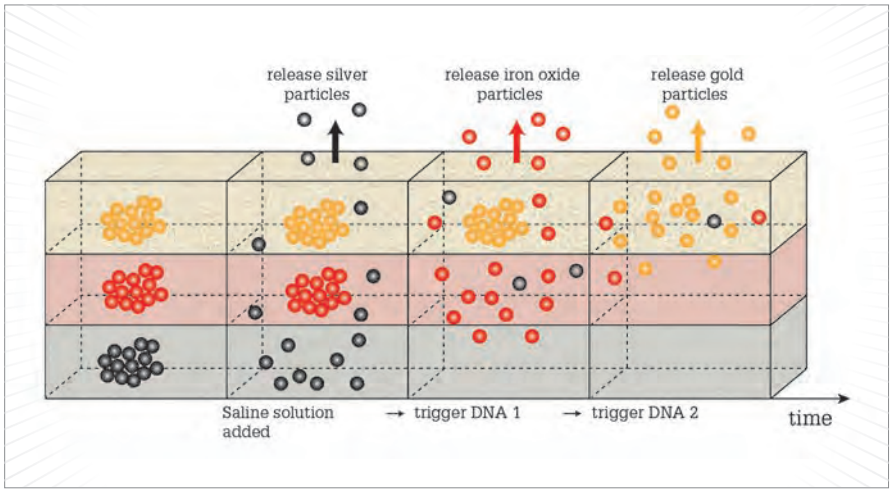

Figure 2. A simplified version of Lieleg's approach.

"With our DNA-based approach, we can already create a successful release cascade of three different nanoparticle species from the same hydrogel."

cluster type and so on. It is like opening a set of Matryoshka dolls – you only get access to the second doll once you have opened the first one. The first opening event gives access to the key needed to trigger the second opening event.

With our DNA-based approach, we can already create a successful release cascade of three different nanoparticle species from the same hydrogel. We can even design the system such that the particles located at the bottom of the gel exit first, and the ones closest to the surface exit last. Also, we showed that this DNA-based release mechanism acting on particles (for example, drug carriers) can be combined with other drug release control strategies acting on small molecules without causing unwanted interference. Thus, it is possible to control the release kinetics of molecules by classical methods (retarding their diffusive exit by employing binding interactions between the drugs and the hydrogel constituents) independently from the release of drug carrier objects (using our DNA-based strategy).

One of our next steps will be to apply a similar DNA-based control strategy to biopolymer-based nanoparticles that are actually loaded with drugs. Our hope is that we achieve a similar level of precision over the release process that we already obtained with inorganic, metallic nanoparticles so far.

What consideration have you given to cost and increased scale?

At this point of our research, we have focused on the general feasibility of obtaining a sequential, ordered release cascade. I do not think that, at this time, the synthetic DNA sequences we employ are cheap enough to be used in a commercial product, such as an ointment or gel. However, with the field of DNA nanotechnology quickly evolving and with other groups from this field also tapping into application-oriented research areas, novel strategies are also being developed that aim to produce defined, artificial DNA strands at lower cost; for example, by making use of biotechnological methods and DNA amplification in microorganisms. With such developments, our mechanism might become affordable relatively soon.

What are the limitations of your approach?

At the moment, our strategy targets the release of different nanoparticles in a controlled, sequential fashion. Even though we have used metallic nanoparticles for our experiments, the DNA-based control mechanism can also be applied to other particles, such as liposomes or biopolymer-based nanoparticles – as long as their surface can be functionalized with DNA strands. However, this is a limitation of our approach, as it relies on such drug carrier objects. On the other hand, this also means that there are no specific requirements for the drugs themselves – they only need to be encapsulated into a certain type of drug carrier so that they can be integrated into our DNA-controlled release cascade.

What types of therapies would benefit from being combined?

I believe that our DNA-based release strategy might be most useful for regulating a time-separated release of different therapeutic agents from a hydrogel that is applied to a body location that is not easily accessible for self administration. I imagine that sensitive wounds, such as burns or internal wounds created after surgery, could benefit from such an approach. Here, it may be possible to release an antibiotic first and then, later, a drug stimulating cell proliferation. Moreover, with our mechanism, it is also possible to release three doses of the same drug, but at distinct, separated and well-defined time points. For this to happen, each drug carrier particle would need to be loaded with the same drug.

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Hidden Analytical Advantages

Contract laboratories need to be treated as equal partners rather than service providers to optimize the benefits of outsourced pharmaceutical analysis

By Greg Thiele

How do you choose which properties to measure when it comes to characterizing APIs, excipients, or even the formulation? The identification of critical quality attributes (CQAs) and critical material attributes (CMAs) is an integral component of Quality by Design (QbD) but decisions around how best to measure them are not always easily made in-house. QbD places emphasis on process and product understanding, and is intended to reduce risk. Though potentially demanding, it facilitates a more flexible regulatory approach – an important consideration when putting together the robust submission package required. The knowledge accrued is also helpful for ensuring secure optimization of the supply chain (1). And beyond CQAs and CMAs may lie many additional variables – powder flowability, porosity and specific surface area, for example, depending on the pharmaceutical product type, can affect development and manufacturing and are, therefore, valuable to measure.

The challenges are significant, so many companies choose to outsource their analytical testing. In fact, in 2018, the global pharmaceutical analytical testing outsourcing market was valued at $5.59 billion and is set to grow by 8.1 percent over the next seven years (2). The accrual of savings holds value for many as the need to invest in and use new instrumentation and train staff falls away. Choosing a good contract laboratory or analytical service gives you access to a broad range of equipment as well as in-depth expertise.

Though companies hold the expectation that outsourcing partners will be able to provide high-quality data in a closely specified timeframe – at competitive prices – a question remains: how do you develop a relationship that best draws upon the strengths of both parties? In my experience, making broad requests of a contract lab offers their experts greater scope to contribute as an equal partner in the research process. Rather than dictating conversations with requests like, "I'd like to measure the particle size of these granules by laser diffraction", companies should consider making more open-ended requests such as, "I'd like to characterize these granules to develop correlations between their properties and those of tablets manufactured from them".

The risk of making such requests, however, is that that they may drive up the cost of outsourcing. But establishing a more comprehensive package of measurements for APIs or formulation is entirely consistent with the QbD approach, and can pay dividends throughout the lifetime of a product. In reality, demonstrating a robust product understanding not only underpins a successful submission but also lays the foundation for the effective supply selection and process troubleshooting needed for long-term economic manufacture.

"In an API, higher specific surface area is usually associated with faster dissolution but for flow additives such as magnesium stearate the situation is less straightforward."

Mercury intrusion porosimetry is a good example of a technique that may be excluded from a narrowly prescribed analytical schedule, but can add value to more comprehensive characterization of granules for tableting and/or finished tablets (3). This core physical technique robustly quantifies internal structure, but tends to be underused by the pharmaceutical industry because of the health and safety concerns associated with working with mercury and a lack of understanding of the benefits of the technique. Casting a wider analytical net can also provide solid evidence of a company's understanding of the factors affecting the integrity of critical measurements. For instance, as shown in Figure 1, particle size (an important variable for many pharmaceutical products because of its influence on characteristics such as bioavailability and dissolution behavior) can be measured using several techniques. But each technique has different strengths and weaknesses, which make it well

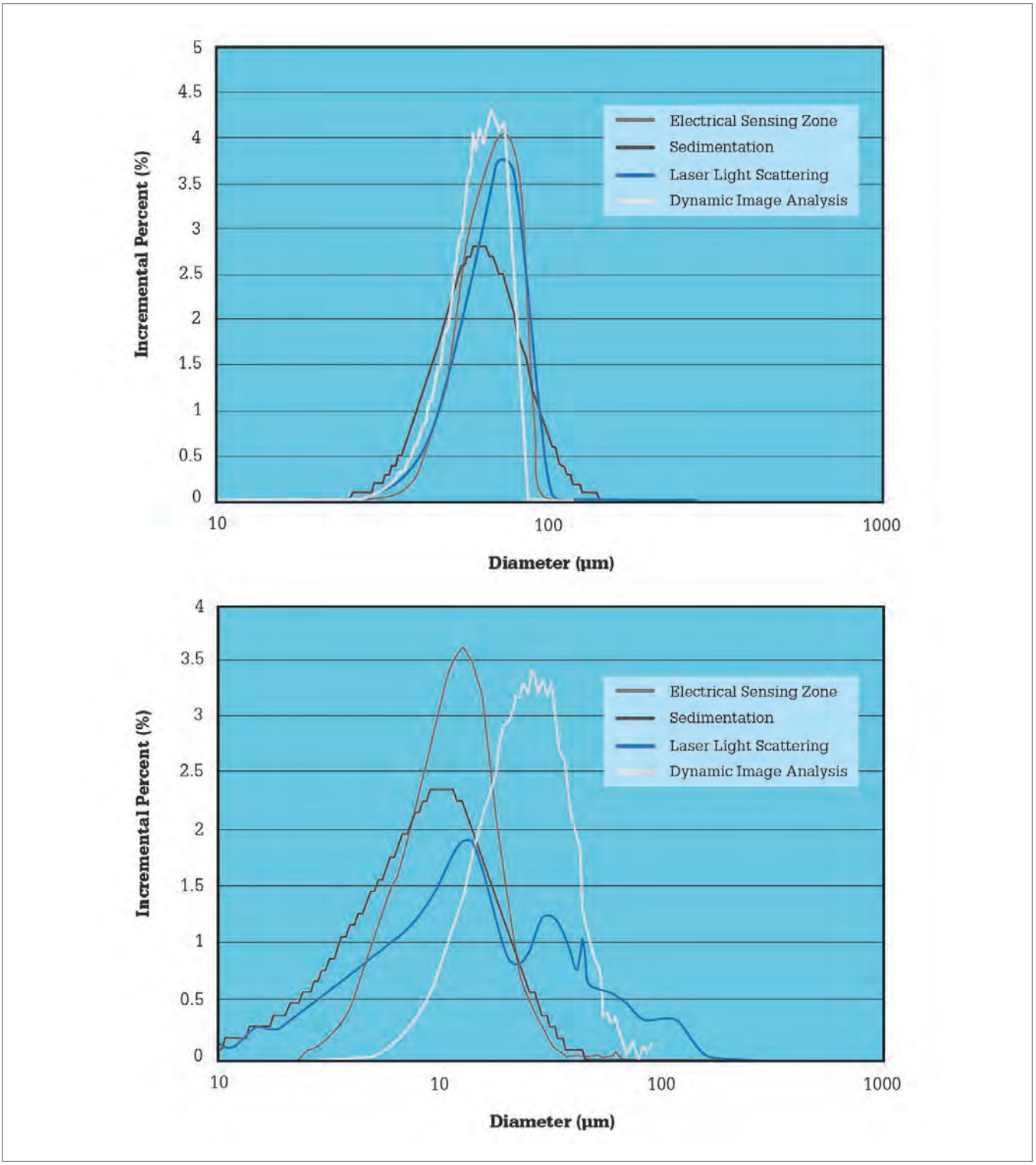


Figure 1: A change in particle shape from spherical (left) to rod-shaped (right) creates a divergence in the particle size distribution data reported by different particle sizing techniques.

PARTICLE SIZE (VOLUME DISTRIBUTION)					
MATERIAL	LOT	MEAN	D90	D50	D10
SuperTab 21AN	10678881	132.874	299.980	118.163	1.286
	10640579	123.902	278.460	111.046	1.184
	10680069	137.314	298.012	128.024	1.399
	Mean	131.363	292.151	119.078	1.290
	%RSD	5.2	4.1	7.2	8.3
SuperTab 11SD	10614997	59.168	117.334	53.639	4.146
	10643209	67.634	124.826	65.090	11.091
	10341963	69.883	136.195	64.786	7.324
	Mean	65.562	126.118	61.172	7.520
	%RSD	8.6	7.5	10.7	46.2
Pharmacel 101	00100016	51.810	98.606	49.353	7.824
	00100014	55.109	103.303	53.231	9.020
	00100018	57.587	105.306	56.397	11.028
	Mean	54.835	102.405	52.994	9.291
	%RSD	5.3	3.4	6.7	17.4

Table 1: High sensitivity laser light scattering analysis picks up significant variability in the level of fines in the three excipients (all results reported in microns).

suited to a particular application – or ill suited to another (4).

Spotting superior supplies

Analytical data is also important when considering the supply chain. The supply chains of the modern pharmaceutical industry are global and complex, and though drugs under patent enjoy some protection with respect to their ability to make profits, generic competition creates fierce pressure, cutting the prices of many drugs. Being able to quantify the potential of a particular supply chain makes it possible to choose the premium products that will stand the test of time and deliver in terms of profitability. One factor that directly impacts the value of supply for specific processes is the fact that certain bulk powder properties like compressibility or flowability are rarely included, or measured, in a formal specification or market contract. Powder testing is an area that has seen considerable advances in the last decade, and those leading the way in its application routinely use multi-faceted characterization based on dynamic, shear and bulk property measurement to maximize insights. Experience suggests that this approach can be highly productive in identifying materials that will exhibit superior process performance from supplies that seem relatively similar (5).

Tables 1 and 2 show data measured for commercially available excipients: anhydrous lactose (SuperTab 21AN), spray-dried lactose (SuperTab 11SD), and microcrystalline cellulose (Pharmacel 101) (all DFE Pharma). These provide further insight into how supplies marketed under the same specification can be usefully differentiated on the basis of superior analytical data. These excipients are

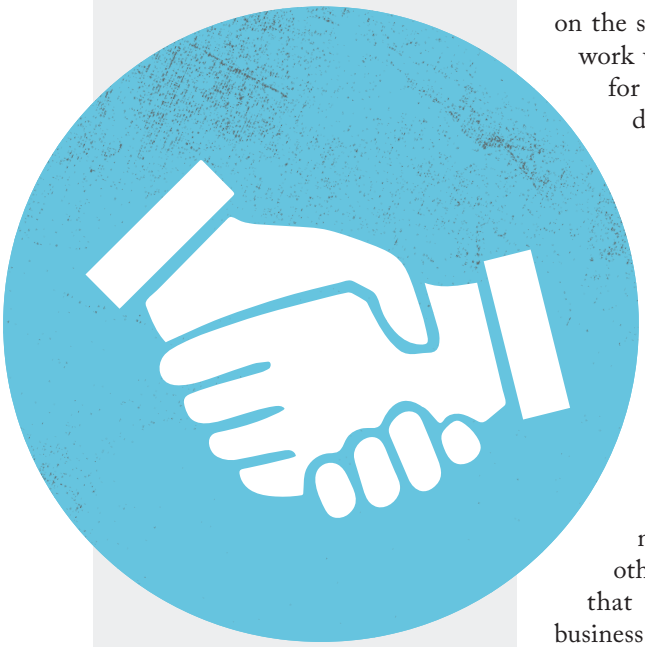
MATERIAL	LOT	DENSITY (g/cc)	POROSITY (%)	SURFACE AREA (M^2/G)
SuperTab 21AN	10678881	1.5821	8.5783	0.3490
	10640579	1.5810	8.5917	0.3442
	10680069	1.5798	11.1114	0.3452
	Mean	1.581	9.4271	0.3461
	%RSD	0.07	15.5	0.73
SuperTab 11SD	10614997	1.5389	3.4083	0.2172
	10643209	1.5391	2.8102	0.2207
	10341963	1.5384	3.0303	0.1892
	Mean	1.5388	3.0829	0.2090
	%RSD	0.02	9.8	8.26
Pharmacel 101	00100016	1.5495	18.6942	1.3805
	00100014	1.5545	16.3986	1.3345
	00100018	1.5527	16.9754	1.3792
	Mean	1.5522	17.3561	1.3647
	%RSD	0.16	6.9	1.92

Table 2: Adding less routinely measured parameters into the characterization mix can be a relevant and valuable way to differentiate suppliers.

highly likely to be associated with a particle size specification, but the static light scattering system used for the measurements (Saturn Digisizer II, Micromeritics) delivers higher resolution than most commercial systems. This is achieved by using a charge coupled device to detect the light scattering pattern produced by the sample, rather than the photo diode array deployed by standard instruments. The results suggest that there is considerable variability in the particle size of the supplies, most notably in terms of the D10 figure – the level of fines. Where fines impact process performance, high sensitivity particle size analysis may, therefore, be useful in identifying a superior supply.

Table 2 shows the results of applying an extended range of material characterization techniques to measure properties which, unlike particle size, may not be routinely considered. These include density (helium pycnometry), porosity (mercury intrusion porosimetry), and specific surface area (gas adsorption using krypton gas). These results show that all three substances exhibit relatively high variability with respect to porosity; SuperTab 11SD also exhibits a relatively high %RSD for specific surface areas. These properties may be neither measured, nor controlled during manufacture, but they may be relevant to a specific application. For example, the specific surface area of magnesium stearate has been securely correlated with the dissolution performance of tablets (6). Magnesium stearate is routinely used in very low concentrations to improve the flow properties of tableting blends, and more generally as a lubricant to enhance the efficiency of tableting processes. It is a naturally sourced excipient, manufactured via a range of different processes, and supplies on the open market consequently exhibit significant variability.

"Outsourcing analysis is becoming an increasingly popular decision, but success relies on developing fruitful working relationships with contract laboratories."



In an API, higher specific surface area is usually associated with faster dissolution but for flow additives such as magnesium stearate the situation is less straightforward. The mechanisms by which magnesium stearate enhances formulation behavior are complex, but the use of sources with a higher specific surface area has been associated with a slow-down in the dissolution of certain APIs (6). This effect may be attributed to more effective coating of the API by the hydrophobic magnesium stearate. Recent research has also identified particle morphology as affecting the impact of magnesium stearate on dissolution performance (6). When choosing between magnesium stearate supplies, a rigorous physical profile is essential to efficiently avoid one that could detrimentally affect product quality.

The right advice

Outsourcing analysis is becoming an increasingly popular decision, but success relies on developing fruitful working relationships with contract laboratories that recognize and draw on the strengths of each partner they work with. Though there is a place for closely prescribed, narrowly defined "analysis to order," an exchange of expertise will add value to the working relationship. For example, many pharma companies wouldn't necessarily appreciate the extent to which analytical data could valuably differentiate very similar and reputable excipient suppliers, but a partner who is an expert in this area will be able to provide more insight – as well as offering other advice about analytical data that can contribute to additional business decisions!

By working collaboratively with a partner and keeping an open mind to suggestions around analytical testing, you'll be able to obtain data that can help accelerate development, demonstrate the understanding needed for a robust regulatory submission, troubleshoot effectively, and even develop a better supply chain. Most importantly, analytical data and expertise give companies the opportunity to establish detailed material profiles that will last for a lifetime.

Greg Thiele is General Manager at Particle Testing Authority, a Micromeritics company.

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Passion for Advancement

Sitting Down With… Trevor Jones, Director of Arix Bioscience, e-Therapeutics and Respiratory Innovation Wales, UK.

Where did your career begin?

I was a lecturer at the University of Nottingham, set on becoming a professor – I had no plans to get into industry. But, one night at the cricket club, the Head of Research at Boots told me they were getting a new Head of Development – and that it was me! So I had to rethink my plan... It was actually incredibly interesting to come from academia into an applied environment. I found that I was given the freedom to actually mold and change the way things worked.

What career highlights give you the most pride or satisfaction?

I've held a variety of roles in many different associations and companies over the years, and I've been able to help many patients in the developing world. One of my biggest career highs was at Wellcome as R&D Director. We discovered and developed an array of drugs, including AZT (zidovudine) – which was launched right at the beginning of our understanding of the HIV epidemic. I was also a founding member of the not-for-profit venture, Medicines for Malaria Venture (which recently held its 20th anniversary in Geneva), which I am very proud of. It has developed a portfolio of malaria products built on good science, and the organization has helped an enormous number of patients who wouldn't be alive without it.

In the UK, I've been fortunate to have had prominent roles that have given me the opportunity to shape the country's pharma industry. When medicine regulation was being developed, I was part of the UK Government's regulatory agency, the Medicines Commission, which set the parameters as to whether a medicine should be approved. I was also Director General of the Association of the British Pharmaceutical Industry (ABPI) for 10 years, representing pharmaceutical companies in front of UK and European governments. I learned a lot of negotiating skills with the Association! I had the difficult task of negotiating how much the industry could charge for their medicines. The resulting scheme – the PPRS – not only allowed industry to be incentivized to invest in research, but also gave the NHS value for money.

Out of all the awards and accolades you have received, which stand out the most?

The first recognition I received was the Harrison Memorial Award from the Royal Pharmaceutical Society of Great Britain. I didn't work for it, or expect it! In 2006, I got the Scrip Lifetime Achievement Award; I value it highly – especially as it was the first such award bestowed by Scrip. I was especially delighted when the Queen honored me with a CBE in 2003. More recently, I became a fellow of the Academy of Medical Sciences. We work on how we can help the professions and government organizations think through some of their dilemmas in medicine, science, and delivery of health. I put this one after my name with my CBE because I am so proud of it.

What areas in the pharma industry interest you the most?

One area in particular that I am passionate about is how machine perception – "artificial intelligence" – can be used in drug discovery and lead to better therapies. Every patient is different, with some drugs working well in one patient and not in another. AI can show us what is unique about these patients, potentially allowing us to find more precise and effective medicines – indeed "cures". Ultimately, AI will transform how patients are diagnosed and how therapeutic outcomes are monitored in the real world. Overall, we can expect better therapy and more efficient healthcare.

I also like to get involved with discussing industry trends and advances at conferences. One of my most recent conferences was Pharma Integrates in the UK where I interviewed Andrew Witty, CEO of Optum, and Menelas Pangalos, Executive Vice President of Biopharmaceutical R&D at AstraZeneca.

What changes would you like to see?

We need to get the focus of the industry back on discovering and making medicines. Over the years, there has been a fair amount of diversification – or "di- worse-ification" – in pharma, with many company shareholders and boards having a short-term vision on return on investment. We need to bear in mind that it takes a considerable amount of time to develop a new drug. Some companies have split off their pharmaceutical innovation groups so they can concentrate on this activity. My feeling is that the best way of restructuring pharma is to put the focus back on drug discovery and development.

What advice would you give to those following in your footsteps?

For students or those just starting their careers: often you pass through a series of funnels into very specific areas of biology or chemistry. You get your degree – often a very good degree – but you have no understanding of the wider perspective of where all that fits. My advice is to get out of your narrow discipline and to seek a broader understanding. I give a series of "popular science" lectures to help broaden people's interests and to show them how diverse science is and where a career can really go. A couple of my students at King's College have taken sudden career changes based on that.

For academics, don't neglect the visionary work. There is a temptation for academics to be tempted to focus on solely business by launching start-ups. There are some fantastic start-ups that make significant contributions to the health and wealth of our nation, but there is a danger: losing sight of "new" science.

In terms of industry – be a good listener. At the academic–industrial interface, sometimes industry does not really listen to what academia is truly saying. Industry and academia operate in very different worlds. But there is a wonderful connection that you can form when you listen to one another and work together to advance science and understanding.

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