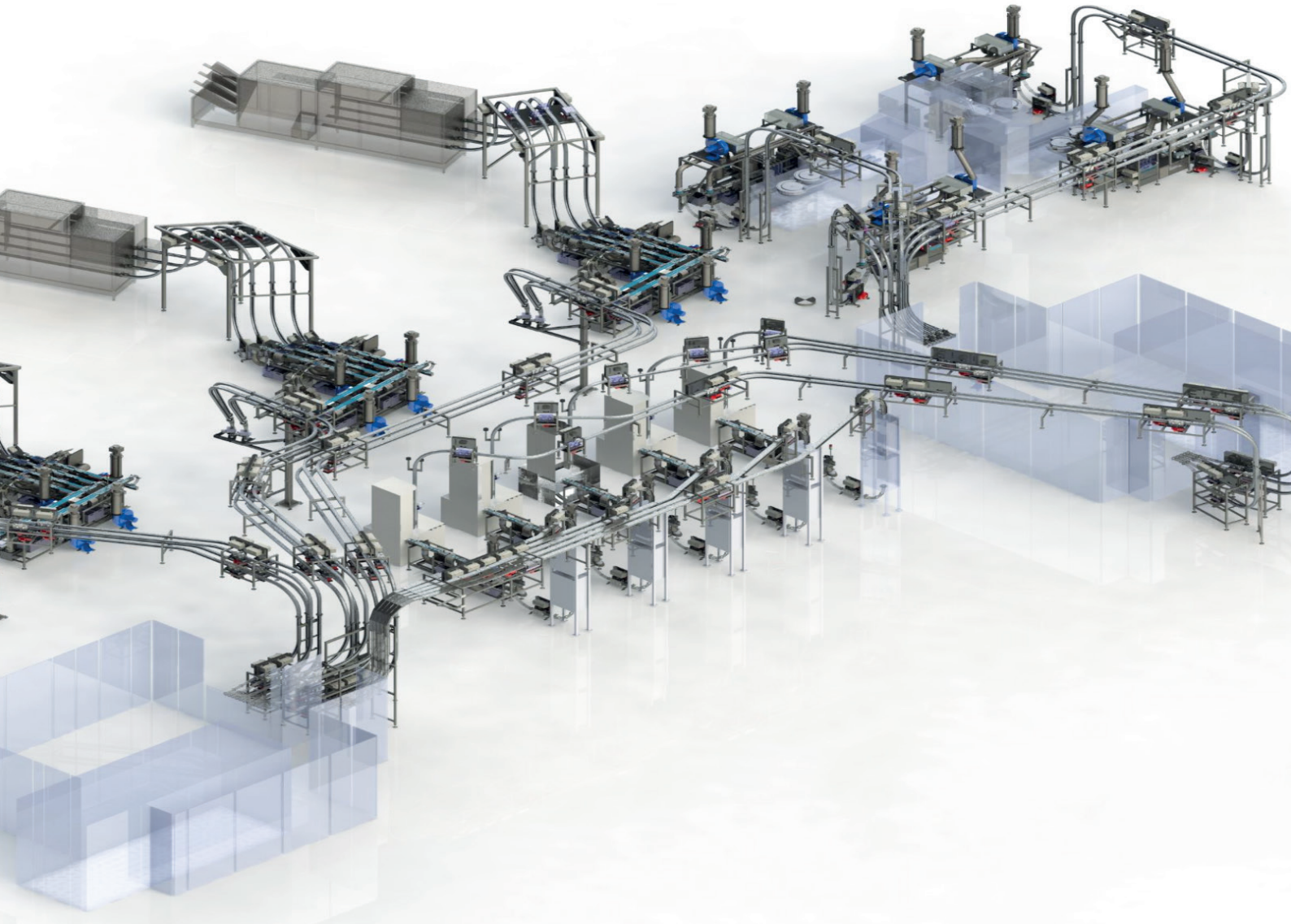
INDUSTRIALISING DRUG DELIVERY

ON drugDELIVERY



AUGUST 10TH 2022 • ISSUE N° 136

DCA

Helping our clients achieve success through great product design

Pen injector for concentrated insulin

www.dca-design.com

CREDENCE MEDSYSTEMS

INNOVATION WITHOUT CHANGE HAS ARRIVED

THE CREDENCE COMPANION

Credence MedSystems, Inc. - +1-844-263-3797 - www.CredenceMed.com

This product has not yet been evaluated by FDA

Contents

ONdrugDelivery Issue N° 136, August 10th, 2022

INDUSTRIALISING DRUG DELIVERY

This edition is one in the ONdrugDelivery series of publications. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field.

EDITORIAL CALENDAR

Sep 2022	Wearable Injectors
Oct	Prefilled Syringes & Injection Devices
Oct/Nov	Drug Delivery & Environmental Sustainability
Nov	Pulmonary & Nasal Drug Delivery
Dec	Connecting Drug Delivery
Jan 2023	Skin Drug Delivery: Dermal, Transdermal & Microneedles
Feb	Prefilled Syringes & Injection Devices
Mar	Ophthalmic Drug Delivery
Apr	Pulmonary & Nasal Drug Delivery
Apr/May	Drug Delivery & Environmental Sustainability
May	Injectable Drug Delivery: Formulations & Devices
Jun	Connecting Drug Delivery
Jul	Novel Oral Delivery Systems
Aug	Industrialising Drug Delivery

EDITORIAL:
Guy Furness, Proprietor & Publisher
E: guy.furness@ondrugdelivery.com

CREATIVE DESIGN:
Simon Smith, Creative Director (Freelance)
E: simon.smith@ondrugdelivery.com

SUBSCRIPTIONS:
Audrey Furness (subscriptions@ondrugdelivery.com)
Print + Digital subscription: **£99/year + postage**.
Digital Only subscription: free.

ADVERTISING:
Guy Furness (guy.furness@ondrugdelivery.com)

ONdrugDelivery is published by
Frederick Furness Publishing Ltd
The Candlemakers, West Street, Lewes
East Sussex, BN7 2NZ, United Kingdom
T: +44 1273 47 28 28

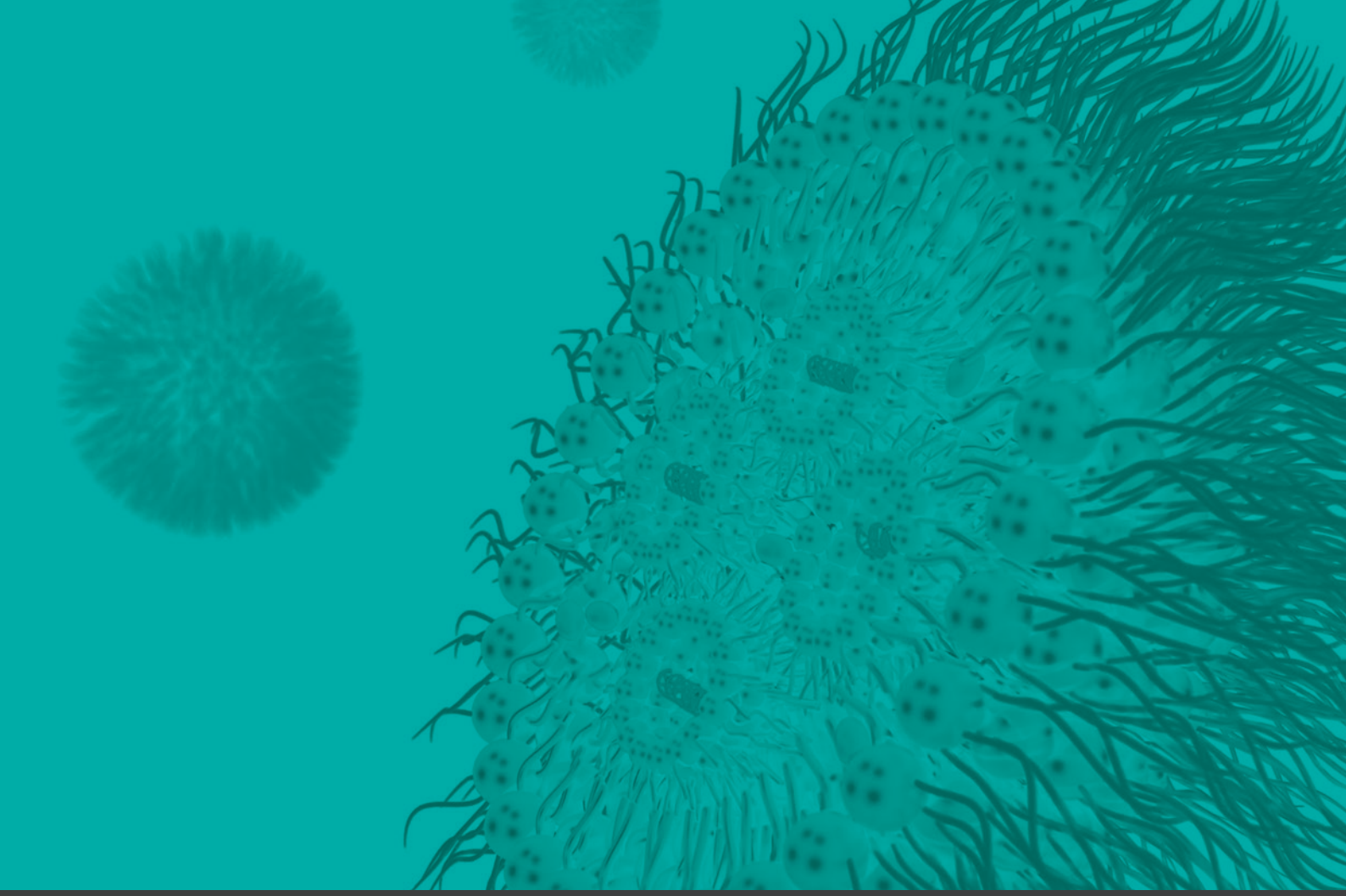
Registered in England: Company No 8348388
ISSN 2049-145X print / ISSN 2049-1468 pdf

RECYCLED
Paper made from recycled material
FSC® C022819
www.fsc.org

WORLD LAND TRUST™
www.carbonbalancedpaper.com

ONdrugDelivery Magazine is printed sustainably by Newman Thomson Ltd, West Sussex, UK, using Forestry Stewardship Council® certified recycled paper, vegetable-based inks, biodegradable laminates and carbon balanced materials offset via the World Land Trust™ following ISO140001 processes.

Front cover image, "3D visualisation of machinery production data enables real-time tracking of markers", courtesy Stevanato Group (see this issue, Page 18). Reproduced with kind permission.



YOUR LNP RESEARCH PARTNER

FOR CUSTOM LIPID SYNTHESIS & BULK LNP COMPONENTS

By partnering with Cayman, you have access to lipid experts with 40 years of experience designing and synthesizing lipids suitable for lipid-based drug delivery systems. We also provide lipids in bulk quantities to help assist with your R&D needs.

LEARN MORE AT

CAYMANCHEM.COM/CUSTOMSYNTHESIS

Cayman CHEMICAL

INDUSTRIALISATION AND SCALE-UP OF DRUG DELIVERY DEVICES

Here, Barry McDermott, PhD, MSc, CEng MIEI, Director, Industrialisation Services, and Shari Krusniak, Director, Strategic Marketing, Contract Manufacturing & Integrated Solutions, both at West Pharmaceutical Services, look at the manufacturing processes involved in bringing a new drug delivery system and formulation to market.

Over the last five years, revenue coming from biologics and biosimilars has increased significantly. This rapid growth has inspired many pharmaceutical companies to invest in biotherapeutics. However, these drugs are sensitive and complex and require expertise in their development, containment and delivery systems. In fact, these drugs commonly start in a standard format but evolve into more convenient prefilled syringes or combination product wearable devices with the goal of improving market share, product differentiation, and patient experience and adherence. For these complex devices, meeting these goals requires great expertise and reliance on a strong supply network.

Drug delivery devices often include technology that must meet regulatory standards and remain current in the fast-paced and evolving market. When considering a novel drug delivery system combined with a new formulation – with either one or both requiring the development of manufacturing processes – considerable challenges are involved in meeting the required quality standards and scaling up the required resources while containing costs and minimising time to market.

Typically, pharmaceutical companies focus on their expertise in the development of the therapy itself and then collaborate with manufacturing partners to research, design and develop the containment and delivery system of the drug to meet those requirements. A successful partnership between these companies is essential for the manufacturing of a safe, effective and competitive therapy to accelerate market entry and to respond quickly to the constantly changing landscape (Figure 1).

COLLABORATION IS CRITICAL

To reach the goals of your development programme, it is important to partner with a trusted device supplier or contract manufacturing organisation. From concept to design, the partnership needs to include early and frequent collaboration and communication, protection of intellectual property and consideration of the patient's full journey. Both partners also need to be aware of challenges that can arise and address root issues through close collaboration.

Many challenges can hinder progress towards delivering innovative, patient-centric products, but those that arise when there is conflict between a pharmaceutical company and its manufacturing provider are often overlooked until they begin to slow

> "With patient safety on the line, it is essential to collaborate successfully and communicate regularly to address problems when they arise."

Dr Barry McDermott
Director, Industrialisation Services
T: +353 86 8249770
E: barry.mcdermott@westpharma.com

West Pharmaceutical Services
Carrickpherish Road,
Waterford
X91 R9V6
Ireland

Shari Krusniak
Director, Strategic Marketing, Contract Manufacturing & Integrated Solutions
T: +1 480 281 4549
E: shari.krusniak@westpharma.com

West Pharmaceutical Services
14677 N 74th Street
Scottsdale
AZ 85260-2403
United States

www.westpharma.com

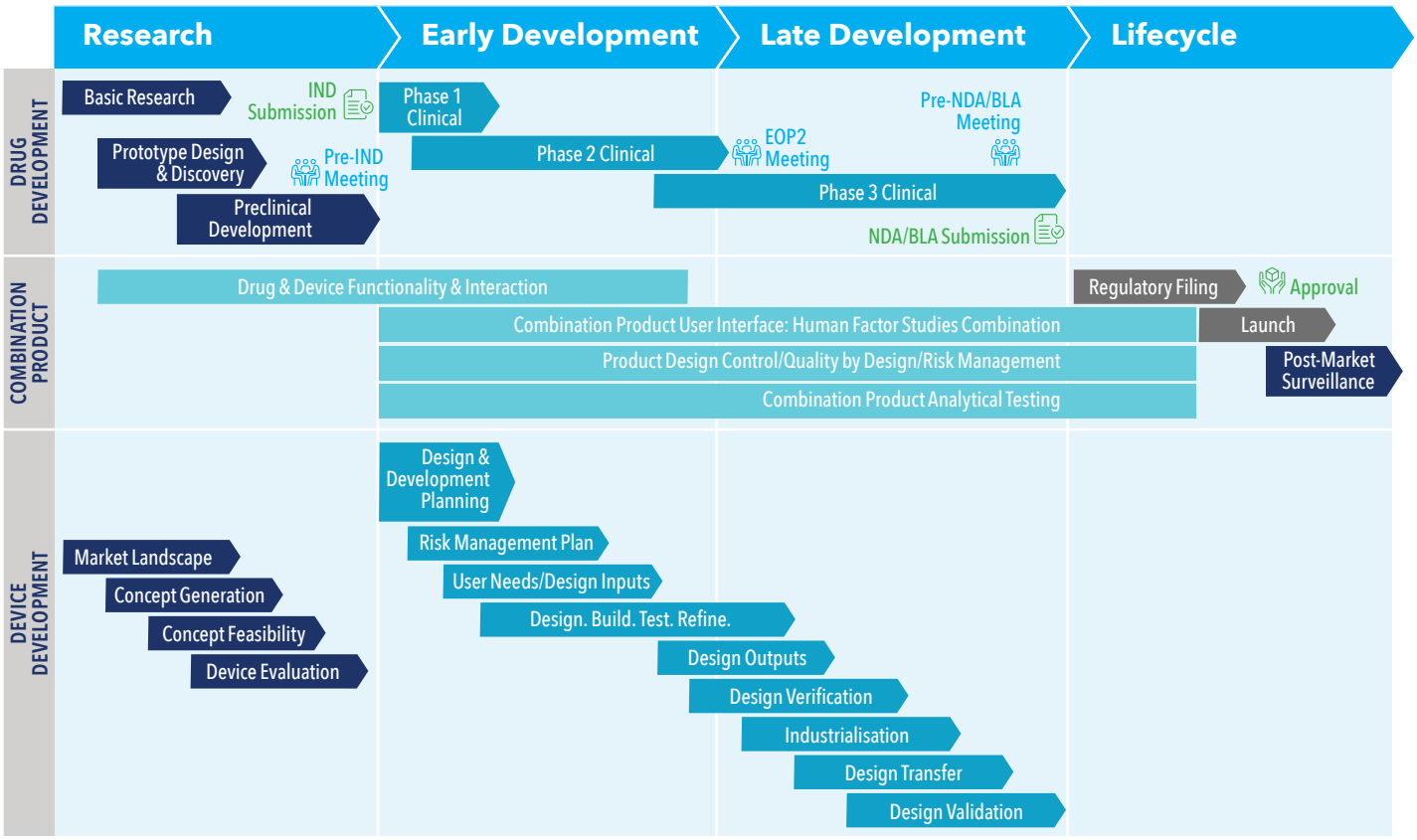


Figure 1: Combination product development process. Bringing a biologic to the market requires that the drug development process and the device development process come together as early as possible. Considering drug and device separately can introduce significant risk.

the process. These issues can arise in any partnership and can be compounded when teams come from different companies and work cultures. Misaligned goals, processes and expectations need to be addressed early to establish a successful partnership. Lack of accountability and decision making, as well as poor communication and problem solving, are common issues that may lead to missed deadlines and/or poor-quality products. With patient safety on the line, it is essential to collaborate successfully and communicate regularly to address problems when they arise.

YOUR DRUG AND ITS DELIVERY DEVICE: A CO-ORDINATED DESIGN, DEVELOPMENT AND MANUFACTURING PERSPECTIVE

Biopharmaceutical companies tend to focus on the molecule of interest and its functional characteristics, but it is equally important to consider how ultimately that molecule will be manufactured from lab to commercial scale, taking into consideration its containment system and how it will be delivered to the patient. As a manufacturing partner, West offers solutions for the design of drug delivery devices that optimise manufacturability. The company understands the importance of transitioning a device from development to the manufacturing stage, which must be done with an understanding of the regulatory needs, scale and expansion of the product in the best interest of the customer. These priorities and West's decades of experience have made the company a trusted solutions provider for many successful pharmaceutical companies. West's approach to manufacturing involves several key aspects:

- Strong programme management
- High standards of quality through design for reliability and capability (DRC)
- Knowledge of changing regulations
- Analytical testing and data to satisfy regulatory agencies
- Capacity for product scalability
- Proper drug handling and cold chain solutions.

Strong Programme Management

Programme management refers to the ability to manage risks while providing timely solutions to immediate challenges and anticipating future needs. A programme kick-off meeting will clarify the needs of both partners and the drug delivery device, and a strong management practice will help to incorporate those needs into the project plan. The programme manager oversees all phases of programmes, from inception through completion, ensuring projects are completed on time and within budget. This person is responsible for scheduling and technical performance and performs the following duties:

- Co-ordinates cross-functional project/programme teams from design to delivery of fully developed healthcare products ready for customer use
- Provides technical support in executing the project plan to meet customer requirements
- Monitors performance and recommends schedule changes, cost adjustments or resource additions
- Co-ordinates the design, build and validation of tooling, assembly line and supply chain.

High Standards of Quality Through DRC

As a global contract manufacturer in the development of devices supporting the pharmaceutical industry, West works with customers to ensure its devices are designed

"Moving through the development process, West optimises the key critical attributes for quality to confirm a robust design and capable processes."

for reliability and capability. Reliability refers to product reliability and robustness, while capability refers to the ability of a product to be assembled and manufactured and to function for its indicated use.

As DRC starts at the research/concept phase of the product development process, West incorporates quality and robustness from the very beginning and, ultimately, optimises the product design and associated manufacturing process for scale-up. West follows its defined DRC methodology, starting with understanding the voice of the customer and translating that voice to concept and component generation and selection while incorporating its design for manufacture and assembly expertise for internal and external supply.

Moving through the development process, West optimises the key critical attributes for quality to confirm a robust design and capable processes. As manufacturing plans are established and product design validation testing and process qualification is completed, the company prepares for production and commercial supply. This established methodology manages the risks of time and cost creep by anticipating and managing potential issues, as well as building quality into the design of the customer's new product. Thus, moving from problem solving to problem prevention.

The process collects vast amounts of data to reveal even subtle changes that affect product integrity, and this approach is consistent across both the product and process development. Data collected as part of the product development and manufacturing process are integral to optimising product and process design and in developing leading, rather than lagging, metrics that guide product and project management, training, infrastructure and capital needs. The DRC methodology, which incorporates data collection and analysis, can provide critical insights that:

- Identify defects earlier
- Reduce manufacturing scrap
- Reduce product variation
- Improve outgoing quality and on-time delivery
- Increase customer satisfaction.

"West designs modern devices and, with early and frequent collaboration with the pharmaceutical company, can adapt them to meet changing regulations that may arise during the manufacturing process."

Knowledge of Changing Regulations

One challenge to anticipate is the ever-changing regulatory landscape for drugs and their delivery systems. West stays up to date with these changes and aims to manufacture devices that exceed current standards in both the physical and technological design of the system. As wearable devices and self-administered products employ the most current technology, West is constantly researching the regulations, including those outside the drug industry, that your product and its electronics must meet to reach the market quickly and safely. West designs modern devices and, with early and frequent collaboration with the pharmaceutical company, can adapt them to meet changing regulations that may arise during the manufacturing process. By leading with the company's quality-by-design process, this requirement is met even through design adaptations to provide safe and effective drugs.

CASE STUDY: NOVEL DRUG DELIVERY DEVICE

A pharmaceutical company and their product design partner chose West as their manufacturing solutions provider for a breath-actuated inhaler with an incorporated dose-counter mechanism and a metered canister of pressurised drug suspension to treat patients with asthma and chronic obstructive pulmonary disease. Thinking ahead, the development team designed and manufactured the device to become a platform technology for future therapies.

West provided support in device development, injection moulding, tooling, supply chain logistics and the scale-up automation strategy. This support resulted in improved risk mitigation, speed to market and a simplified supply chain during the process of manufacturing these devices at clinical trial scale, with the capacity to scale up to meet the needs of the commercial market. However, the success of the partnership and final combination drug manufacturing did not come without challenges and the need to adapt to changing requirements.

Challenges included scaling up from single-cavity tools to multi-cavity tools, adhering to tight tolerances, moulding and assembling multiple components with new materials while meeting customer specifications, meeting critical processing parameters, developing an integrated automation solution for the device assembly and verifying the device's functionality. These challenges were addressed through West's comprehensive plan that included conceptualisation, design, mould manufacturing and adherence to regulations.

The final respiratory device consisted of 12 injection-moulded components produced from four different resin groups through a process that involved building seven components into a dose-counter assembly. Engineering verification testing then involved design alterations to ensure the robustness of the device during typical patient use.

The result achieved by West was the delivery of 11 of the 12 multi-cavity tools to progress to the quality control stage. This involved design of experiments, metrology, steel cuts if required, process capability and corner process studies, and metrology development and review. The development also included automation of the assembly to ensure scalability, all while adhering to the highest standards of compliance and quality.

Analytical Testing and Data to Satisfy Regulatory Agencies

Access to robust analytical testing services is critical for successful commercialisation of biologics. Most pharmaceutical and biotech companies outsource these services because of the need for highly specialised staff and equipment to perform injectable package testing to satisfy regulatory demand. West has extensive experience in extractables and leachables, particle analysis, container closure integrity, and performance and packaging/delivery systems, among other methodologies. The company's dedicated packaging and performance testing group works with customers to develop custom protocols specific to their needs – and the needs of the combination drug product. West partners with clients and understands the current regulations and standards as well as ensuring the proper study design and interpretation of the results.

Capacity for Product Scalability

With a product designed and manufactured, scalability must also be considered. It is important to understand the needs of the market for your specific drug and if there are potential hurdles in the supply chain that may slow the process of scaling its production. As an experienced solutions provider, West knows how to anticipate hurdles and designs products, including the required tooling, equipment, facilities and clean room capacity, from the start to minimise such risks.

Proper Drug Handling and Cold Chain Solutions

In addition to the supply chain for the device itself, you and your manufacturing partner must consider the requirements for the drug's delivery and storage. Biotherapeutics are sensitive drugs typically containing unstable molecules that require temperature-controlled handling, storage, transportation and dispensing. It is crucial that your contract manufacturing provider can ensure proper cold chain solutions so as to not compromise the integrity, efficacy, safety or security of the drug.

WEST IS A TRUSTED MANUFACTURING PARTNER

Today, biotherapeutic drug delivery is trending towards self-administration and improved patient experience, requiring sophisticated drug delivery devices, such as self-administered injectables and other types of combination products. The industrialisation needs of modern delivery systems are more complex and require an experienced manufacturing partner and a proven track record of helping pharmaceutical companies bring medicines and products to the market.

With over 100 years of experience providing packaging, transportation, storage and manufacturing of drug delivery devices, West has collaborated with pharmaceutical and biotech companies around the world to create market-differentiating drug delivery systems for their products. The success of these partnerships has resulted in the use of more than 112 million West components and/or devices each day, with eight out of 10 of the biggest-selling biologics relying on West packaging.

ABOUT THE COMPANY

West Pharmaceutical Services is a leading provider of innovative, high-quality injectable solutions and services. As a trusted partner to established and emerging drug developers, West helps ensure the safe, effective containment and delivery of life-saving and life-enhancing medicines for patients. With approximately 10,000 team members across 50 sites worldwide, West helps support its customers by delivering over 45 billion components and devices each year.

ABOUT THE AUTHORS

Barry McDermott is Director of Industrialisation Services at West Pharmaceutical Services, a provider of pharmaceutical delivery and packaging systems. He has 30 years of experience in research and development, engineering and programme management.

Shari Krusniak is Director of Strategic Marketing at West Pharmaceutical Services, a provider of pharmaceutical delivery and packaging systems. She has more than 15 years of experience in medical device manufacturing, sales and marketing.

12TH ANNUAL

PODD®

PARTNERSHIP OPPORTUNITIES IN DRUG DELIVERY

OCTOBER 24-25, 2022 • THE WESTIN COPLEY PLACE, BOSTON

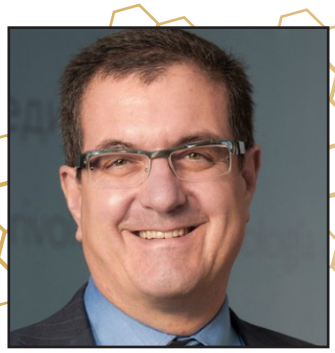
Co-Chairs, Keynotes and Zeitgeist Speakers

Co-Chair
Shawn Davis, PhD
AstraZeneca

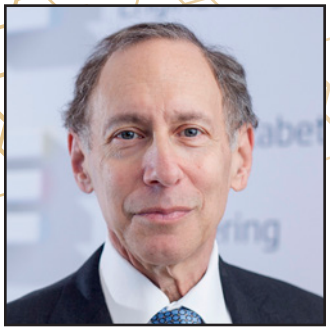
Co-Chair
Ann Daugherty, PhD
Genetech

Co-Chair
Mark Schiebler, PhD
Roche

Co-Chair
Uri Baruch
Cambridge Design Partnership



Keynote
John Maraganore, PhD
Formerly Alnylam Pharmaceuticals



Keynote
Robert Langer, PhD
MIT

Zeitgeist
Nicholas Warne, PhD
Pfizer

Key Topic Areas

- The Future of RNA Delivery
- Payer Perspective on Drug Delivery Differentiation
- Meeting the Demands for At-Home Drug Delivery
- Challenging the Cost of Drug Delivery Maufacturing
- Subcutaneous Formulations and Technology
- Next-Generation on Connected Devices
- Oral Delivery of Biologics
- Adaptive Drug Delivery
- Targeted Drug Delivery
- Connected Devices
- Combination Product Strategies

15% Discount with Code ONDD15

2 for 1 Pharma Rate Available
Learn more at: www.poddconference.com

MITIGATE RISK WITH THE RIGHT PARTNER

Responsive to the unique needs of biologic, pharma and generic drug product, West is by your side to:

- Reduce development and supply risk
- Accelerate your path to market
- Minimize the total cost of ownership
- Improve the patient experience

FOR MORE INFORMATION VISIT **WWW.WESTPHARMA.COM/DERISK**

NORTH AMERICA 1-800-345-9800 OPTION 8
SOUTH AMERICA +55 11 4055 6061
EUROPE +49 (0) 2403-7960
INDIA +91 40 49401111
ASIA PACIFIC +65 6862 3400

IMPROVE YOUR BIOPHARMACEUTICAL WORKFLOW: SIX BENEFITS OF SINGLE-USE SYSTEM TECHNOLOGIES

In this article, Sara Dorman, Global Biopharma Market Manager at Roquette, discusses the benefits of single-use systems, including how they help accelerate a drug product's journey to market securely and more sustainably.

Bringing valuable drug products to market quickly and safely remains a challenging process. To meet the needs of patients globally, the pharmaceutical industry continues to face pressures to speed up production, scale up manufacturing, simplify workflows and improve efficiencies to lower costs – without compromising on quality or safety. At the same time, implementing robust processes that offer adaptability and fluctuating capacity has become a primary focus for drug developers and innovators, especially in the biopharmaceutical industry.

This was first necessary to meet rising demand for biological therapies, but has become even more pressing following the emergence of covid-19 and the need for rapid and flexible vaccine development.

Single-use systems (SUS) – like precision dispensing technologies – offer manufacturers a way to streamline bioprocessing operations and maximise production efficiencies by increasing throughput and making scalability easier.

TIME TO RETHINK BIOPHARMACEUTICAL WORKFLOWS?

The biopharmaceutical method of developing drugs continues to grow in popularity. It became an especially high-profile topic during the covid-19 pandemic, which necessitated swift manufacture of the mRNA vaccine and monoclonal antibodies for the treatment of the disease, both of which are made using biopharmaceutical processes. This, combined with the global re-emergence of infectious diseases (requiring antibodies) and increased rates of cancer (demanding novel therapies), contributes to the need for more targeted biopharmaceutical therapeutics on the market.

> "Biopharmaceutical manufacture can bring significant operational and technological challenges."

However, biopharmaceutical manufacture can bring significant operational and technological challenges. Producing these large and complex molecules in a reliable manner at industrial scale requires sophisticated manufacturing capabilities, long process durations, low yields and costly raw materials. Additionally, there is a need for highly skilled operators, making it very expensive to manage production facilities. To meet rising demand for biotherapeutics, there is therefore a necessity for more flexible workflows that allow for rapid scale-up and reduced production costs. Disposable bioprocessing equipment – like SUS – helps to address this and, consequently, it has become increasingly established in the modern biopharmaceutical processing of therapeutic drugs.

WHAT ARE SINGLE-USE TECHNOLOGIES?

SUS refer to disposable biopharmaceutical manufacturing (or bioprocessing) equipment lines, that are designed to be used during the production process of a single batch of therapeutics. Precision dispensing solutions are an example of a SUS, which enables the precise, yet flexible supply of raw materials. An alternative to traditional stainless-steel systems, SUS offer many advantages over reusable and partially disposable systems. This is linked to their unique ability to enhance production flexibility, limit operational costs and reduce overall management of the workflow – while minimising risk of contamination. As such, they are viewed increasingly as a commercially viable approach to achieving maximum process efficiency and productivity during biopharmaceutical manufacturing.

Sara Dorman
Global Biopharma Market Manager
E: sara.dorman@roquette.com

Roquette
Rue de la Haute Loge
62136 Lestrem
France

www.roquette.com

"It is predicted that SUS will soon be in place for most biopharmaceutical production lines, especially since the focus on bioprocesses and batch manufacturing continues to grow."

Single-use (or disposable) bioprocessing systems already dominate the precommercial market, but there is a trend for increased adoption of SUS for commercial-scale manufacturing too. As such, it is predicted that SUS will soon be in place for most biopharmaceutical production lines, especially since the focus on bioprocesses and batch manufacturing continues to grow. This is evident when you consider the numbers. The global single-use bioprocessing market size was valued at US$15.8 billion (£13.1 billion) in 2020 and is expected to expand at a compound annual growth rate of 16% from 2021 to 2028, illustrating the significant uptake of SUS by manufacturers.[1]

Are you keen to understand the reasons behind the rapid adoption of disposable bioprocessing equipment? Here are six ways that SUS, such as precision dispensing technologies, improve biopharmaceutical workflows.

SIX BENEFITS OF CHOOSING SINGLE-USE TECHNOLOGIES

1. Reduce handling time

Traditionally, the process of handling and weighing biopharmaceutical ingredients is time and labour intensive, and requires additional procedures to be put in place, increasing the risk of contamination. The implementation of SUS, like precision dispensing technology, can directly address these challenges. Here, single-use packaging and right-size weighing capabilities can allow processors to discharge raw materials seamlessly into the bioreactor; helping to streamline and eliminate entire steps of the production process, such as clean-in-place (CIP) procedures. As well as increasing efficiencies and limiting risk of cross-contamination, this removes many manual processes that can introduce unintentional human errors, such as weighing raw ingredients incorrectly.

2. Cost savings

Traditional stainless-steel systems are reusable, durable and able to withstand exposure to the powerful chemicals used to sanitise pharmaceutical processing systems. However, because stainless-steel systems necessitate stringent sterilisation regimes, these workflows involve harsh chemicals (which are often harmful to the environment) and result in considerable energy and water consumption. This can be costly and time consuming, while the risk of contamination still remains. Similarly, partially disposable systems – which can be used more than once, depending on the therapeutic being manufactured – must undergo cleaning and disinfection, as well as ongoing maintenance, since they can deteriorate over time.

"While SUS require repeated purchase per batch, the costs of these systems are generally offset by the avoidance of cleaning, sterilisation and validation, time saved and improved flexibility versus stainless-steel equipment."

Figure 1: A greener, more cost-effective solution: SUS, like precision dispensing technologies, significantly reduce cleaning times, resulting in lower water and energy usage.

SUS are championed for their role in cost reduction largely due to fewer cleaning steps because these systems remove the need for cleaning between every manufacture cycle while ensuring a sterile system for every drug batch, reducing production contamination and generating greater throughput. In addition, SUS can also decrease labour costs, as additional hold times and validation steps can be eliminated. Moreover, with much less facility infrastructure required, including less plumbing or an in-house water-for-injection (WFI) plant, investment and construction costs are lower and the plant's footprint much smaller.

Thus, while SUS require repeated purchase per batch, the costs of these systems are generally offset by the avoidance of cleaning, sterilisation and validation, time saved and improved flexibility versus stainless-steel equipment.

3. Increased productivity

By reducing the amount of time needed for raw material approval, sampling, dispensing and processing, SUS, like precision dispensing technologies (Figure 1), can significantly optimise turnaround times and accelerate the journey to market for novel, life-saving drug products. Crucially, with single-use equipment, process turnaround and set up of new processing lines are much quicker. This links back to the fact that these technologies reduce the significant system downtime needed to clean, sterilise and validate product containers and transfer assemblies, greatly reducing changeover times between processes and batches. Furthermore, this enables facilities to process more batches per year, resulting in increased productivity, efficiency, capacity and profitability.

4. Easily integrated into existing workflows

Equipment like single-use packaging for precision dispensing can be easily and quickly integrated into existing manufacturing processes, and is adaptable across a diverse range of workflows, including stainless steel or hybrid. As such, it provides the flexibility needed to keep pace with the ever-changing pharmaceutical landscape while remaining cGMP and US FDA compliant. Because precision

dispensing offers a "plug-and-play" solution, it also reduces the amount of operations and machinery training required after implementation. In turn, this further reduces the number of hours a facility must invest in material handling and streamlining workflows, bringing more process efficiencies.

5. Better customisation, compliance and control

Packaging for precise dispensing, and single-use pharma charge bags, are designed with the end user in mind and are purpose built to meet exact customer needs. For example, SUS packaging is usually available in a wide range of weights and custom fills, and product features can be matched to the desired chemistries and operational architectures. Packaging and outlet port size can be flexible to suit the application too, with suppliers allowing for customer input and customisation.

In terms of compliance, precision dispensing packaging can be procured from a vertically integrated organisation with a single point of audit, enabling high levels of transparency, easy compliance and extensive in-house knowledge about packaging production and material provenance. There are also two main regulations impacting components used in single-use systems: material biocompatibility and leachables and extractables. Biocompatibility testing requirements fall within USP 87, USP 88, USP 1031 and ISO 10993, depending on the application, while extractable and leachable tests run on the finished products used in SUS. To ensure minimal risk of contamination from the packaging itself, it is important that precision packaging for precision dispensing complies with extractables and leachables regulations for single-use technologies.

6. Promote a greener future

The bioprocessing industry continues to take steps to guarantee a greener, more sustainable future in which resources can be saved, products are profitably used and, at the end of their life, materials are recycled. Single-use technologies exhibit lower environmental impact than reusable systems and are subsequently determined the more environmentally friendly option. This is primarily because they eradicate the need for chemicals and resources – like energy and water – to sterilise reusable systems. Calculations suggest that converting from stainless steel to single use results in an approximate 85% reduction of both water use and waste generation.[2] Furthermore, manufacturers can choose to recycle or repurpose disposables, for example, by incinerating them for energy recovery. As SUS advance further, it is predicted that production efficiencies will continue to improve over time, further reducing their environmental footprint.

A LOOK TO THE FUTURE

As the biopharmaceutical market continues to grow, there is a need for increased efficiencies within existing processes – this requires a rethink of prevailing workflows. With batches needing to be produced more frequently, it will be necessary for biotherapeutic manufacturers to be accurate with their raw material requirements, as well as flexible with their scale-up and scale-down capabilities. To keep pace with these developments while ensuring business profitability and productivity, there will likely be a continued rise in the adoption of SUS – such as precision dispensing technologies – to facilitate the safe and efficient production of specialised pharmaceuticals. And while there will always be a place for stainless-steel and hybrid technologies, the importance of SUS continues to grow.

ABOUT THE COMPANY

Roquette is a family-owned global leader in plant-based ingredients, a pioneer of plant proteins and a leading provider of pharmaceutical excipients. Founded in 1933, the company currently operates in more than 100 countries, has a turnover of €3.9 billion, and employs more than 8,000 people worldwide. Life and nature have been the company's sources of inspiration for decades; all its raw materials are of natural origin and enable a new plant protein cuisine. The company offers pharmaceutical solutions that play a key role in medical treatments and develops innovative ingredients for food, nutrition and health markets, unlocking the potential of nature to improve, cure and save lives. Roquette is committed to improving the wellbeing of people all over the world, and puts sustainable development at the heart of its concerns, while caring for resources and territories in a bid to create a better and healthier future for all generations.

ABOUT THE AUTHOR

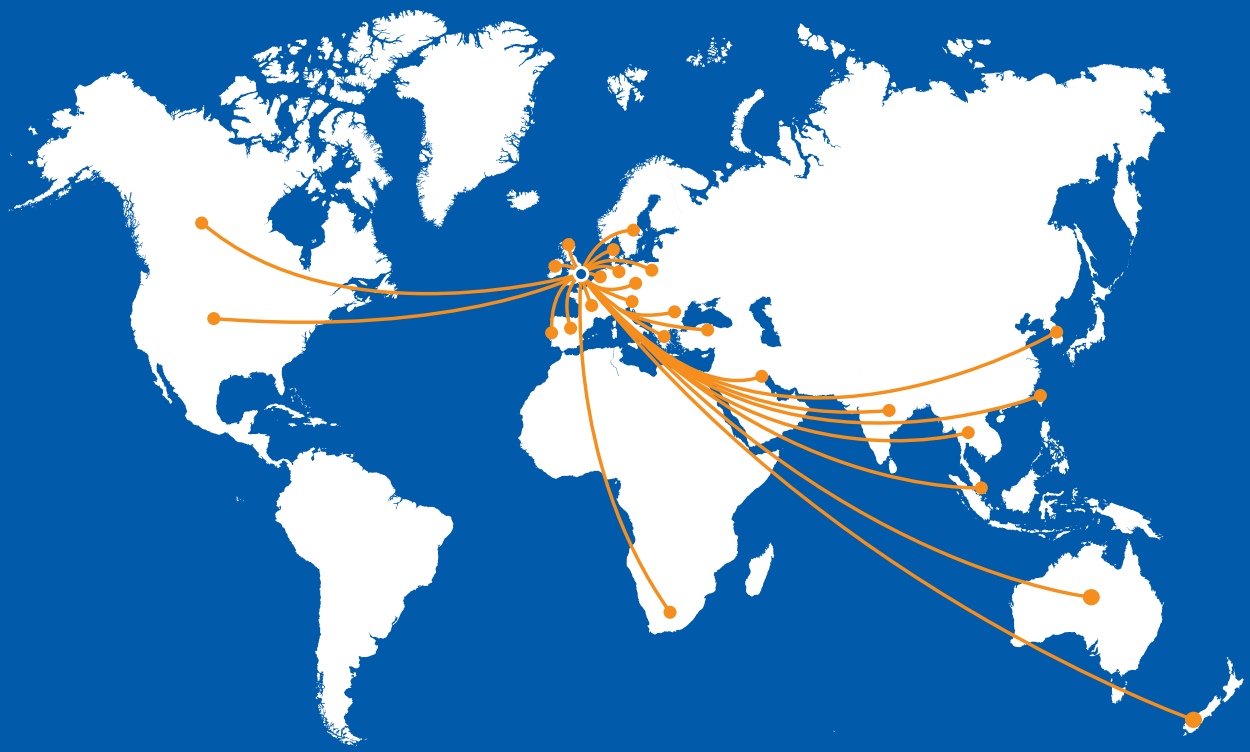
Sara Dorman is a Global Biopharma Market Manager at Roquette, a global leader in plant-based ingredients for the pharma industry. Ms Dorman holds an MSc in Molecular and Cellular Biochemistry from Loyola University in Chicago (IL, US) and a BA in Biology from Lawrence University, Appleton (WI, US). She has over 20 years of experience in the biopharmaceutical, micro/diagnostic and fermentation industries.

REFERENCES

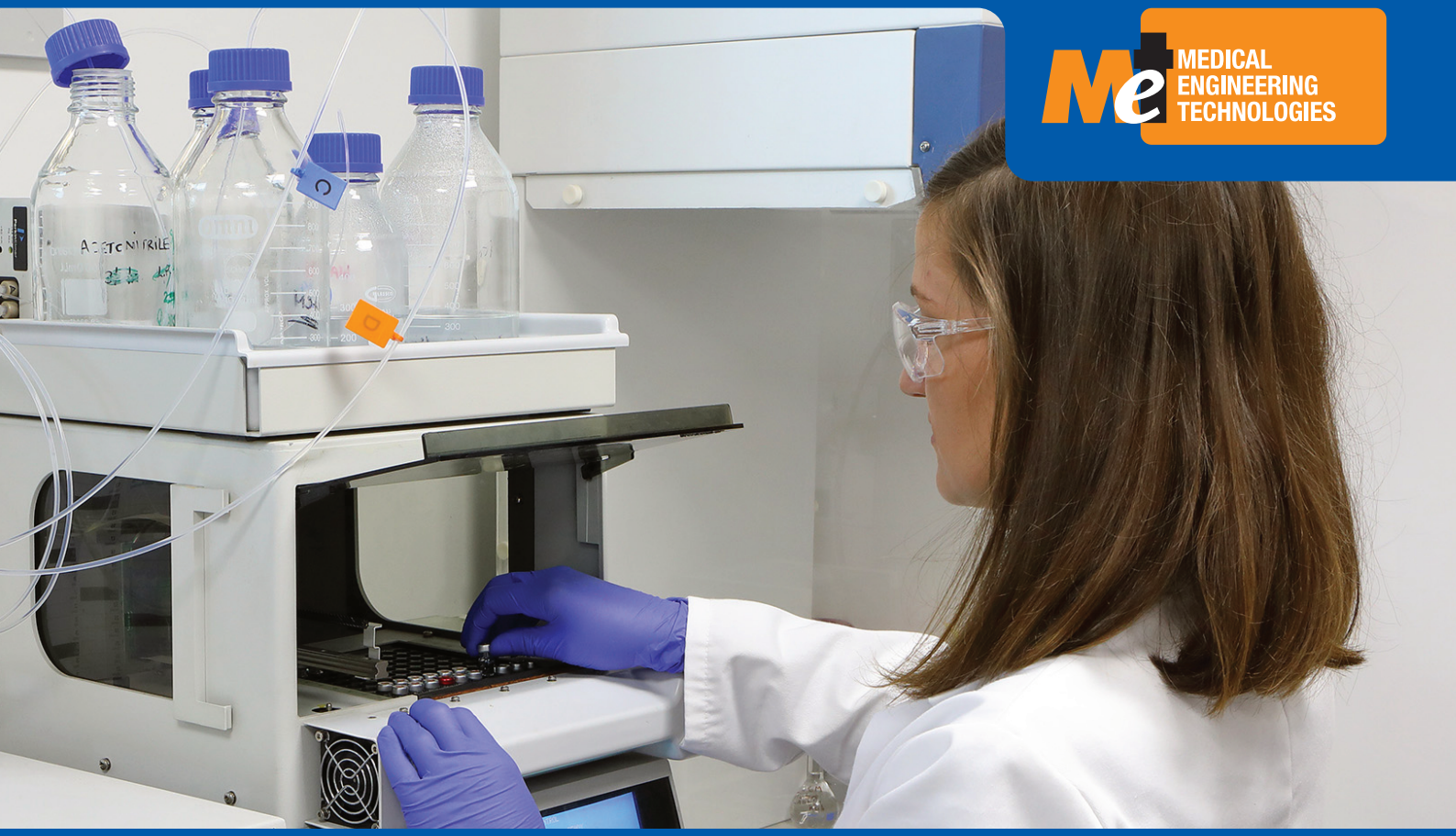
1. *"Single-use Bioprocessing Market Size, Share & Trends Analysis Report By Product (Probes & Sensors, Simple & Peripheral Elements), By Workflow (Downstream, Upstream), By End-use, By Region, And Segment Forecasts, 2021 – 2028". Research Report, Grand View Research, accessed Jul 2022.*
2. *Hodge G. "The economic and strategic value of flexible manufacturing capacity". ISPE Strasbourg Conference, Sep 28–29, 2009.*

Analytical Chemistry Testing

Medical Engineering Technologies is the destination for combination device batch release and chemical analyses testing. Clients from across the globe have found our laboratory services to be rapid, precise and very effective.



Global Excellence in Combination Device Chemical Analyses



MEDICAL ENGINEERING TECHNOLOGIES

Analytical Chemistry

- Drug Stability & Container Compatibility
- Residual Solvents ICH Q3C & USP <467>
- Single-use Technologies Residual Analysis
- Determination of Nitrosamine
- Cannabinoid (CBD) Analysis
- SUS Production System Analysis
- GC/MS & Headspace GC/MS,
- HPLC/MS, HPLC/PDA, HPLC/RI & HPLC/UV

ISO 10993 Biological Evaluation of Medical Devices

- Extractables & Leachables
- Chemical Characterisation
- Degradation Studies
- Toxicological Risk Assessment

ISO 18562 Breathing Circuits

- Particulates Matter released by Breathing Devices
- VOC's released by Breathing Devices
- Leachables in condensate
- Toxicological Risk Assessment

Our chemical analysis capabilities encompass a very wide range of techniques and applications. The technical skills and equipment within MET can be applied to your combination devices and formulations to verify safety and effectiveness.

Careful protocol development and implementation will ensure effective and efficient execution of a test programme that will satisfy the needs of all regulatory authorities. This is a result of our excellent training and experience along with a team of chemists who care.

Medical Engineering Technologies Ltd
Unit 16, Holmestone Road,
Dover, Kent. CT17 0UF
UNITED KINGDOM

www.met.uk.com
t +44 (0)1304 213223
t +44 (0)845 458 8924
e sales@met.uk.com

ISO 17025 QUALITY SYSTEM

Stevanato Group

EMBRACING OPPORTUNITIES PRESENTED BY DIGITALISATION: USING DATA TO DRIVE PERFORMANCE

In this article, Otto Abildgaard, System Owner Digitalisation, and Sebastian Berninger-Lund, Assembly and Packaging Automation Chief Designer, both at Stevanato Group, review the four-stage process the company has developed to bring improvements in time to market through optimised manufacturing. They present how machine design and assembly is being enhanced through developments such as the digital twin – and discuss how the collection and use of data throughout the manufacturing process can drive improved performance.

As an industry, pharma is renowned for innovation, responsiveness to unmet needs and a determination to continuously improve. Whether it is the development of more personalised drugs to treat complex diseases or the implementation of connected devices to track and improve patient adherence, many recent advances have come from greater insight supported by data. Nowhere is this striving for improvement seen more than in device manufacturing, where the momentum for more rapid deployment of products through the digitisation of manufacturing is gathering real pace (Figure 1).

Across all sectors, healthcare and pharma included, covid-19 has accelerated underlying digital change. In doing so, it has accelerated the pace of business, with research from global consulting firm McKinsey & Company suggesting that business practices considered best-in-class in 2018 would today be regarded as slower than average.[1]

> "Organisations must embed smarter thinking throughout their business and couple it with continued investment in innovative technologies."

To achieve the higher levels of operational agility now required to sustain competitive advantage, organisations must embed smarter thinking throughout their business and couple it with continued investment in

Figure 1: Harnessing digitalisation for a new era of pharma manufacturing.

Otto Abildgaard
System Owner Digitalisation
E: otto.abildgaard@stevanatogroup.com

Sebastian Berninger-Lund
Assembly and Packaging Automation Chief Designer
E: sebastian.berningerlund@stevanatogroup.com

Stevanato Group
Via Molinella 17
35017 Piombino Dese
Padova
Italy

www.stevanatogroup.com

"Continual improvements are fuelled by the systematic capture and purposeful analysis of relevant data."

innovative technologies. Harnessed correctly and used in the right way, such technologies have the potential to enhance accuracy, efficiency and productivity while limiting risks and costs.

At Stevanato Group, the potential of technology to advance pharmaceutical manufacturing environments is a key focus. While this incorporates the digitisation of individual activities and specific processes, there is an opportunity for stakeholders to collaborate and innovate together on a more fundamental transition to digitally integrated environments, where continual improvements are fuelled by the systematic capture and purposeful analysis of relevant data.

The company is developing a four-stage framework to support its pharmaceutical partners in realising this transformation, resulting in manufacturing processes and workflows that are digitally optimised. This framework can help achieve gains in operational performance while sustaining consistency of product quality, minimising demands on resources and avoiding costly disruption.

The first element of the framework relates to machine design, where a digitally led approach can be used to simplify and derisk the journey from prototyping to the point at which components and equipment are engineered into existence. The focus here is on exploiting all the advantages afforded by a virtual environment by developing a digital twin of the machine. This combines physical computer-aided design (CAD) with machine behaviour – using a programmable logic controller (PLC) – enabling iterations to be made quickly and cost effectively before the transition is made to three-dimensional (3D) reality.

The digital twin technology creates a copy of the machine, precisely mirroring within a digital environment what can be expected of the physical version. This means that process optimisation can be incorporated into the design phase, where new developments on a machine are tested and validated before they are manufactured. This has the benefit of accelerating implementation and reducing potential disruption, since component and software changes can be validated virtually in parallel with the actual machine. This approach reduces the likelihood of iterative real-world developments and therefore reduces waste in terms of materials and time. All the while, machine owners are left with a comprehensive digital record of their equipment that can also be employed as a platform for virtual training.

The second element of the Stevanato Group framework encompasses the digitisation of machine assemblies. This involves using high-definition cameras to record in critical detail the machinery within an entire assembly line at the point at which it is validated on the shopfloor. From these source images, an accurate 3D model of the set-up can be rendered using CAD software and, because the virtual image is a precise replica of the delivered system, it can be cross-referenced against a digital "blueprint" to interrogate and highlight any discrepancies between the two.

This process is conducted using an on-screen, colour-coded "heat map" that visualises any deviations and highlights where attention might be required. At a component level, it will show, for example, areas of wear and tear that might have an influence on performance.

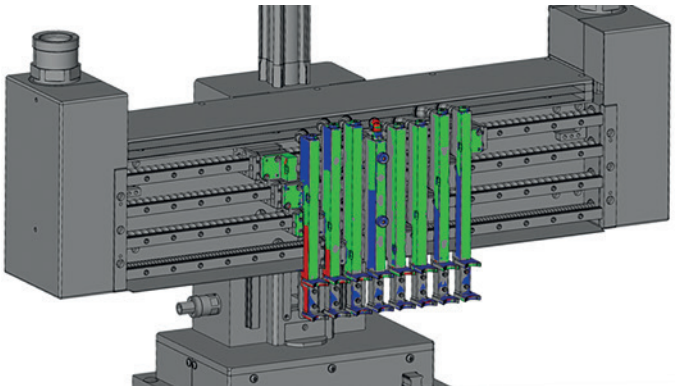


Figure 2: Colour-coded "heat map" indicating where to pay attention, based on any deviations.

On high-performance production units, such deviations can impact a machine's productivity but are too subtle to be detected via manual inspection. By digitising the machinery, however, issues can be identified, diagnosed and corrected through interactive remote analysis, speeding up the process and minimising downtime while ensuring consistency of quality is maintained and failure rates are kept to a minimum.

In Figure 2, the parts with blue marking should be adjusted inwards by the assembly engineer and areas with a red marking should be adjusted outwards for ideal operation of the equipment module.

Knowing that the machine is designed, assembled and performing correctly as a result of the first two stages, the focus is then on the area of digital surveillance and the collection of data from various operational phases, including running-in, factory acceptance testing, site acceptance testing and production. Subsequently, the collected data can be used and analysed for continual improvement.

Regarding collection – the third stage – Stevanato Group can facilitate high-level data capture through data monitoring and measuring. The data-collection platform has been designed on the principles of compatibility and interoperability to ensure it can be integrated with equipment from any major supplier – not just Stevanato Group's own machinery – and with software interfaces provided by third-party providers across the market.

The data-collection platform conforms to the rule of "garbage in, garbage out" – if the data capture and recording process is not performed at the highest level, then its usefulness will necessarily be diminished. It follows, therefore, that enabling the collection of item-level, batch-traceable, high-integrity data at a superior sampling rate allows the insights derived – and their resultant value – to be significantly enhanced.

Typically, there are a variety of hurdles to establishing a framework and process for the collection of such data. The platform addresses many of the key challenges here, with no additional coding required inside the process code, and the advanced filter set-up ensures only data of value is captured at a high sampling rate of each PLC scan, with item-level traceability to inform diagnostic activity. The vendor-agnostic nature of the data-collection platform also means that the end user does not require multiple suppliers to manage and maintain a series of separate data interfaces – nor are they burdened with creating such interfaces in-house. In this way, it creates a unified interface for end users in the pharma industry, simplifying IT systems and, therefore, reducing ongoing maintenance requirements. Simultaneously, machine builders are provided with access to a broad range of data interfaces, databases and analytics without investing in internal competences.

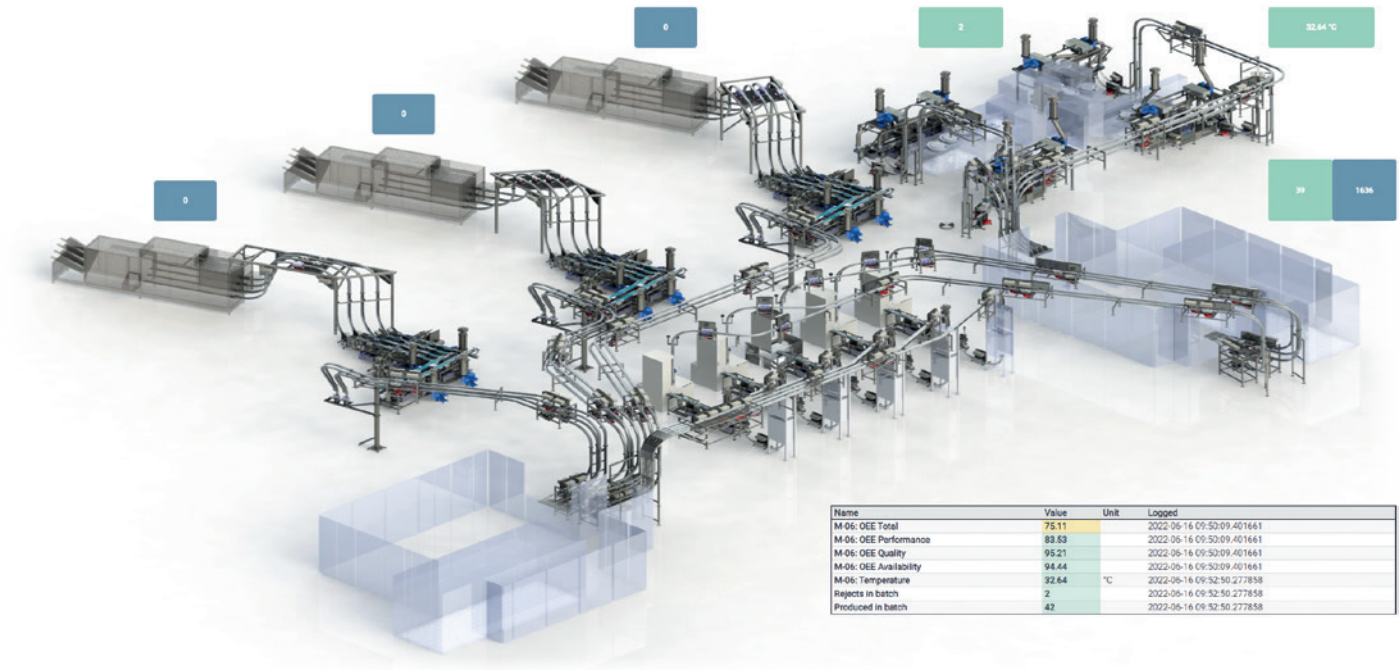


Figure 3: Real-time tracking of markers through 3D visualisation.

Value creation by data analytics and visualisation occurs in this final stage, which is predicated on creating meaningful, actionable insight from the collected data. To achieve this, it is essential for the data not to be considered as an abstract asset, held away from the organisation, but rather for it to be "plugged in" at an operational level and made available to people in specific roles who can act upon it accordingly.

Operators, for example, can create maximum value if they are provided with immediate feedback from equipment in a live setting. Maintenance teams, meanwhile, are seeking underlying machine operation data provided over a period of time to feed into root-cause analysis and long-term optimisation strategies. Line managers will require different datasets or analysis patterns to assess trends in shopfloor operations, while quality managers will benefit from insight into the components sourced from providers across the supply chain.

Sifting through a continuously generated "fire hose" of production data to arrive at these various tailored insights makes for a challenging task. However, this task can be simplified by translating the acquired data into dynamic, 3D visualisations accessed via a dashboard, giving users at all levels access to the information they need in a digestible, graphical form (Figure 3).

This provides operators with access to near-real-time tracking of markers such as temperature and process speed, while those with a focus on longer-term performance can track machine-level issues over time to inform iterative improvements. As such, it neatly dovetails with the Six Sigma approach adopted within many manufacturing environments to sustain quality of performance and limit defects, as measured by process capability index (Cpk) values.

Traceability adds an important layer of value in these circumstances because data values are associated with recorded imagery that can act as reference evidence. Video feeds from the constant surveillance tools used on production lines, for example, can be accessed where deviations are highlighted, presenting an opportunity for deeper analysis.

This example highlights the interlinked nature of truly digital systems, and the benefits that can be realised when the thread of digital thinking is embedded throughout all stages of the production chain, from design and operation to support and performance analysis. As an enabler within this chain, Stevanato Group integrates at whatever point its tools and equipment can be employed to optimise certain processes or functions. For some partners, this will mean an exclusive focus on the collection of data that can be digested and interpreted within their own systems, while others will take

advantage of associated stages of the Stevanato Group offering to support engineering design or facilitate data analysis.

This open, integrated alignment of capabilities among partners is fundamental to the digital philosophy that pharmaceutical companies must adopt for their operations to adapt quickly to the production challenges associated with rapidly deploying new products to market. Under these intensified conditions, where defects and deviations from a desired target can extend timeframes and costs exponentially, the answers to sustained performance enhancement will exist within the data. Uncovering them is not simply a case of data gathering but, rather, ensuring that systems are designed to manage the flow, capture and analysis of high-volume, high-integrity data, and then making it come alive in the eyes of the individual who can act upon it.

ABOUT THE COMPANY

Founded in 1949, Stevanato Group is a leading global provider of drug containment, drug delivery and diagnostic solutions to the pharmaceutical, biotechnology and life sciences industries. The Group delivers an integrated, end-to-end portfolio of products, processes and services that address customer needs across the entire drug life cycle at each of the development, clinical and commercial stages. Stevanato Group's core capabilities in scientific research and development, its commitment to technical innovation and its engineering excellence are central to its ability to offer value-added solutions to clients.

REFERENCES

1. *"The new digital edge: Rethinking strategy for the postpandemic era". Survey, McKinsey & Company, May 26, 2021.*

ABOUT THE AUTHORS

Otto Abildgaard is System Owner Digitalisation at Stevanato Group. He gained his experience from high-technology manufacturing processes as a specialist and technical project manager. He specialises in combining sensor technology and data science with his passion for making digital products visible and valuable. With a strong foundation in both physics and engineering, Mr Abildgaard excels at leading, communicating and developing new digital solutions from idea to product – and, by that, leading Stevanato Group to new heights.

Sebastian Berninger-Lund is Assembly and Packaging Automation Chief Designer at Stevanato Group. Through his background in automation and project management, Mr Berninger-Lund gained fundamental experience to deliver quality and validated machines across high-technology industry branches. His passion for quality, structure and standardisation perfectly meets GMP needs, leading him to push Stevanato Group's product quality to new levels.

PDA
Parenteral Drug Association

pda.org/2022ups

2022 PDA Universe of Pre-Filled Syringes and Injection Devices Conference

REGISTER BY 21 AUGUST TO SAVE!

The New Normal in Injectable Drug Delivery

Excitement is Growing for the Return to In Person!

Stay a step ahead of the future of pharmaceutical devices! This year's plenary sessions will take you on a journey, starting with an overview of the current status of the field, followed by a look at the importance of partnership and cross-industry collaboration, a patient perspective, and finally, an in-depth exploration of what the future holds.

Concurrent sessions will delve into hot topics, such as:

- Autoinjectors
- Clinical to Commercial
- Deep Cold Storage
- Digital Health
- Human Factors
- Large Volume Injectors
- Manufacturing
- New Technologies
- Regulatory Affairs and Standards
- Sustainability

Don't miss the return of this popular conference to an in-person format to take advantage of networking opportunities and the chance to connect with numerous vendors and suppliers in the Exhibit Hall!

Join us to be the first to know about the advances that will push the industry forward.

Visit *pda.org/2022ups* to learn more!

18-19 OCTOBER | PALM SPRINGS, CALIFORNIA

EXHIBITION:18-19 OCTOBER
ANNEX 1 WORKSHOP: 20-21 OCTOBER
TRAINING COURSES: 20 OCTOBER
#PDAups

CONNECTING PEOPLE SCIENCE AND REGULATION®

Your trusted partner for contract manufacturing services of drug delivery devices

At Stevanato Group, we understand the rigorous requirements to produce components and sub-assemblies for drug delivery systems.
Leading players trust our state-of-the-art manufacturing capabilities and scalable production solutions within the pen injector, auto-injector, wearable, and inhaler markets.

INTERVIEW

In this interview, Renan Joel of Easyfairs talks with ONdrugDelivery about the upcoming inaugural Connect in Pharma conference in Geneva. Mr Joel gives insight into what the conference has to offer attendees, the organiser's track record and future ambitions for Connect in Pharma.

RENAN JOEL, DIVISIONAL DIRECTOR, EASYFAIRS

Renan Joel is Divisional Director of Packaging at Easyfairs, working across an international portfolio of agenda-setting packaging events in the UK, France, Switzerland and Italy. His comprehensive approach to connecting suppliers with key players has helped build a platform that will drive collaboration and business for Europe's pharmaceutical community.

"Attendees can expect to find a programme that includes a range of opportunities to learn about the latest advances and trends through plenary conferences, workshops and networking events."

Q To begin, could you give us an overview of the Connect in Pharma conference? What should attendees expect to experience and what should they expect to take away after having attended?

A Connect in Pharma is a new event for the pharmaceutical and biotechnology community, organised by Easyfairs, a leading international events company. It is the first event exclusively dedicated to the entire pharmaceutical manufacturing value chain, with the inaugural event taking place in Geneva on September 14-15, 2022.

Attendees can expect to find a programme that includes a range of opportunities to learn about the latest advances and trends through plenary conferences, workshops and networking events. This new event presents pharma companies and their suppliers with an unrivalled opportunity to discover and shape the future of their products and the wider sector.

Like all Easyfairs events, Connect in Pharma aims to ensure people feel energised by the conversations and mix of people in the room. We have a track record of bringing a buzz and excitement to our event spaces. This also means ensuring that visitors find plenty of opportunities to network and mingle. Visitors will find a champagne bar right in the middle of the hall, a photography exhibition, an awards ceremony highlighting innovations in sustainable packaging and more.

The photo exhibit is something I am particularly excited about. We are working with SbD Creative (Mold, UK) to launch a multimedia exhibit called "Days of Rare", which will feature photos and video interviews with individuals affected by rare diseases. It is part of a charity initiative we have formed with EspeRare (Geneva, Switzerland), a not-for-profit organisation that develops and promotes access to life-changing treatments and technologies for patients affected by rare diseases. For every visitor who walks through the conference doors, Easyfairs and Connect in Pharma will donate five Swiss francs to EspeRare.

I think everyone who attends Connect in Pharma can expect to find something that inspires them, someone who has a solution to a technical challenge and a host of new ideas to take away with them.

Q Could you talk about how you decided on packaging, drug delivery and contract manufacturing as the scope for Connect in Pharma? Also, please could you tell us why you decided on Geneva as the location for this year's show?

A We worked closely with a newly formed advisory board to identify four key areas in the European pharmaceutical market. These main themes – innovative packaging, drug delivery systems, contract manufacturing and the filling and assembly process – are key areas that players in the pharmaceutical sector are increasingly focusing on, looking towards integrated solutions to reduce time to market. This event looks at everything downstream of the molecule. In other words, once the science has been done, companies need to invest in getting that molecule into a form that can be delivered in a safe and reliable way to a patient.

Modern pharmaceutical businesses are looking for the most effective way to bring their products to market against the backdrop of an expanding and ageing population, growing disruption in international supply chains and a growing trend towards small batch production. Having the right drug delivery system, filling and finishing vials in a sterile environment, packaging and outsourcing are all important components of that process. There is a vibrant community in Europe making extraordinary advances across all these areas.

"It quickly became clear that Connect in Pharma would have to be in Geneva, given its geographical proximity to so many important players in the sector, from large corporations to small start-ups and biotech clusters."

It is crucial that businesses in the pharmaceutical space find the best solutions for drug delivery devices and packaging, and that they find out about the latest innovations to remain competitive in a fast-paced global market. Geneva is the perfect location to bring together key influencers from leading pharmaceutical groups, biotech companies, industry clusters and suppliers. Before deciding to launch any new event, our team at Easyfairs conducts thorough market research to map out our target audience, and it quickly became clear that Connect in Pharma would have to be in Geneva, given its geographical proximity to so many important players in the sector, from large corporations to small start-ups and biotech clusters. It is the geographical heart of pharmaceutical production in Europe.

Q The key attractions at Connect in Pharma are the conference agenda and the exhibition, can you give us some more detail on each of these?

A The exhibition hall will host about 100 exhibitors, including BD (NJ, US), Essentra Packaging (Nottingham, UK), Unither Pharmaceuticals (Aimens, France), Catalent Pharma Solutions (NJ, US), Gerresheimer (Düsseldorf, Germany) and many more. This is the ideal location to explore solutions for pharmaceutical packaging, medical devices and manufacturing challenges.

The plenary conferences are all about helping us think about the European pharmaceutical sector of tomorrow. Organised as four half-days, the conference programme will give the floor to experts working at the forefront of pharmaceutical development in the main areas of the pharmaceutical supply chain: packaging, medical devices, sub-contracting and equipment. Visitors can hear from experts on a range of topics, from cybersecurity, through patient-centric design to the economics and geography of innovation.

The workshops are 45-minute sessions, giving visitors access to experts who can provide insight and advice on finding technical solutions to problems. This part of the programme is intended to provide representatives from pharmaceutical and biotech companies with the opportunity to interact with different suppliers to better understand the best practices and challenges of their suggested solutions.

> "Our aim is to make Connect in Pharma an annual event that is not to be missed."

We are also dedicating a portion of exhibitor space to highlight innovation. This will allow participants to hear from exhibitors demonstrating their latest innovation or technology in short, 15-minute segments. This will be a way for visitors to learn about the latest innovations and find new suppliers and partners.

Q As Connect in Pharma is a brand-new event, can you tell us a little more about the organiser, Easyfairs?

A At Easyfairs, we organise over 200 face-to-face events in 14 countries, primarily in Europe. We have a long-standing track record of running events in the packaging world, so we knew we were well placed to serve the pharmaceutical sector as well.

We serve communities by giving them a vision of their future, helping them foster connections and offering them a life-changing experience through a core focus on new technologies and innovation.

The team at Easyfairs is passionate about "easifying" the life of our customers. What this means is that we are looking to increase the return on time and investment for professional communities through our "all-in" formulas, advanced technology and customer-centric approach. At Easyfairs, our goal is to harness new technology and innovate to make "being there" an exciting experience.

Our digital features and initiatives provide these communities with excellent opportunities to network effectively and do business throughout the year. We listen carefully to create compelling online formats that meet customers' constantly evolving needs.

Q What are the medium-to-long-term plans for Connect in Pharma? Where do you see the event in four or five years' time?

A We know it usually takes a few years for any new exhibition to become established, but we are confident this edition will be a huge success for us and we are ready to invest in the medium and long term to ensure this happens with Connect in Pharma. Nevertheless, we are very impressed by the results we have already achieved in our first year. While we expect to have about 100 exhibitors this year, the venue at Palexpo has the capacity to accommodate larger exhibitions, and we anticipate that the number of exhibitors and visitors will grow by 50% for Connect in Pharma's second edition.

We are always looking at ways to build our community. While Connect in Pharma will remain a live, in-person, Geneva-based event, we are looking at ways to use technology to create meaningful and useful information services around the event.

In four or five years' time, we expect to be the market leader in this space. Our aim is to make Connect in Pharma an annual event that is not to be missed by suppliers, specifiers and other influencers involved in pharma and biopharma packaging, devices and production. Easyfairs is an ambitious company and, when we enter a market, we are in it for the long run.

Connect in Pharma will take place in Geneva, Switzerland, on September 14-15, 2022. Follow the link to find out more: www.connectinpharma.com

CONNECT IN PHARMA

Renan Joel
Divisional Director Packaging – UK, France, Italy & Switzerland
E: renan.joel@easyfairs.com

Easyfairs
Rue Saint-Lambert 135
1200 Brussels
Belgium

www.easyfairs.com

ON drugDELIVERY

2022/23 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
September 2022	Wearable Injectors	Deadline passed
October	Prefilled Syringes & Injection Devices	Sep 8, 2022
Oct/Nov	Drug Delivery & Environmental Sustainability	Sep 15, 2022
November	Pulmonary & Nasal Drug Delivery	Oct 6, 2022
December	Connecting Drug Delivery	Nov 3, 2022
January 2023	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Dec 1, 2022
February	Prefilled Syringes & Injection Devices	Jan 12, 2023
March	Ophthalmic Drug Delivery	Feb 2, 2023
April	Pulmonary & Nasal Drug Delivery	Mar 2, 2023
April/May	Drug Delivery & Environmental Sustainability	Mar 16, 2023
May	Delivering Injectables: Devices & Formulations	Apr 6, 2023
June	Connecting Drug Delivery	May 4, 2023
July	Novel Oral Delivery Systems	Jun 8, 2023
August	Industrialising Drug Delivery	Jul 6, 2023

CONNECT IN PHARMA

THE FUTURE OF
PACKAGING, DRUG DELIVERY &
CONTRACT MANUFACTURING

14 & 15 September 2022 | Geneva, Switzerland

The new event at the heart of European pharma
dedicated to innovative packaging, drug delivery systems, CDMO/CMO and filling & assembling processes



REGISTER TO ATTEND
USING THE CODE 2050
connectinpharma.com

Founding partners

BD · ESSENTRA PACKAGING · UNITHER · KÖRBER · Catalent · BIOCORP · gerresheimer · Uhlmann UHLMANN GROUP

by EASYFAIRS

gerresheimer

INDUSTRIALISATION OF PHARMACEUTICAL AND MEDICAL DEVICES IN THE SCIENTIFIC MOULDING APPROACH

Here, Thomas Rudolph, Global Team Lead, Process Engineering, Markus Reil, Head of Plant Quality & Global Quality Engineering, Stefan Schumann, Engineer Advanced Technology Moulds, and Tobias Weigert, Global Team Lead Metrology, all of Gerresheimer, discuss the company's strategy for managing potential risks across the entire product lifecycle, including the identification of all parameters within the injection moulding process using highly precise measurement technology.

There are very few other industrial sectors where reliable quality plays such a crucial role as in the drug delivery device sector. Every faulty product can put the efficacy of a therapy and, in extreme cases, the life and health of the patient at risk. With this in mind, Gerresheimer made a paradigm shift years ago (Figure 1). The goal of the company's quality strategy is no longer to weed out faulty products at the end of the production process (quality by inspection) but instead to design the entire product lifecycle around preventing faulty products in the first place (quality by design). In so doing, Gerresheimer reduces the risk of rejected batches, ensures interruption-free product delivery for its customers and benefits patients, who can rely on flawless primary packaging and reliably functioning devices.

RISK-BASED APPROACH

A deciding factor for successful quality by design is to recognise all the relevant risks in the product lifecycle, classify them according to their severity and develop appropriate strategies for mastering them. By identifying, rating and prioritising these risks, Gerresheimer lays a reliable foundation for all stages of the product engineering process. This approach can be split into three pillars:

1. Risk management, in the form of targeted, prioritised management of risks performed as a continuous task
2. Control strategy in production, which ensures that the quality levels corresponding to the risks are met in series production over the long term
3. Validation strategy, which acts as the link between the other two pillars, accounting for the fact that long-term data from series production are, statistically, always worse than the short-term data from the validation phase.

By taking a risk-based quality approach, producer and consumer risk can be clearly limited. The customer's requirements for the product are translated into key figures, which enable precise measurement of the required properties. During the product

> "By identifying, rating and prioritising these risks, Gerresheimer lays a reliable foundation for all stages of the product engineering process."

Thomas Rudolph
Global Team Lead,
Process Engineering
T: +49 9431 639 6973
E: thomas.rudolph@gerresheimer.com

Markus Reil
Head of Plant Quality &
Global Quality Engineering
T: +49 9431 639 7684
E: markus.reil@gerresheimer.com

Stefan Schumann
Engineer Advanced
Technology Moulds
T: +49 9431 639 77545
E: stefan.schumann@gerresheimer.com

Tobias Weigert
Global Team Lead Metrology
T: +49 9431 639 6685
E: tobias.weigert@gerresheimer.com

Gerresheimer Regensburg GmbH
Oskar-von-Miller-Str. 6
92442 Wackersdorf
Germany

www.gerresheimer.com

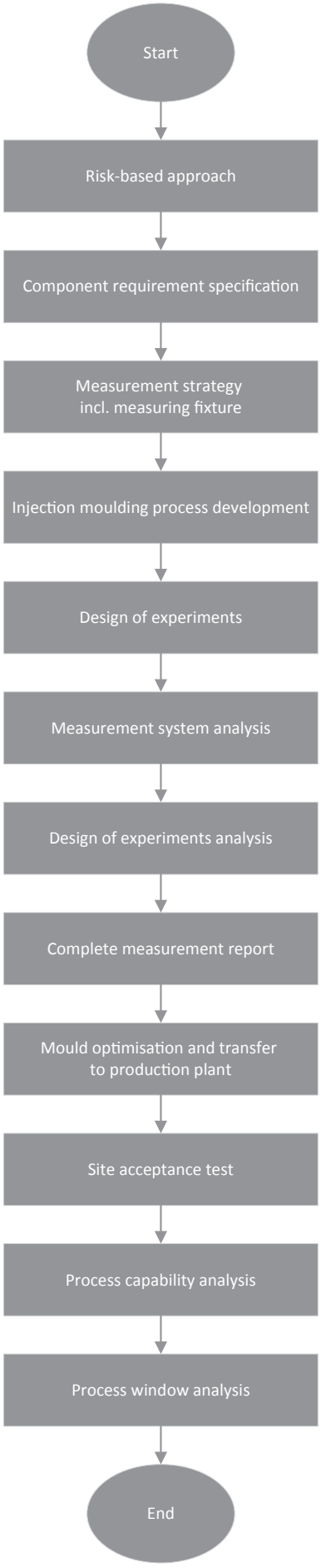


Figure 1: Quality by design flowchart.

engineering phase, a strict validation strategy is defined based on the severity of the product risks determined in the linked failure modes and effects analyses and the acceptable business risks. In turn, the control strategy during production is determined by product risks and residual risks. The outcome is a production process where the customer can rely on product properties and quality without reservation.

Gx INNOSAFE – INTEGRATED PASSIVE SAFETY SYSTEM FOR PREVENTING NEEDLESTICK INJURIES

With their exposed cannulas, used syringes present an omnipresent source of danger in medical practices, laboratories and hospitals. Existing needle protection systems reduce the risk of injury for end users but require additional effort both during filling and when using the syringe. With Gx InnoSafe (Figure 2), Gerresheimer offers a syringe with an integrated passive safety system that is optimised for processes at pharmaceutical companies, preventing accidental needlestick injuries and reuse.

For users, injections are performed as usual. The syringe body is visible so users can check that it is filled and that the contents are pure, as well as optimally monitoring administration. After removal of the sealing cap with an integrated flexible needle shield, the syringe is placed at the site of injection, the cannula inserted into the tissue and the active agent injected. Accidental triggering of the safety system is ruled out as the mechanism is not activated until the cannula is inserted, and the safety mechanism is automatically and permanently locked once the syringe is removed from the site of injection. In this way, the cannula is reliably concealed and syringe reuse is prevented.

For the pharmaceutical company, the Gx InnoSafe offers all the benefits of the ready-to-fill (RTF) syringe filling process. During production, the safety system is assembled on Gx RTF glass syringes in the cleanroom just as with a standard needle shield. The syringes are packed with the safety system in a 100-hole nest and tub format, then sealed and sterilised with ethylene oxide. They can be processed on existing filling lines without additional preparation and assembly steps.

> "Due to the impossibility of inline testing, quality assurance for the sealing mechanism must take place via statistically analysed samples."

MEASUREMENT TECHNOLOGY – KEY COMPETENCE FOR THE SCIENTIFIC MOULDING APPROACH

Gx InnoSafe was developed to prevent needlestick injuries, which is one of the greatest residual risks for syringe-based injections. A quality level adequate for the risk plays a decisive role when it comes to success in clinical practice. However, this is anything but trivial when it comes to mass production of a product. While the whole range of quality criteria can be fully checked inline during production, this does not include the most critical function of Gx InnoSafe – the irreversible sealing of the needle.

Due to the impossibility of inline testing, quality assurance for the sealing mechanism must take place via statistically analysed samples. For the product, maximum reliable (worst-case) error rates were defined for series production based on the risk management severity. The testing strategy for series production was then determined based on the required sample sizes and acceptance criteria. For validation, the sample sizes and acceptance criteria were tightened, based on internal quality processes, to ensure that a quality level corresponding to the application risks is reached over the long term. Risk-based product reliability values exceeding 99% and a statistical confidence level of 95% were applied.

To achieve reproducible measurement results during function tests, measurement methods were developed and optimised for use in series production, then qualified in Gerresheimer's metrology and quality lab. The test and functional parameters defined by quality engineering in the component requirement specification (CRS) have to be measurable using jigs on co-ordinate-measuring equipment. Gerresheimer relies on Zeiss Contura G2 and Zeiss O-Inspect CMMs (Carl Zeiss, Oberkochen, Germany) as standard for tactile and optical measurements to ensure department and location-independent reproducibility.

In parallel with mould making, a measurement strategy is developed and co-ordinated with the customer or quality

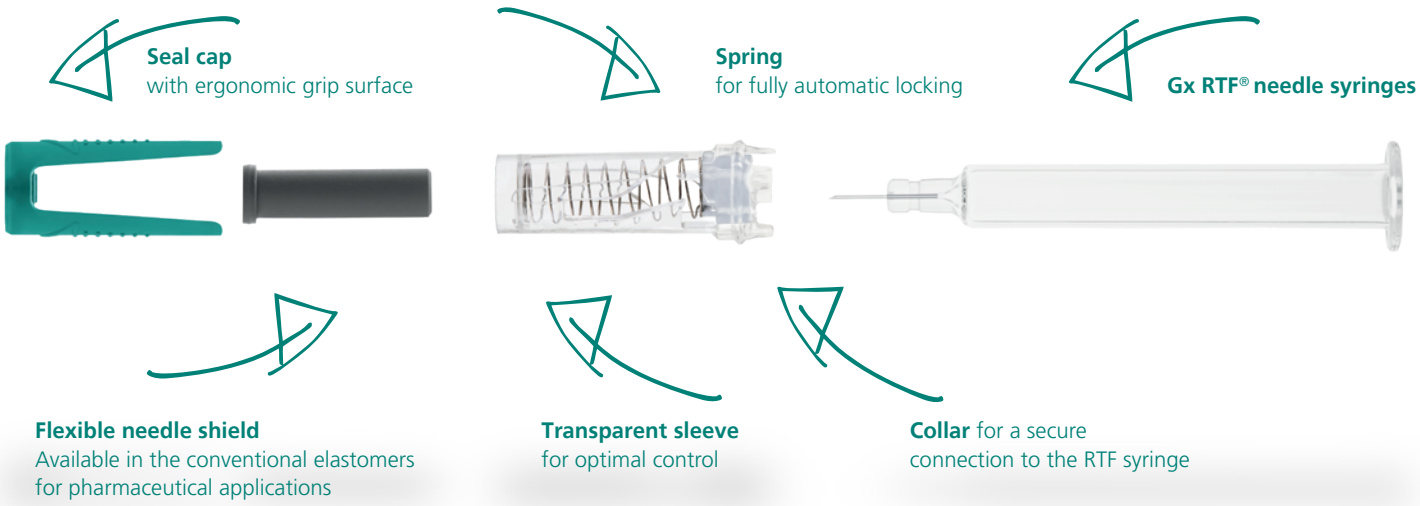


Figure 2: Gerresheimer's Gx InnoSafe safety system.

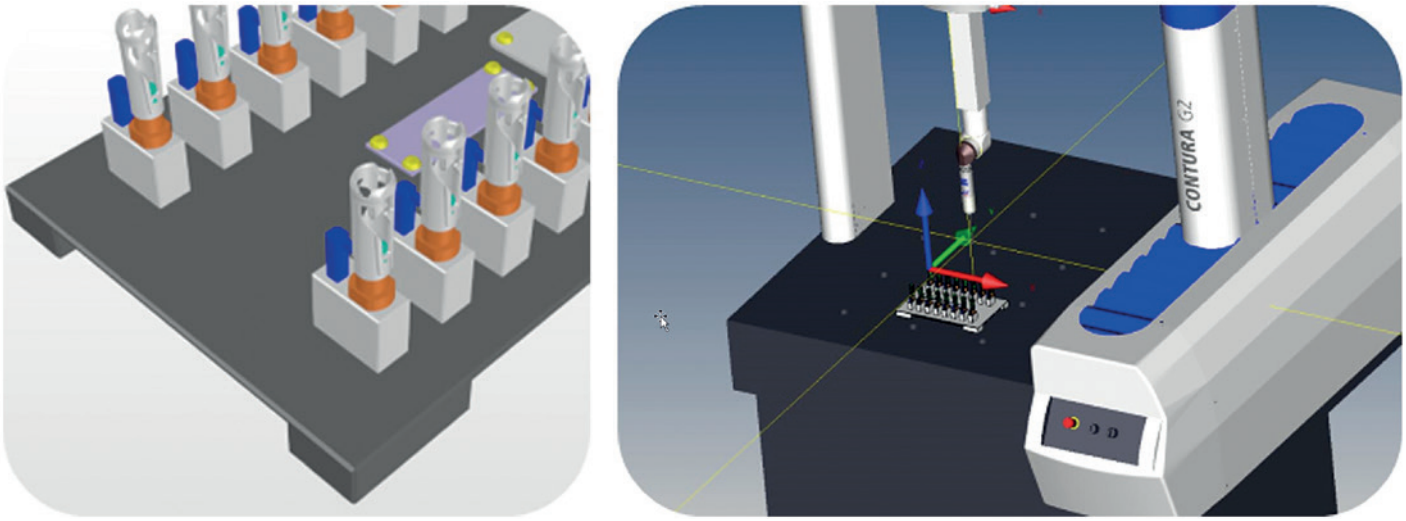


Figure 3: Virtual test programs are created in parallel for qualifying standard probes.

engineering. As a result, a measuring device can be derived, which is available for measuring the first test samples in Gerresheimer's Technical Competence Center in Wackersdorf. The creation of the test programs takes place virtually, in parallel, to ensure that the defined standard probes can be used. (Figure 3).

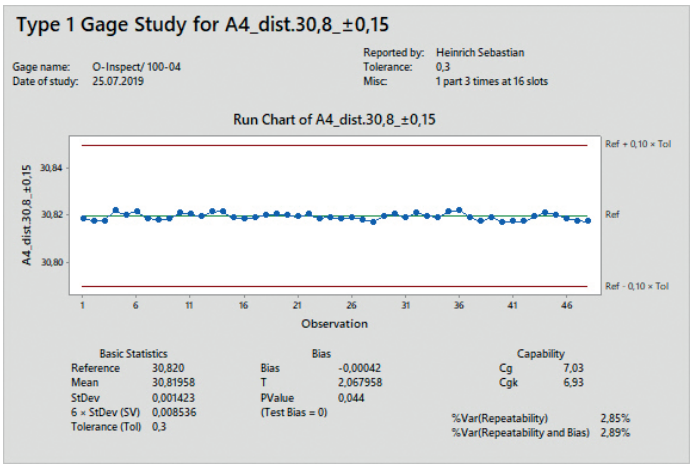
SCIENTIFIC MOULDING APPROACH

Quite a number of process variables define an injection moulding process and must be considered when establishing a robust process for achieving consistent part quality. Application of a scientific moulding approach helps in understanding the characteristics of each parameter and its influence on a specific part. The goal is to analyse the whole injection moulding process, from the time the resin enters the injection moulding machine to when it leaves the mould as a finished part, with the ultimate aim of establishing a process that minimises variation in part quality.

> "The goal is to analyse the whole injection moulding process, from the time the resin enters the injection moulding machine to when it leaves the mould as a finished part, with the ultimate aim of establishing a process that minimises variation in part quality."

During the first step, the back pressure, suck back, cavity balance, injection rate via viscosity curve, holding time, switch over point, clamping force and cooling time parameters are analysed. Whenever it is possible, in-cavity pressure sensors are used to optimise the process.

This is followed by a parameter screening to determine an aesthetic process window within which visually acceptable parts can be produced. As standard procedure, the four parameters of melt temperature, mould temperature, injection speed and holding pressure are varied. This provides information about the performance and limitations of the mould, as the chosen variables are stretched to their limits to determine the inherent limits of the mould. The wider the limits are, the bigger the process window is and the more robust is the process. As the screening provides a window for visual appearance of the part, dimensional data must be taken afterwards.



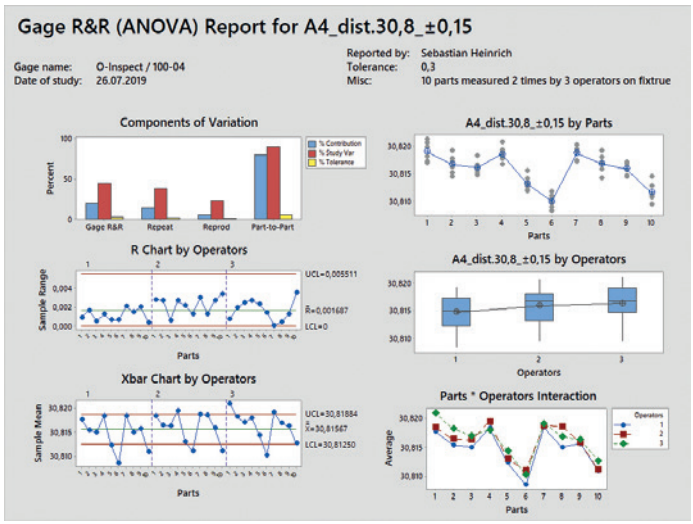


Figure 4: Two MSAs are conducted as part of tool qualification.

Once the process parameter limits have been determined, a fraction factorial design of experiments (DoE) is performed to investigate main effects and parameter interactions on the most critical and functional dimensions, as defined in the CRS. DoE can be performed on serial machines or pilot plant injection moulding machines of various types and sizes, as well as from different manufacturers.

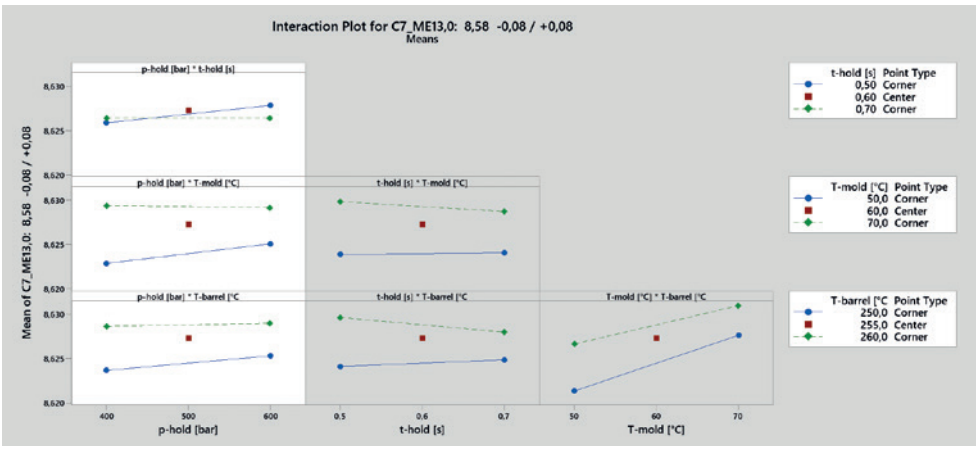
After the measuring jig has been produced and delivered by the in-house tool shop, it is then qualified with the test program. This means that a defined and co-ordinated qualification plan is used to ensure that production has taken place according to specifications. It also includes the successful completion of two measurement system analyses (MSAs). A CG value of >1.33 applies as the acceptance criterion for MSA 1 along with a gage R&R value of <20% for MSA 2 (Figure 4). This ensures that identical measurements are generated across all fixture positions and that the operator influence is kept to a minimum.

After completing all qualification sections, the system is approved for tool qualification and can be used for all further measurements, including DoE, measurement report and process capability. As soon as the tool qualification is completed, the equipment is sent to the respective production site and used for in-process control.

Statistical analysis of the dimensional results of the DoE is then used to filter out the significant parameters for the considered dimensions and gives a deeper understanding of how the part behaviour depends on several parameter combinations (Figure 5). Based on the results of this analysis, either the mould steel will be adjusted to move dimensions to the centre of the process window or a parameter setting is chosen that already gives the best results regarding robustness.

Once the DoE analysis has revealed which combinations of parameters should be selected for a given tool, the components are measured according to the drawing. In addition, virtually all other dimensions defined on the drawing are measured using an X-ray scanner. At Gerresheimer, this is done on a Zeiss Metrotom 800, which scans and identifies the components based on a barcode as part of a fully automated process. Additionally, comprehensive test programs, which are programmed at the start of mould making, autonomously measure all the plastic components for each mould cavity. As a result, digital product data and measurement reports are available.

> "The use of CT scans to fully measure plastic components is a key point and serves as a means of creating initial sample test reports at high speed and at a consistently high quality."



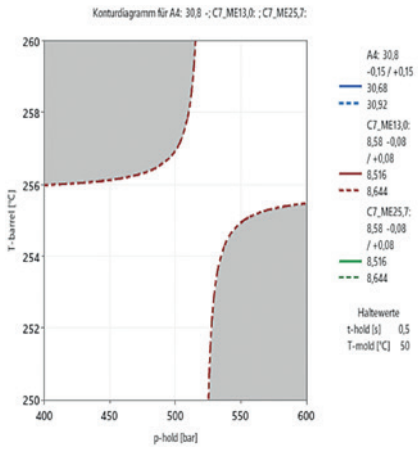


Figure 5: Interaction between process parameters.

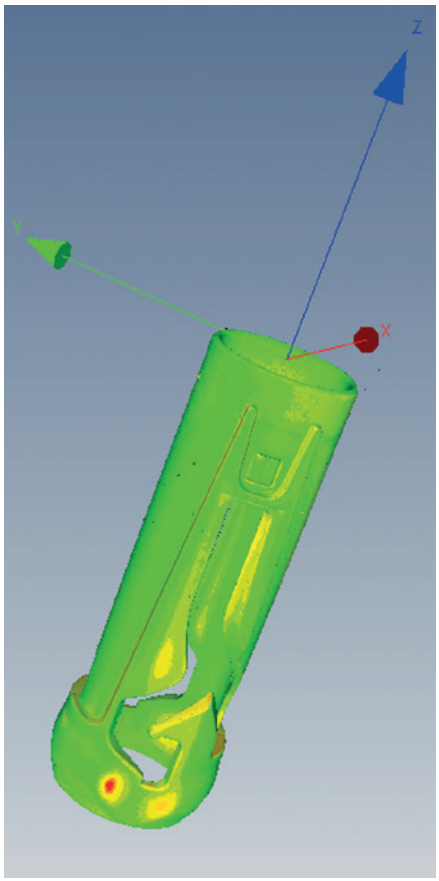


Figure 6: X-ray data is used to show the difference between the measurements taken by different tools and deviations from the CAD model.

The use of computerised tomography (CT) scans to fully measure plastic components is a key point and serves as a means of creating initial sample test reports at high speed and at a consistently high quality. This is due to the fact that components can be measured without any possible warpage during clamping and in sequence ("one-shot measurement"). Gerresheimer also takes advantage of this when using jigs to measure test and functional dimensions.

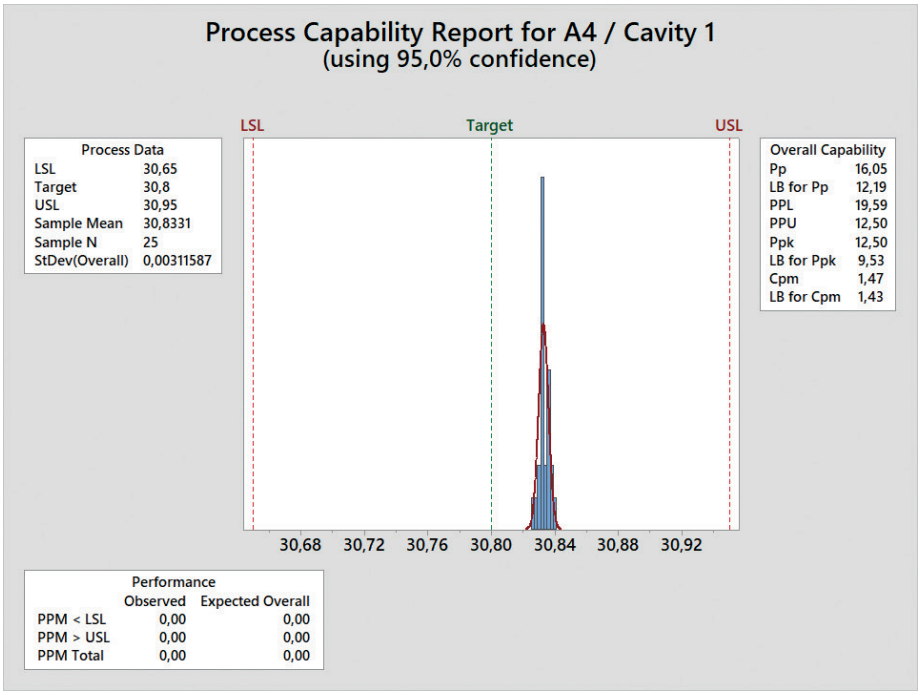


Figure 7: Process capability report.

A comparison ensures that the measurement results from the X-ray scanner are comparable those of the jigs. The X-ray scanner makes it possible to show deviations from the computer-aided design (CAD) model or between the results of different tools in false colours (Figure 6). The digitisation of the produced parts enables reverse engineering by comparing the component with the CAD model or 2D design drawings. Unlike with physical products, digitised products are not subjected to environmental factors or post-shrinkage. For example, this allows changes to the components since tool creation to be tracked precisely. Function or defect analyses of components and assemblies are made significantly easier by using CT scans.

In the course of industrialisation, the moulds go through optimisation loops and finally pass several qualification runs on the serial machine. When necessary, the process can be adapted through additional DoEs. Alternatively, adjustments can be made based on the in-cavity pressure curve in the mould evaluated on the pilot plant IMM as it contains all the necessary information on the flow of the molten plastic and solidification phases in the mould. Matching that fingerprint delivers parts with the same and consistent quality, as well as being machine independent.

Qualification runs on the serial machine are performed at low and high levels based on the nominal process setting. With these runs, the natural variation of the key process parameters can be considered,

allowing for a following analysis to confirm the process capability of the critical dimensions at the chosen limits. To perform a preliminary process capability analysis, at least 25 components of each cavity have to be measured. The Ppk value required by the customer serves as the acceptance criterion. A typical value for this kind of standard distribution with a confidence interval of ±3s is 1.67. This means that the probability that components meeting the quality requirements are produced is 99.73% (Figure 7).

Besides the lab for dimensional measurement of components, assemblies and finished products, Gerresheimer also has a lab for function testing. It is equipped with a 4K digital microscope, a high-speed camera, a test station for metering accuracy, a 3D printer for rapid prototyping and three material test machines from Zwick Roell (Ulm, Germany), a six-axle robot and two climatic test chambers.

CONCLUSION

At Gerresheimer, quality is no longer ensured by sorting out faulty parts after production but is instead established systematically in the products and processes during the development and industrialisation phases. During all phases of product engineering, the quality assurance department works closely with all the other departments involved. In this way, quality by design is not only the safest but also the most efficient way to launch medical products on the market.

ABOUT THE COMPANY

With a wide range of products for pharmaceutical packaging and drug delivery devices, Gerresheimer is a global partner in the areas of pharmaceuticals, health, wellness and biotech. With locations in Europe, the US and Asia, Gerresheimer produces hundreds of millions of successful drug delivery systems and primary packaging components quickly, cost-efficiently and with a high standard of quality each year. In the area of drug delivery devices, Gerresheimer covers the entire range of drug delivery, from inhalers, through autoinjectors and pen injectors, to needle-free injection systems, all the way to classic injection systems. Just as comprehensive is Gerresheimer's service offering, which covers the entire value chain, from the initial idea to product development with in-house tooling and special machine engineering, to large-scale production, assembly and international distribution. Close collaboration with the customer results in products that safely and reliably deliver the customer's active agents to patients.

ABOUT THE AUTHORS

Thomas Rudolph holds a Dipl-Ing in Mechanical Engineering with a focus on plastics technology. He started at Gerresheimer's Technical Competence Center in Wackersdorf in 2005 and heads a global team of injection moulding process engineers. He and his team are responsible for developing robust injection moulding processes with the help of scientific methods and the transfer of qualified injection moulds to the global production sites.

Markus Reil studied machine engineering at the Amberg-Weiden University of Applied Science (Amburg, Germany) with a special focus on laser technology, graduating in 2003. Between 2003 and 2007, he worked in several positions to gather professional experience. In 2007 he took part in an in-house education programme at Gerresheimer's Technical Competence Center in Wackersdorf and received a certificate as "Six-Sigma Black Belt (Grundig Akademie)". In 2017 Reil was appointed as Head Plant Quality & Global Quality Engineering.

Stefan Schumann started a dual master's degree in plastics technology in combination with an apprenticeship as a Process Mechanic for plastics and rubber technology at Gerresheimer. From 2016 to 2017 he performed research in the field of innovation-focused mechanical engineering. After successfully completing his degree, he started as an Expert in Injection Moulding in the Mould Process Engineering department of Gerresheimer's Technical Competence Center in Wackersdorf. Since May 2021 he has been working as an Engineer in Advanced Technology Moulds in the Global Mould and Process Engineering department and is responsible for innovative technology projects in the area of mould development.

Tobias Weigert started his professional career with an apprenticeship as Mould Maker for jigs at Mühlbauer Group (Roding, Germany). In parallel with joining Gerresheimer in October 2013 as a Measurement Engineer, he completed his state certification in Mechanical Engineering. After that, he started his BA in Industrial Engineering, which he completed in 2019. Since 2018, Mr Weigert has led Gerresheimer's Global Metrology Team within Germany, the US and China for the Technical Competence Centers. Since the start of of 2021 he has also been part of the "Formula GT" programme, which is an internal Gerresheimer programme for employees with high potential.

We turn your visions into components and products ready-for-market

Customized Solutions

Gerresheimer – your international one-stop-partner for drug delivery systems. Whether start-up or Fortune 500 company, we provide a service offering as individual as your active ingredient, patient or user.

Explore our services!

- Concept, product and process development
- Industrialization
- Contract Manufacturing

gerresheimer.com

gerresheimer
innovating for a better life

SCHERDEL
medtec North America

FROM SIMULATION TO SPRING SATISFACTION

In this article, Drew Jelgerhuis, Business Development Manager, Medical, at Scherdel Medtech North America, discusses the power of simulation to enhance a drug delivery device design project, including faster development times and reduced costs.

Development engineers are constantly trying to understand how their design will perform under various conditions, environments and applications. Simultaneously, project managers are trying to reduce the project's time to market and cut costs to beat the competition. Serving both these aims, simulation services are a great tool with which to test and evaluate designs and thus improve time to market and reduce overall costs before even making a prototype.

> "Simulation services are a great tool with which to test and evaluate designs and thus improve time to market and reduce overall costs before even making a prototype."

Scherdel Medtec is committed to providing the best engineering for your medical device components. The company's simulation services include statics/dynamics, fatigue, metal forming, fluid dynamics, temperature, electromagnetics, multiphysics, optimisation, mechanical engineering and injection moulding (Figure 1). In addition to these simulation services, Scherdel supplements this analysis with a wide range of physical testing.

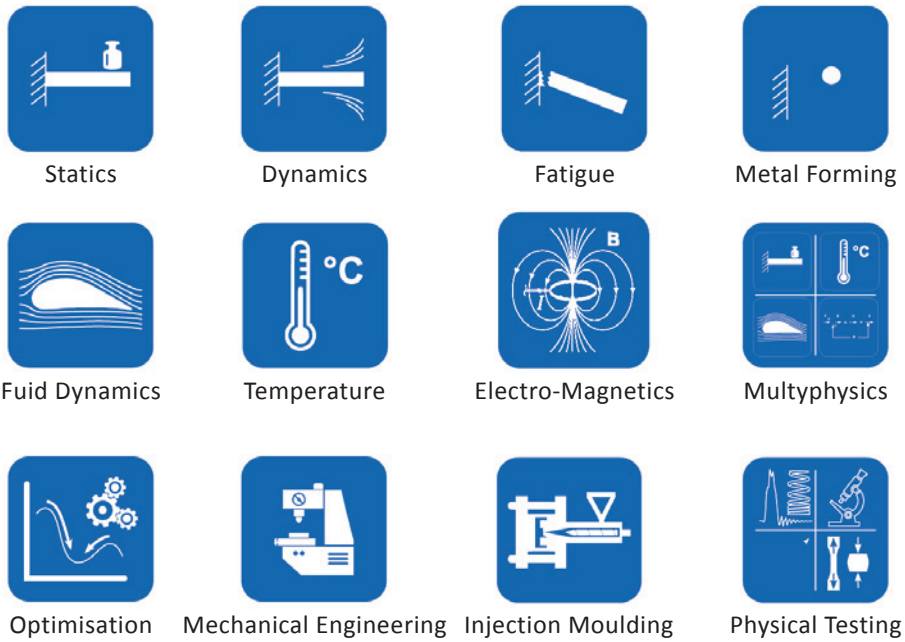


Figure 1: Scherdel's simulation capabilities.

Drew Jelgerhuis
Business Development Manager, Medical
T: +1 231 777 6173
E: drew.jelgerhuis@scherdel.com

Scherdel Medtec North America LLC
3440 E Laketon Avenue
Muskegon
Michigan
49442
United States

medtec.scherdel.com

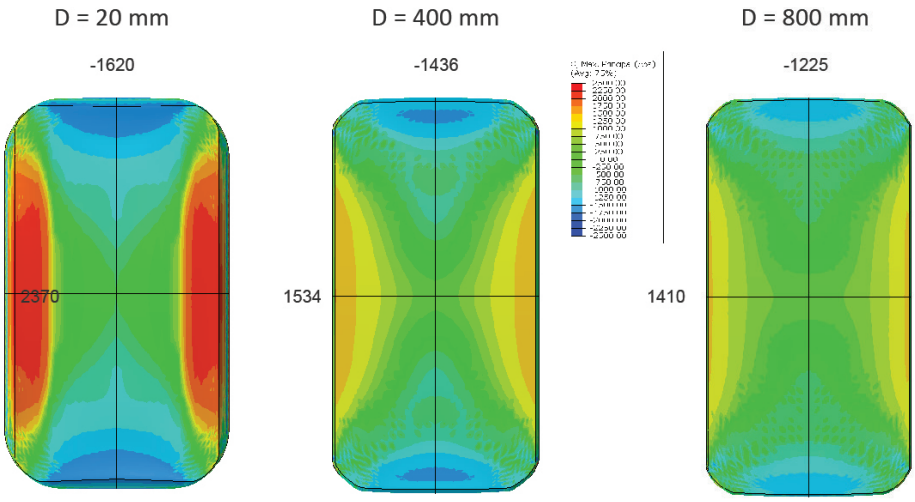


Figure 2: Simulating variation of a wire roller's diameter.

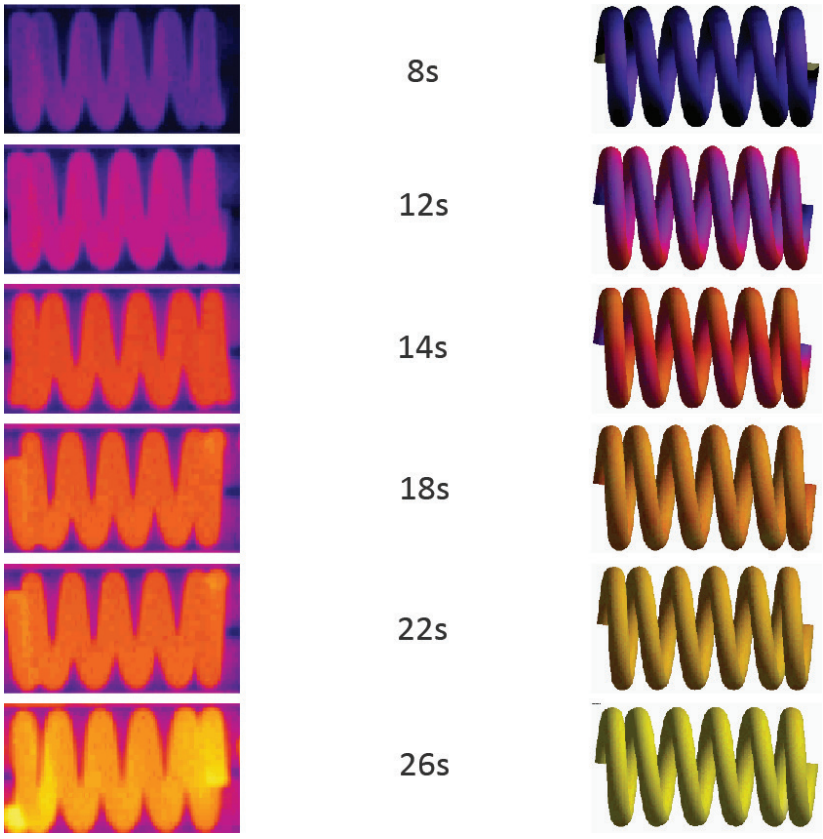


Figure 3: Simulation showing yellow/purple conduction.

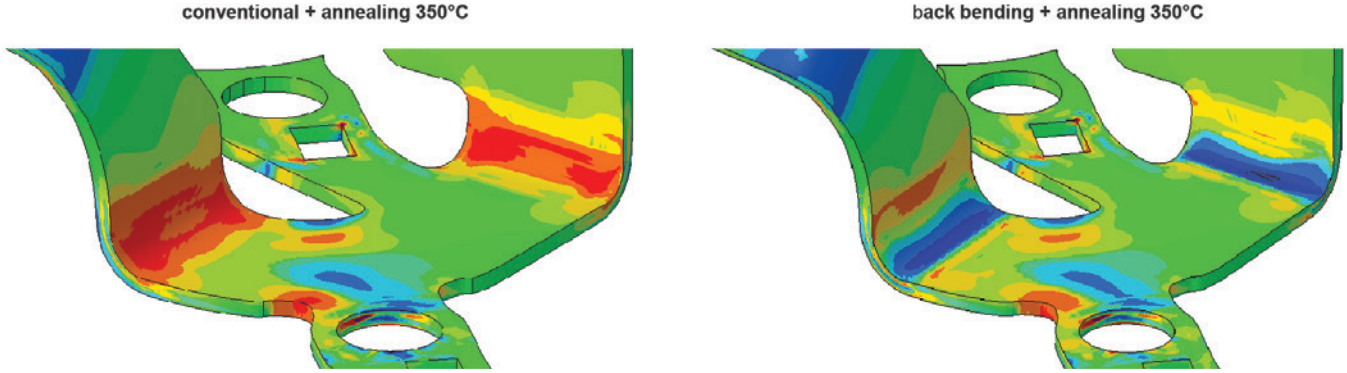


Figure 4: Annealing dispersion using temperature simulation.

Scherdel's simulation team performs hundreds of simulation projects every year, and the number of these numerical simulation tasks continues to grow year on year as the value of the results they offer improves with the continual advancement in software, algorithms and engineering knowledge. Over the past five years, the company has increased its number of simulation projects by over 30% annually. This is, in part, due to the significant value that it provides but also due to the growing number of types of simulation that Scherdel can perform.

Taking a simple compression spring as an example, Scherdel can simulate the wire drawing process to determine the stress levels throughout the wire before even beginning to form it into a spring. Controlling the variables from the first process can help determine and improve the performance of the simulation after the final process. For example, by simulating the diameter of the wire roller, it is possible to understand the effects on the internal stress (Figure 2). This saves expensive and time-consuming experimenting.

Progressing into the coiling and conductive heating process, Scherdel can then determine and optimise the process for best results based on the specifications of the given spring (Figure 3). The next process may involve annealing, which Scherdel can simulate in its temperature simulation (Figure 4). Another process often used in the manufacture of springs is shot peening, where Scherdel's manufacturing simulation can provide analysis of the process to optimise it for distribution and wear reduction.

The process of precision stamping presents many opportunities to use simulation to test various methods of manufacturing processes to improve the robustness of a given component. One such example is elucidating the difference between processes and the improvement in critical bending areas.

Another process that can be simulated for compression springs is stroke stress (Figure 5). This circumvents the need to make springs and test them over millions of cycles, and avoids the subsequent lab tests required to understand the stresses present.

The benefits that result from numerical simulation are as follows:

- Deviation between simulation and testing is less than 10%
- First-time-right prototypes are made a reality
- Simulation speeds up development times
- Simulation finds better solutions
- Simulation is always faster than trial and error with prototypes
- Simulation provides greater insight
- Simulation costs are investigations in fault prevention
- Co-ordinated use of simulation and testing is the fastest way to new products.

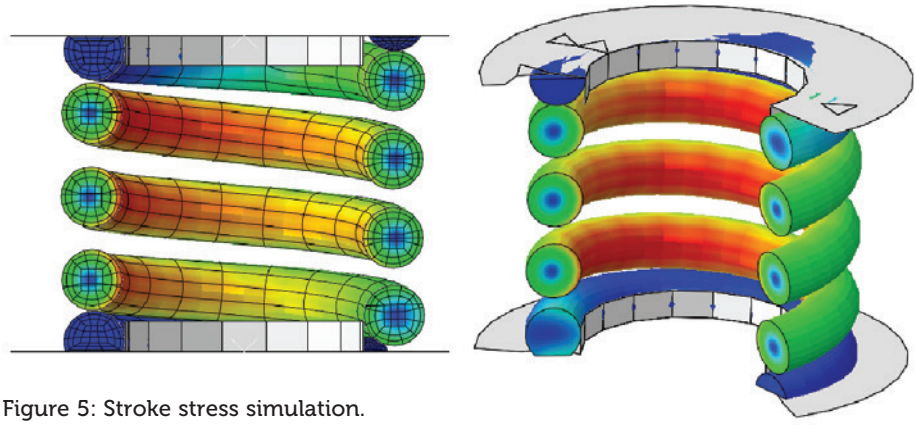


Figure 5: Stroke stress simulation.

Scherdel Medtec has world-class software, engineers and the experience to tackle design challenges and shorten development cycles while improving the quality of the product and saving prototype and testing money in the project's budget.

ABOUT THE AUTHOR

Drew Jelgerhuis is the Business Development Manager for Scherdel Medtec North America. With over 15 years of business development experience in the medical device sector, Mr Jelgerhuis leads the North American Medtec team growth in co-operation with the other global Medtec leaders. Mr Jelgerhuis holds a BS in Mechanical Engineering from Dordt University (IA, US) with a minor in Business Administration. He enjoys solving technical problems for customers by providing solutions for their medical device component requirements.

ABOUT THE COMPANY

Scherdel Medtec is part of the Scherdel Group. With about 5,800 employees at 32 locations worldwide, Scherdel Group is a leading, family-owned company in the field of metal forming, with core competence in the production of engineering springs, stamping parts and assemblies for the pharmaceutical and automotive industries.

Nemera
we put patients first

HOLISTIC DEVELOPMENT AND INDUSTRIALISATION OF DRUG DELIVERY DEVICES AND COMBINATION PRODUCTS

In this article, Mark Tunkel, Global Category Director, Services, and Niyati Sapatnekar, Global Communications Manager, both of Nemera, discuss the company's holistic approach to development and industrialisation.

Doctors have always known that healthcare isn't a one-size-fits-all business – it requires a personalised, value-based approach.[1] Whilst the healthcare landscape continues to evolve, accelerated by the covid-19 pandemic, it is increasingly important to keep up with the surrounding changes, including climate change, geopolitics and vulnerable populations.

Over the past few years, new insights in biology, chemistry and engineering have led to the discovery of new molecules and drugs. This, in turn, has increased the necessity of well-adapted drug delivery device solutions to ensure their maximum efficacy, as well as the best patient outcomes. Staying on top of healthcare trends is critical not only for well-established drug providers but also for those smaller players intervening in and around the space. Industrialising new devices and introducing them to the market requires a rigorous process that navigates a variety of factors and strengths in contract development and manufacturing expertise that can be applied in a flexible manner.

AN INCREASINGLY COMPLEX LANDSCAPE FOR COMBINATION PRODUCTS

The complexities involved in selecting or developing the correct device for a combination product have never been more challenging. A convergence of trends, including significant growth in the global drug development pipeline, the need for more complex delivery devices to address targeted applications and drug attributes, and increased migration of care from the clinic to self-administration in home settings have driven demand for a wide range of solutions. This is coupled with a crowded and competitive landscape in the biologics, biosimilars and generics segments, where speed to market, differentiation, patient centricity and value creation are critical.

> "The complexities involved in selecting or developing the correct device for a combination product have never been more challenging."

Beyond the patient, this includes an ecosystem of stakeholders including not only providers (healthcare professionals) but also health systems, payers (to consider factors such as value-based care) and regulators, as the market for product introduction and the intended filing approach can affect device selection and development strategies. These factors then need to be considered within the available or emerging technology landscape.

Mark Tunkel
Global Category Director, Services
E: mark.tunkel@nemera.net

Niyati Sapatnekar
Global Communications Manager
E: niyati.sapatnekar@nemera.net

Nemera
20 Avenue de la Gare
38290 La Verpillière
France

www.nemera.net

"It is critical to fully understand the patient journey as well any related clinical processes."

Therefore, developers need to adopt a holistic approach to developing a device strategy that is focused on the entire combination product, spans development stages and requires specialised expertise at every step of the process – all balancing a variety of factors and influences that need to be considered. This leads to better near- and long-term decision making across the lifecycle of drug products (Figure 1).

INTEGRATING THE VOICE OF THE PATIENT INTO DEVELOPMENT

At the earliest stages of establishing the functional requirements and user needs for a new device application, it is critical to fully understand the patient journey, as well any related clinical processes. Use of a method called "applied ethnography" can achieve this goal. This relies on interviews and in-context observations of practices, processes and experiences within the patient's home or use environment.

Potential use cases are looked at broadly, beyond the administration event or complying with instructions for use. This starts from when a patient is diagnosed and continues through the entire process of receiving their device, then preparing and administering their medication, to final disposal of the device, as well as considering the times in between treatment, to understand how the process changes over time and fully how frequency of administration may affect the patient experience.

It is equally important to gain an understanding of the experience of healthcare professionals to consider relevant settings in clinical environments. This is important in applications where care is being provided in both at-home and clinical environments; consider the migration of care from settings with significant support systems, such as an oncology ward, to an environment of self-administration where clinical personnel are not present and the burden of support falls to a family member or caregiver.

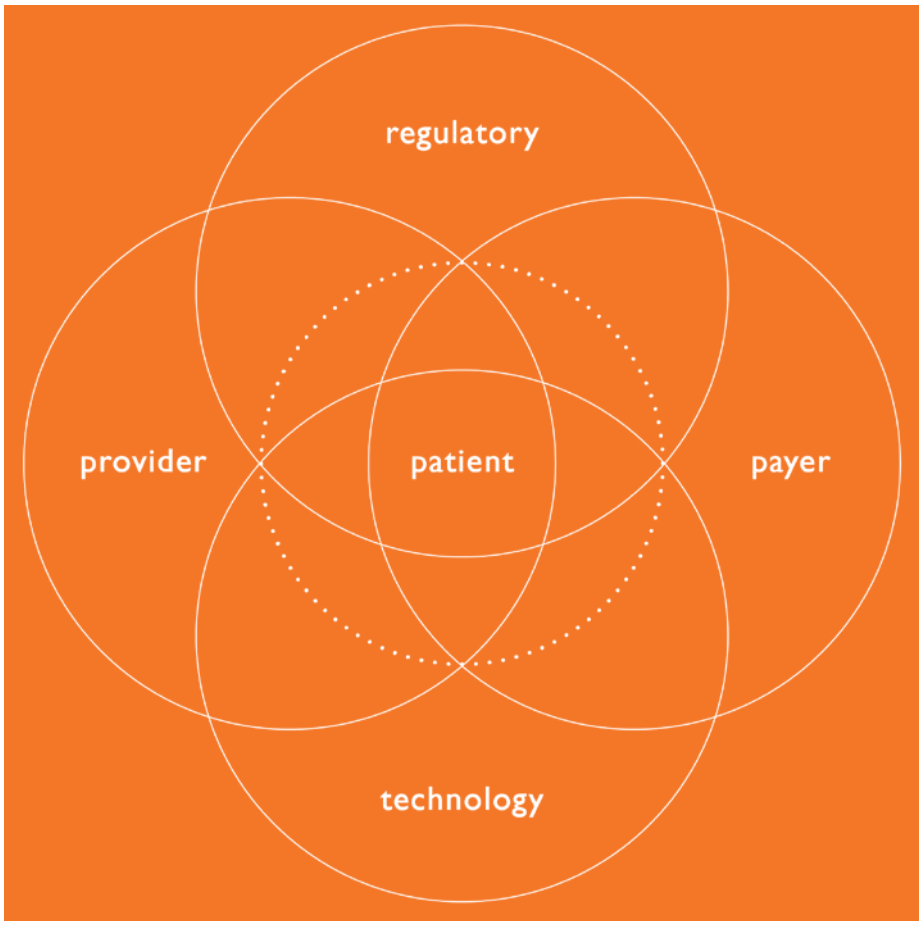


Figure 1: The combination product ecosystem.

The outputs of this process include patient journey maps, clinical process maps, an understanding of prioritised user needs and values and pain points that can be leveraged to improving the patient and provider experience.

These outputs support meeting needs holistically while also assessing the technology landscape to identify existing intellectual property (IP) or platforms that may be fit for the intended device function and combination product attributes. Alternately, this can lead to the need for the development of a novel delivery system, for which this foundation can be used to establish user needs and functional device requirements (Figure 2).

INNOVATIVE CONTRACT DEVICE DEVELOPMENT & PRECLINICAL SUPPLY

In applications that are not best suited for existing platform devices, there is an opportunity to develop a new device with a customised user experience and technical functions that addresses the whole of the device usage process and broader patient journey, and also results in an original IP that is owned by a developer. This requires an innovative design development partner with broad experience with various devices and a wide range of patient populations and applications. Multiple scenarios for optimising care through user interaction or technical function can be considered, as well as design for sustainability. In some cases, background "technology bricks" can be used as a base for development to accelerate development cycles and to simplify the development of critical technical functions and navigation of the IP landscape. Ideally, there should be an option for fast-to-completion, small-series production for internal development or registration with agile assets for manufacturing and assembly that integrate the know how of a proven manufacturing partner and planning for later stages.

This results in innovative devices that have a manufacturing strategy integrated from the earliest stages of development for all necessary supply. This ensures innovation is balanced with user based and technical risk identification and mitigated early to reduce the risk of transition to manufacturing and end users upon market introduction.

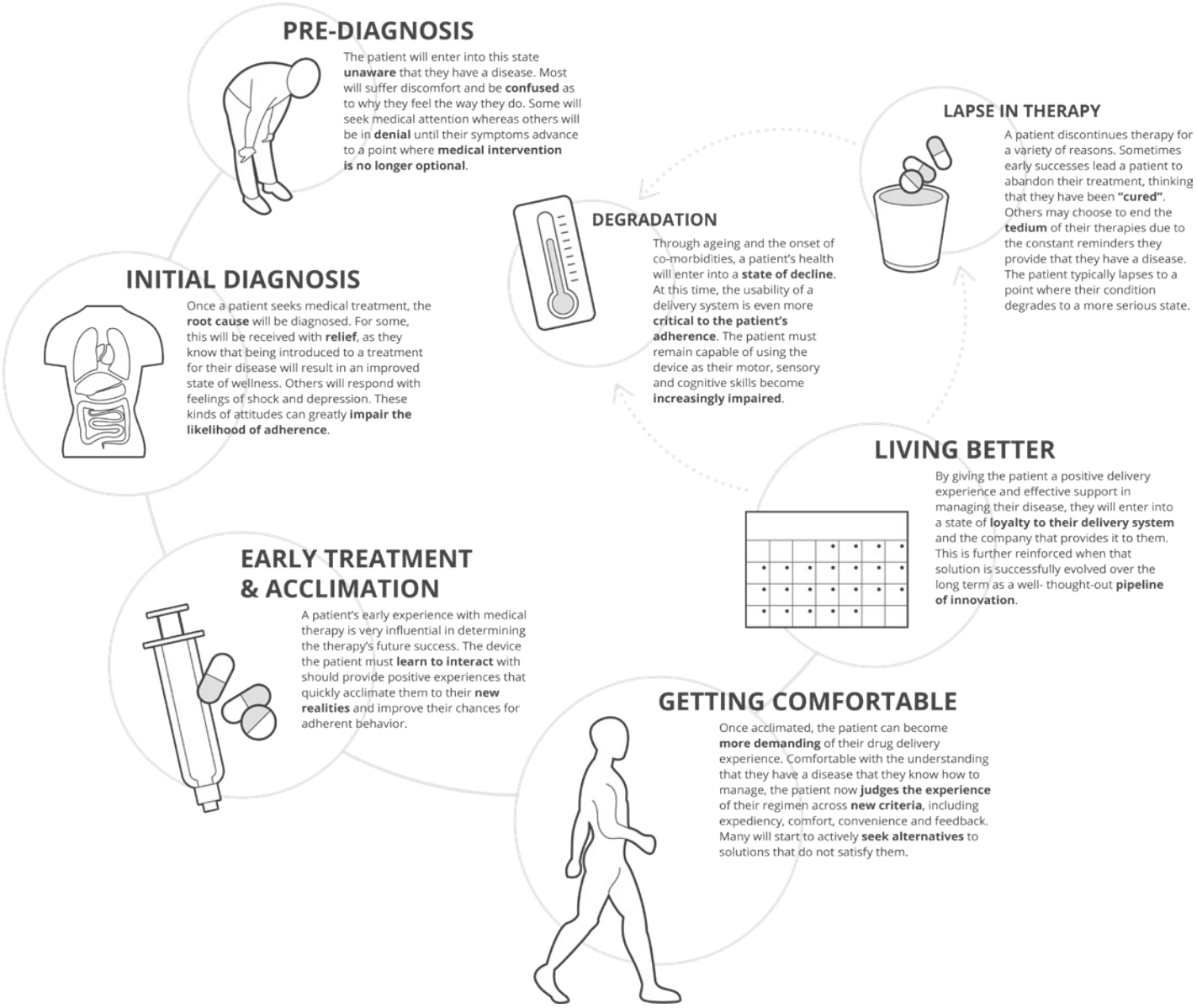


Figure 2: Key milestones along the patient journey and implications for delivery device design.

SAFE, EFFECETIVE AND DIFFERENTIATED COMBINATION PRODUCTS

Any device development programme must include human factors and patient experience activities. It is critical to ensure that the selected device, in combination with the drug, is appropriate, safe and effective for the target population and suitable for the chosen regulatory strategy. This also extends to optimising the patient experience to create competitive differentiation and ensure adherence and engagement with patients and clinical stakeholders.

A good example of this approach might be the consideration of a biosimilar application where competitors are targeting the same reference drug and devices. Alternately, for new drug applications and new device development programmes, the company needs to project what a future use case might look like and anticipate areas of risk to ensure that development is tailored to mitigate them. In both instances, the company needs to be sure that it is addressing the defined user group populations and early use-related risk analysis activities to define the human factors and usability programme.

As part of the overall regulatory management strategy for the device in the relevant markets, human factors must be addressed from planning and initial risk analysis to conducting formative and summative usability testing for the device. This includes the production of human factors engineering report documentation for use in regulatory submissions as part of the larger documentation set required. This also includes instructions for use and value-added packaging, as well as leveraging digital-health-related add-ons to support patient engagement and adherence. It is crucial this is all completed holistically.

CUSTOMISED INDUSTRIALISATION AND COMMERCIAL MANUFACTURING

Every application is unique, so process development and requirements for clinical and large-scale manufacturing need to be aligned to these specific goals leveraging broad experience with many device types. This includes definition and selection of the proper assembly and automation approach, as well as a global approach to mould development with a proven supply base. Custom approaches for all aspects of the manufacturing process that can deployed at a variety of global manufacturing sites should be considered.

A diverse team of experts should ensure that all learnings from the development to date are integrated in the most effective way possible. Any initial approaches for preclinical or small-series manufacturing can later be scaled up to a high-volume manufacturing setup or ideal manufacturing location with the appropriate assets and expertise once initial development objectives have been met. This approach speeds up time to market and enables deferment of capital expenses. The team should also integrate all necessary aspects of reliability and quality planning as early in the process as possible. The result is a reliable and repeatable process that is as unique as the device that has been developed (Figure 3).

Figure 3: Agile industrialisation.

BENEFITS OF PARTNERING WITH AN INTEGRATED SERVICE PROVIDER

Nemera's integrated development, consulting and manufacturing services allow customers to achieve the outcome of a successful regulatory submission and commercial launch of a safe, effective and differentiated combination product with a single partner applying an agile process across the device and combination product value chains. This support is provided from definition of the programme and requirements through to sustained delivery of commercial supply. This will drive patient centricity, reduction of risk and decreased time to market.

This approach can be applied to Nemera's established IP platforms or to organic development and allows customers to focus on their core business related to their drug assets. Furthermore, Nemera's procurement teams strive to embed sustainable criteria in their approach with suppliers and other stakeholders from the earliest stages of the process. This helps limit the impact on the planet.

ABOUT THE COMPANY

As a world-leading drug delivery device solutions provider, Nemera's purpose of putting patients first enables it to design and manufacture devices that maximise treatment efficacy. The company is a holistic partner and helps its customers succeed in the sprint to market for their combination products. From early device strategy to state-of-the-art manufacturing, Nemera is committed to the highest quality standards. Agile and open-minded, the company works with its customers as colleagues and goes the extra mile to fulfil its mission.

ABOUT THE AUTHORS

Mark Tunkel is Global Category Director, Services, at Nemera. He was previously a partner at Insight Product Development, which was acquired by Nemera in 2019 and became the Insight Innovation Center. With more than 20 years of global business development experience and a deep understanding of the marketplace challenges and trends impacting the pharma industry, Mr Tunkel has advised many of the world's leading companies on their product development and innovation strategies, with an emphasis on driving realisation and the most favourable business outcomes.

Niyati Sapatnekar is Global Communications Manager at Nemera. Along with the team, her goal is to support the vision, mission and ambition of the company through engaging and impactful communications. With two master's degrees, including one in Communications from Sciences Po Rennes (Rennes, France), she believes that a focus on healthcare communications is the best way to nurture her passion for language, science and people.

REFERENCE

1. *"2022 Healthcare Industry Trends That Will Make a Difference". UCF Online, accessed Aug 2022.*

Nemera

we put patients first

Your Drug Delivery Device Solutions Partner

CONTINUOUS IMPROVEMENT: FROM ABSTRACTION TO REALITY

In this article, Tracy Pedreso, Head of Continuous Improvement at SHL Medical, discusses the company's strategy for making continuous improvement a reality.

In various highly competitive industries where the quality of products and services is critical, the practice of using marketing ploys to double as a mask for imperfection is rampant. While something being built to perfection may seem too good to be true, much less is done to challenge such claims. As demands from consumers and regulators increase over time, challenging the notion of a company's constant state of perfection becomes increasingly important.

For example, when a developing company undergoes an expansion journey, it may see an upgrade in its infrastructure and operational capacity, but also an increase in required manpower and operational processes. In the foreground, we think that these are all attributable to growth, but a critical analysis may prove otherwise. Over time, continuous improvement (CI) has been an emerging driver for businesses to achieve a lean manufacturing process, thereby creating value for their customers and the best-in-class products in their respective industries. Still, for many, "to improve continuously" is more commonly said than done; the pursuit of perfection or "continuous improvement" is an abstract vision that is given top-down by business leaders.

QUALITY INNOVATION IN A HIGHLY REGULATED INDUSTRY

In many ways, the need for constant innovation in the pharma and medtech industries is also a reflection of the need for CI in these sectors. As the demand for safe, effective and high-quality treatment modalities continues to rise, the regulatory framework that serves as the healthcare industry's checks and balances becomes more stringent, too. Nonetheless, in the age of 21st-century medicine, it is inarguable that pharma and medtech must continue to innovate life-saving technologies and products. However, given the present regulatory underpinnings, innovation is a risky process in itself. A seemingly obvious paradox exists between the need to innovate and the responsibility to ensure quality but derisked products and services not only for the patients but throughout the value chain. How do you meet the global regulatory requirements for innovation in a highly regulated, risk-averse business such as pharma/medtech? This is where continuous improvement takes centre stage at SHL Medical.

A DEFINITION OF CI

CI is a cultural mindset of constantly looking for opportunities to improve product quality, services, processes and workplace safety. In a management context, CI means a never-ending effort to uncover and eliminate the root causes of problems or to reduce lean waste in all operational processes. Usually, it involves gradual or small-step improvements rather than a single inordinate change. For the Japanese, CI is a business culture. It involves people across all levels of an organisation, with the goal of finding and eliminating waste in materials, machineries and operational processes, as well as improving workplace organisation methods and safety.

Notably, the Japanese word "kaizen" is contextually treated as synonymous with the term CI. Kaizen comes from the Japanese characters kai, meaning "change", and zen, meaning "good". Taken literally, kaizen means improvement or "change for the better". Outside Japan, kaizen has been adopted by various industries in the West and

Tracy Pedreso
Associate Director and
Head of Continuous Improvement
T: +886 3 217 0303 ext 6036
E: tracy.pedreso@shl-medical.com

SHL Medical
36, Liufu Rd
Luzhu District
Taoyuan City 338
Taiwan
ROC

www.shl-medical.com

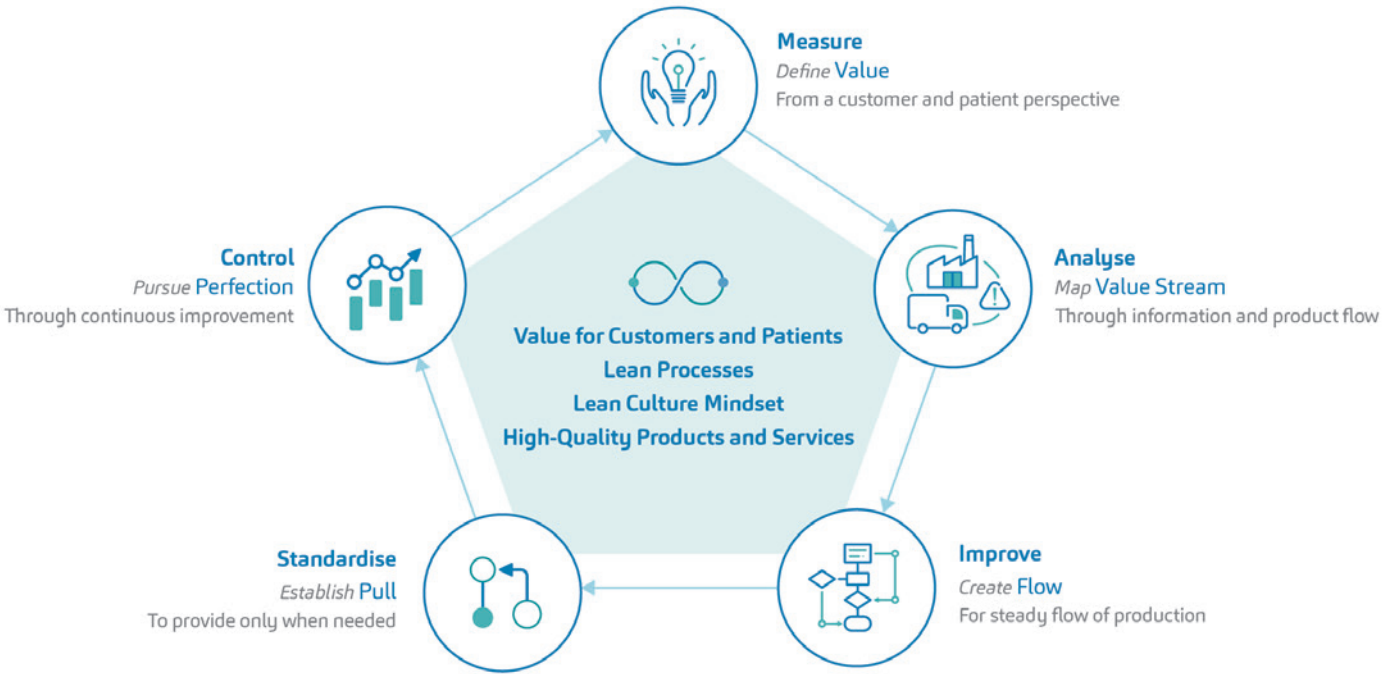


Figure 1: The CI-lean transformation approach strategy at SHL Medical.

has since branched out into other distinct yet similar principles, such as just in time (JIT), the Toyota Way, Six Sigma and lean manufacturing. Although the names of these disciplines seem disparate, this article refers to CI as the archaic term encompassing the foundational concepts, methods and frameworks to constantly improve products, services or processes over time.[1]

CI IN THE PHARMA AND MEDTECH INDUSTRIES

In 2002, the US FDA launched the Pharmaceutical Quality for the 21st Century initiative to "encourage adoption of innovative technologies that would lead to an agile and flexible pharmaceutical manufacturing industry". From there, the pharmaceutical sector witnessed progressions in this initiative, with a couple of guidelines being published back to back just two years later. Alongside its published guidance and reports on cGMP and process analytical technology (PAT), the FDA also released an exploratory paper on its "proposed next steps towards the desired state of pharmaceutical manufacturing".

It could be said that such a move by the FDA in 2004 heralded the formalisation of a drive towards CI in the industry. However, this is not to say that pharma was keen to embrace the concept of CI – in practice, the rate of uptake was slow. In fact, 19 years on, although CI has already proven advantageous and exhibited prime importance in manufacturing operations across various industries, much is yet to be achieved on the medtech industry's CI journey.[2,3,4]

AN EMERGING NEED TO COMMUNICATE CI INITIATIVES

Conducting an unfiltered Google search using the keywords "continuous improvement + autoinjector OR medical device OR drug delivery systems" would yield extremely few relevant results. Being aware that CI is also referred to as "operational excellence," the same internet search was conducted, with similarly few results.

SHL Medical sees a need for the medtech industry to actively communicate its cognisance of practising continuous improvement. With the rise of combination products, a mutual subscription to CI by pharma and medtech would go a long way to enabling the independence of patients who rely on the treatments these industries co-develop.

> "Sustainable positive change over time is the true essence of timeless operational or business excellence."

Globally, regulatory bodies and the standards that they institute exist to ensure the safety and efficacy of the medicines and treatment modalities that reach the hands of patients. Utmost compliance to such is the norm but does not reflect a business organisation's full subscription to CI in any significant way. "Operational excellence" is a common buzzword in many other manufacturing sectors but, in truth, the industry standards, knowledge and principles carried over from the past may no longer be representative of the superlatives of the present. For example, a modularised platform strategy for autoinjector development offers optimisation unseen in traditional platform strategies. SHL Medical understands that the pursuit of excellence and perfection is a never-ending journey and that sustainable positive change over time is the true essence of timeless operational or business excellence.

GLOBAL CI STRATEGY AT SHL MEDICAL

A transformative CI journey requires a transformative vision. SHL Medical's CI strategy (Figure 1) is anchored within the following philosophies, which are aligned to its core values:

1. **Focus on customer:** create value for customers and patients
2. **Drive simplicity:** create lean processes
3. **Learn and improve:** create a lean culture mindset and drive continuous improvement
4. **Deliver together:** collaborate and work as one team to achieve a common goal with the utmost quality.

The key to systematised CI work is moving from the idea of abstract to tangible objectives. SHL's vision of value creation for patients and customers is entwined with values that are qualifiable and quantifiable at the same time.

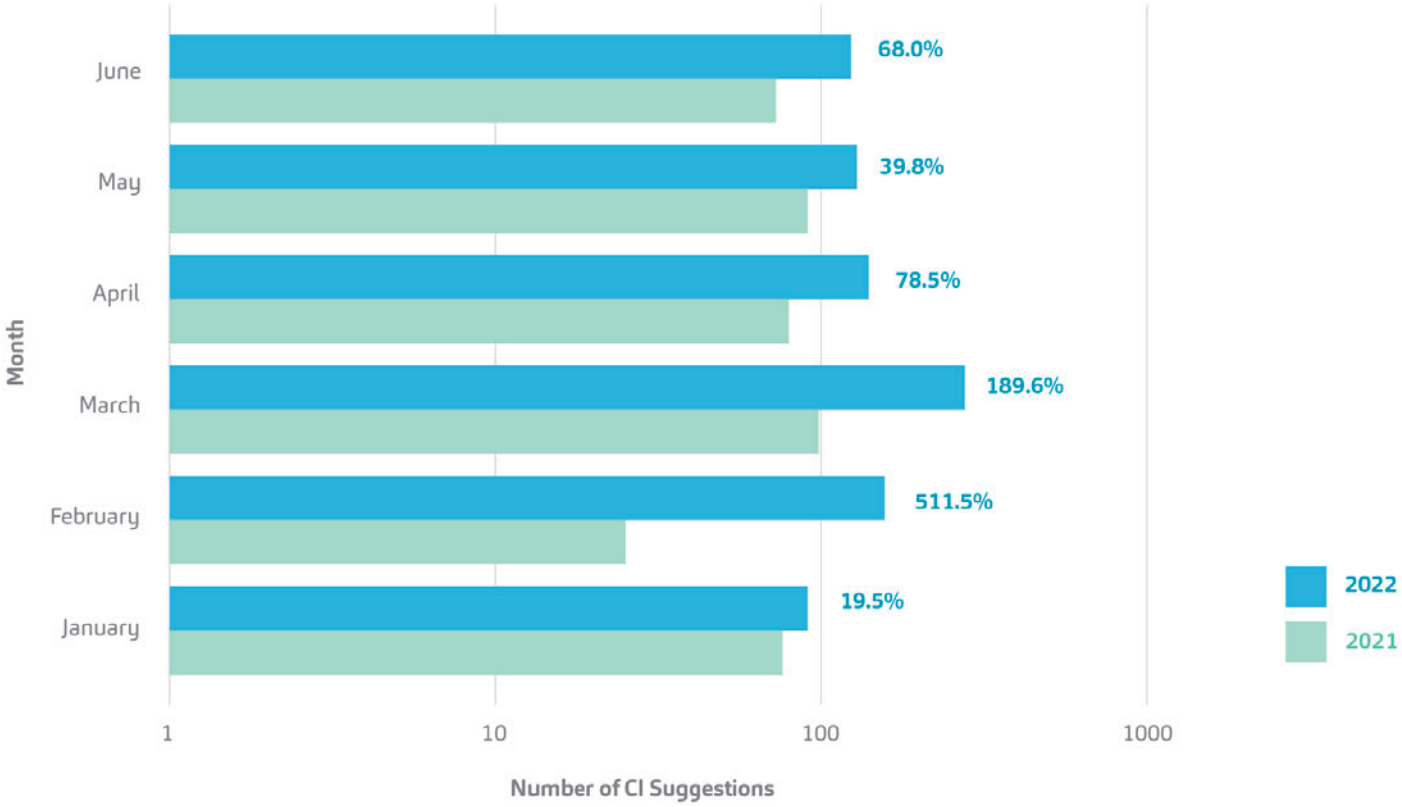


Figure 2: A comparison of the number of CI suggestions made at SHL Medical for the first half-year of 2021 and 2022. The graph uses a logarithmic scale with the percentage change from 2021 to 2022 displayed.

When it came to creating a sustainable CI function at SHL Medical, the first step was building a foundation of lean culture across the entire organisation. The CI team was formed based on globally accepted lean principles that were tailored to SHL's vision as a leading medtech company. The team, composed of CI engineers and lean champions representing various departments and functions, advocates for a systematised and organised approach to shape lean culture and sustain CI-building initiatives across the organisation. After all, just like the scientific method, CI programmes require empirical evidence as a basis for decision making.

A TOP-DOWN AND BOTTOM-UP APPROACH

SHL understands that CI is not a one-way street. A successfully functioning CI programme requires leadership commitment, with lean champions to guide and empower their peers. However, in spite of a firm vision from leadership, colleagues might find CI to be esoteric, acting as an adversary to their work or its principles. Given that buy-in from colleagues is a key cornerstone to making CI sustainable across an organisation, SHL has been proactive in establishing a lean mindset across its workforce instead of overloading employees with jargon. In fact, SHL's CI team solicits ideas from manufacturing line operators, who are considered a critical source of insight into the demands of real-time production. As with maintaining equilibrium, providing the right tools and resources is key, and the active participation of colleagues in knowledge building is incentivised.

> "A successfully functioning CI programme requires leadership commitment, with lean champions to guide and empower their peers."

Figure 2 shows a comparison of the number of CI suggestions submitted for the first half of 2021 versus 2022, including the percentage change between the time periods. A sustainably healthy CI programme should show variance in time-based trends. That is, successful CI-building initiatives are not forced. A key factor in maintaining a healthy CI programme is the alignment of CI initiatives and programmes with departmental key performance indicators (KPIs). Embedding CI initiatives into departmental KPIs helps accelerate the cultural transformation towards having a lean mindset across an organisation. Consequently, it should be remembered that such CI activities are always bound to the idea of surpassing whatever is best in class today. This way, value for customers and their patients is constantly maximised while a positive change is created for operations, processes and the people involved. After a constant flux of CI suggestions, the time will come when it reaches a plateau – a normal phenomenon as CI programmes mature.

CI ACROSS ALL OPERATIONS

While some may believe that CI programmes are not universally beneficial for all customer autoinjector development projects, SHL embeds CI in its operations differently. SHL's more than two decades of infrastructure development allow the company to use platform modularity as its contemporary industrialisation approach. Platform modularisation allows the company to leverage both historical data and its communal moulding, testing and assembly machines. As such, SHL is able to implement CI programmes that

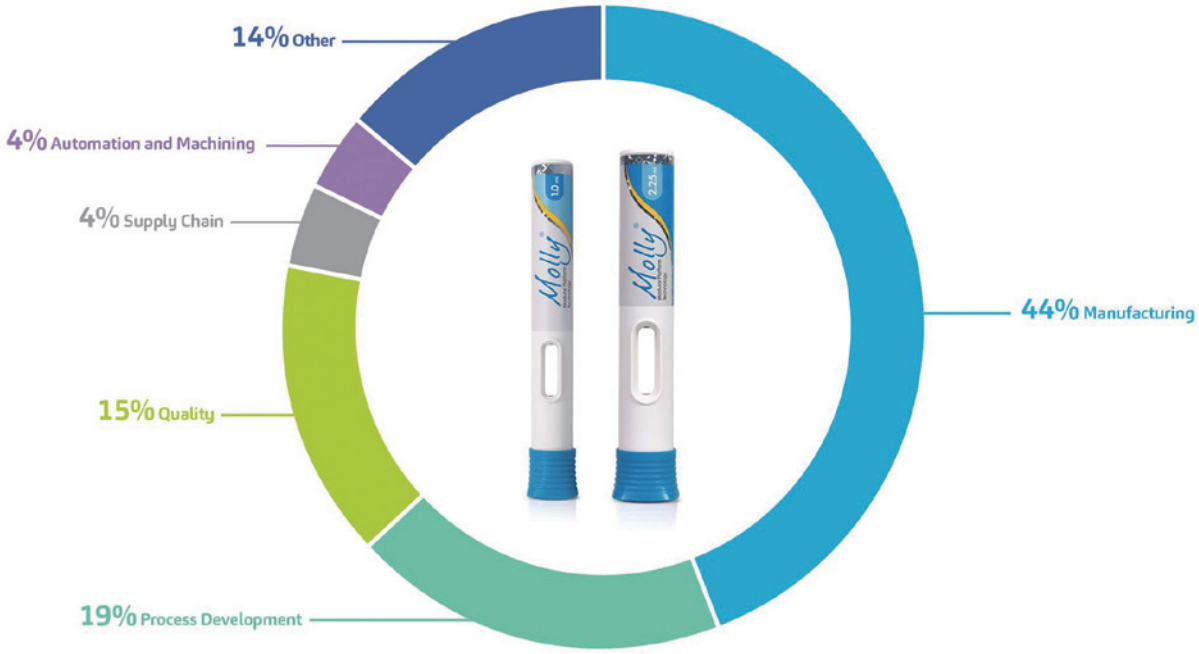


Figure 3: Percentage graph showing the top five focus areas where CI has been implemented across SHL's operations. The goal of operational excellence is to exceed the customer's expectations by creating lasting value and embedding top quality for all the products and services being offered.

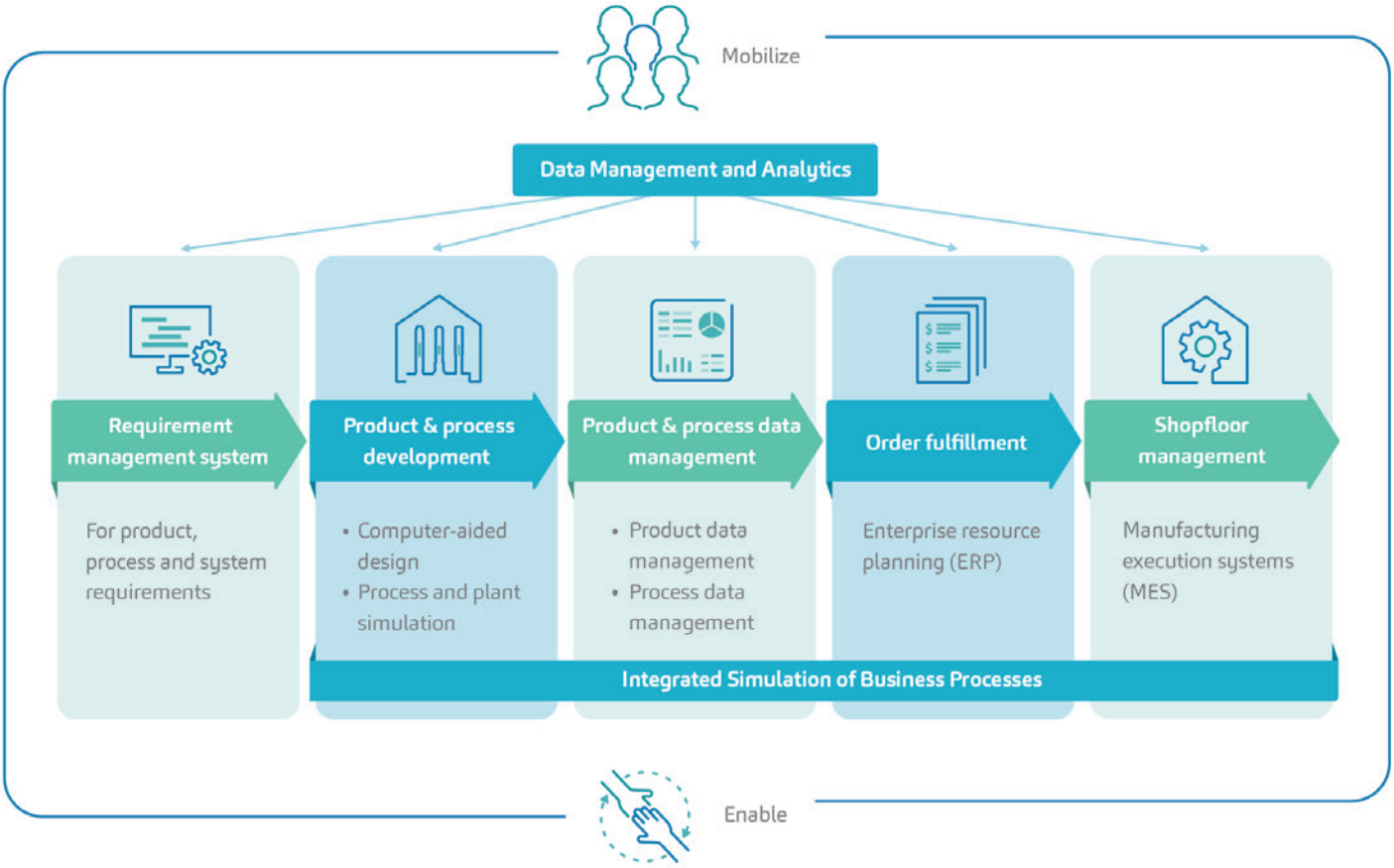


Figure 4: A condensed overview of SHL's digitalisation programme. SHL found a way to tailor its digital transformation in a direction that pursues operational excellence.

continuously optimise the root processes it uses across multiple customer projects. A closer look at the focus areas for CI ideas that were submitted and implemented (Figure 3) points to the ultimate pursuit of operational excellence, encompassing both process development and manufacturing excellence.

CI IN ACTION

Value-stream mapping (VSM) is a fundamental CI-lean manufacturing method for analysing the state of the stream of events that transforms raw materials into the products that reach the customer and their

patients, as well as considering how that state may be improved in future. Here, value creation should not be misconstrued as meeting the bare minimum nor the fulfilling of norms – exceeding cGMP regulations and industry standards is always a first priority for SHL.

For example, from 2020 onwards, SHL's manual assembly machine (MAM) operations underwent a transformative journey that has not only benefited its staff but also maximised value creation for customer projects. SHL had a clear vision for redefining its manual assembly line conventions of productivity, efficiency, quality and resource maximisation, all of which are supported by real data. Clinical to commercial readiness in autoinjector development starts with a robust manual assembly process, so SHL fortified its already robust MAM operations framework to support an even shorter manufacturing lead time. To make this happen, shopfloor processes were further optimised and lean documentation procedures were practised, resulting in a continuous-flow process, as well as enabling a paperless assembly operation. During the process of lean transformation, most non-value-added activities were reduced by more than a third, further maximising SHL's assembly line productivity and capacity. To increase organisational confidence in adherence to schedules, e-dashboards were made available across the assembly lines. These are evident of SHL's commitment to redefining what is best in class in terms of autoinjector manufacturing.

AUTOMATION AND DIGITALISATION AS A SUBSET OF OPERATIONAL EXCELLENCE

For SHL, the fourth industrial revolution (Industry 4.0) did not mean joining the bandwagon of simply digitising and automating anything and everything. Rather, it was an opportunity to look at the bigger picture and see where the company could generate most value from creating a lean manufacturing process as the foundation for implementing digitalisation and automation in its operations. As such, in pursuit of CI and lean manufacturing, SHL also found its way into a digital transformation journey, during which it developed an end-to-end digital framework that spans all its data, products and processes. SHL's digital transformation features an architecture where a data management and analytics system automatically creates feedback loops based on data from all product and process levels (Figure 4).

CI HERALDS SUSTAINABLY POSITIVE CHANGE

SHL understands that sustainability and positive change across operations can be attained through the consistent, committed and systematic participation of people across the value chain. It has shown that CI is more than an abstraction, and that value can be created in a way that both supports the workforce and maximises benefits for customers. In an industry where the safe and effective delivery of drugs and treatment modalities to patients is of prime importance, SHL believes in a future built upon present action towards CI.

> "Value can be created in a way that both supports the workforce involved and maximises benefits for customers."

ABOUT THE COMPANY

SHL Medical is a solutions provider in the design, development and manufacturing of advanced drug delivery devices, such as autoinjectors and pen injectors. The company also provides final assembly, labelling and packaging services for leading pharmaceutical and biotech companies across the globe. With locations in Switzerland, Taiwan, Sweden and the US, SHL Medical has successfully built a strong international team of experts that develops breakthrough drug delivery solutions for pharma and biotech customers. These include advanced reusable and disposable injection systems that can accommodate large-volume and high-viscosity formulations – and connected device technologies for next-generation healthcare.

REFERENCES

1. *"Continuous Improvement". Encyclopedia.com web page, accessed Jul 2022.*
2. *Yu L et al, "FDA's new pharmaceutical quality initiative: Knowledge-aided assessment & structured applications". Int J Pharm X, 2019, Vol 1, Article 100010.*
3. *"Pharmaceutical cGMPs for the 21st century – a risk-based approach". US FDA Report, Sep 2004.*
4. *"Guidance for Industry: PAT — A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance". US FDA, Oct 2004.*

ABOUT THE AUTHOR

Tracy Pedreso is an Associate Director at SHL Medical and currently heads the CI department, based in Taiwan. In his latest role, he leads a team of CI engineers, along with an extended team of lean champions who drive lean manufacturing and business excellence across the organisation. Prior to this, Mr Pedreso was the head of SHL's manufacturing assembly operations across Taiwan. He was previously a Focus Factory Manager at ResMed (Singapore), where he worked for 11 years. Mr Pedreso holds bachelor degrees in both Electronics and Communication Engineering, and Engineering Technology. He is Lean Six Sigma Green Belt and Black Belt certified and has been a catalyst of CI in multifaceted industries for more than 20 years.

SHL MEDICAL

Modular designs

Allowing flexibility in design and manufacturing

Learn more:
www.shl-medical.com

INTERVIEW

In this interview, Piyush Agarwal of Tjoapack talks with ONdrugDelivery about the current state of the injectable pharmaceuticals market and how working with a specialist contract packaging organisation can help pharma companies navigate their product through this rapidly evolving sector and deliver their product to market on time.

PIYUSH AGARWAL, TECHNICAL SOLUTIONS & SUPPLIER MANAGER, TJOAPACK

Piyush Agarwal heads Technical Solutions and Supplier Management at Tjoapack. He has been with Tjoapack since early 2019 and has executed multiple functions, including business development and project implementation. His team is responsible for finding operationally feasible and commercially viable solutions for pharmaceutical companies to pack their products on time. He is also responsible both for managing contracts and negotiations with existing suppliers and for onboarding new suppliers. He holds a Bachelor's degree in Engineering and a Master's in Business Administration.

Q To begin, let's discuss the major trends, aside from patient-centricity, in the prefilled syringe (PFS) and injection sphere. First, are there any new devices or innovations in syringe design that are becoming more popular among pharmaceutical companies?

A The demand for PFSs has been steadily increasing over the past decade. Alongside this, other injectable devices that improve the injectable medicine administration experience have been developed in tandem. For instance, autoinjectors, injection pens and infusion pumps have also been actively increasing their share in the sterile manufacturing market.

As for syringe components, engineers are actively exploring integrated safety systems that can be applied to the PFSs. These tend to focus extensively on needle safety, usability and multi-barrel options. Specialists are actively expanding syringe portfolio ranges with respect to product volume options and needle sizes.

Q In your opinion, what is the current position of PFSs in the pharmaceutical space?

A PFSs have become the primary alternative to multi-vial solutions when it comes to biologics and biosimilars. On the current market, PFSs are extensively used for antithrombotics, vaccines, biologics and small molecules. The use of PFSs in these areas helps to improve the manufacturing process, avoid waste and ensure that the correct dose is administered.

> "A large and diverse group of manufacturers are investing in the development and commercialisation of biosimilars. This, in turn, is facilitating the demand for new packaging solutions for injectables."

The current pharma market has seen a significant shift towards therapeutic segments like immunology, oncology and gene therapy. As such, biologics are now being given a higher priority in the pharmaceutical industry's pipeline. The administration of biologics is mostly performed via injection, as alternative routes of administration often drastically lower their effectiveness.

Within biologics, monoclonal antibodies (mAbs) have the largest market share, followed by vaccines and insulin. For small-molecule injectables, the leading segments are oncology and anti-infectives. mABs accounted for one quarter of the total revenue share in biologics in 2019, primarily due to the expanding product pipeline and a high rate of approvals by the US FDA and EMA. Additionally, according to the recent filings, the most prominent growth areas are oncology and immunology.

In general, a large and diverse group of manufacturers are investing in the development and commercialisation of biosimilars. This, in turn, is facilitating the demand for new packaging solutions for injectables. When we look at the current pharmaceutical pipeline and, in particular, clinical and preclinical trials, small molecule and mAB therapies are dominant. Additionally, we're also seeing the preferred delivery route change along with this shift in pipeline priorities. There is a decrease in the oral delivery route, while the injectable route increases.

Q Do you expect upcoming new regulations to impact the use of PFSs?

A Currently, supportive government regulations, such as needlestick legislation, are providing a boost to PFS market growth. This legislation promotes the widespread implementation of PFSs with integrated safety systems to reduce the rate of needlestick injuries.

Additionally, the recent Institute for Safe Medication Practices (ISMP) guidelines heavily support an increased use of ready-to-administer (RTA) syringes. The ISMP guidelines have increased awareness and guidance regarding the use and manufacture of RTA syringes. In their guidelines published in 2020, the ISMP once again addressed the main downsides of admixing faced by clinicians during emergency situations, introducing new safe practices that include the use of RTA products. Similar guidelines are also being released by other regulatory bodies and serve as an additional driver for the PFS market.

Q Can you tell us about any new approaches to the packaging of PFSs and other injectable devices?

A As PFSs and other devices become more sophisticated, their packaging needs have shifted from solely carton-based packaging to a more stable and durable packaging solution. While carton-based packaging does offer some form of structural stability with the inclusion of paper-based custom inlays to keep the devices in place, there are alternate approaches to packaging injectable devices in cartons. Two such approaches are placing them in an unsealed blister with a clamp-in option and a sealed blister with or without a clamp-in option.

These trends are leading companies to adopt various non-standardised solutions. Forward-thinking contract packaging organisations (CPOs) are addressing these needs by investing in secondary packaging capabilities so that they can be flexible in order to meet market requirements. The services such companies can offer range from manual customised package assembly to automated packaging of PFSs into blisters.

Advanced blistering lines can automate the secondary packing of injectables, including vials, ampules and PFSs, into rigid PVC with high thermoformability. These PVC blisters are then sealed, ensuring that all components remain intact. The blister, along with a patient information leaflet, is then placed inside a carton that can be serialised later or aggregated based on market-specific requirements.

Q How does a CPO manage the transfer of the product from the contract manufacturer or the pharmaceutical company to its facility for packaging PFSs?

A First, the quality and integrity of the product needs to be ensured. The key considerations for this are analytical tests (performed by certified third parties at the client's wish); identifying key components (safety device and format parts for plunger rods, backstops or finger flanges); identification of necessary packaging materials (such as foils and films) with subsequent stability studies executed by a certified third party; and quality validation to ensure that each step of the PFS assembly process is safe for the end-product and patients to use.

The packaging of PFSs differs from the packaging of other dosage forms, such as oral solids and vials (Box 1). Oral solids are primarily packed into blisters, bottles and similar, and therefore have different in-process controls to ensure that there is no contamination. Since oral solids come in different sizes and shapes, there is not always one standard solution that fits all. However, for PFS packaging, the key

> "For PFS packaging, the key considerations are the type of PFS assembly (with or without a safety device) and format parts for plunger rods, backstops or finger flanges."

BOX 1: PACKAGING PROCESSES STEP-BY-STEP

PFSs
- Manual infeed of syringes
- Plunger rod insertion station
  - Infeed of plunger rods
  - Sorting of plunger rods
  - Plunger rod insertion
  - Syringe rotation with adjustable speed and torque to allow fine adjustment
- Labelling
  - Labelling is done via a separate unwinding unit
  - Labelling is synchronised with the rotation speed of the syringes
- Label printing
  - Label printing is done via thermal transfer to include variable data
- Safety device station (optional)
  - Infeed of safety device
  - Pick-up and pushdown of device
  - Finger flange assembly station
- Backstop assembly station
  - Infeed of backstops
  - Sorting
  - Assembly
- Blistering
  - Thermoforming pockets for placing PFSs
  - Feeding PFSs, vials and/or needles into pockets
  - Lidding and sealing
- Carton unit
  - Placing sealed blister into the carton with a leaflet
- Serialisation unit
- Automated case packer
  - Placing cartons into shipper
  - Optional aggregation
- Tertiary packaging.

ORAL SOLIDS (BLISTERING)
- Bulk feeding
- Blistering
  - Thermoforming pockets for placing tablets
  - Lidding and sealing
- Carton unit
  - Placing sealed blister into the carton with a leaflet
- Serialisation
- Tertiary packaging.

ORAL SOLIDS (BOTTLING)
- Bulk feeding
- Bottling
  - Tablet counting
  - Bottle feeding
  - Induction sealing (if applicable)
  - Adding silica gel (if applicable)
  - Adding space filler (if applicable)
  - Capping (snap-on or twist-off)
- Carton unit (if applicable)
  - Placing sealed blister into the carton with a leaflet
- Serialisation
- Tertiary packaging.

VIALS (SECONDARY PACKAGING)
- Manual infeed of vials
- Labelling
- Label printing
  - This is done via thermal transfer to include variable data
- Inlay station
  - Adding an inlay for single or multi-vial packs (optional)
- Carton unit
  - Placing inlay or single vials into the carton with a patient information leaflet
- Serialisation unit
- Tertiary packaging.

"It is key to have a packaging partner that can support with scalability from clinical trial to product launch to commercial high-volume batches."

considerations are the type of PFS assembly (with or without a safety device) and format parts for plunger rods, backstops or finger flanges. Identifying the optimum foil with deep stretch properties to hold the PFS in its blister and a suitable lidding foil are some of the other key considerations.

Q How can a CPO support its customers in managing these issues?

A An established CPO can leverage its own experience, along with that of its suppliers, to create a tailor-made solution for its customers. It's also important to include a dedicated project and technical team in the production team to ensure that all the equipment is correctly installed and that operators are sufficiently trained with the equipment. It is also prudent for the CPO to provide a management team dedicated to finding technically feasible and commercially viable solutions for clients that help them meet their requirements, as well as a dedicated project management and implementation team to ensure that products are delivered to the patient on time.

Q What is the best way for pharmaceutical companies to address the unique challenges they face when packaging their products?

A When it comes to packaging, the current challenges faced by pharmaceutical companies include securing key components for format parts and/or equipment and key packaging materials for secondary and tertiary packaging, as well as having the agility to ensure that new products are launched to new markets on time and the flexibility to adapt to different regulatory, market, equipment and process requirements. To meet these challenges, it is key to have a packaging partner that can support with scalability from clinical trial to product launch to commercial high-volume batches.

Q What are the challenges facing pharmaceutical companies when ensuring the traceability of their products?

A Nowadays, the serialisation process is well-established and implemented within all key markets. However, challenges still arise from the differences in serialisation requirements across different markets, such as Europe, the US, India, China and Russia. For example, while serialisation within Europe is uniform (except for Italy and Greece), many companies come across difficulties when they decide to go international. The differences are concentrated around medicine verification systems, the extent of required "Track & Trace", pick processes for different markets and mandatory aggregation.

Q Could you explain the challenges of the labelling process for treatments?

A Different markets have different language requirements, which makes stock-keeping unit artwork management critical. There is also the consideration that some markets, such as Switzerland and the Benelux countries, have multiple language requirements, which leads to more complex booklets and labels. Lastly, it's critical to realise that the varying temperature requirements of products makes choice of label and adhesive material crucial.

Q How can CPOs overcome the challenges of labelling in cold and ultra-cold environments?

A Standard labelling process are often done under ambient conditions in the range of 15–25°C. However, for cold-chain products (2–8°C), it is prudent to follow the product guides of "Time Out of Range" to ensure that the end-product temperature conditions are met. Optimum label materials should selected to ensure proper adhesiveness even under condensation. For ultra-cold environments (-20°C), one solution is to label and pack products on dry-ice trays.

ABOUT THE COMPANY

Tjoapack is a global CPO specialising in primary and secondary pharmaceutical packaging and supply chain management services. The company is dedicated to shaping the future of the pharmaceutical supply chain to be safer and more reliable for its customers and for patients. With a track record of almost 30 years in contract packaging, Tjoapack uses its knowledge and experience to offer flexible solutions to its customers' challenges and uses the latest technologies to improve its operations continuously. The company now supplies products to over 40 countries across all continents.

Tjoapack

Piyush Agarwal
Technical Solutions & Supplier Manager

Tjoapack
Nieuwe Donk 9
4879 AC Etten-Leur
The Netherlands

T: +31 (0)889871 100
E: info@tjoapack.com

tjoapack.com

Medical Technology Ireland

21-22 September 2022, Galway Racecourse

Showcasing innovative medical technology products and solutions for the Irish medical device design and manufacturing industry.

Unmissable **Two-day** Conference

FREE Entry

Women in MedTech Forum

220+ Exhibitors

1200+ Attendees

Research & Innovation **Showcase**

Register NOW

2000+ FREE car parking spaces!

Our Partners:

cúram SFI Research Centre for Medical Devices

OÉ Gaillimh NUI Galway

Ollscoil Teicneolaíochta an Atlantaigh Atlantic Technological University

Medical Technology UK 22-23 March 2023 Coventry Building Society Arena

Register NOW for FREE entry at **www.medicaltechnologyireland.com**

If you are interested in exhibiting, contact **jason.moss@medicaltechnologyireland.com**

SINGLE USE SYSTEMS – THE FUTURE OF BIOPHARMACEUTICAL PROCESSING

Here, Jeff Lowe, Product Manager at Trelleborg Healthcare & Medical, considers single-use systems and looks at their role in the future of biopharmaceutical processing.

Based on an article that originally appeared in Medical Design Briefs in February 2022.

Single-use systems (SUS) represent the future in biopharmaceutical processing of therapeutic drugs with significant advantages over traditional reusable stainless steel systems.

Seemingly the antithesis to a whole world trying to move away from disposable products and processes, SUS actually promote sustainability by eradicating the chemicals and resources, such as water and energy, needed to sterilise reusable systems. Perhaps, most critically, with little cost and process time, SUS virtually eliminate the risk of cross-contamination, as the product flow path is discarded and replaced after each batch.

MANUFACTURING PROCESS SYSTEMS

Within the biopharmaceutical industry, three types of processing systems are used to create therapeutic drugs.

The first type involves **stainless steel systems**. These are reusable, durable and able to withstand exposure to the chemicals used to sanitise pharmaceutical processing systems, usually at extreme temperatures. These require stringent sterilisation regimes that involve harsh chemicals and require considerable energy consumption to bring systems up to the extreme temperatures required for effective cleaning.

The second types are partly **disposable systems**. These use some parts of the processing system more than once, depending on the therapeutic being produced. Reused parts undergo cleaning regimes similar to those used to sterilise stainless steel systems, and maintenance is required as reusable elements deteriorate over time.

Both stainless steel systems and the reusable parts of disposable systems contain an inherent risk of contamination unless cleaning and sterilisation regimes are thoroughly performed.

SUS, the third type of biopharmaceutical processing system, are designed to be used for the duration of the production process of a single batch of therapeutics and then discarded.

The rise in the adoption of single-use technologies is proving to reduce product cross-contamination risks. In addition, SUS are highly efficient and cost-effective. According to a study conducted by Single Use Support (Endach, Austria), SUS lower operating costs by offering 46% water and energy requirement reductions, a 35% more favourable CO_2 footprint due to lower facility emissions and a 40% lower initial investment cost. They also allow pharmaceutical manufacturers to push products to market faster by increasing throughput and making scalability easier.

THE SHIFT TO SINGLE-USE SYSTEMS

Single-use bioprocessing systems have gained significant traction due to the rapid adoption of disposable technology by pharmaceutical manufacturers. According to Allied Market Research, the value of the global single-use bioprocessing market was US$2.8 billion (£2.4 billion) in 2016, and the projection is for it to reach $9.3 billion by 2023, at a CAGR of 18.7% over the period.

The technology is primarily applied in disposable freezing of pharmaceuticals, sterile filling of drugs, transportation of drug products, culture media preparation and

> "Both stainless steel systems and the reusable parts of disposable systems contain an inherent risk of contamination unless cleaning and sterilisation regimes are thoroughly performed."

Jeff Lowe
Product Manager

Trelleborg Healthcare & Medical

T: +1 774 764 1272
E: jeffrey.lowe@trelleborg.com

www.trelleborg.com/healthcare

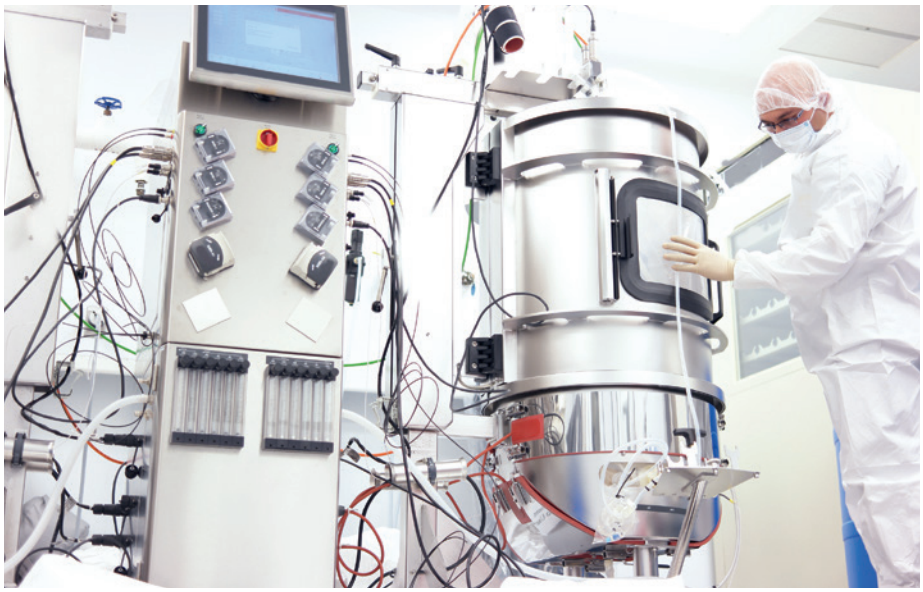


Figure 1: In SUS, all process parts are replaced with a new set so the system is quickly back up and running.

buffer preparation for bioprocessing. Most biopharmaceutical companies therefore use SUS to manufacture vaccines using large-scale bioreactor bags (Box 1), monoclonal antibodies (mAbs) and other pharmaceutical components on a commercial scale (Figure 1).

However, there are challenges in developing SUS relating to gaining regulatory approval of component materials, navigating the nuances of material compatibility with process fluids and maintaining the supply chain. For these reasons, suppliers must provide assurance that their products deploy operational best practices and are certifiably and regulatorily safe.

VALUE OF QUALITY AND MATERIAL EXPERTISE

One major advantage of SUS is single approval. Traditionally, after pharmaceutical manufacturers produce a batch of drugs, they must sterilise all the equipment and submit the equipment to the US FDA for approval between batches. This is a very costly and time-consuming process. Everything must be sterilised, and the seals in equipment connections often need to be replaced. Companies incur labour and supply costs when sanitising the system and experience extended downtime during cleaning.

In SUS, all process parts, including hoses, bags and seals, are disposed of and replaced with a new set so the system is quickly back up and running. Pharmaceutical manufacturers only need to gain approval from the FDA once. This not only saves time and money but also involves less risk of contamination and generates greater throughput.

A trusted and experienced supply partner can provide therapeutic manufacturers with all the data needed to support the quality of the component materials and parts for approval by the FDA. This may include the production of parts in a cleanroom and independent laboratory testing.

While there are no industry standards specifically for SUS, components, including seals, should comply with certain standards and technical guides. Some specific examples are the ASTM Standard F838-05 on Sterilizing Filtration, the ANSI/AAMI/ISO Standard 11137 on Sterilization of Healthcare Products – Radiation, and the ANSI/AAMI/ISO Standard 13408 on Aseptic Processing of Healthcare Products.

The Bio-Process Systems Alliance (BPSA) is a leader in developing new best practice guides for SUS. This is stimulating the development of standards and guides

"In SUS, all process parts, including hoses, bags and seals, are disposed of and replaced with a new set so the system is quickly back up and running."

BOX 1: A BRIEF HISTORY OF TRADITIONAL VERSUS THERAPEUTIC DRUGS

Synthesised and made from chemicals, traditional drugs, such as aspirin, process and attach to a certain gene. mAbs are laboratory-made proteins that mimic the immune system's ability to fight off harmful antigens, such as viruses.

Therapeutic drugs made in biopharmaceutical processing using mAbs teach the human immune system how to protect itself if introduced to a disease or illness.

Biopharmaceuticals include a wide range of products, such as vaccines, therapeutic proteins, blood and blood components and tissues. In contrast to chemically synthesised small-molecule drugs, which have a well-defined structure, biopharmaceuticals derive from living materials (human, animal, micro-organism or plant) and are much larger and more complex in structure.

Because biopharmaceuticals work with the immune system and do not contain chemical-based drugs, there is greater acceptance of biopharmaceuticals to treat a range of diseases, and the market is growing quickly. In addition, an increasing ageing population in Western countries, rising costs of healthcare globally, widespread presence of chronic ailments, technological advancements and manufacturing and contamination factors are all driving the rise in biopharmaceutical market demand.

The biopharmaceutical method of making drugs is an especially high-profile topic due to the global covid-19 pandemic and the use of the mRNA vaccine, which is made using a biopharmaceutical process.

by other organisations, such as ASTM-BPE, PDA and ISPE. BPSA guides cover irradiation and sterilisation validation, determination of extractables and leachables and disposal of SUS.

EXTRACTABLES AND LEACHABLES

To select processing materials that avoid risk, it is important to understand the chemical nature of extractables and leachables. Extractables are compounds emitted from a packaging component, delivery system or manufacturing surface during aggressive testing. Leachables are compounds that migrate into the drug over time from contact with system components and manufacturing surfaces.

An interaction of extractables or leachables with drugs or other media can be harmful to individuals and have possible long-term effects on the human body. Thorough testing is required to ensure that products are suitable for high-risk applications, such as drug delivery devices, combination products and long-term implants. For example, extensive testing must be conducted with all components to determine the extraction levels of substances under different conditions (Figure 2).

CONCLUSION

Single-use bioprocessing technology has gained significant traction due to the rapid adoption of disposable bioprocessing equipment by pharmaceutical manufacturers. SUS help pharmaceutical manufacturers save time and money while minimising the risk of contamination. Additionally, pharmaceutical manufacturers can select processing materials that limit extractables and leachables and rest assured that they meet all regulations by partnering with an experienced components supplier.

Figure 2: SUS have significant advantages over traditional reusable stainless steel systems.

By monitoring the market and staying in tune with customer needs, components suppliers can help therapeutic manufactures choose the right material for the right application. When components suppliers have global reach and material development expertise, they can demonstrate a comprehensive understanding of product applications. This allows them to collaborate with therapeutic manufacturers to understand their needs and provide the best solution.

ABOUT THE COMPANY

Trelleborg Healthcare & Medical helps pharmaceutical and medical device companies improve patient quality of life. It does this by forming lasting partnerships with customers to develop innovative, reliable engineered polymer solutions for demanding medical, biotech and pharmaceutical applications. From a single global source, backed by the expertise of a worldwide engineering and manufacturing network, it partners with its customers in all stages of development, from concept to serial production, providing the optimum solutions to meet all their partners' polymer-based healthcare and medical application challenges. Trelleborg Healthcare & Medical combines a number of operations from within Trelleborg Group that are focused on this industry.

ABOUT THE AUTHOR

Jeff Lowe, Product Manager at Trelleborg Healthcare & Medical, supports the effort to build additional biopharma capabilities into Trelleborg's Healthcare & Medical facility in Northborough (MA, US). He has a background in Operations and Product Management within medical device manufacturers.

DISSECTING THE DELICATE DELIVERY PROCESS FOR OCULAR GENE THERAPY

Here, Yongdong Zhou, MD, PhD, Head of Ophthalmology Team, Senior Director, at WuXi AppTec, considers the challenges of ocular gene therapy delivery approaches.

Gene therapy has emerged as one of the most promising areas of medicine in recent years. Not a year goes by without multiple breakthroughs in the field, and nowhere is there so much potential as in ocular gene therapy.

One of the major challenges of gene therapy has always been its delivery. It is incredibly difficult to insert genetic code into the correct cells, and consensus over the best means of delivery has evolved in recent years. This is particularly true for the eyes, where delivery is immensely complex.

The human eye is particularly suited to gene therapy because it is immune-privileged, meaning tissue grafts, foreign antigens and therapeutics can thrive without the body's immune system attacking them. But that does not make it any easier to administer, particularly when dealing with injections and pharmaceutical applications around one of the human body's more fragile organs.

Ocular gene therapy has the potential to treat diseases previously considered untreatable and restore hope to millions of patients suffering from ocular issues. But because of its complexity – particularly for delivery – practitioners need to ensure they make the right choices about the correct treatment path and delivery method for each patient.

"Ocular gene therapy has the potential to treat diseases previously considered untreatable and restore hope to millions of patients suffering from ocular issues."

VIRAL VERSUS NON-VIRAL VECTORS

Gene therapy is delivered via one of two systems: viral or non-viral. These two methods can address all types of treatment purposes: suppression, enhancement or replacement of a disorder-related gene. Viral delivery systems are the most common delivery methods in US FDA-approved ocular gene therapy. A viral vector is delivered into or near the target tissues or cells, either by an injection, where the target is in the eye, or pharmaceutically, where the target is near the eye's surface.

Viral vectors are built using a blueprint of a virus. They use the parts of the virus that help deliver genetic materials and exclude the parts that cause disease. They are widely considered to be more effective than non-viral vectors but do have some drawbacks – they are limited by their immunogenicity, oncogenicity and the small amount of DNA they can transport.

Adenoviruses, once a popular viral vector, have been largely abandoned for having strong immunogenicity and short expression duration. Lentiviruses bring an increased risk of oncogenesis (where healthy cells are transformed into cancer cells) because they naturally integrate into host genomes. Adeno-associated viruses (AAVs) are the most commonly used viral vector for ocular gene therapy. This is because they have three advantages over competing procedures:

1. An ability to transduce multiple retinal cell types
2. A relatively low immunogenicity
3. Low oncogenicity because they do not integrate into the host genome like lentiviruses.

Non-viral vectors are less effective than viral vectors, but they are safer, less costly to develop, more reproducible and they do not have a DNA size limit issue. However, excluding those actively studied *in vivo*, non-viral delivery methods (either physical or chemical) have not been used as much as viral delivery systems.

Dr Yongdong Zhou
Head of Ophthalmology Team,
Senior Director
E: zhou_yongdong@wuxiapptec.com

WuXi AppTec
1318 Wuzhong Avenue
Wuzhong District Suzhou
215104
China

labtesting.wuxiapptec.com

The most actively researched non-viral vectors are chemical disruption, electroporation and polymer-based vectors. Electroporation is a physical form of non-viral delivery method and involves using pulses of electricity to create temporary pores in a cell membrane. These pores then enable genetic materials to be delivered into the cell to take effect. Electroporation has been explored *in vivo*, but the most recent applications have been on cells outside the body. The other method of delivering a non-viral vector is chemical, where lipid nanoparticles (LNPs) are used.

LNPs have membranes made from lipids similar to the molecules in cell membranes. Their main strength is versatility. They can be used to deliver DNA or messenger RNA, which can instruct cells to block a protein or make more of it. They have been described as a platform technology on which genetic solutions can be built quickly and loaded into the appropriate LNP.

When researchers are considering which kind of vector to use for gene therapy delivery, there are several things they must consider. Effectiveness, safety, the size of genetic materials, the duration of gene expression, the target cells, accessibility and cost all make the list of considerations. But the decision making does not end there. There is also the question of whether to use injected or pharmaceutical means to administer the ocular gene therapy. There are benefits and challenges to both but selecting the right one is crucial.

THE PHARMACEUTICAL APPROACH

Conventionally, drug delivery routes for treating an ocular disease have included systemic (oral delivery and intramuscular or intravenous injection), topical (eye drops, ointments) and injections in and around the eye.

> "The purpose of ocular gene therapy treatment is to put genetic material into the target cells, so the delivery method depends on where those cells are located."

The purpose of ocular gene therapy treatment is to put genetic material into the target cells, so the delivery method depends on where those cells are located. If they are near or on the eye's surface, topical administration can work, but if the cells are in the eye, an injection is the best method.

Drug delivery via systemic or topical administration presents three major challenges. First, a tissue-specific delivery method needs to be developed. Secondly, doctors need to maintain a high local concentration of the genetic material. Lastly, the blood-retinal barrier can often block the drug from passing into the retina via systemic circulation.

Most genetic diseases associated with the eye are either a form of retinopathy (a disease in the retina) or neuropathy (damage or disease in the nerves). The target cells in both cases are in the eye itself, so it is incredibly difficult to use a pharmaceutical approach, meaning that injections are necessary. However, injection is an invasive approach and comes with its own challenges.

THE INJECTION APPROACH

There are several different types of injections in and around the eye – subconjunctival, retrobulbar, intracameral, intravitreal, subretinal and suprachoroidal. Intravitreal and subretinal injections are the most popular administration routes, but others can be used, and new methods are emerging. For example, an intracameral injection can be applied if a genetic disorder involves the corneal endothelium, or if a gene therapy is being used for glaucoma.

The suprachoroidal injection route has been actively studied and potentially used in gene therapy for retinal or choroidal diseases, ocular oncology and steroid delivery. This new approach is being developed to target the posterior segment of the eye. This route has the potential to achieve chorioretinal concentrations 10 times greater than those obtained with intravitreal injections. It also avoids the need for vitrectomy and retinotomy, as is required for subretinal delivery. A suprachoroidal injection also reduces the drug's exposure to the vitreous and anterior segment, potentially mitigating the side effect of increasing intraocular pressure found with steroids.

The process of administering an ocular injection is complex. A subretinal injection includes the following steps:

- First there is the vector preparation, then a transconjunctival puncture through the sclera and into the vitreous using a vitrectomy trocar.
- Next, leave the drive pipe in the sclera to facilitate the injection and conduct vitrectomy to remove the vitreous. If a vitrectomy is not conducted, the next step is a paracentesis of the anterior chamber, releasing aqueous humour for intraocular pressure control.
- After that, the practitioner must insert the 23-gauge subretinal injection needle into the vitreous, accessing the subretinal space while avoiding the major retinal vessels. At this point, the vectors are injected, generating a bleb beneath the neurosensory retina.
- Finally, the needle is pulled out, the drive pipe removed and the incision is sealed if necessary.

Challenges with Injections

Injections in such a delicate part of the body will always be complex. It can be even more challenging if the target cells are in the retina, which is a very subtle tissue. The procedure needs to be practiced often before it can be administered appropriately.

Scientists need to consider that while injection is currently the most common route for delivering gene therapies, it is not ideal. There is a risk of injury and infection from ocular injection. The most common injuries involve the iris, lens and retina and cause bleeding, cataract and retinal detachment. Intraocular pressure (IOP) needs to be monitored or prevented for intraocular injections by an anterior chamber paracentesis. A high IOP can cause damage to the retina and optic nerve, which is part of the mechanism of glaucoma.

To mitigate risks, trained surgeons or technologists should perform the procedure only after as much practice as possible. They should ensure that they are using qualified devices and instruments, conduct a strictly sterile operation to avoid infection and inflammation, monitor or prevent IOP, avoid injecting near blood vessels or touching the lens, and consider using steroids or immune-inhibiting medications.

> "Developing new non-invasive means to deliver gene therapy would be highly worthwhile."

If a non-invasive route exists, it is always preferable to something as invasive as an injection. Therefore, developing new non-invasive means to deliver gene therapy would be highly worthwhile.

It is also important to consider how to best control toxicity when delivering ocular gene therapy. Producing too much toxicity can be mitigated by selecting the appropriate viral vectors, or non-viral vectors where suitable, a lower dose or concentration and applying an anti-inflammation treatment.

CONSIDERATIONS FOR DRUG DEVELOPERS AND SPONSORS

Drug developers and sponsors should consider all the above but also keep in mind a few other factors. They should note that the success rate of ocular injections and the level of experience with such procedures are critical when choosing a drug development partner.

On the practical side, they need to remember that spare animals may be needed for replacements in the case of failures, and steroids and immune-inhibiting medicines should be on hand to treat inflammation caused by the injection of vectors. And for viral vector delivery studies, a biosafety level-2 lab is required and may cost more when working with a lab testing partner.

It is also worth remembering that a number of factors determine the success of ocular gene therapy, some of which are out of the hands of drug developers. The effectiveness of gene therapy for ocular diseases can change depending on whether it is a single-mutation disorder or a multi mutation disorder. Then key decisions are made before treatment, which can also affect how a patient reacts. This can include establishing the appropriate method to ensure that the vectors are delivered to or near the target cells. It is also important to choose appropriate AAV capsids for gene therapy. Different serotypes of AAV provide different tropisms for different retinal cell types.

Other factors determining the outcome include the successful transduction rate of the vectors, the expression/transduction in the desired target cells and the expression duration. The patient's immune reaction to the vectors will also determine success or failure, as will the proportion of functional cells remaining when the gene therapy is administered.

In vivo and *in vitro* studies suggest gene therapy will work best for people with single-mutation-induced disorders and more functional cells remaining and where there is high transduction, low immunogenicity and robust expression in the target cells.

A FINAL WORD ABOUT OCULAR GENE THERAPY

Ocular gene therapy is an exciting branch of medicine and promises to give hope to people worldwide suffering from conditions previously thought untreatable. The potential upsides for drug developers and sponsors interested in pursuing ocular disease treatments are substantial.

However, they must recognise the complexity of many factors, including delivery methods. Those looking into this topic seriously should first make a list of single-mutation disorders, explore orphan drug designation from the FDA as an option for rare genetic disease research, and choose a delivery system that ensures high transduction and low immunogenicity in the eye.

Finally, drug developers and sponsors need to ensure they collaborate with a team experienced in gene therapy studies and drug delivery techniques.

ABOUT THE COMPANY

As a global company with operations across Asia, Europe and North America, WuXi AppTec provides a broad portfolio of R&D and manufacturing services that enables the global pharmaceutical and healthcare industry to advance discoveries and deliver groundbreaking treatments to patients. Through its unique business models, WuXi AppTec's integrated, end-to-end services include chemistry and drug CRDMO (Contract Research, Development and Manufacturing Organisation) services, biology discovery, preclinical testing and clinical research services, cell and gene therapies CTDMO (Contract Testing, Development and Manufacturing Organisation) services, helping customers improve the productivity of advancing healthcare products through cost-effective and efficient solutions. WuXi AppTec received an AA ESG rating from MSCI in 2021, and its open-access platform is enabling more than 5,800 collaborators from over 30 countries to improve the health of those in need, and to realise the vision that "every drug can be made and every disease can be treated".

ABOUT THE AUTHOR

Yongdong Zhou, MD, PhD, Head of Ophthalmology Team, Senior Director, WuXi AppTec, is a board-certified ophthalmologist with 21 years of experience in clinical diagnosis and surgery. Dr Zhou brings ten years of experience from the Neuroscience Center of Excellence, Louisiana State University Health Sciences Center in New Orleans (LA, US) and the Doheny Image Reading Center, Doheny Eye Institute in Los Angeles (CA, US), as an assistant professor and an investigator and supervisor of an ocular image-reading team. He has tremendous experience in ophthalmic preclinical exploratory research, animal model development and application, clinical trials of new agents, technologies and devices.

- Design more compact, intricate components for connected wearable devices
- Integrate electronic functionality into structural components
- Increased patient utility, comfort and concealment
- LCP resins deliver exceptional flow in thin-wall molding to enable smaller parts and free up more internal space
- Manage overall device costs with rapid cycling and more parts produced per hour

Visit us at **healthcare.celanese.com** to learn more!