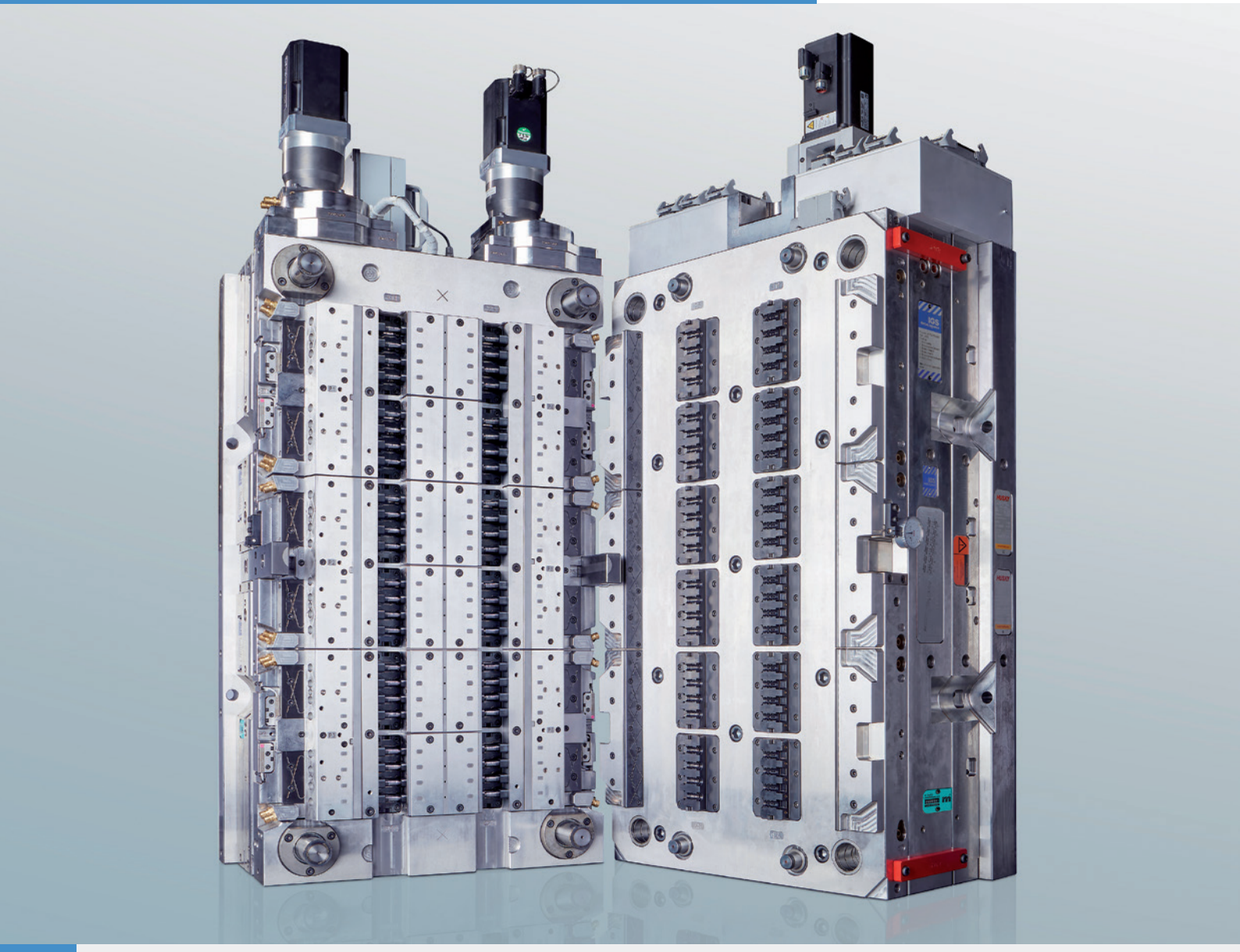
INDUSTRIALISING DRUG DELIVERY

ON drugDELIVERY



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ONdrugDelivery Issue N° 150, July 3rd, 2023

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

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Oct	Prefilled Syringes & Injection Devices
Oct/Nov	Drug Delivery & Environmental Sustainability
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Jun/Jul	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:
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Front cover image, "An IGS Mould", courtesy IGS GeboJagema (see this issue, Page 31). Reproduced with kind permission.

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Owen Mumford
Pharmaceutical Services

DFM & DFA: THE DIFFERENCES, BENEFITS AND HOW TO IMPLEMENT THEM

In this article, Phil Sampey, Senior Design Engineer at Haughton Design, discusses the principles associated with design-for-manufacture and design-for-assembly methodologies as applied to drug delivery device design, giving an overview of what each involves and key areas of focus to ensure that the full benefits of these approaches can be realised.

Two concepts that frequently arise in current industry discussions are "DFM" and "DFA". These concepts should be given consideration from the outset of a project through to after a product or device has been manufactured. So, what do they mean? What are the differences? How important are they? How can each one be correctly implemented in medical and drug delivery device development?

DESIGN FOR MANUFACTURE

DFM stands for "design for manufacture", the process of designing parts with a particular manufacturing process in mind. Designing parts for manufacture is a crucial aspect of device development. DFM involves designing parts that are not only functional and meet the required specifications but that are also optimised for efficient and cost-effective production. The DFM process can be broken down into four areas:

- Chosen manufacturing process
- Part design
- Material selection
- The environment to which the parts will be exposed.

Consideration must be given to each of these areas. If just one area is neglected, it could lead to costly product failures further down the road.

The chosen manufacturing process and part design areas of DFM go hand in hand. When designing a component, both the desired function and design intent of the component should be considered whilst keeping the chosen manufacturing process in mind. The component should be designed to conform to the good manufacturing principles for the chosen manufacturing process. This will include considerations from the physical size and shape of a component to the specific geometry of individual features.

For example, when designing for injection moulding, the part should be designed in a specific way, following the common design rules for injection moulding, such as using fillets and radii wherever possible to reduce stress concentrations, adding a split-line to the part, using draft angles on areas of the part geometry to aid the release from the tool and ensuring that there are no thick/thin sections or undercuts in the design. However, if it is decided that the part is to be computer numerical control (CNC) machined instead, then the design features of a CNC machined part would not necessarily need to incorporate most of these injection moulding design rules (Figure 1).

When it comes to material selection, choosing the final materials for the components of a device can have a big impact on the DFM considerations. Not only will the chosen manufacturing process play a part in selecting the right materials, but the specification and use case of the final product will help guide the selection of the best materials for the device. The following questions are just some key

> "When designing a component, both the desired function and design intent of the component should be considered whilst keeping the chosen manufacturing process in mind."

Phil Sampey
Senior Design Engineer
T: +44 1785 848530
E: pas@haughtondesign.co.uk

Haughton Design Ltd
5 Parker Court
Dyson Way
Staffordshire Technology Park
Stafford
ST18 0WP
United Kingdom

www.haughtondesign.co.uk

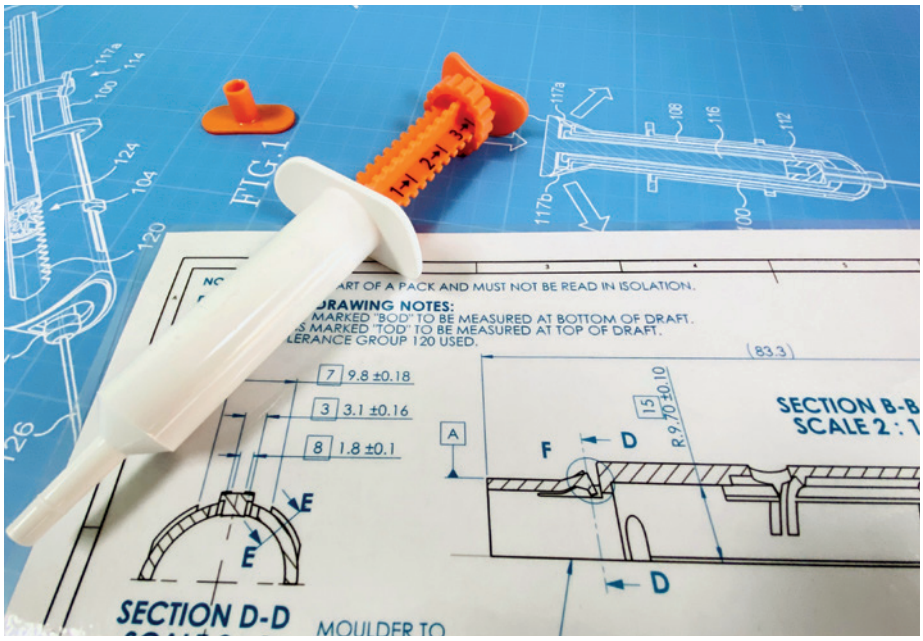

Figure 1: Part design and chosen manufacturing process go hand in hand, the considerations of one feed back into the other.

considerations for material selection:

- Will it need to withstand a load?
- Will there be any living hinges incorporated into the design?
- Will there be any snap-fits or clips?
- Does the chosen material need to be medical grade, sterilisation safe, food contact safe or hold a certain USP classification?
- Will the final device face have prolonged exposure to harsh chemicals, lipids or other biologicals?

In practice, the chemical resistance requirements of a device's chosen final materials often take the top spot of importance when selecting final materials, trumping mechanical requirements. These are all important areas that can drive the material selection aspect of DFM and should be looked at holistically and in detail.

Material data sheets are a fantastic resource, filled with useful information that can help with understanding material properties. Polymer datasheets provide detailed information about the physical, mechanical and chemical properties of a given polymer. This information can help determine whether the material is suitable for the intended application.

> "Material data sheets are a fantastic resource, filled with useful information that can help with understanding material properties."

A section of polymer datasheets that is often overlooked is the thermal properties of the material. This section plays a huge part in ensuring that the final device can survive and operate in a particularly low- or high-temperature environment if required. The best design in the world won't survive if the device's features cannot perform within the specified operating temperatures of the application. Knowing the application and the environmental conditions that the device will be subjected to can be key to selecting the correct material.

DFM is an important part of any device development cycle. It should be considered early in the process to maximise cost and time savings. Appreciating and considering these four areas of the DFM process will ensure that a device is engineered and manufactured so that it performs to a high standard with robust, lasting performance. Addressing potential issues at the early stages of product development will help get it right the first time, or at least require less prototyping and fewer product iterations.

In conclusion, designing parts for manufacture is an essential aspect of product development. By understanding the manufacturing process, optimising for material properties, minimising complexity and considering tolerances and testing requirements, devices can be engineered so that they are not only functional but also optimised for efficient, cost-effective production.

> "Although DFA and DFM principles are often looked at as one combined subject, they are quite separate methodologies."

DESIGN FOR ASSEMBLY

DFA stands for "design for assembly", a process by which products and devices are designed with ease of assembly in mind. For example, if a product contains fewer parts, it will take less time to assemble, thereby reducing assembly time and costs. DFA is an essential aspect of engineering and manufacturing that plays a critical role in ensuring the successful and efficient assembly of complex devices. Properly designed components can reduce assembly time and cost, improve quality and reliability and enhance overall product performance.

Although DFA and DFM principles are often looked at as one combined subject, they are quite separate methodologies. DFA is the optimisation of the device and the assembly process, while DFM focuses on the manufacturing process and material selection. The aim of DFA is to make the assembly process easier, faster and more consistent to increase productivity. Some of the main principles of DFA to keep in mind are:

- Minimising part count
- Built-in fasteners
- Use of standard parts
- Part symmetry
- Poka-yoke assembly-specific design features.

Applying these principles throughout the design process will ensure the right path to achieving an efficient and successful device (Figure 2).

Minimising part count is an easy way to ensure that devices are quick to assemble. Well-designed devices that have fewer parts usually end up being more durable, as well as easier to assemble and repair. Keeping the part count down will not only cut assembly times, and therefore assembly

Figure 2: Following DFA principles can lead to reduced assembly time and costs for a device, as well as improved reliability and quality.

costs, but also prevent confusion during assembly and result in fewer assembly issues. However, be mindful that overly complex components might unnecessarily increase manufacturing costs.

It is highly beneficial to have a close relationship with the chosen manufacturer. Communication between designers and manufacturers is key to resolving complex part issues and helps to ensure that parts are designed efficiently and cost-effectively. Every manufacturer has their own way of doing things, so having a cohesive relationship with a chosen manufacturing partner is one of the biggest potential efficiency boosts for any design project.

Built-in fasteners should always be a consideration when designing efficient products. Although bolts, screws and rivets are relatively inexpensive, the installation of these fixings is very time-consuming. Built-in fasteners, such as snap-fits, speed up the assembly of the final device. Snap-fits don't require any special production equipment and can make assembly quick and simple.

Using standard off-the-shelf parts instead of costly custom-manufactured parts, such as bushings and gears, will increase repeatability, save time during the assembly process and reduce assembly costs. Incorporating off-the-shelf parts into devices will also speed up the design process, as there are fewer custom parts to design and engineer.

Designing symmetric components is another way to ensure an efficient DFA methodology. This makes the assembly process easier for workers as it reduces the time spent trying to identify which way round similar looking components should be mounted.

Finally, incorporating assembly-specific design features into parts, such as physical obstructions to prevent components being fitted wrongly, or adding physical or graphical identifiers to parts that make them easier to identify and assemble, is one of the easiest ways to reduce assembly time. One of the simplest but most effective poka-yoke design features is the UK electrical plug and socket; the three-prong design for the plug and socket ensures that the plug can only be connected to the socket in the single correct orientation. Incorporating these poka-yoke design features into the component design will make sure devices can't be assembled incorrectly and will avoid many potential issues down the line.

Designing parts for assembly requires a comprehensive understanding of the manufacturing process, product requirements and assembly considerations. By following the principles of DFA – standardisation, minimising part count, ease of assembly, modular design and material selection – designers can create parts that are optimised for assembly, which can result in improved product performance, reduced assembly time and cost and increased patient satisfaction.

A FINAL WORD

Hopefully this brief overview of the value that DFM and DFA principles have in device design has highlighted the importance of following these practices. Implementing these two methodologies can not only help reduce the time to market and costs of devices, but also be a guide to designing a more robust and effective device that can stand the test of time.

ABOUT THE COMPANY

Haughton Design is a UK-based design consultancy that specialises in providing medical device design, development and engineering services for global healthcare, medtech and pharmaceutical clients. The company's mission is to responsibly accelerate its clients' medical device development programmes by developing devices that are grounded in robust engineering, manufacturability, usability and sustainability. Haughton Design's clients in the drug delivery space value its innovative approach, technical expertise, fresh ideas and improved time to market. The company's services are designed to make the medical device design and development process easier for its clients and their teams.

ABOUT THE AUTHOR

Phil Sampey graduated with a degree in Automotive Technology before working for a global market leader specialising in quick turnaround plastic injection mould tooling and CNC machined parts. Using his early manufacturing knowledge and experience, Mr Sampey has since worked on an extensive range of medical and drug delivery device projects such as inhalation devices, prefilled syringes, feed tube sets, autoinjectors, trainer devices and ostomy products. He has extensive experience in a wide range of manufacturing and industrialising techniques from prototype manufacturing to full-scale volume production. Mr Sampey is Haughton Design's DFM and DFA champion alongside assisting with the management of the company's ISO:13485 and ISO:9001 QMS accreditations and network of approved manufacturers.

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September	Wearable Injectors	Aug 3, 2023
October	Prefilled Syringes & Injection Devices	Sep 7, 2023
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June	Connecting Drug Delivery	May 9, 2024
Jun/Jul	Industrialising Drug Delivery	May 23, 2024

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Particle Works

HIGH-THROUGHPUT SCREENING TO ACCELERATE NANOMEDICINE DISCOVERY

In this article, Ben Knappett, PhD, Head of Science and Applications at Particle Works, discusses how the successful combination of microfluidics with automation can provide rapid and cost-effective high-throughput lipid nanoparticle technology formulation screening, and how this approach could play a significant role in advancing the development of new nanotherapies.

The widespread introduction of covid-19 mRNA vaccines was underpinned by lipid nanoparticle (LNP) technology, and the success of this rapid roll-out has solidified the viability of nanomedicines, attracting new funding and interest in this area. The market continues to boom, and recent scientific breakthroughs have proven LNPs to be highly effective drug delivery systems for a range of therapy types. The ability to screen large numbers of different formulations is essential for optimising numerous performance characteristics that depend on a specific particle size, shape and structure. Automated systems are ideal for this screening, surmounting the challenges associated with typical low-throughput LNP preparation methods.[1]

EXPLORING THE POTENTIAL OF NANOMEDICINES

The field of nanomedicine holds promise for overcoming the undesirable properties of many conventional drugs that limit their clinical use, including poor pharmacokinetics, restricted bioavailability and high toxicity.[2] Using LNPs as drug delivery systems is a revolutionary way of improving the therapeutic index of a drug, and the viability of this technology has recently been validated by the successful development of LNP-mRNA covid-19 vaccines. As a result, this approach has received significant research interest and offers key advantages over other drug delivery options, enabling the encapsulation of a range of payloads with high efficiency, stabilising the API and helping to deliver it to target cells (Figure 1).

The success of LNP medicines is widely acknowledged to lie in the specific formulation of the particle, as this can significantly affect the therapeutic efficacy. The optimal formulation for each application is vital to turn promising biologics into effective and viable therapeutics – whether for a vaccine, gene therapy or cancer treatment – and reproducibly creating uniform particles with

"The field of nanomedicine holds promise for overcoming the undesirable properties of many conventional drugs that limit their clinical use, including poor pharmacokinetics, restricted bioavailability and high toxicity."

Dr Ben Knappett
Head of Science and Applications
E: info@particle-works.com

Particle Works
Unit 1, Anglian Business Park,
Orchard Road, Royston,
Hertfordshire
SG8 5TW
United Kingdom

www.particle-works.com

Figure 1: Novel systems combining microfluidics with automation provide high-throughput LNP formulation screening to accelerate the creation of pioneering genetic medicines and cancer treatments.

finely tuned performance characteristics is vital to achieving this.[3] Furthermore, nanomedicines are intended for clinical applications, meaning that LNPs must be consistent and safe for use in humans.

FINDING THE PERFECT BALANCE

LNPs must be carefully engineered to ensure that they can perform the complicated series of actions necessary for effective drug delivery – including transport across cell membranes and intracellular release – while keeping their therapeutic cargo intact. Several different factors may affect the success of an LNP, and must be controlled by altering the liposomal formulation of the particles to achieve the ideal performance criteria. Particle size affects both uptake and delivery – with the best performing formulations being between 75 and 95 nm in diameter[4,5] – and the polydispersity index, a measurement of the uniformity of particle sizes, must have a value of 0.2 or below to be deemed acceptable.[6]

Lipid type	Options in Clinical Use
Ionisable	SM-102 MC3 9A1P9
Phospholipid	Phospholipon-90G DSPC
PEGylated	DMG-PEG_{2000} DOPE-PEG_{2000} DSPE-PEG_{2000} DSPE-PEG_{5000}
Cholesterol	–

Table 1: Lipid categories.

The biological performance of an LNP largely depends on four lipidic components: ionisable lipids, phospholipids, PEGylated lipids and cholesterol.[1,7] Both the molar ratio and type of lipid material can be altered, with multiple options currently in clinical use (Table 1).

Many different LNP factors can be fine-tuned, such as cargo concentration, length or sequence, as well as the charge ratio of the particle itself. Process parameters – including total flow rates, reagent mixing kinetics, pH and type/concentration of buffer – can also be adjusted. To identify the "sweet spot" of particle performance, small quantities of every permutation of formulation parameters must be synthesised. Physiochemical characterisation of each batch is then screened, before the most promising nanoformulations are selected to take forward. This cumbersome process is largely reliant on trial and error, and requires potentially billions of investigations. The experimental process must also be consistent and validated, quickly racking up high materials and consumables costs, as well as incurring heavy demands on labour and time.

> "There is a clear demand for a platform that can rapidly synthesise trial nanoformulations in a controlled manner, allowing efficient screening and process parameter adjustments."

AUTOMATION FOR IMPROVED THROUGHPUT AND CONTROL

Low-throughput, manual screening introduces large workflow bottlenecks, delaying downstream assays and characterisation steps. In the absence of automation in both upstream and downstream stages, there is a danger of missing the perfect nanoformulation, hindering discovery.[3] There is therefore a clear demand for a platform that can rapidly synthesise trial nanoformulations in a controlled manner, allowing efficient screening and process parameter adjustments.

Microfluidic devices can achieve this by manipulating fluids on the microlitre scale, generating reproducible and monodisperse nanoformulations possessing tightly controlled physical properties. However, most microfluidic systems used for formulation screening only allow one experiment to be performed at a time before experimental parameters need to be changed manually. As a result, this method had not been able to offer sufficient automation until recently.[8]

The latest automated microfluidic platforms overcome this to enable effective and efficient high-throughput generation of numerous LNP formulations. These innovative platforms significantly accelerate screening timeframes, offering superior process consistency, increased automation and minimised running costs (Figure 2). They are compatible with 96-well plate formats – completing up to 96 experiments in as little as six hours – to seamlessly fit with existing upstream and downstream workflows, permitting easy sample transfer between all stages of particle production.

These platforms feature reusable glass microfluidic chips and automatic washing between experiments to ensure that there is no cross-contamination, which enables

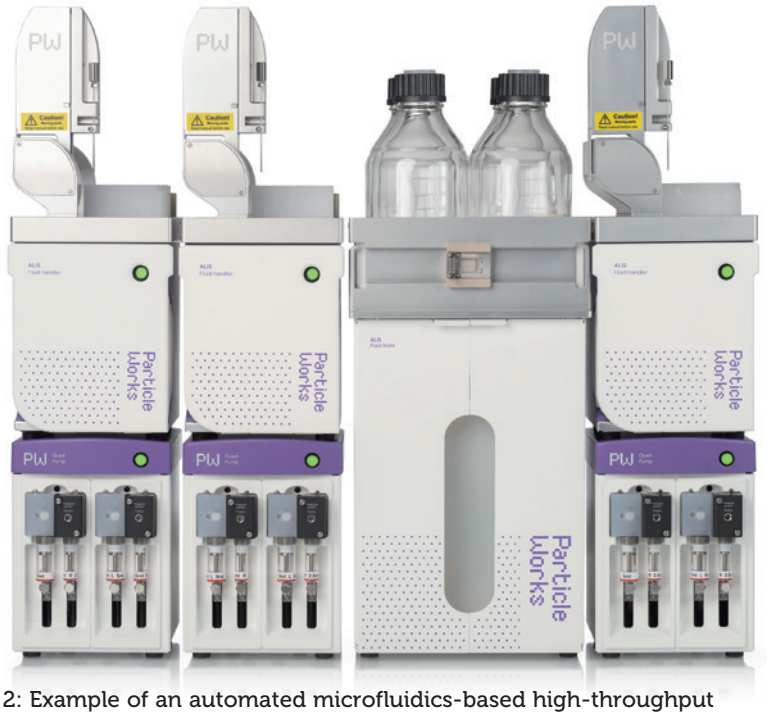

Figure 2: Example of an automated microfluidics-based high-throughput formulation screening platform.

complete system recovery and highly reproducible LNP formulation following the addition of unstable samples (Figure 3). They therefore offer high levels of flexibility with minimal manual intervention by the user. A single system can be used for both process optimisation and continuous production, simplifying the transfer from early-stage particle screening to scaled-up production and empowering researchers to accelerate nanomedicine discovery.

> "LNP medicines have the potential to transform patient care in the near future."

A HOPEFUL FUTURE FOR NANOTHERAPIES

LNP medicines have the potential to transform patient care in the near future, and encapsulating biological material is now an integral part of the early-stage development of genetic medicines and vaccines. To bring an LNP-based therapeutic to the global market, researchers need to consider how quickly they can go from screening nanoformulations to the clinic and, ultimately, on to commercialisation. To synthesise LNPs reliably and reproducibly with optimal performance characteristics, there is a clear requirement for automated high-throughput platforms that offer excellent synthesis control. Novel microfluidics systems meet this need, combining controlled synthesis of LNP formulations with automated high-throughput formulation screening to minimise costs and shorten development timelines. These innovative platforms are already helping to accelerate the development of therapeutics that rely on lipid-based drug delivery mechanisms, advancing the creation of genetic medicines and cancer treatments to help address some of the world's urgent healthcare challenges.

ABOUT THE COMPANY

Particle Works combines a strong heritage in engineering with nanoparticle knowledge, microfluidic expertise and in-house microfluidic chip fabrication. The company designs and manufactures state-of-the-art particle engineering platforms, paving the way to particle perfection. Its technology is used in a wide range of applications, including the production of nanoparticle-based vaccines, medicines and therapeutics. Recently spun out of the Dolomite Microfluidics brand, Particle Works was born as a dedicated and focused drug delivery brand. The company has been at the forefront of this rapidly

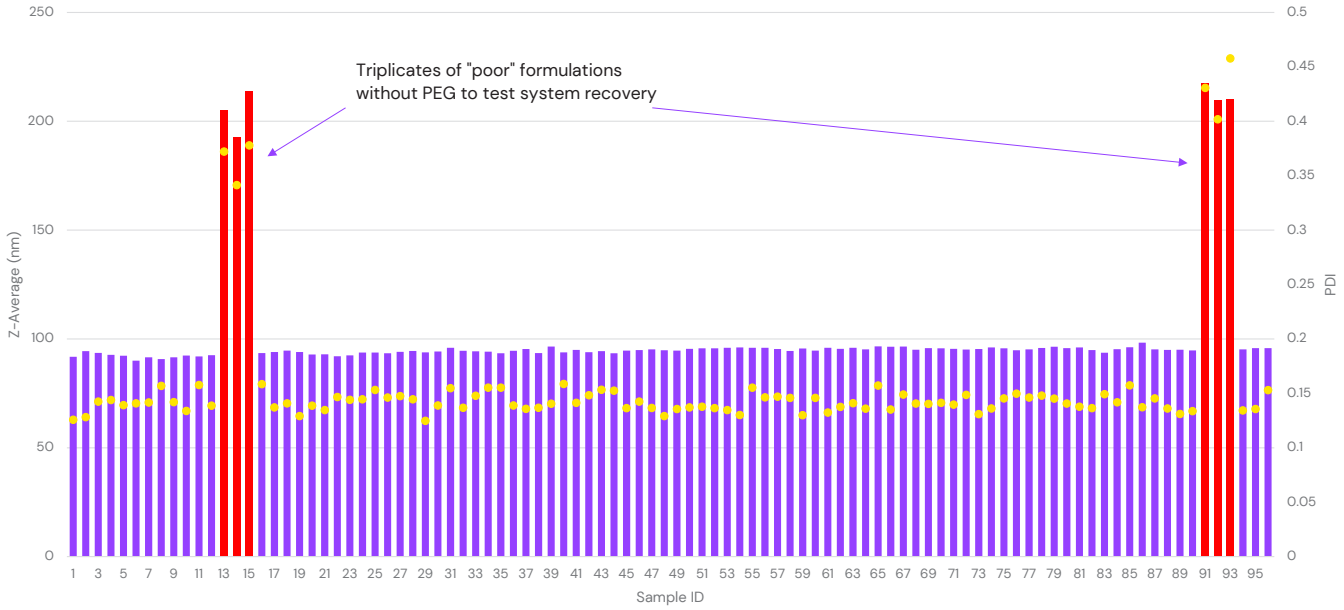

Figure 3: System recovery of the ALiS automated microfluidic platform was tested by the addition of six spike sample formulations with no PEGylated lipid. There was a null effect on the reproducibility of subsequent samples, demonstrating the efficacy of the automated wash between experiments.

changing science, listening and adapting as its customers' needs have evolved. Particle Works' platforms enable scientists to formulate particles faster, ensuring they are ready for their next breakthrough and the scale-up of discoveries.

Particle Works is part of Blacktrace Holdings Limited – a world leader in Productizing Science™ – and is based in Royston (near Cambridge) UK. The company has offices in the US, Japan and Vietnam, and worldwide distributors offering technical assistance and support.

REFERENCES

1. *Cui L et al, "Development of a high-throughput platform for screening lipid nanoparticles for mRNA delivery". Nanoscale, 2022, Vol 14, pp 1480–1491.*
2. *Beltrán-Gracia E et al, "Nanomedicine review: Clinical developments in liposomal applications". Cancer Nano, 2019, Vol 10, p 11.*
3. *Zaslavsky J, Bannigan P, Allen C, "Re-envisioning the design of nanomedicines: Harnessing automation and artificial intelligence". Expert Opin Drug Deliv, 2023, Vol 20(2), pp 241–257.*
4. *Tenchov R et al, "Lipid Nanoparticles from Liposomes to mRNA Vaccine Delivery, a Landscape of Research Diversity and Advancement". ACS Nano, 2021, Vol 15, pp 16982–17015.*
5. *Hassett KJ et al, "Optimization of Lipid Nanoparticles for Intramuscular Administration of mRNA Vaccines". Mol Ther Nucleic Acids, 2019, Vol 15, pp 1–11.*
6. *Danaei M et al, "Impact of Particle Size and Polydispersity Index on the Clinical Applications of Lipidic Nanocarrier Systems". Pharmaceutics, 2018, Vol 10(2), p 57.*
7. *Hald Albertsen C et al, "The role of lipid components in lipid nanoparticles for vaccines and gene therapy". Adv Drug Deliv Rev, 2022, Vol 188, p 114416.*
8. *Zhao X et al, "Microfluidic Generation of Nanomaterials for Biomedical Applications". Small, 2020, Vol 16(9), p 1901943.*

ABOUT THE AUTHOR

Ben Knappett, PhD, received his MChem degree from Durham University (UK), and completed a PhD in nanoparticle synthesis and characterisation at the University of Cambridge (UK). He started working for Particle Works in 2016, developing nanoparticle and microparticle products using microfluidics technology. Dr Knappett moved into his current position as Head of Science and Applications in 2021, leading a team of scientists who specify and test new Particle Works systems, create content for applications and support customers with installation and training. Dr Knappett and his lab team also run proof-of-principle studies to demonstrate the capabilities of Particle Works' systems with customer materials.

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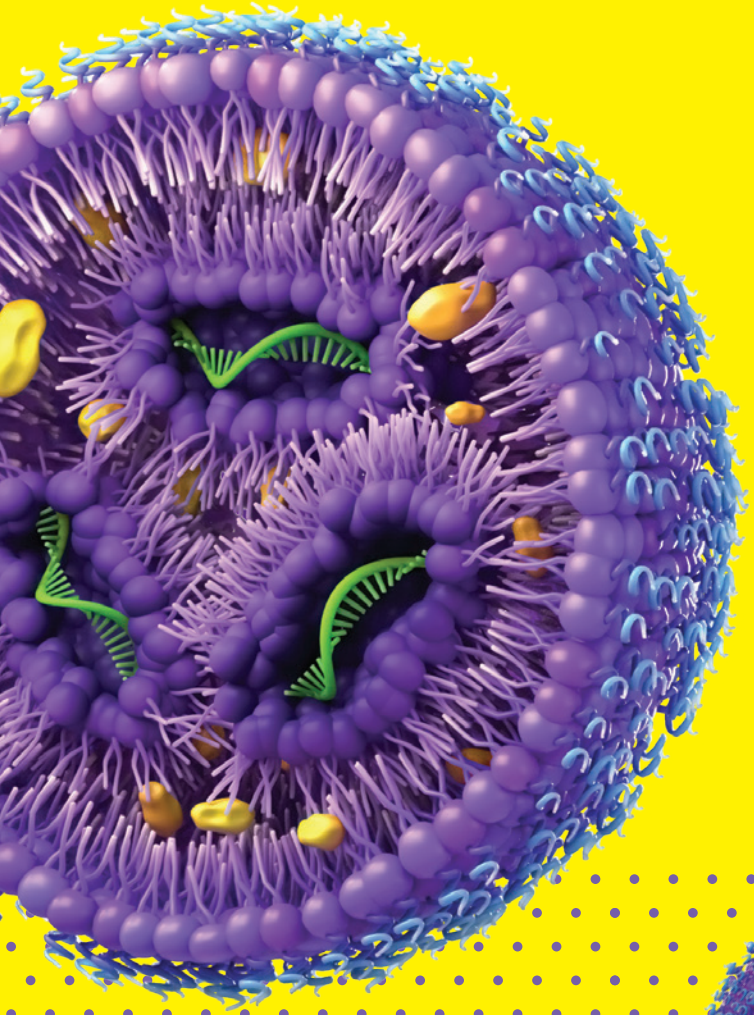

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SUCCESSFUL INDUSTRIALISATION REQUIRES SOLID FOUNDATIONS

Here, Jennifer Riter, Senior Director, Business and Technical Operations, and Victoria Morgan, Director, Biologics Marketing, both at West Pharmaceutical Services, discuss the importance of choosing the right containment system at the start for successful industrialisation of an injectable drug product.

In recent years, pharmaceutical manufacturers and regulatory authorities have increased their scrutiny of the supply chain's ability to deliver even greater levels of quality – all in the expectation of delivering improved patient safety and compliance. This expectation is against a backdrop of more complex and costly drugs being developed, as well as an ongoing drive for greater efficiency in manufacturing.

To address these complex issues, containment system and drug delivery system manufacturers have developed components that not only ensure quality, safety and efficacy throughout a drug product's lifecycle, they also mitigate the risks and maximise the efficiencies of fill-finish processing.

In this article, we will discuss how choosing the appropriate quality of containment systems from the outset is critical to the successful industrialisation of an injectable drug product. We will review some of the challenges associated with injectables – most notably extractables, leachables and particulates – which are some of the primary reasons for a product recall.

We will then showcase how West Pharmaceutical Services has addressed these challenges with an integrated offer of NovaPure® components, coupled with analytical testing services. Together, this portfolio delivers pharmaceutical manufacturers the reassurance they need that extractables and leachables, particle analysis, container closure integrity, product performance and processing considerations have been addressed appropriately and that they have the data they need for a successful approval.

We will then review the implications of the European Medical Device Regulation (MDR), specifically regulation 2023/607, for pharmaceutical manufacturers, particularly in terms of the data needed. Finally, we will present a case study on how West's integrated technical document package can assist in reducing the time, cost and risks associated with MDR submissions.

ENORMOUS COMPLEXITY

It might be argued that the simplistic terminology within drug development is failing us. Talk of pathways, roadmaps and journeys accurately conveys the process, but these succinct terms are truly insufficient to express the enormous complexity involved in guiding a molecule from research and development through to regulatory approval and manufacture at scale.

> "Formulation, materials, machinery, technology and human factors must all be synchronised in harmony."

Jennifer Riter
Senior Director, Business and Technical Operations
E: jennifer.riter@westpharma.com

Victoria Morgan
Director, Biologics Marketing
E: victoria.morgan@westpharma.com

West Pharmaceutical Services
530 Herman O West Drive
Exton
PA 19341
United States

www.westpharma.com

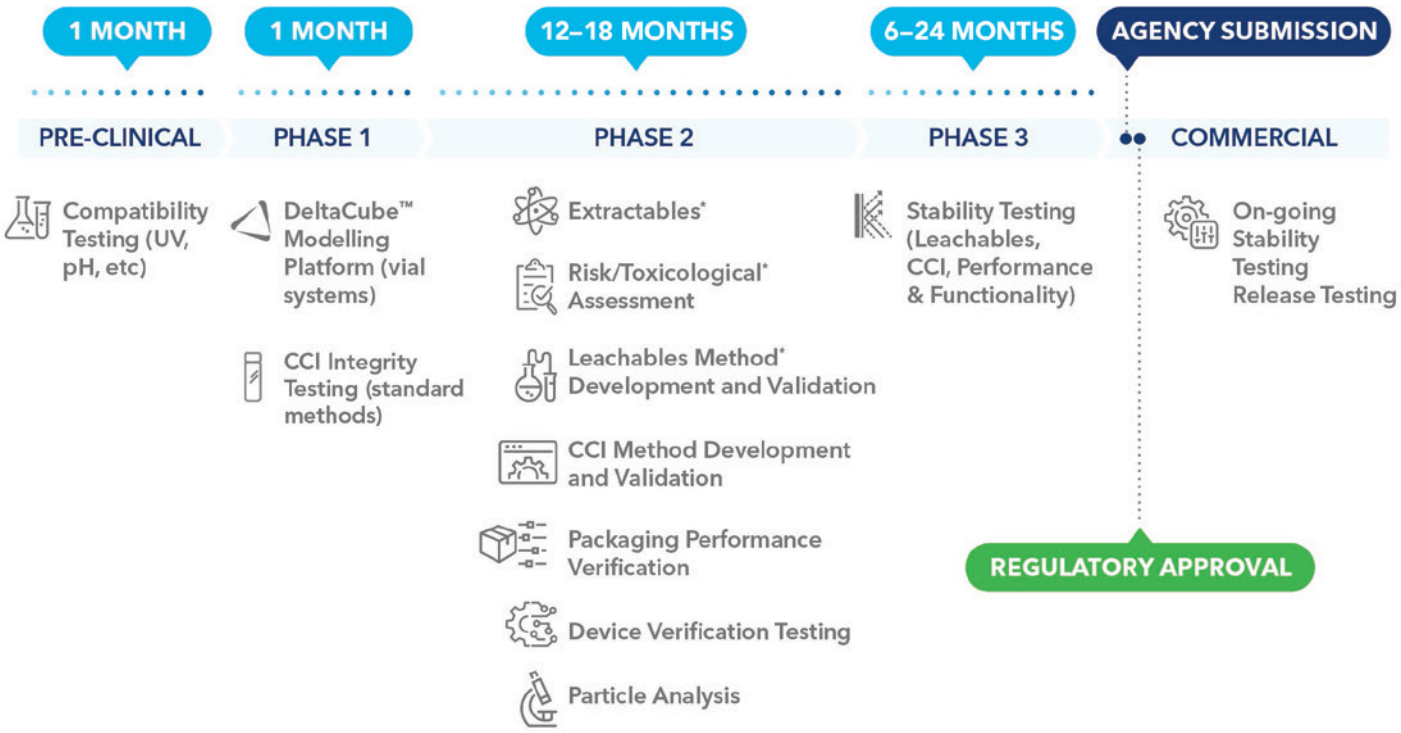

Figure 1: Planning drug product packaging testing with drug product development can help reduce delays to your regulatory submission. *Extractables, risk/toxicological assessment and leachables are performed sequentially and therefore require the greatest amount of time of 18 months.

The ultimate goal of industrialising a product requires pharmaceutical manufacturers to orchestrate a range of variables into a delicately co-ordinated and closely managed process to realise the associated economic benefits. Formulation, materials, machinery, technology and human factors must all be synchronised in harmony. At the same time, however, each one of these elements has the potential to undermine the entire process and, therefore, to compromise the output.

For a drug product, any such compromise can present a danger to patient safety and introduce the possibility of a recall, which carries both financial and reputational consequences. When the process is industrialised at scale, such risks are amplified. The same multiplier effect that allows productivity gains to be unlocked can mean the damage is exponentially more significant.

MITIGATING THE RISK

Managing the quality of every element in an industrialised process is therefore crucial to mitigate the risk of any problems occurring, either at the point of development, during production or later in the product's lifecycle. Integrated combination products, such as prefilled syringes (PFSs), already address many risk-mitigation factors by delivering an accurately measured ready-to-administer dose of a drug product in single-use form. This reduces the risk of human error associated with administration, while also avoiding the possibility of coring of the elastomer stopper when it is punctured by a needle, which can inherently cause the patient to not get the appropriate dose of their drug product.

> "The plunger plays a critical role because it is in direct contact with the drug formulation."

Maintaining drug integrity within a PFS places particular emphasis on the primary packaging components that will remain in contact with the drug product following fill-finish and on into transportation and storage. Among these, the plunger plays a critical role because it is in direct contact with the drug formulation, meaning there is an imperative for this part of the containment system to demonstrate qualities that will avoid, or significantly limit, the potential for formulation integrity to be compromised. Any impairment in terms of purity, sterility or stability can, in turn, impair the product's efficacy and safety.

West's NovaPure plungers have been designed and manufactured using quality by design (QbD) principles to address these risks and meet the exacting requirements for performance and patient safety. In the case of NovaPure plungers, these proven benefits are realised through a combination of the enhanced design, the elastomeric formulation and the FluroTec™ barrier film.

The specification of a component such as a NovaPure plunger ensures a key building block is in place for industrialised production, but components cannot be considered in isolation when establishing a quality-based, large-scale manufacturing process. This also relies heavily on testing and evaluation to verify the sustained compatibility between the drug product and containment system from both a physical and chemical perspective. Among the main objectives is providing evidence that extractables, leachables and particulates are kept to an absolute minimum while container closure integrity (CCI) is securely maintained (Figure 1).

ANALYTICAL TESTING

At West, analytical testing services are delivered as part of a wider quality-focused approach, complementing components such as NovaPure plungers to ensure

compatibility between the packaging system and drug product is evaluated at an early stage and will minimise any risk or concerns when production is scaled. Working closely with pharmaceutical manufacturers, West provides an initial assessment of the risk of extractables and leachables – and develops a comprehensive series of analytical tests that will elicit data on any continued risk presented by these elements over the shelf life of a drug product.

Parallel analysis will be carried out to test the CCI of the PFS system. This is achieved using a variety of deterministic methods, including high-voltage leak detection, to provide pharmaceutical partners with a comprehensive, data-backed understanding of the materials and components that comprise the system, as well as the mechanics of how they function together to protect against issues such as leakage and ingress over time. Separate analytical testing will also be carried out to assess the risk of contamination from particulates, evaluating the potential for packaging components, manufacturing processes or extrinsic environmental elements to result in the presence of visible or sub-visible particles within the contained dose.

The provision of such extensive analytical testing methods, dovetailed with the supply of quality products, affords pharmaceutical manufacturers a holistic view of the entire drug containment system. It provides a platform to evidence data and compliance with regulatory standards, such as MDR, at all levels – from components through to the finished product. Crucially, there is also consideration from the very beginning of how those standards can be met in the context of scalability and the continued need to apply rigorous quality control during volume production.

COMPLIANCE

The process of demonstrating compliance has, of course, become more involved for pharmaceutical companies in recent years as regulators tighten controls around product quality and patient safety. In the EU, for example, the EU MDR (2017/745/EU), first published on April 5, 2017, introduced several changes designed to safeguard device quality. This was implemented in the wake of the PIP breast implant scandal, where the fraudulent manufacture of implants using unapproved silicone gel left many patients at increased risk of rupture.[1] Compared with the EU directive it replaced (93/42/EEC), the MDR places far greater emphasis on patient safety and sets out a far more comprehensive set of enforced requirements for pharmaceutical manufacturers to follow.

Implementation of the regulation was already subject to a phased transition before being disrupted by the pandemic in 2020 and finally coming into force on May 26, 2021. Subsequent challenges, however, including the increased demands placed on marketing authorisation holders and the need for capacity-limited notified bodies to fulfil a more involved role in device approvals, led the European Commission to propose extensions to the transition periods stipulated in Article 120 of the regulation. For Class IIB non-implantable devices, Class IIA and Class I devices, which encompasses PFSs, this now means the deadline for transition has been extended to December 2028.

This "relief" has been balanced with stringent conditional requirements to actively implement compliance measures. This includes the need for a device manufacturer to establish a quality management system (QMS) by May 26, 2024 and for that QMS to be audited and approved as compliant by the relevant notified body no later than September 2024. Conformity assessments carried out by notified bodies incorporate a detailed review of technical documentation compiled to evidence a device's general safety and performance requirements (GSPRs) as well as interrogation of the clinical evaluation report, which contains testing data on the clinical use of a device. As part of a wider information-gathering process, these documents are reviewed in light of Annex I of the revised MDR to inform the risk-based assessment conducted by the notified body.

ASSESSING CONFORMITY

Because of its rigorous nature, the process of assessing conformity is not necessarily a straightforward one, and this can result in delays to the marketing authorisation holder receiving a notified body opinion. Problems can relate to incomplete submissions, where there is insufficient information provided to demonstrate compliance with MDR, or simply the fact that the supplied technical documentation is poorly structured, which complicates the notified body's already arduous task of appraising all the supplied materials.

"Because of its rigorous nature, the process of assessing conformity is not necessarily a straightforward one."

At West, a commitment to QbD principles means it can support pharmaceutical partners at each stage along this updated and extended approval pathway. The company's knowledge of the process and the nature of the information and data required puts it in an ideal position to compile and co-ordinate all necessary technical information relating to its components for efficient filing in a timely manner. In streamlining this process, West's overarching objective is to empower pharmaceutical manufacturers in their engagement with a notified body and, ultimately, the EMA, ensuring all documentation and certification is available to demonstrate compliance with the updated regulatory framework.

TECHNICAL DOCUMENT PACKAGE

This service offering has been encapsulated as the Technical Document Package (TDP). Borne out of first-hand experience, it comes after West conducted a successful pilot programme to support a pharmaceutical customer with an MDR filing for a new drug product delivered via a PFS system incorporating a NovaPure plunger. The aim of the programme was to address the recognised challenges associated with the filing process, including the need for cross-organisational stakeholder management and the co-ordination of consistent responses.

Working closely together with the customer, West adopted a strategic approach to gathering, assimilating and presenting the required data at a level of detail and in a format that would satisfy scrutiny by the notified body. By focusing efforts on the "right-first-time" delivery of high-quality and highly relevant information connected to the specific GSPRs, West was able to minimise requests for supplemental information, avoid complex multi-document iterations and truncate the entire certification process.

In turn, this positive outcome has given West a robust platform from which to develop a transferrable template for supporting a successful filing in a time-efficient manner

in the form of the TDP. This offering currently supports applications for 1–3 mL NovaPure plungers by incorporating more than 30 documents, including component technical summaries, quality statements and compliance bulletins, into a single, integrated information package. Future developments will see the offering extended further into West's range of leading primary packaging components.

The changes to MDR, while specific to the EU, offer an indication of the continual drive among regulatory bodies to address novel technologies and ensure patient safety. For pharmaceutical manufacturers navigating the many challenges involved in bringing an integral drug product to market at industrial scale, the TDP provides a reassuringly efficient platform to demonstrate compliance. Furthermore, it provides an effective reminder that, whether in the provision of individual components or supporting analytical services or entire drug delivery systems, a strategy rooted in quality can allow risks to be controlled and production to flourish.

At West, this quality philosophy has been deep rooted for decades, a point perhaps best illustrated by the fact that all the top 10 best-selling global injectable drugs in 2022 used West packaging.

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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 10,000 team members across 50 sites worldwide, West helps support customers by delivering approximately 47 billion components and devices each year.

ABOUT THE AUTHORS

Jennifer Riter is Senior Director, Business and Technical Operations for the Services and Solutions organisation at West Pharmaceutical Services. Her experience spans 27 years of West's components, containment and delivery systems, with hands-on experience of providing technical support and analytical solutions to the company's multinational customers. Ms Riter has also spoken at several symposiums on analytical testing of parenteral packaging components, devices and combination products. She has a BSc degree in Biology/Chemistry from Lock Haven University (PA, US) and an MBA in Pharmaceutical Business from the University of the Sciences in Philadelphia (PA, US).

Victoria Morgan is Director, Biologics Marketing, with global marketing responsibility for the biologics business, which strives to develop high-quality products and services to help pharma companies serve unmet patient needs with biologic molecules. She brings a wealth of knowledge about scaling drug development through to and beyond commercialisation, predominantly in injectable drug delivery products, including vials and combination products. She has a BSc degree from the University of Wales (UK) and an MBA from INSEAD Business School in Paris (France).

REFERENCES

1. *"PIP breast implants". Web Page, UK NHS. (www.nhs.uk/conditions/pip-implants, Accessed, Jun 1, 2023)*

MITIGATE RISK WITH THE RIGHT PARTNER AND THE RIGHT PRODUCT

NovaPure® plungers from the industry leading partner to help de-risk the transition to combination products

NovaPure® plungers and the West Analytical & Regulatory Services teams help support filings to EU MDR 2017/745 because:

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- You get a robust, proven process for supporting GSPRs from an experienced supplier

Minimizing risk during development and filing processes can lead to an expedited path to market.

TO LEARN MORE ABOUT MDR 2017/745, WATCH OUR RECENT WEBINAR AT **WESTPHARMA.COM/NEWS-AND-EVENTS/WEBINAR** OR VISIT **WESTPHARMA.COM/DERISK.**

GLOBAL EXPANSION AND A DEEP COMMITMENT TO PRECISION DRUG DELIVERY DEVICE COMPONENT MANUFACTURE

– AN INTERVIEW WITH JULIEN MARTINS & DAVID PHILBRICK OF PARAGON MEDICAL

In this exclusive interview, Julien Martins and David Philbrick talk with ONdrugDelivery about Paragon Medical's recent expansion. They discuss a wide range of topics, including the services Paragon Medical can provide the drug delivery industry, its wider business operations, the company's expanded facilities in the US and Europe, and its new Advanced Surgical Innovation Center.

Julien Martins is Director of Business Development – Europe at Paragon Medical. With an Engineering degree he joined Paragon Medical 15 years ago, and has held various roles in engineering, operations and business development. He is responsible for developing the drug delivery market in Europe for Paragon Medical.

David Philbrick is the New Business Development Manager for Paragon Medical. Mr Philbrick supports various Paragon Medical engineering and commercial team members with new product development tasks. He also interfaces directly with customer teams through early-stage project development. His experience of over 43 years in engineering management and product development, including disposable medical devices, has led to numerous manufacturing innovations that have earned him many shared patents with Paragon Medical's customers and partners.

Q To begin with, please could you provide an overview of Paragon Medical as an organisation? What does the company offer and who are its partners and clients both more broadly and specifically in the drug delivery device space?

JM In summary, Paragon Medical is a contract manufacturing organisation (CMO) that works in the life science industry, including drug delivery systems (Figure 1). We are a large, international company with a global footprint, with facilities in the US, Europe and in China; we have 15 campuses in total. All these facilities come from organic and inorganic growth. We have over a century of combined expertise in high-precision manufacturing, advanced engineering, and design support. With facilities across the globe, we can lean on the varying expertise within each of our locations in order to provide an integrated, end-to-end supply chain solution for our customers.

> "With drug delivery being one of our most important segments, we want to be able to support our customers locally the same way we have been doing in the US."

We have experience working with Top Five OEM companies in each of the medical industries we operate in.

DP Our work with drug delivery is interesting. We find that a lot of design and engineering for drug delivery devices, such as wearables and autoinjectors, is based in Europe, but the production manufacturing is more global. For example, for a North American launch, we would have to have direct manufacturing in the US to support American production. On the other hand, if the products are going to launch in Europe or Asia, then we would want to target launching production there.

JM It's worth mentioning that part of the reason for this is to align with local regulatory standards, as well as proximity to our customers and the target market. So far, Paragon Medical has been pretty successful in the drug delivery devices market, but we did that primarily from the US. However, we've seen that, as a global contract manufacturer, best results require proximity to our customers, which is what we do in the other segments we operate in. So, with drug delivery being one of our most important segments, we want to be able to support our customers locally the same way we have been doing in the US.

We have also seen that having local operations is key to sustainability objectives. This is becoming an increasingly important consideration for our customers in the industry, so we need to be able to provide local manufacturing – Europe for Europe, US for US, Asia for Asia. This is the direction we're steering in today.

Q What sectors does Paragon Medical operate in outside drug delivery?

JM Paragon Medical initially started in the orthopaedic industry, where we make implantable

Figure 1: Paragon Medical serves a broad market crossing multiple anatomical, technological, and procedural segments.

components, instruments and cases & trays. Since the acquisition by MW Industries, we are also active in other life science segments, such as robotics, cardiovascular and dental. We now have a much larger portfolio of capabilities and services that we can offer across the different life sciences.

DP Not only are we a contract manufacturer ourselves, but we also support some of the very largest contract manufacturers in the world in the drug delivery space – we work for everyone. We own the relationships. Even when we're supporting a project with a CMO and we're not the engineering firm, we end up owning a relationship with the original equipment manufacturer as an outcome of the relationship.

Q Can you give us some examples of the metal components Paragon Medical provides to the drug delivery industry?

JM We produce a wide variety of components. For example, our facility in Southington (CT, US) has extensive expertise in making springs and stamped metal parts and components of different complexities and sizes. However, we also make other types of components, such as hypodermic needles, and we have support for connected devices that require electronic components. We have also a facility in Bridgeport (CT, US) that works together with Southington when there is a need to do assemblies in a cleanroom environment, or when there is a need to do some moulding.

> "Not only are we a contract manufacturer ourselves, but we also support some of the very largest contract manufacturers in the world in the drug delivery space – we work for everyone."

We have the advantage that we have a lot of sister facilities that have different capabilities. For example, Southington is the expert for wire forming, coiling and metal stamping, but we also have facilities that are expert in moulding or expert in computerised numerical control (CNC) machining, such as turning, grinding or milling. This means that we can use the expertise of the sister facilities as necessary to support the needs of each individual project.

Q How would you say Paragon Medical is uniquely positioned to serve the requirements of its drug delivery device partners and clients?

JM In large part it's thanks to our global footprint and the different life science segments that we cover. We have a large portfolio of capability and knowledge at Paragon Medical that we can use to support drug delivery system developers. We have CNC knowledge, we have moulding knowledge, we are experts in coiling and stamping, and we can use all that knowledge and expertise together under the same roof, which is the key to how we can help our customers to reduce their supply chains. If you have a project that needs spring stamping parts, CNC parts, moulding parts and hypodermic needles, rather than going to four or five different suppliers, you can get everything from Paragon Medical. We deal with the supply chain because our sister facilities can simplify everything. The advantage is that Paragon Medical only operates in the medical and life science industries, so we are ISO 13485 certified for every single facility and we have embedded knowledge about the requirements and the regulations required for life science manufacturing.

DP One of the key drivers that really brought a lot of our success is the engineering support that we provide up front. For a lot of products or projects we get involved in, we're usually providing engineering support for one to two years before we even get to run our first validation. We provide all of our customers with this direct engineering support up front as the project progresses through design verification. Our customers ask us, "Are you in it for the long haul? Are you going to stick with us and help us until we get this thing commercialised?" We provide that service directly for our entire global network of companies in addition to regulatory support.

JM We also understand our customers' need to have trusted partners that can help them in developing their projects from ideation. We understand that there is a lot of validation to run, there is a lot of complexity, there will be a lot of changes, etc. To support this, we can take the expertise that we've gained across the different industries we work with and draw out the best of each and use those lessons to inform current projects.

For example, we have an innovation centre in Warsaw (IN, US), initially focused on the orthopaedic market – that has been so successful and so in demand by our customers

Figure 2: In Spring 2023, Paragon Medical opened its 65,000 square foot manufacturing facility in Siechnice, Poland, as part of its ongoing effort to serve the European and worldwide markets.

that we have decided to open a second innovation centre focused on drug delivery. We started to build that last year. Now, it is up and running and is a perfect example of the benefits Paragon Medical can offer – helping our customers to develop processes, undertake rapid prototyping and launch their products to market as soon as possible, all while reducing costs. We want to accompany our customers from the very beginning up to the launch of the product.

Q Could you give us a rundown of Paragon Medical's expansion programme and the benefits it offers to drug delivery device partners and customers?

DP We expanded our Southington facility about three years ago. We had to expand because we outgrew our footprint and there wasn't enough physical space to build out a building big enough to double or triple the size, which was the scale we required. Instead, we ended up selling our building and moved about a mile away into an approximately 24,000 square metre building, which essentially tripled our capacity for manufacturing there. Our company invested in additional machinery as well as moving our existing equipment. It's been pretty exciting to see a modern, state-of-the-art facility doing the precision work that we do.

A lot of the drug delivery projects that we work on also demanded that we increase capacity on very popular products. Before we moved to our new building, we had around 10% of our overall equipment dedicated to specific drug delivery products; now, we have approximately 45% of our equipment dedicated to this market segment, even in an environment where we added 30 or 40 more machines. They're all dedicated machines for certain product lines. It's pretty exciting to see.

As this market continues to grow, even our competitors have to invest because the global manufacturing footprint doesn't have enough equipment to meet the expanding demand in the drug delivery segment. We all have to continue to invest to meet the current growth.

JM Alongside moving into the new building in Southington, another thing that we've done is to put presence in Europe for our European customers. The first thing that we've done is to add the team that we have here in Lausanne, Switzerland, which is a sales and business development team. That's where I'm based, with a focus on developing our drug delivery market in Europe.

We've also decided to expand our existing facility in Poland, which was primarily working on orthopaedics. We've bought the building next to our current building, which is 6,000 square meters, and we completed the building work earlier this year – we had a grand opening back in March of this year (Figure 2). This new facility is going to be dedicated to serve the surgical and drug delivery sectors as needed. We've already received the first coiling and wire forming machines to make springs for drug delivery devices.

"The goal is to continue expanding our capacity for drug delivery projects; we're listening to our customers in Europe to see what they're looking for, what they're missing and how we can help them from there."

The goal is to continue expanding our capacity for drug delivery projects; we're listening to our customers in Europe to see what they're looking for, what they're missing and how we can help them from there. Our plan is to use the same strategy that we have in the orthopaedic industry, which is having a local presence in the EU to help our customers in Europe, having a local point of contact and a local contract manufacturer that is just a one- or two-hour flight from them. It makes everything easier – they can visit our facilities, while our team is working in the same time zone, and a number of other benefits.

DP It's going to be very easy to grow our European footprint in Poland. Poland is just getting started, but the equipment is all state-of-the-art manufacturing equipment that's a good fit for the work that we're going to do

"The ASIC's objective is to help customers develop new products, provide rapid prototyping and facilitate a smooth transition from ideation to prototype and from prototype to launch."

there. So, it's going to be very easy for our European sales team to provide manufacturing services on products that are going to launch in Europe. We're going to have the capability to launch in the Americas or in Europe, depending on what market the customer wants to serve first.

Q Can you tell us about recent advances with Paragon Medical's Advanced Surgical Innovation Center (ASIC)?

JM The ASIC is a new product development centre we've built at our Southington facility. We have something similar for our advanced orthopaedic industry operation in Indiana, so we decided to do the same for our advanced surgical and drug delivery business because we see the intrinsic value to our customers (Figure 3). The ASIC's objective is to help customers develop new products, provide rapid prototyping and faciliate a smooth transition from ideation to prototype and from prototype to launch. We're going to have state-of-the-art machines there. It's going to be completely independent from the production facility, but will have the same type of machines; this is where the advantage comes from because we build the prototype on the ASIC machines and then, when the process is created, easily transfer it to the machines and processes in the main production facility during scale-up.

Figure 3: With an expected grand opening in late Summer 2023, Paragon Medical's ASIC offers 4,000 square feet of space dedicated to new enterprise innovation, rapid prototyping, process and equipment development, production and assembly.

The ASIC has some of our most knowledgeable people in terms of skills – the best designers, engineers, etc. These are the people who are going to create the concept, create the process and then deliver to the other facilities. So, this centre is going to support not only Southington but also our facilities in Bridgeport, Mansfield and Poland with the same service.

DP The equipment that we've brought in so far includes wire machines, CNC hole popper machining centres and three axis machining centres, and we've got another dozen pieces of equipment that we'll be moving in over the next two weeks. The ASIC is going to be a completely built-out facility. Their entire project board is already completely full for the next month and a half on projects with all types of customers. It's really fascinating to watch how quickly this is happening.

Customers come to us when they know they want to get high-precision products that can be commercialised through the DFM process. We help them make the process acceptable for the required robustness of their device. We're the ones that can run the design verification tests or pre-production to verify the process is accurate. You can't get that in a prototype house. You'd have to go to the source where you're going to do your manufacturing.

Thanks to our experience, we know what it takes to commercialise a product – it requires investment, and a CMO has to be prepared for that growth cycle. One of the strengths of our entire organisation is our SIOP process where we manage a customer's forecast. We even help the customer build

a forecast even if they don't have one themselves, which helps us predict when we have to buy equipment and machinery at any given point in the growth cycle, which is a really important factor that you have to pay attention to.

Q Can you elaborate on who at Paragon Medical is driving your European expansion in the drug delivery market?

JM Regarding our European operations, I've worked for Paragon Medical for 15 years in different roles. I started as an engineer, then I moved to project management and business development. I'm located in Lausanne, together with Kees De Louw, who is our sales director for Europe. He has extensive experience in the orthopaedic and life science industry. Both of us report to Greg Hall, who is our Director for International Business Development, meaning that he's responsible for all business development activities outside the US. Greg has worked for Paragon Medical for over 30 years; he was one of the first employees and, again, has extensive experience in the industry. That's our core business development team.

Then we have Dave, who probably has the most experience in the drug delivery space. We all have experience in the life science industry, but when it comes to drug delivery specifically, Dave is probably the one who has the most, coming from a very technical background. Dave brings several things to the table; he knows a lot of people in the drug delivery industry, he has a thorough understanding of industry trends and his technical background is very helpful. His support is key when it comes to helping customers with developing new products. That's the core team. There are a lot of others who are helping to develop our European presence, but if I had to name the core team for the development of drug delivery outside United States, it's the four of us.

> "It's pretty amazing to watch our global reach continue to grow. We've got a very, very strong team."

DP Naturally, our customers are global in nature too. So, if they choose to source in America, that's fine, but we're getting very established and able to support projects anywhere in the world. We also export a great deal of products to Asia. It's a very exciting time for us; we have both Japanese and Canadian customers coming on board. In Latin America we already have a strong relationship with several facilities in Mexico, the Baja Peninsula and the Caribbean. It's pretty amazing to watch our global reach continue to grow. We've got a very, very strong team.

Q Any final thoughts you'd like to share with our readers?

JM I'd like to elaborate a little on our expansion at our Poland facility. A major driver behind the increase in capacity is to provide local manufacturing for our European customers, but that doesn't mean that the Poland facility is solely going to serve the European market. It can also serve the US and global market and act as an extension of Paragon Medical's Southington operations. Say, for example, we have customer with an insulin product that's growing with a big ramp-up. With the Poland expansion, we're going to be in a position to provide that customer with a mitigation plan by dual sourcing the product using both the Poland and Southington facilities.

DP We currently have 15 business locations, including some that have multiple buildings on a campus, and we're continuing to expand and invest. This month we are celebrating the grand opening of a new building on our Pierceton (IN, US) campus where we have an additive manufacturing facility offering 34,000 square feet of manufacturing and operational space dedicated to 3D printing.

I'd also like to mention our Automation Equipment Services (AES) briefly – one of our locations has a team with dedicated engineers building automation equipment for our plants, including sub-assembly of components for drug delivery. A lot of our AES work is around drug delivery assemblies and specialised packaging to help our customers be efficient with how they want to introduce our products to their automation lines. It gives us the ability to support all of our locations with an automation team that builds specialised equipment.

At Paragon Medical, we are in a good spot right now and we have great customers. Our customers don't just come to us once; they come to us over and over again for their next development project. It's a constant cycle of new things. It's a very exciting time for us.

ABOUT THE COMPANY

In today's challenging healthcare environment, the right contract manufacturer can help simplify the complexities of supply chain management and expedite product commercialisation. Paragon Medical is a trusted partner for the drug delivery industry, serving as an extension of development teams by delivering world class operational excellence and sales, inventory and operations planning with over a century of combined expertise in high-precision manufacturing, advanced engineering and design support.

Paragon Medical is a strategic partner for medical device manufacturing, offering an end-to-end supply chain solution from initial concept and product development to verification and validation testing, final production, assembly and ongoing strategic demand planning, with differentiated and personalised solutions designed to exceed expectations every time.

Paragon Medical

Julien Martins
Director of Business Development – Europe
T: +41 78 314 13 14
E: julien.martins@paragonmedical.com

Paragon Medical
Av de l'Avant-Poste 4
CH-1005 Lausanne
Switzerland

David Philbrick
New Business Development Manager
T: +1 860 621 7358
E: dave.philbrick@paragonmedical.com

Paragon Medical
75 Aircraft Rd
Southington
CT 06489
United States

www.paragonmedical.com

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STREAMLINING DRUG DELIVERY DEVICE DEVELOPMENT FOR INDUSTRIALISATION SUCCESS

In this article, Hans Arts, Chief Sales Officer, Jan-Willem Den Hollander and Ron Cisliek, Director of Business Development – USA, all of IGS GeboJagema, discuss the value of bringing an industrialisation partner on board early in product development and how working with a single manufacturing specialist can preserve insights and learnings throughout the product development lifecycle and deliver additional value and quality.

FROM PROTOTYPE TO PRODUCTION

The core challenge in the production of drug delivery devices is how to combine exceptional quality with cost-effective manufacturing. It is critical to guarantee the flawless operation of every single device, potentially up into billions of units, while also optimising costs to ensure affordability.

Industrialisation is key in taking on this challenge. This article discusses how each of the four development phases of a product mould can be optimised for industrialisation, advocating for a forward-thinking approach, where proactive and strategic investments into design and engineering lay the foundation for successful industrialisation. As part of this approach, considerations for industrialisation should be taken into account from the earliest stages of product development.

THE FOUR PHASES OF AN INJECTION MOULD FOR DRUG DELIVERY DEVICE

Before exploring how to optimise product development for industrialisation, it is important to understand the phases of product development. While different approaches are possible, the development of most devices consists of four main phases.

Phase 1: Proto-tools

The goal in the first phase of development is to create a concept that proves the device's functional viability. To keep costs low, the product design is iterated upon with 3D printed device samples and single-use silicone moulds. At the conclusion of this phase, a proto-tool is produced. This is typically a "soft mould" made from aluminium or non-hardened steel (Figure 1).

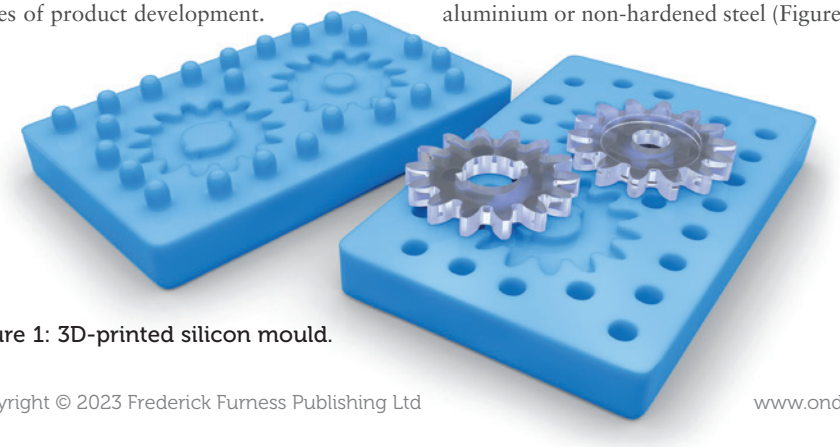


Figure 1: 3D-printed silicon mould.

Hans Arts
Chief Sales Officer
T: +31 40 2647500
E: hans.arts@igsgebojagema.nl

Jan-Willem Den Hollander
Business Development Manager
T: +31 40 2647500
E: jw.denhollander@igsgebojagema.nl

Ron Cisliek
Director of Business Development – USA
T: +1 727 215 4143
E: ron.cisliek@igsgebojagema.nl

IGS GeboJagema
Esp 430
5633 AJ Eindhoven
The Netherlands

www.igsgebojagema.nl

Phase 2: Submission Tool

To ready the device for submission to the US FDA or EMA, "pre-production" moulds are required. These moulds are made out of hardened steel and tend to have between one and four cavities. These submission tools are suitable to produce the first few millions of devices, after which they often serve as back-ups.

Phase 3: Launch

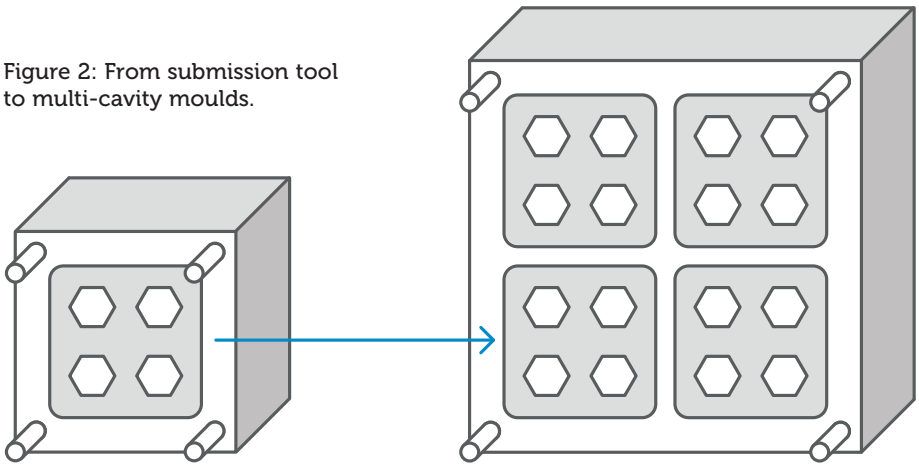
After approval, the new drug product is put on the market. After the long approval and testing process, there is a high degree of confidence that the product will be successful. For this reason, original equipment manufacturers (OEMs) tend to opt for multi-cavity moulds in order to have sufficient production capacity (Figure 2).

Phase 4: Ramp Up

Once the drug has proved successful, it is time to scale up the production capacity. At this point, OEMs can either decide to use repeat moulds or moulds with a higher number of cavities.

"IGS GeboJagema has shown many times how cost-effective industrialisation starts in the earliest stages of product development."

Figure 2: From submission tool to multi-cavity moulds.



OPTIMISING EACH DEVELOPMENT PHASE FOR INDUSTRIALISATION

At first glance, it might seem like industrialisation becomes most relevant only after the drug product is approved, in Phases 3 and 4. However, as a high-precision mould maker, IGS GeboJagema has shown many times how cost-effective industrialisation starts in the earliest stages of product development.

During Phase 1, the primary objective is to design a product that is both easy to use for patients and effective in delivering the drug. IGS GeboJagema supports its customers in this phase by sharing its design for manufacturing (DFM) expertise. This is where the IGS team optimises the product design for efficient production further down the line. For example, seemingly small product design changes can reduce cycle time or significantly lower mould costs – adjustments in this early stage can have a significant impact on a project's bottom line (Figure 3).

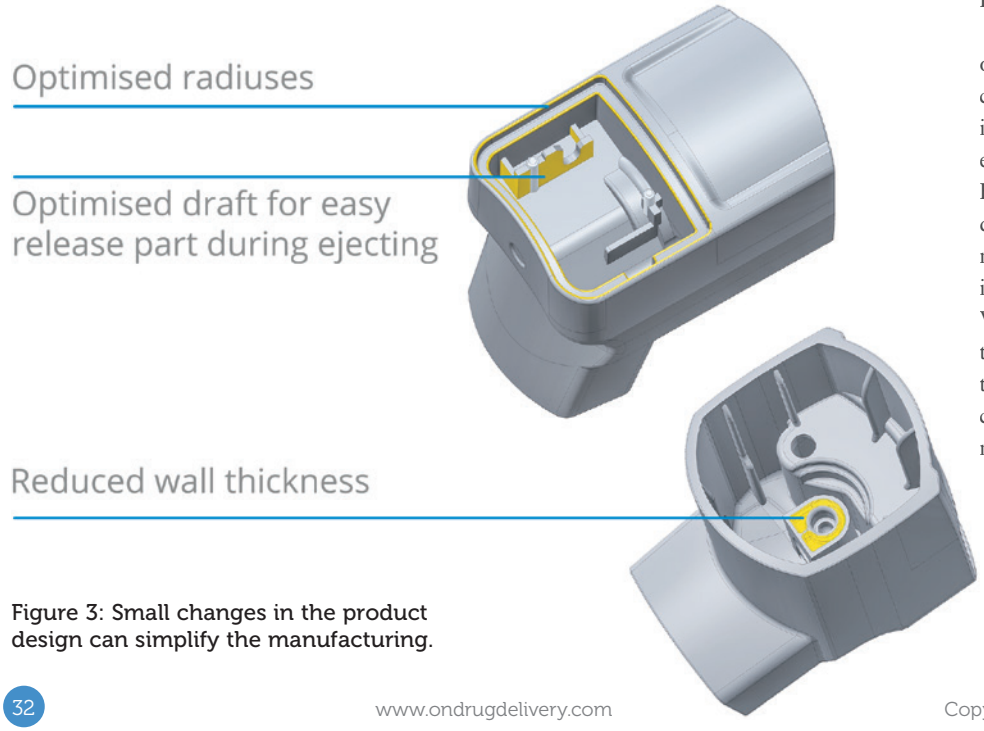


Figure 3: Small changes in the product design can simplify the manufacturing.

"While there will be some learnings from the development of the single-cavity mould, the larger cavity stack will introduce new challenges. In practice, this means that much of the work is done twice."

As a rule of thumb, it is advisable to involve industrialisation-focused partners for 75% of the first product design. Furthermore, IGS GeboJagema works together with automation companies to ensure that the product design is suitable for efficient assembly, which is known as "design for assembly". More information about DFM can be found in IGS GeboJagema's white paper on the topic.

As described, in Phase 2 OEMs usually opt for a mould with no more than four cavities. The advantage of this is that it saves costs and time at this relatively early stage of the product development. However, the drawback is that it requires designing and programming a new, multi-cavity mould when the product is ready to be launched in Phase 3. While there will be some learnings from the development of the single-cavity mould, the larger cavity stack will introduce new challenges. In practice, this means that much of the work is done twice.

For this reason, when OEMs are confident that their drug will be approved, IGS GeboJagema often suggests a different approach. Instead of engineering a single- or low cavity mould, the company designs and programs a 16- or 32-cavity tool

(Figure 4). This involves almost the same amount of work as developing a single-cavity mould. After completing that mould engineering concept, it is fairly straightforward to take the cavity stack and manufacture a smaller injection mould for it. This approach is an investment that is highly beneficial during the launch of the product in Phase 3, allowing the client to take advantage of 100% of the learnings of the pre-production tool. Moreover, the submission cavity stacks can be reused in the multi-cavity mould or be kept as a spare.

After the drug has successfully entered the market, production needs to be scaled up in Phase 4. Production capacity can be expanded through repeat moulds, but for most products it is more cost-effective to employ moulds with 48, 64, 96 or 128 cavities. These high cavity moulds significantly improve output and reduce the total cost of ownership. The challenge, however, is to deliver the same product quality in these high-cavity moulds. With more products produced per shot, it is difficult to achieve the same process capability index (Cpk) value. To maintain the same high quality, extreme precision is required in every aspect of the mould, including cavity-to-cavity variation, gate design, gate accuracy and even the cooling channels.

IGS GeboJagema's approach to tackling this challenge starts with an industry 4.0 production environment. Eliminating human hands from the mould production process allows the company to achieve an extremely low cavity-to-cavity variation. IGS GeboJagema also uses gates that are identical down to a single submicron. This ensures that the resistance is the same across the entire tool during the moulding process and improves the filling balance of the tool.

Additionally, during mould validation, the company uses an advanced version of PRO-OP – software initially developed by Cambridge University (UK) and optimised by IGS GeboJagema for high-precision mould qualification. The program is used to identify the injection-moulding process settings that produce the highest possible quality. In short, through extreme precision mould making, the most cost-effective production can be combined with high quality.

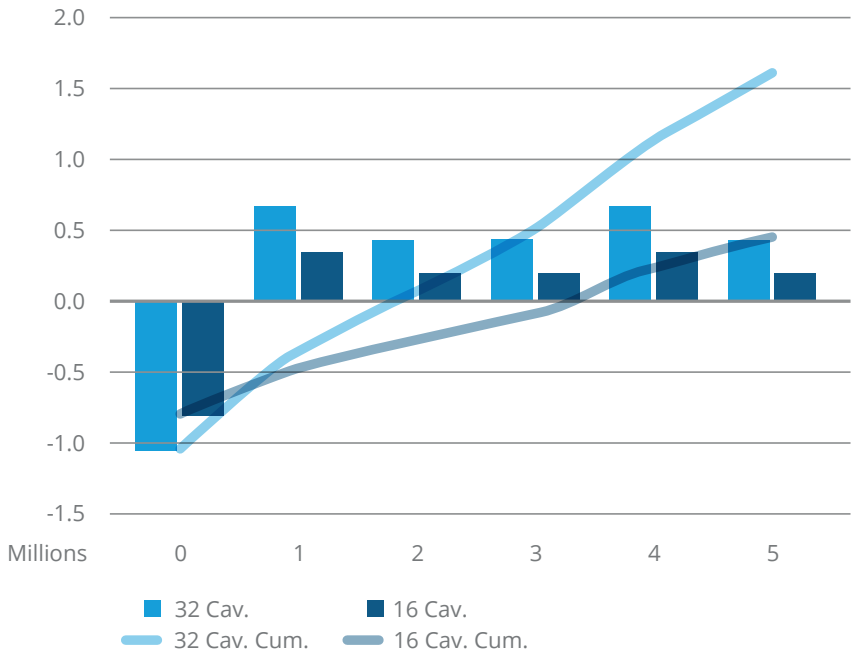


Figure 4: Choosing a 16- or 32-cavity mould.

AVOID BREAKING UP THE LEARNING CURVE

There is one more best practice for OEMs that want to optimise their product for industrialisation. It is common for OEMs to collaborate with different partners during development. For example, during Phases 1 and 2 they may work with a shop for rapid prototyping soft tools, while working with a larger, industrialisation-focused mould manufacturer in the later phases. The downside of this approach is that it breaks up the learning curve. Different teams work on the development of the mould, which inevitably means that learnings and insights are lost when they are passed from one organisation to another. To avoid this, IGS GeboJagema works together with rapid prototyping and automation equipment partners, allowing OEMs to work with a single partner from Phase 1 to 4. As the same team can now collect all the learning and experience, this enables a more streamlined engineering process, resulting in a superior product that reaches the market more rapidly.

> "IGS GeboJagema works together with rapid prototyping and automation equipment partners, allowing OEMs to work with a single partner from Phase 1 to 4."

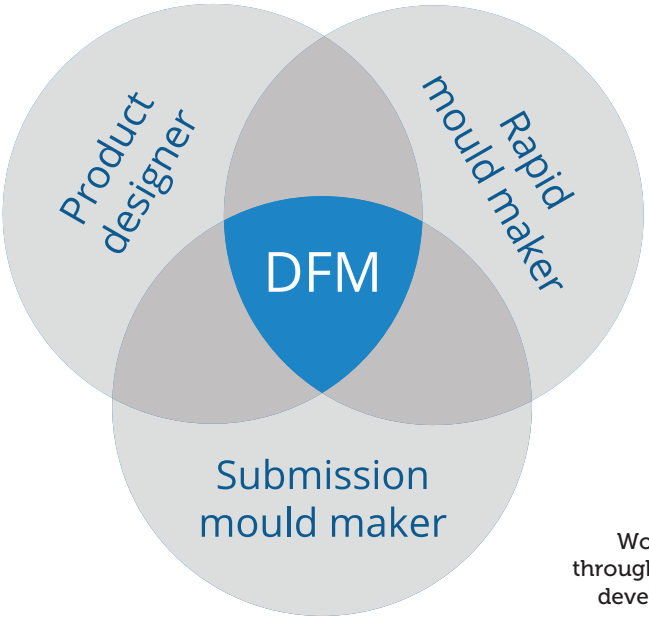


Figure 5: Working together throughout the entire development cycle.

A FORWARD-THINKING APPROACH

In this article, IGS GeboJagema has argued for a forward-thinking approach. By collaborating with an experienced partner throughout the entire development cycle, OEMs can ensure that critical learnings and insights are retained and applied effectively. This approach maximises the potential for cost-effective production and reduces the total cost of ownership and lead times. It simplifies the development process while maintaining the highest standards of quality and performance for the end-user (Figure 5).

ABOUT THE COMPANY

IGS GeboJagema is a high-precision mould maker that designs, manufactures, validates and maintains moulds for products where extreme precision is vital, from glasses and contact lenses to asthma inhalers, insulin pens and blood diagnostic devices. The company specialises in collaborating with medical OEMs early in the product lifecycle, allowing its exceptional engineering team to develop innovative moulding solutions.

ABOUT THE AUTHORS

Hans Arts is the Chief Sales Officer at IGS GeboJagema. With extensive industry experience, his focus is on understanding the evolving needs of the market and ensuring that the company continues to deliver innovative, best-in-class solutions to meet those needs.

Jan-Willem Den Hollander serves as the Business Development Manager at IGS GeboJagema. His position involves building strategic partnerships and identifying new business opportunities. His collaborative approach has been crucial in fostering early engagement with medical OEMs, setting the stage for the development of pioneering moulding solutions.

Ron Cisliek is Director of Business Development – USA at IGS GeboJagema, responsible for the commercial development and sustaining relationships with healthcare customers. He has a keen focus on attention to detail using his profound understanding of what it takes to design, construct, and operate effective part solutions for global healthcare OEMs and CMOs. He has more than 35 years of international experience in the injection-molding industry and has worked for IGS GeboJagema since 2022.

IGS GeboJagema

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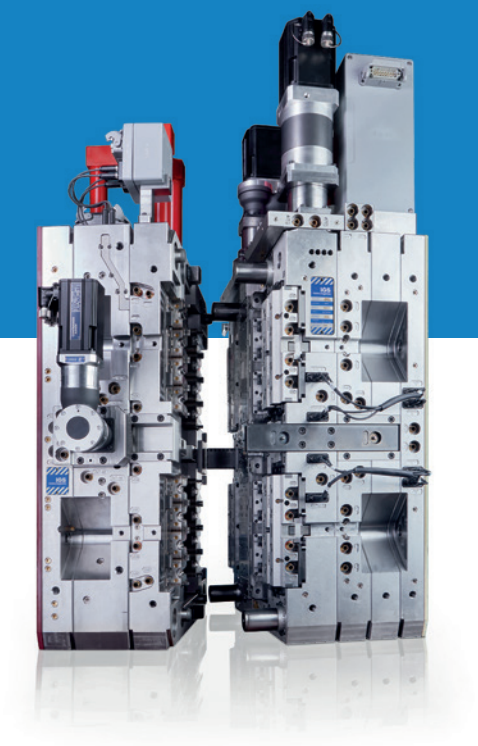

IGS GeboJagema combines unrivalled technical expertise, smart innovations and rigorous testing with the latest technology and the highest specifications of materials. By working closely with medical OEMs early in the product life cycle, we allow our clients to take full advantage of our engineering power. It's how we deliver unique, innovative solutions that give our clients an edge over their competitors.

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HOW A FLEXIBLE APPROACH TO AUTOINJECTOR ASSEMBLY EQUIPMENT CAN DELIVER A COMPETITIVE ADVANTAGE

In this article, Mads Keinicke Hansen, System Owner Process at Stevanato Group, presents an overview of the company's Standard Autoinjector Assembly Machine platform, providing an in-depth examination of its key features and advantages to illustrate how it is transforming autoinjector assembly processes in the pharmaceutical industry.

Whether managing a chronic condition or dealing urgently with a life-threatening allergic reaction, patients today play an increasingly central role in their own medical care through the self-administration of essential drugs.

By enabling patients to take drug delivery into their own hands, technologies such as autoinjectors are key facilitators of this shift, and innovation in this space means the range of devices on the market continues to expand in terms of specification and application. From a manufacturing perspective, capitalising on new autoinjector opportunities relies not only on high-precision engineering capabilities but also having the agility and flexibility to answer increasingly diverse production requirements at speed and minimal cost. To address these needs, Stevanato Group introduced the revolutionary Standard Autoinjector Assembly Machine platform that, through its cutting-edge design, delivers a more versatile and scalable approach to efficient autoinjector assembly.

FLEXIBILITY AND SCALABILITY TO SUPPORT AUTOINJECTOR FORMATS

Flexibility and scalability are at the heart of the Standard Autoinjector Assembly Machine platform, which has been designed for seamless future expansion of production capacity through the addition of new equipment to existing process modules. This feature provides users with the freedom to scale up their operations as needed without completely overhauling the assembly line at each iteration. The platform also provides support for collaborative in/outfeed robots that can assist manual operators by automating the transportation of products from pallets to in/outfeed modules.

> "The Standard Autoinjector Assembly Machine platform is designed to support a wide range of popular autoinjector device platforms, including 1.0 and 2.25 mL."

The Standard Autoinjector Assembly Machine platform is designed to support a wide range of popular autoinjector device platforms, including 1.0 and 2.25 mL. By using a single, versatile assembly line for multiple autoinjector device platforms, manufacturers can streamline their production process, reduce costs and optimise efficiency.

STANDARDISATION FOR FASTER AND MORE EFFECTIVE PROJECT EXECUTION

By embracing standardisation, the Standard Autoinjector Assembly Machine platform offers faster and more effective project execution compared with fully customised assembly lines. Standardisation eliminates

Mads Keinicke Hansen
System Owner Process
E: mads.hansen@stevanatogroup.com

Stevanato Group
Via Molinella 17
35017 Piombino Dese
Padova
Italy

www.stevanatogroup.com

the need for lengthy customisation processes, significantly reducing lead times. It also means that maintenance and repairs can be carried out more efficiently, helping to limit any downtime. In the fast-paced pharmaceutical industry, this ability to accelerate time to market and turnaround time can help manufacturers gain a competitive edge.

The ability to switch between different products swiftly is crucial for pharmaceutical manufacturers seeking to maintain production efficiency. The Standard Autoinjector Assembly Machine platform excels in this aspect, boasting a remarkably fast changeover time. With minimal downtime, manufacturers can transition between autoinjector device platforms seamlessly, maximising productivity and minimising production delays.

To optimise efficiency and use of resources, the Standard Autoinjector Assembly Machine platform enables multiple devices to be assembled on the same line. This innovative feature eliminates the need for separate assembly lines for each autoinjector format, reducing costs and floor space requirements. As a result, manufacturers can achieve higher productivity and economies of scale, ultimately enhancing their competitiveness in the market.

CUSTOMISABLE FEATURES TO ANSWER DIFFERENT MARKET NEEDS

Stevanato Group's Standard Autoinjector Assembly Machine platform offers the option of in-line laser engraving. This capability allows manufacturers to add essential product identification information, such as branding or batch numbers, directly onto the autoinjector. The in-line laser engraving feature ensures accurate and permanent marking, enabling serialisation on the assembly line and enhancing product traceability and compliance. This is achieved by engraving a 2D barcode onto the device, which enables full product provenance throughout the lifetime of the product. This can be integrated with the company's data-collection platform for a data-driven, real-time monitoring approach to component traceability. Additionally, an independent laser engraving module can be installed in extension of the labelling module, which provides the ability to engrave customer-specific data onto various label heights, with the machine able to inspect and reject any labels that do not meet quality standards. It also ensures that the labels are accurately applied to the autoinjectors.

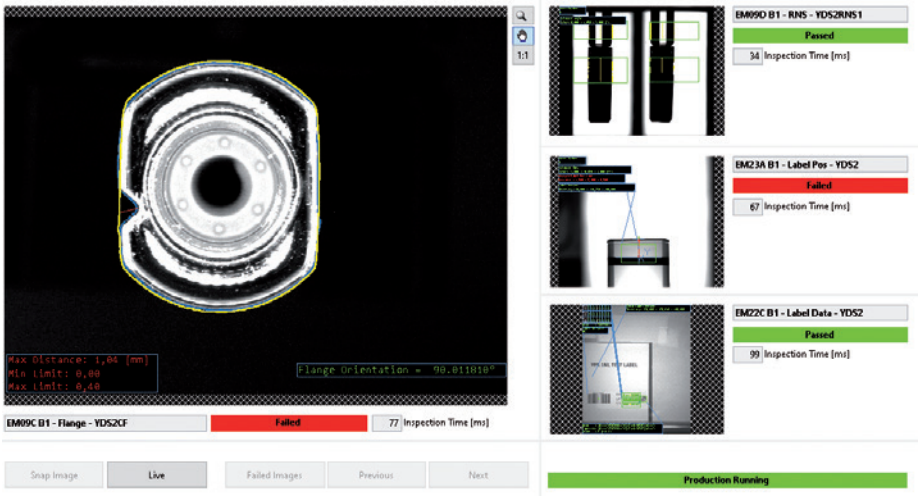

Figure 1: Inspection module with a variety of device verification checks.

In addition to its flexibility in handling multiple autoinjector formats, the Standard Autoinjector Assembly Machine platform is also designed to accommodate various tray sizes for infeed and outfeed. This means the machine can handle different tray sizes without requiring extensive modifications or changes to its set-up, making it easier for operators to switch between different products, saving effort and time.

LINE CLEARANCE AND LINE OPERATOR FRIENDLINESS FOCUS

The machine's design prioritises operator safety and ease of use, which aims to promote a more comfortable and productive work environment. All assembly machines designed on the BasiQX XTV – Stevanato Group's flexible platform based on a vertical transport system – have a clear distinction between the production side and the operator side to make line clearance easier. Additionally, the standard autoinjector platform can perform an automatic format-set check on critical points, which enhances productivity and machine safety by preventing collisions and avoiding a potential production stop.

DEDICATED SYRINGE INFEED AND VERIFICATION MODULE

By having a dedicated syringe infeed module on the assembly platform, it is possible to verify the syringe on a plethora of parameters and provide local rejection of faulty components before they are assembled with other autoinjector components. In production, the platform supports the use of multiple syringe formats, with the sole requirement of changing format parts on the infeed module and not on the main assembly line.

The inspections include checks for plunger position, rigid needle shield (RNS) presence, position and alignment, colour code, radio frequency identification, major chips and cracks, and debris on the plunger, as well as cut-flange orientation. The figure above shows an inspection module where the device is inspected for multiple precision factors between assembly sequences. If the configuration does not meet the requirements, the device will be rejected at the end of the assembly sequence (Figure 1).

PREPARED FOR DIGITALISATION

The platform is designed with high-frequency force and path monitoring systems for assembly verification and data

"By having a dedicated syringe infeed module on the assembly platform, it is possible to verify the syringe on a plethora of parameters and provide local rejection of faulty components before they are assembled with other autoinjector components."

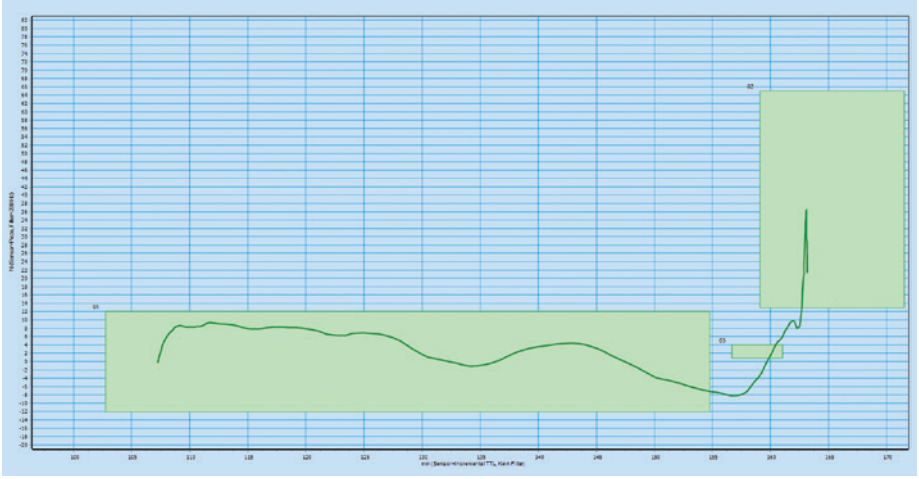

Figure 2: High-frequency force distance verification system where the configuration meets the requirements.

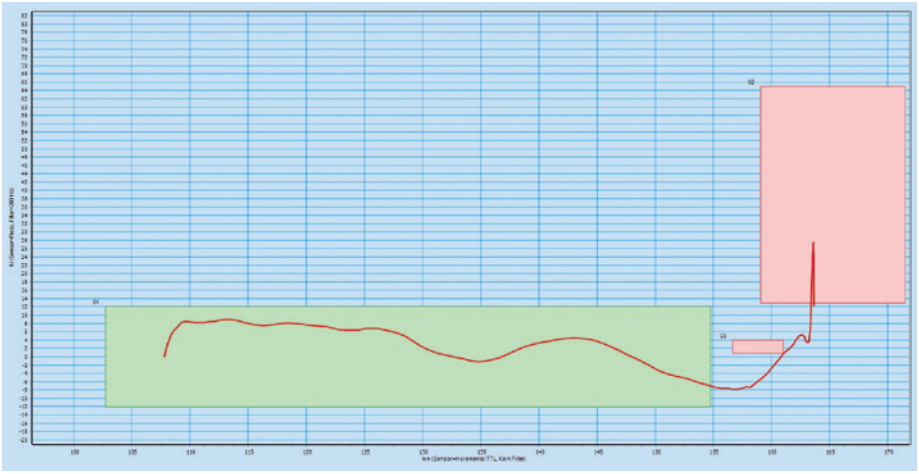

Figure 3: High-frequency force distance verification system where the configuration does not meet the requirements.

collection, providing product provenance throughout the lifetime of the autoinjector. The data picked up by these systems can be used for diagnostics through the data-collection smart production interfaces. The green boxes in the high-frequency force distance verification graphs above illustrate the minimum and maximum force for four different checks during the assembly process (Figures 2 & 3).

Graphs, such as the one above, are available for every module of the assembly process that includes a high-frequency force and path monitoring system, and the data is prepared for Stevanato Group's data-collection platform for a data-driven approach and real-time monitoring.

CONCLUSION

In summary, the Standard Autoinjector Assembly Machine platform is a flexible, scalable and efficient solution for the assembly of a wide range of autoinjector formats. Its standardised design enables faster and more effective project execution compared with fully customised assembly lines, while its modular construction allows for seamless upgrades and modifications to accommodate changing production requirements.

The machine's fast changeover time, ability to run multiple devices on the same assembly line and optional in-line laser engraving and labelling features further enhance its versatility and suitability for a range of production scenarios. Its focus on operator safety and convenience, as well as its dedicated syringe infeed and verification module, ensure that the finished product is of the highest quality and reliability.

Overall, the Standard Autoinjector Assembly Machine platform is an excellent choice for pharmaceutical manufacturers looking to improve the efficiency, flexibility and quality of their autoinjector assembly process. By investing in this advanced technology, manufacturers can stay ahead of the competition and meet the demands of an ever-changing industry.

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. Stevanato Group delivers an integrated, end-to-end portfolio of products, processes and services that address customer needs across the entire drug lifecycle 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.

ABOUT THE AUTHOR

Mads Keinicke Hansen is System Owner Process at Stevanato Group. He is a skilled mechanical engineer with more than 25 years of experience within Stevanato Group. He has a deep understanding of drug delivery devices and every day he contributes valuable input to a plethora of projects to ensure the best possible solutions are delivered to customers.

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RFID-BASED UNIT-LEVEL TRACEABILITY: COULD IT BE THE KEY TO OPERATIONAL EXCELLENCE FOR FILL-FINISH LINES?

In this article, Yacine Haddadi, Senior Global Marketing Manager, and Herve Soukiassian, Associate Director – R&D Product Development, both at BD, look at how the company's track & trace model can help manufacturers improve their fill-finish operations.

Fill-finish operations are the final, critical phase before distribution of a pharmaceutical product. With its radio frequency identification (RFID)-based unit-level tracking solution for prefilled syringes (PFSs), Becton Dickinson is positioned to help pharma manufacturers address key risks and costly bottlenecks related to the fill-finish process. The BD solution for track & trace[1] (T&T) has now been derisked through evaluation by a major pharmaceutical company, confirming several use cases, and is now ready to start large-scale implementation. Key use cases include the mitigation of mix-up risks, automation of the reconciliation process and elimination of over-segregation.

TIMES ARE CHANGING – FILL-FINISH OPERATIONS NEED TO KEEP UP

With the industry adopting a platform approach to drug products, and with more products and dosages being filled in the same type of container on the same fill-finish lines,[2] the risk of product mix-up is evolving, challenging current processes and manufacturing flows. The colour-coding systems typically used to prevent drug product mix-ups are reaching their functional limits. Today, pharma manufacturers need to adapt their approach to risk mitigation in the face of new demands on modern fill-finish operations.

> "Pharma manufacturers need to adapt their approach to risk mitigation in the face of new demands on modern fill-finish operations."

Regulatory guidelines, existing and emerging, are also pressuring pharma to adapt fill-finish operations. To address quality problems that impact product availability and lead to product shortages,[3] regulators are calling for more visibility of the manufacturing process,[4] while also applying new scrutiny to how manufacturers ensure the integrity, quality and identity of their drugs. Examples include US FDA regulation 21 CFR610.14 that states that the manufacturer must ensure product identity after labelling, and USP Chapter <1790> concerning visual inspection, which requires manufacturers to determine the normal reject rate and investigate root causes.[5] Furthermore, with the new Quality Management Maturity approach, the FDA is looking to reward companies that go beyond the cGMPs and implement solutions to ensure that "every dose is safe and effective and free of contamination and defects".

Yacine Haddadi
Senior Global Marketing Manager
E: yacine.haddadi@bd.com

Hervé Soukiassian
Associate Director –
R&D Product Development
E: herve.soukiassian@bd.com

BD
11, rue Aristide Bergès
ZI des Iles – BP4
38801 Le Pont de Claix
Cedex
France

www.bd.com

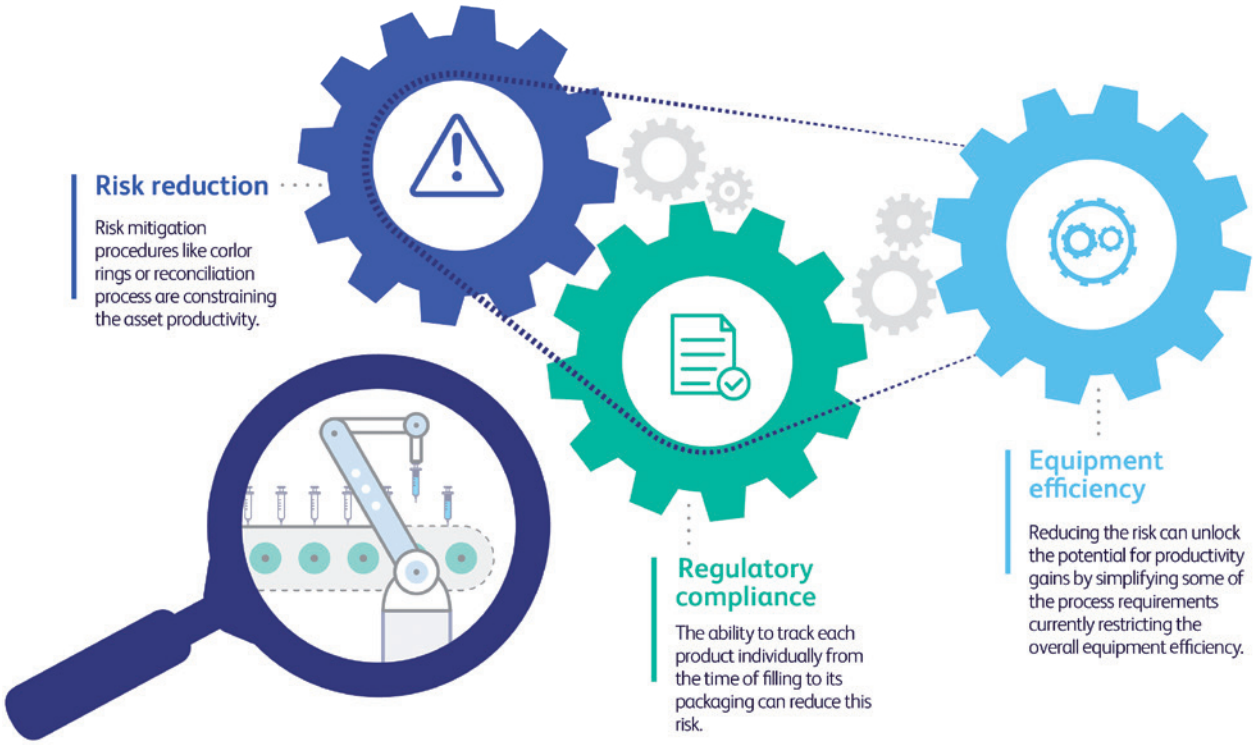

Figure 1: Interconnection between risk reduction, compliance and equipment efficiency.

The EU EMA is following the same rationale and has also initiated a working document to explore how digital innovations in manufacturing can help address the vulnerabilities of the medicine supply chain.[6] Looking beyond the manufacturing site, end-to-end dose-level drug traceability is emerging as a likely next step of drug serialisation requirements.

Manufacturers also face pressure to align their fill-finish operations with new digital technologies as they seek to increase quality, lower the cost of goods manufactured (COGM), reduce batch release lead times and improve overall equipment effectiveness.[7] According to a January 2023 report by McKinsey,[8] the manufacture of sterile pharmaceutical products is set to grow by more than 50% over the next seven years, driven by new demand for recombinant antibodies and small molecules initiated during the covid-19 pandemic. Because of the time required to create and qualify new sterile manufacturing lines, pharma manufacturers must be prepared to tap the unused capacity of their existing lines. Attaining the additional yields necessary to respond to market growth will require new levels of operational excellence on fill-finish lines – something that is challenging without process automation and digitalisation.

SLAY SILOS WITH A HOLISTIC APPROACH

Risk mitigation, regulatory alignment and yield optimisation are often addressed as separate challenges, each requiring a different set of solutions. However, when examined carefully, these challenges are actually interconnected in fill-finish operations. Asset productivity is constrained by regulatory requirements that intend to mitigate the risk of releasing flawed products to market (Figure 1). The ability to track each product individually from the time of filling to its packaging can reduce this risk. And, by extension, doing so can unlock the potential for productivity gains by simplifying some of the process requirements currently restricting overall equipment efficiency (OEE).

These challenges could all be addressed by the unit-level identification of primary containers. This would help pharma manufacturers build trust in their fill-finish processes by providing unit-by-unit accountability for each and every container on the filling line – and beyond. It would support manufacturers in addressing the barriers to quality and productivity inherent in many fill-finish processes, but which have not, until recently, been the focus of industry scrutiny. Unit-level traceability and precision would be at the heart of more efficient deviation management and reduce batch-level complexities to the clarity of a "batch of one" – replacing guesswork, inaccuracies and labour-intensive investigations with precise, continually updated unit-level data that can help resolve issues before they become subjects for investigation. This would also position manufacturers to build end-to-end value chains leveraging unit-level traceability from glass manufacturing to point-of-care (POC) applications.

"The BD solution for T&T consists of RFID-tagged syringes, tagged nests and cloud-based sharing of aggregation data."

SOLUTION OVERVIEW

The BD solution for T&T (Figure 2) consists of RFID-tagged syringes (the tag is located in the rigid needle shield (RNS)), tagged nests and cloud-based sharing of aggregation data (syringe-nest aggregation). Each RFID tag will incorporate a container unique identifier (CUID). At the end of the BD manufacturing process, tagged syringes are sealed into tubs and their CUIDs are read and aggregated to the nest ID. This aggregation of parent and child units is intended to facilitate reading at filling line entry where only the nest ID will be read, with the child CUIDs easily retrieved from the aggregation data. Each CUID will be associated with the current drug filling batch and drug code. The unit's status at each step (i.e. successfully filled, rejected, etc) can be recorded and,

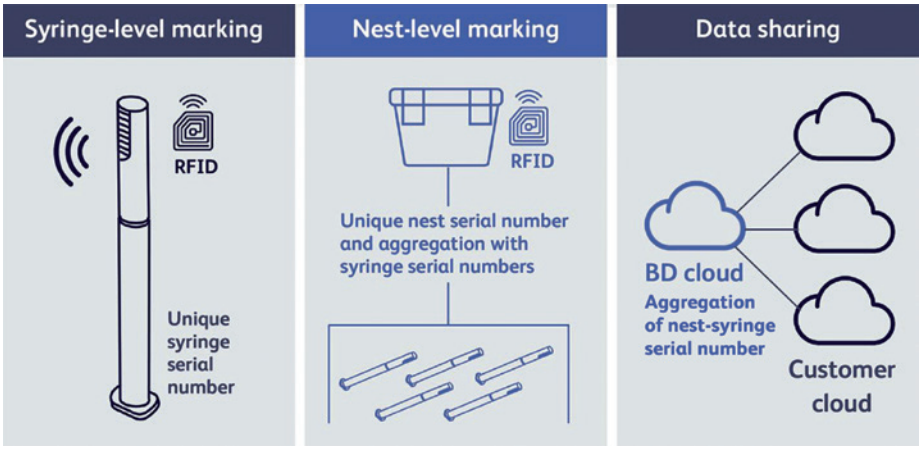

Figure 2: The BD solution for T&T.

at each subsequent process step, the syringe ID can be cross-checked to prevent mix-ups, even after assembly.

Additional manufacturing events can be recorded to build a full syringe pedigree. Prior to release, the drug's pedigree can be confirmed based on its movement through its pharma manufacturing steps. Additionally, the nest RFID tag will activate mass-reading use cases (e.g. read in pallets) thanks to its longer reading range.

The solution aims to offer throughput speeds of up to 1,000 units per minute, ensuring compatibility with the fastest fill-finish process speeds.[9] As the solution uses industry-standard components,* pharma customers can choose their preferred partners for integration with their existing equipment and systems.

CHOOSE RFID TECHNOLOGY WHEN AGILITY COUNTS

RFID technology represents several chief advantages over optical marking. Because RFID readers require no line of sight, their placement is simple and flexible and can be installed outside of isolators. In addition, there is no need to rotate syringes, ensuring compatibility with existing machines and helping to maintain high throughput speeds while eliminating extra process steps and potential sources of error. The RFID tag can be read through autoinjectors, ensuring full visibility across all manufacturing steps.

> "RFID technology represents several chief advantages over optical marking."

Unlike optical marking, the RFID T&T solution requires no modification of the syringe barrel, which could potentially interfere with human- or machine-based visual inspection and detection of visible particles. The RFID unit is incorporated into the RNS without altering the RNS's dimensions, maintaining compatibility with secondary devices such as autoinjectors and safety devices.[10] In addition, the BD solution enables mass reading of units within nests and through secondary devices, cartons and pallets, for instantaneous identification of units at each lifecycle stage.

At the end of the manufacturing process, the syringe RFID tag could be re-encoded to carry drug information that can be used in a hospital setting to automate documentation, track recalls and improve inventory management.[11] The solution has the potential to be extended to provide end-to-end traceability to meet the needs of connected ecosystem strategies including POC applications and the monitoring of patient outcomes.

Use Case 1: Addressing the Growing Risk of Mix-Ups[12]

The BD solution for T&T is intended to offer a robust alternative to the limitations of colour rings. Because it is based on individually identified containers with associated data, the T&T solution is designed to manage unlimited combinations of products/strengths, while colour rings are limited by the ability to distinguish many colours within manufacturing constraints (e.g. speed, light, etc). And because colour-coded rings are applied at the exit of visual inspection, a coverage gap exists when using them, allowing the possibility of mix-ups to occur between filling and inspection. However, with a single and continuous unit-level tracking system covering the entire fill-finish process and beyond, the T&T solution is intended to ensure that there are no gaps in vigilance against mix-ups. Additionally, removing the application of colour rings should streamline the process, supporting greater equipment efficiency.[13]

Use Case 2: Automating Reconciliation

The reconciliation step is intended to ensure that all materials have been accounted for at the end of a batch fill-finish process and that no mix-up occurred. It is a mandatory, labour-intensive step that must be completed before the start of a new filling batch. It requires counting incoming and outgoing units, and the final tally must account for 100% of the units, including rejects, samples and returns. Discrepancies must be investigated, and all units need to be accounted for to clear the line and commence changeover. Reconciliation is a significant pain point for many pharma manufacturing operations. Accounting for 100% of all materials used in a fill-finish process can be challenging and there is a risk of calculation error.

The T&T solution identifies and tracks every PFS unit as it moves through the fill-finish process. Any unit that does not make it out of a particular manufacturing step is identified during the process. Reconciliation issues can be resolved "on the fly", making it possible to "blacklist" missing units, marking them for automatic ejection should they reappear in the process. Issues could be closed quickly, significantly accelerating the reconciliation process, leading to better OEE and faster batch release. With RFID-equipped unit-level PFS tracking, fill-finish operations could convert time previously lost during reconciliation into productivity.

Use Case 3: The End of Over-Segregation

Due to the lack of unit-level visibility of traditional fill-finish operations, when a quality issue occurs, segregating only affected units is challenging. Therefore, to ensure segregation of all affected products, manufacturers often over-segregate or even discard entire batches. The BD solution for T&T is designed to precisely link rejected units to each step of the process, making it possible to identify and segregate only those units affected by a potential quality issue. By eliminating the disposal of non-affected products, manufacturers could be able to optimise product delivery.

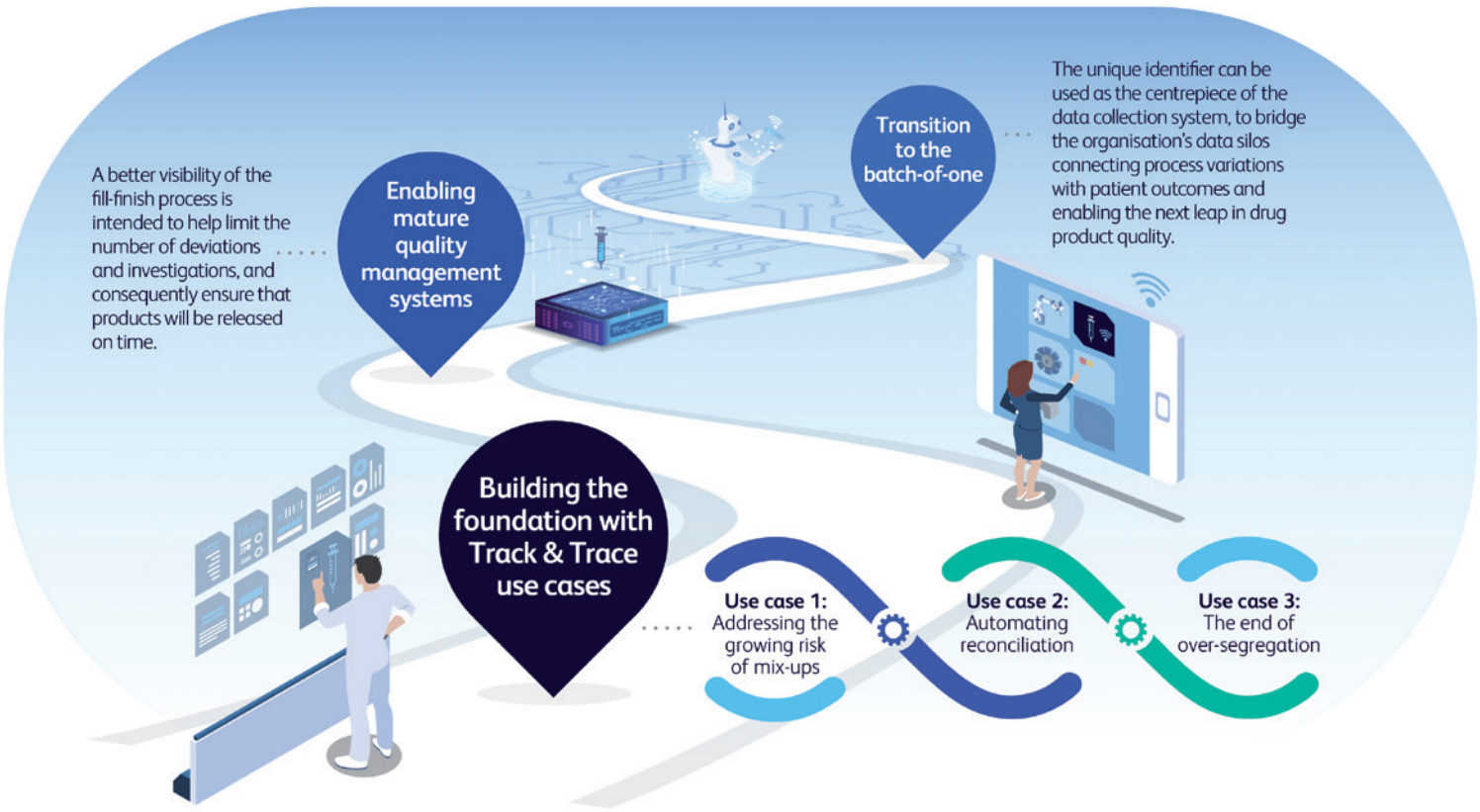

Figure 3: Unit-level identification is a foundation for Pharma 4.0 applications.

ADAPTING TO PRESENT AND EMERGING REGULATORY TRENDS

Pharma manufacturers face the challenge of implementing mature quality management systems that provide better visibility of the fill-finish process and which limit the number of deviations and investigations and, consequently, ensure that products will be released on time. In response to regulatory trends, manufacturers are expected to replace the traditional "detect and reject" approach to quality with proactive practices that enable continuous quality improvement and "right-first-time results". This includes the ability to establish normal rejection rates, detect trends, determine root causes and implement corrective and preventive actions. The BD solution for T&T is intended to provide the process visibility central to reaching these goals.

CREATING VALUE THROUGH PHARMA 4.0

The ISPE** defines Pharma 4.0 as "the era of smart machines, storage systems and production plants that can autonomously exchange information, trigger actions and control operations free of any human intervention", conveying the notion of widespread digitalisation and automation throughout the industry. While companies may be at various levels of implementation of Pharma 4.0 strategies, the large majority are using data to monitor their processes, products and environments. However, as this data is not linked to the physical container, it is only used for a specific process step and cannot be leveraged to build a true end-to-end control strategy that encompasses the primary packaging, the pharma manufacturing steps and the possibility of going all the way to the patient.

Unit-level traceability represents a key digital enabler for a range of Pharma 4.0 applications, both within the manufacturing site and beyond it. The unique identifier can be used as the centrepiece of the data collection system, to bridge the organisation's data silos connecting process variations with patient outcomes and enabling the next leap in drug product quality. Looking further, by providing pharma with access to container metadata (PFS length, flange dimensions, concentricity, etc) at the unit level, and by linking this to pharma manufacturing process data and, ultimately, to patient data, pharma manufacturers could be able to identify how small variations in the primary container or in their process can impact processability, quality and/or the patient experience. Ultimately, by moving scrutiny from the batch to the dose, a new level of trust in the process could be reached thanks to accountability at the unit level, paving the way for a "batch-of-one" approach, enabling real-time release of manufactured doses (Figure 3).

LOWER THE COST OF GOODS MANUFACTURED

BD's RFID T&T solution is intended to support pharma manufacturers in lowering their COGM and increasing OEE. It is designed to address many of the sources of high fill-finish costs, helping pharma companies to:

- Reduce changeover downtime by accelerating line clearance and reconciliation
- Reduce the duration and complexity of investigations to ensure timely batch release
- Put a stop to over-segregation and full-batch discard, and reduce the overall scrap rate
- Mitigate exposure to mix-ups and minimise the risk of human error
- Increase manufacturing flexibility to better handle portfolio growth and prevent expensive changes in supply flows.

TOTAL COST OF OWNERSHIP: A STRONG BUSINESS CASE

BD has undertaken a comprehensive total cost of ownership analysis supporting a strong business case for its solution for T&T. The study can be made available to qualified partners who are evaluating the BD solution.

An Incremental Revolution

The BD solution for T&T can help pharma manufacturers bring new performance to their fill-finish operations in a way that is compatible with their operational and investment priorities. Scalable, flexible and future-proof, the T&T solution is intended to help pharma manufacturers adapt rapidly and cost effectively to the growing demands on their fill-finish operations.

BD invites all interested parties to reserve a visit to its demonstration lab for a proof-of-concept presentation of its RFID-based solution for T&T.

** UHF RFID tag, EPC™/RFID tagging protocol based on GS1 standards. By selecting no proprietary software or rules, GS1 standards enable any allowed supply chain participant across the globe to read data with proper RFID equipment.*
*** International Society for Pharmaceutical Engineering is a non-profit association serving its members by leading scientific, technical and regulatory advancement throughout the entire pharmaceutical lifecycle.*

ABOUT THE COMPANY

BD is one of the largest global medical technology companies in the world and is advancing the world of health by improving medical discovery, diagnostics and the delivery of care. The company supports the heroes on the frontlines of healthcare by developing innovative technology, services and solutions that help advance both clinical therapy for patients and clinical process for healthcare providers. BD and its 75,000 employees have a passion and commitment to help enhance the safety and efficiency of clinicians' care delivery process, enable laboratory scientists to accurately detect disease and advance researchers' capabilities to develop the next generation of diagnostics and therapeutics. BD has a presence in virtually every country and partners with organisations around the world to address some of the most challenging global health issues. By working in close collaboration with customers, BD can help enhance outcomes, lower costs, increase efficiencies, improve safety and expand access to healthcare.

REFERENCES

1. *"Policy paper on traceability of medical products". WHO, March 18, 2021.*
2. *Markarian J, "Automating Biopharma Manufacturing", Pharm Technol. 2022, Vol 46(7), pp 30–33.*
3. *"Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals". US FDA, Jul 2022.*
4. *"Unique identification of primary containers to drive product traceability and quality". ISPE, Feb 1, 2021.*
5. *"Pharma Firm Explores RFID for Prefilled Syringes". PDA Letter, Jun 23, 2020.*
6. *"Commission staff working document – Vulnerabilities of the global supply chains of medicines – Structured Dialogue on the security of medicines supply". European Commission, Oct 2022.*
7. *Schrader U, "Operations can launch the next blockbuster in pharma". McKinsey and Company. Feb 16, 2021.*
8. *"How Sterile Pharma Manufacturers Can Grow Capacity without Capital Investment". McKinsey and Company, 2023.*
9. *"The current state of aseptic processing & fill-finish manufacturing". CRB, Accessed Jan 12, 2023.*
10. *Steffen Y, "RFID in RNS for 100% container traceability". PDA Webinar, Feb 17, 2021.*
11. *"RFID Uses, Benefits, and Costs: Literature Review and Key Informant Interviews". The Axia Institute, Michigan State University, May 2022.*
12. *"Supporting Becton Dickinson in assessing the opportunity for industrial traceability solutions". Study conducted for Becton, Dickinson and Company, Feb 2020.*
13. *"Primary research to assess the value creation for syringe identification". Study conducted for Becton, Dickinson and Company, Jan 2022.*

ABOUT THE AUTHORS

Yacine Haddadi is a Senior Global Marketing Manager at BD Medical – Pharmaceutical Systems, responsible for developing and bringing to market a new digital traceability platform for primary containers. He has over a decade of experience in the healthcare software industry, helping hospitals and pharmaceutical companies transition from paper-based to digital solutions, including cloud-based and mobile applications. Mr Haddadi has actively contributed to the development of multiple innovative projects leveraging data analytics and artificial intelligence to improve operational efficiency and patient outcomes. He joined BD in 2021 and is involved in the ISPE Community of Practice, working on the traceability of primary containers. Prior to joining BD, he worked at Guerbet, where he led the global launches of T&T solutions for contrast media (Contrast&Care®) and radiation doses (Dose&Care®). Mr Haddadi is a pharmacist and holds a master's degree in health marketing from UPMC Sorbonne Université (France).

Hervé Soukiassian joined BD Medical – Pharmaceutical Systems in 2007 and is currently involved in product development pertaining to PFSs for T&T. Under his leadership, the BD Neopak™ XSi™ and the BD Neopak™ XtraFlow™ Glass Prefillable Syringe have been successfully developed and brought to market. He has also contributed actively within the PDA as co-author of both Technical Report 85, "Enhanced Test Methods for Visible Particle Detection and Enumeration on Elastomeric Closures and Glass Containers", and Technical Report 73, "Prefilled Syringe User Requirements for Biotechnology Applications". Prior to joining BD, Mr Soukiassian held various positions at Hewlett Packard, developing expertise in the fields of process engineering and product development for over a decade. He later joined the board of directors of ActiCM, a start-up company specialising in optical co-ordinate measurement machines. He graduated from the Institut National des Sciences Appliquées in Lyon, France, as a mechanical and industrial engineer with a master's degree in material sciences.

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ENTERING THE UK MARKET: A GUIDE FOR US MEDICAL DEVICES COMPANIES

In this article, Matthew Burton, Strategic Development Director at IMed Consultancy, discusses the new EU Medical Device Registration and offers a guide for the UK Responsible Person within companies.

Europe is in full regulatory transition, and with the new EU Medical Device Registration (MDR) causing delays and complications for businesses wanting to place a new device on the European market, many US businesses are understandably starting to turn towards the UK.

In contrast with the EU, in fact, the UK continues to operate with consolidated regulations for the time being and is positioning itself as an ideal market for products that are novel and niche while trying to enhance the medtech sector and develop it as a pillar of industry with the declared objective of attracting innovative products. Specifically, the UK government has recently launched a medtech strategy, to ensure social care systems can reliably access safe, effective and innovative medical technologies.[1] The document states the vital importance of medtech within the UK health and care system, as recently highlighted by the covid-19 pandemic, and the critical role medtech devices will have in shaping the future of the UK health and care system.

Another reason the UK market is appealing to US businesses is its "one provider, one payer" model provided by the NHS, with tenders every four years that increase the chance of successfully positioning medical devices within the NHS framework. In addition, the UK market does not normally require translation and localisation of instructions for use, technical documents and even advertising, as would be the norm for access into non-English-speaking European countries, further speeding up processes without the need for additional investments.

> "The UK continues to operate with consolidated regulations for the time being and is positioning itself as an ideal market for products that are novel and niche."

First and foremost, however, US businesses wanting to enter the UK market in this time of regulatory transition need to understand the UK regulatory landscape and to get familiar with acronyms such as MHRA and UKRP.

UK OR GREAT BRITAIN?

The first important distinction to make is between the UK and Great Britain (England, Scotland and Wales), due to Northern Ireland's unique current regulatory status. Under the Northern Ireland Protocol, in fact, different rules apply in Northern Ireland and in Great Britain.[2]

As of January 2021, businesses wishing to enter the market in **Great Britain** are required to:

- Register with the MHRA
- Appoint a single UK Responsible Person (UKRP) for all of their devices, who will act on their behalf to carry out specified tasks, such as registration
- Comply with relevant product marking and conformity assessment requirements for medical devices.

Requirements for placing devices on the **Northern Ireland market** can instead be summarised as follows:

- The EU MDR and EU IVDR have applied in Northern Ireland since May 2021 and May 2022, respectively
- CE marking is required in Northern Ireland. In addition, the UKNI indication is required if a UK Notified Body undertakes mandatory third-party conformity assessment

Matthew Burton
Strategic Development Director
T: +44 1295 724286
E: matthew@imedconsultancy.com

IMed Consultancy
Bloxham Mill Business Centre
Barford Road
Bloxham
Banbury
Oxfordshire
OX15 4FF
United Kingdom

www.imedconsultancy.com

- Certain devices will require registration with the UK MHRA, including *in vitro* diagnostic medical devices (IVDs), which need to be registered with the MHRA when placed on the Northern Ireland market.

THE MHRA

The MHRA is the entity responsible for regulating the UK medical devices market. Specifically, the MHRA performs market surveillance and can take decisions over the marketing and supply of devices in the UK.

Failure to meet the above requirements will preclude manufacturers from lawfully placing their devices on the UK market.

What is a UKRP?

A UKRP acts on behalf of businesses based outside the UK to carry out all tasks needed to successfully place their device on the UK market and liaise with entities such as the MHRA.

UKRPs need to be physically located in the UK, and their name and address must be included on the product labelling or the outer packaging, or the instructions for use in cases where the UK Conformity Assessed (UKCA) marking has been affixed.[2] They are legally responsible on a par with manufacturers.

A UKRP's responsibilities are detailed in the UK MDR 2002,[3] but can be summarised as follows:

- Liaising and collaborating with the MHRA
- Ensuring the declaration on conformity and all technical documentation have been drawn up
- Keeping available a copy of all relevant documentation, including a copy of the declaration of conformity and relevant certificates
- Immediately informing the manufacturer about complaints and reports from healthcare professionals, patients and users.

> "Choosing the right UKRP, especially when placing a device on the UK market for the first time, can definitely make a difference for medical device manufacturers."

Choosing the right UKRP, especially when placing a device on the UK market for the first time, can definitely make a difference for medical device manufacturers that need to be at least familiar with all the UKRP requirements and responsibilities, as set out in the UK MDR 2002, to ensure they are getting the support required from an eligible UKRP.

Since appointing a single UKRP to act on their behalf is the first, most important thing businesses based outside the UK need to do to place a device on the Great Britain market, choosing the right partner can be the make or break of success in entering the market for medical device manufacturers.

Manufacturers should also be aware that, although there is nothing to prevent an importer or distributor also acting as a UKRP, the newly defined responsibilities of the UKRP require an in-depth understanding of the regulatory landscape for medical devices. Manufacturers should appoint their UKRP carefully and would be well advised to consider UKRP providers that offer experience in dealing with institutions and volatile regulatory environments. US businesses wishing to place one or more devices on the UK market may even decide to rely on not just one expert but on a consultancy to make sure of being assisted by a whole team of experts with broad knowledge and wide access to relevant resources, which can support them in all their regulatory needs.

ABOUT THE COMPANY

Founded in 2012, IMed Consultancy offers a wide range of regulatory and compliance services to the medtech industry, supporting medical device manufacturers through all stages of the product lifecycle from concept and design consultancy through to post-market surveillance activities. IMed Consultancy's team of skilled and experienced medical regulatory professionals offers an outstanding yet flexible service covering regulatory affairs, UKRP and EU Authorised Representative (EUAR) services, PRRC, and quality assurance in medical devices, including Class III active and implantables, companion diagnostics, software as a medical device (SaMD) and IVDs. With extensive hands-on problem-solving expertise, IMed Consultancy's remit is truly global, ensuring that client devices are successfully launched and maintained in total compliance in the UK, EU, US and internationally.

REFERENCES

1. *"Medical technology strategy". Policy paper, Gov.UK, Feb 3, 2023.*
2. *"Regulating medical devices in the UK". Guidance, Gov.UK, Apr 27, 2023.*
3. *"The Medical Devices Regulations 2002". legislation.gov.uk, accessed Jun 2023.*

ABOUT THE AUTHOR

Matthew Burton is IMed Consultancy's Strategic Development Director, with over 12 years' experience in quality assurance and regulatory affairs, specialising in MDD/UKCA and EU MDR. Representing many clients as UKRP, PRRC and with global registrations, he has worked with many devices over his regulatory career.

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