PREFILLED SYRINGES:
THE RISE OF THE DELIVERY DEVICE PORTFOLIO

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"Prefilled Syringes: the Rise of the Delivery Device Portfolio"

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

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Nov	Pulmonary & Nasal Drug Delivery
Dec	Delivering Biotherapeutics
2013	
Jan	Oral Drug Delivery
Feb	Prefilled Syringes
Mar	Transdermal Delivery, Microneedles & Needle-Free Injection
Apr	Pulmonary & Nasal Drug Delivery
May	Injectable Drug Delivery: Formulations Focus
Jun	Injectable Drug Delivery: Devices Focus
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Contact: Guy Furness, Proprietor & Publisher
T: +44 (0) 1273 78 24 24
E: guy.furness@ondrugdelivery.com

MAILING ADDRESS:
Frederick Furness Publishing
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T: (859)225-5375
E: rmollozzi@medprosafety.com

MedPro Safety Products, Inc
145 Rose Street
Lexington
KY 40507
United States

www.medprosafety.com

WHY ONE IS GREATER THAN MANY

In this article, Garyen Denning, Executive Vice-President, MedPro Safety Products, Inc, describes how the single glass cartridge at the heart of the company's needle-stick safety technology has now developed to offer a full platform of delivery devices, including a prefilled syringe, an IV access delivery device and a vial cartridge, all based around the same primary container.

Using one primary container for different types of drug delivery has distinct advantages over current prefilled syringes. A single cartridge can offer the highest level of needlestick safety, IV access, and vial usage. MedPro Safety Products is dispelling the notion that managing the lifecycle of a drug is a multi-faceted process. MedPro has created a platform that uses a standard cartridge to address lifecycle management concerns previously encountered by the pharmaceutical company.

HOW FAST IS FAST ENOUGH?

In today's highly competitive pharmaceutical marketplace it is critical that solutions providers understand the needs of device users and pharmaceutical customers alike. MedPro Safety Products began developing its needlestick safety drug delivery device with technology that uses a standard cartridge as the primary container. During the evaluation of the technology by pharmaceutical companies, MedPro observed the challenges a pharmaceutical company faces during device selection. These challenges all involved the primary container and its validation to the patient. Until now, a stable primary container with multiple points of delivery has been an unmet need to pharmaceutical companies.

Reaction time and speed of innovation to address that unmet need are key to MedPro's success within the industry. What began as a needlestick safety initiative for the company has grown into an entire drug delivery platform (see Figure 1). Today, needlestick safety is still a very important issue and the MedPro technology presents a pharmaceutical company with an opportunity for differentiation by offering what the company believes is the highest level of needlestick safety available for the healthcare

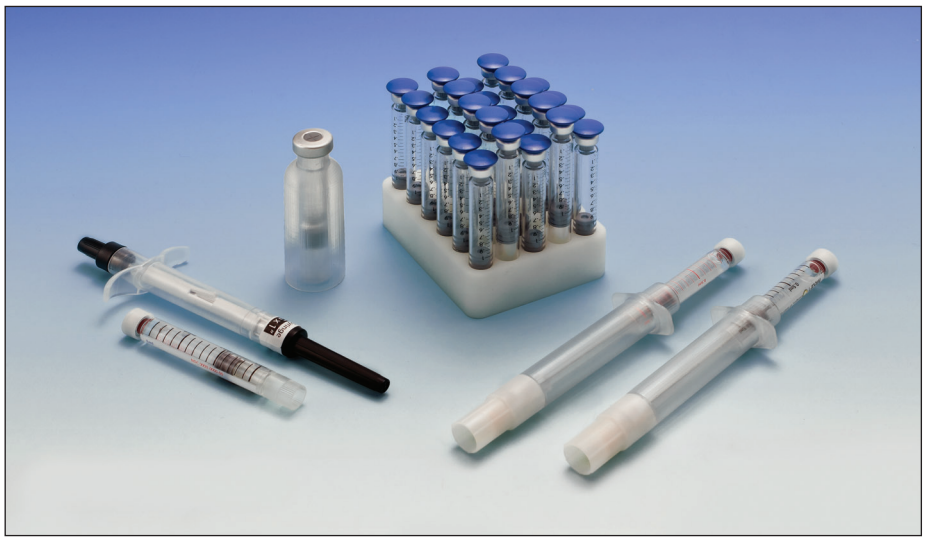

Figure 1: What began as a needlestick safety initiative has grown into an entire drug delivery platform.

Mr Garyen Denning
Executive Vice-President
T: +1 859 225 5375
E: gdenning@medprosafety.com

MedPro Safety Products, Inc
145 Rose Street
Lexington
KY 40507
United States

www.medprosafety.com

professional. Understanding how to use a standard cartridge to make drug delivery simpler and safer, MedPro has been able to create additional opportunities for pharmaceutical companies using that same primary container.

MedPro's success is based on its complete dedication to addressing its customers' needs as quickly and efficiently as possible. MedPro has often been approached by customers with conceptual ideas and the company is able to provide designs, prototypes, manufacturing considerations and intellectual property reviews in a matter of weeks.

A PLATFORM, NOT JUST A SYRINGE

The market for safety syringes for drug delivery is a crowded one. There are many options available to pharmaceutical companies, most of those options being an add-on safety device that requires the healthcare professional to "activate" the safety mechanism. The MedPro Drug Delivery platform is anything but another safety syringe. The platform is based on a standard glass cartridge. The pharmaceutical company can validate that cartridge and then use it in three different ways:

1. As a prefilled syringe with automatic, passive needlestick safety (Figure 2)
2. As an IV delivery device that has compatibility with all needle free valves (Figure 3)
3. As a vial cartridge, allowing the healthcare professional to draw up medicine from the container into a hypodermic syringe (Figure 4)

The ability to use one primary container with these different options changes the game for pharmaceutical companies during device evaluations for a new molecule. The platform allows them to keep their options open and their costs down by requiring one packaging option, versus multiple packaging options such as a vial and a prefilled syringe. From a cost perspective, the ability to keep the primary container simple, and the process requirements within the aseptic core minimised, provide a compelling economic value proposition.

CARTRIDGE SIMPLICITY

The platform allows a pharmaceutical customer to fill the container and finish the packaging in one of two ways. The first is a sterile cartridge with a baked-on silicone application in a nest-and-tub format. This format can be run on a prefilled syringe line. The second option is bulk cartridge filling. Recently, MedPro announced a partnership with Weimer Pharma (Rastatt, Germany). The partnership offers another way for pharmaceutical companies to decrease their upfront investment and have the benefits of the

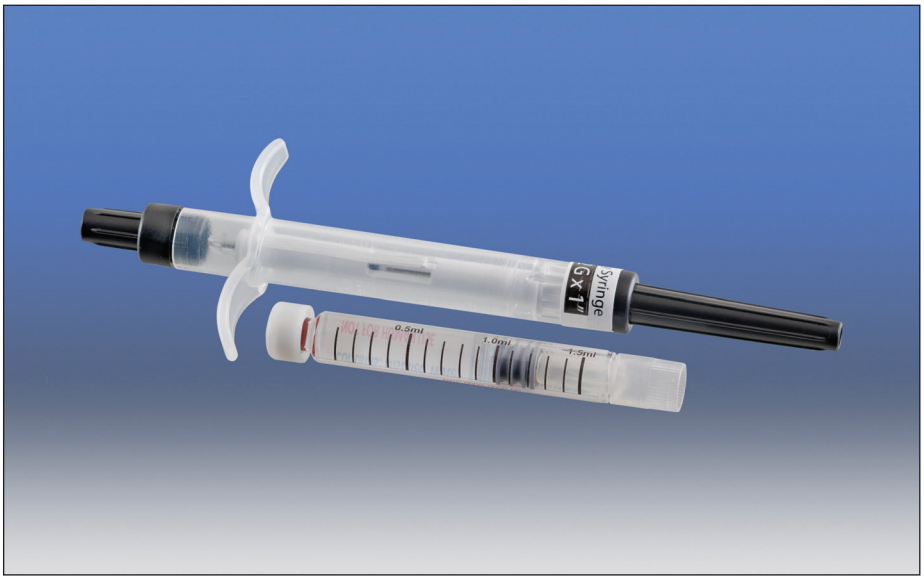

Figure 2: The MedPro prefilled syringe with automatic, passive safety.

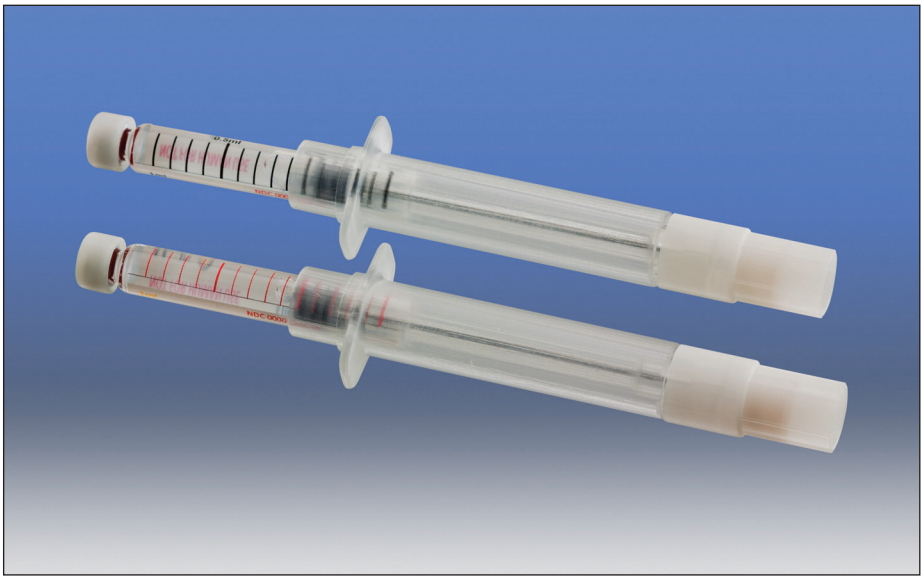

Figure 3: The IV Shuttle is compatible with all needle-free valves.

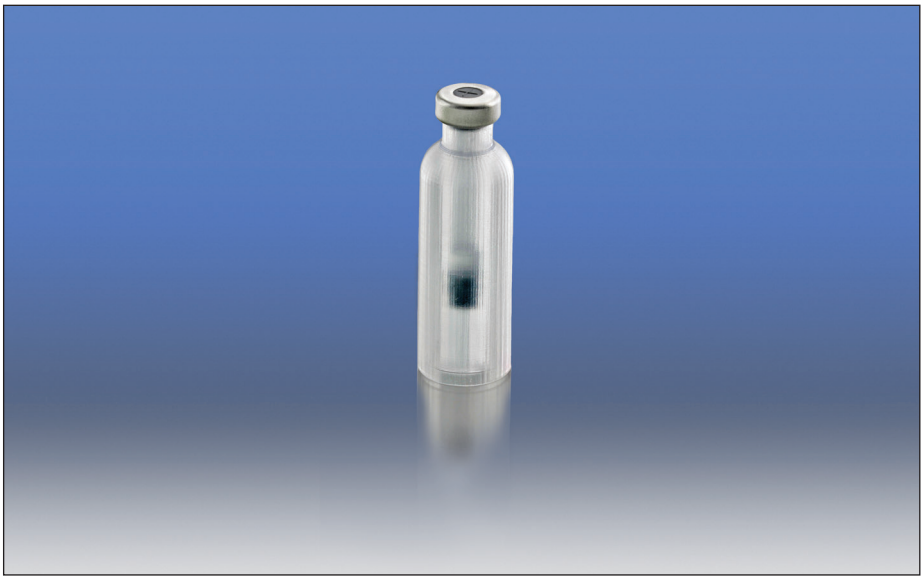

Figure 4: MedPro's vial cartridge allows medication to be drawn up into a syringe.

MedPro platform for their injectable products.

As experts in cartridge filling, Weimer can provide all of the necessary activities around filling a drug cartridge and using it with the MedPro system. The Weimer bulk cartridge filling process offers high process flexibility where baked-on siliconisation and sterilisation is tailored to particular products. The bulk process allows low numbers of transfers of sterilised units and reduces the contamination risk to a minimum. For customers considering a move to a prefilled syringe, Weimer not only evaluates the syringe itself but the additional equipment and validations that will be required to add safety to that syringe.

The Weimer CMO solution or the "ready to fill cartridge" both require less capital investment for the fill finish and for that reason are attractive alternatives. Pharmaceutical customers are constantly evaluating more efficient means of fill-finish and are looking to outsource more of the non-value-add activities. By partnering with an expert in cartridge filling, MedPro is able to offer customers a turnkey solution for device adoption.

Weimer's Business Development Manager, Jürgen Nowak says, "For seventy years, Weimer has been a renowned contract manufacturer and developer for pharmaceutical companies around the world. The innovative MedPro Drug Delivery Platform fits perfectly with Weimer's cartridge fill finish services. Together, our technology offers a new dimension to patient convenience."

DIFFERENTIATION ANYONE?

The MedPro Drug Delivery platform takes the idea of a prefilled syringe and turns it upside down, both literally and figuratively. Practically, this methodology has benefits that healthcare professionals have praised during focus groups and one-on-one interviews:

1. Injectable product visibility – Healthcare professionals can inspect the product prior to injection because they have a clear view of the drug contents. Prefilled syringes today that have safety devices added to them can sometimes add unwanted size and clutter around the drug product.
2. Pre-Activation – By keeping the drug cartridge separate, the healthcare professional can be sure that any safety device will not pre-activate during shipping and handling, which would render the normal prefilled safety syringe useless and cause the drug to be wasted.
3. Cold Chain – For temperature-controlled products, the cartridge can be packaged with a very efficient form factor, and the footprint of the temperature sensitive product can be more than cut in half. This matters for healthcare professionals with limited refrigeration space as well as home health users who can store the device portion in their pantry, while the drug contents take up much less room in their refrigerators.

PLATFORM POTENTIAL

The drug cartridge is a proven container for injectable products. Capitalising on this proven container is the cornerstone of the MedPro platform. The company's intellectual property includes a number of possibilities, which are continuously refined through ongoing development efforts. The use of a cartridge as a dual chamber system or within types of auto-injectors offers additional flexibility and options for pharmaceutical companies.

For pharmaceutical companies that are planning new projects and molecular development, the delivery system is a key component in the success of each project. The MedPro platform can offer the necessary characteristics to ensure the pharmaceutical company is successful with the delivery device.

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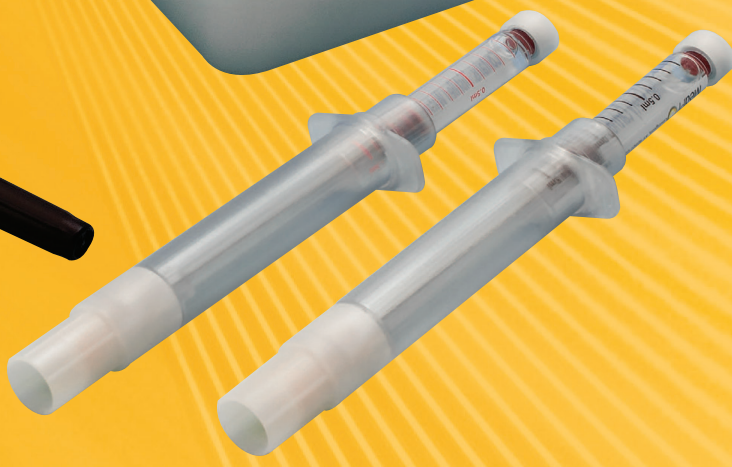
CARTRIDGE PLATFORM

- One Primary Container
- Standard Cartridge
- Baked Silicone Application
- Life Cycle Management Solution



About MedPro

MedPro Safety Products is a leader in innovative devices that increase the level of safety across the continuum of care. This product compliments the company's innovative drug delivery platform that offers passive, automatic needlestick protection and safer IV delivery.

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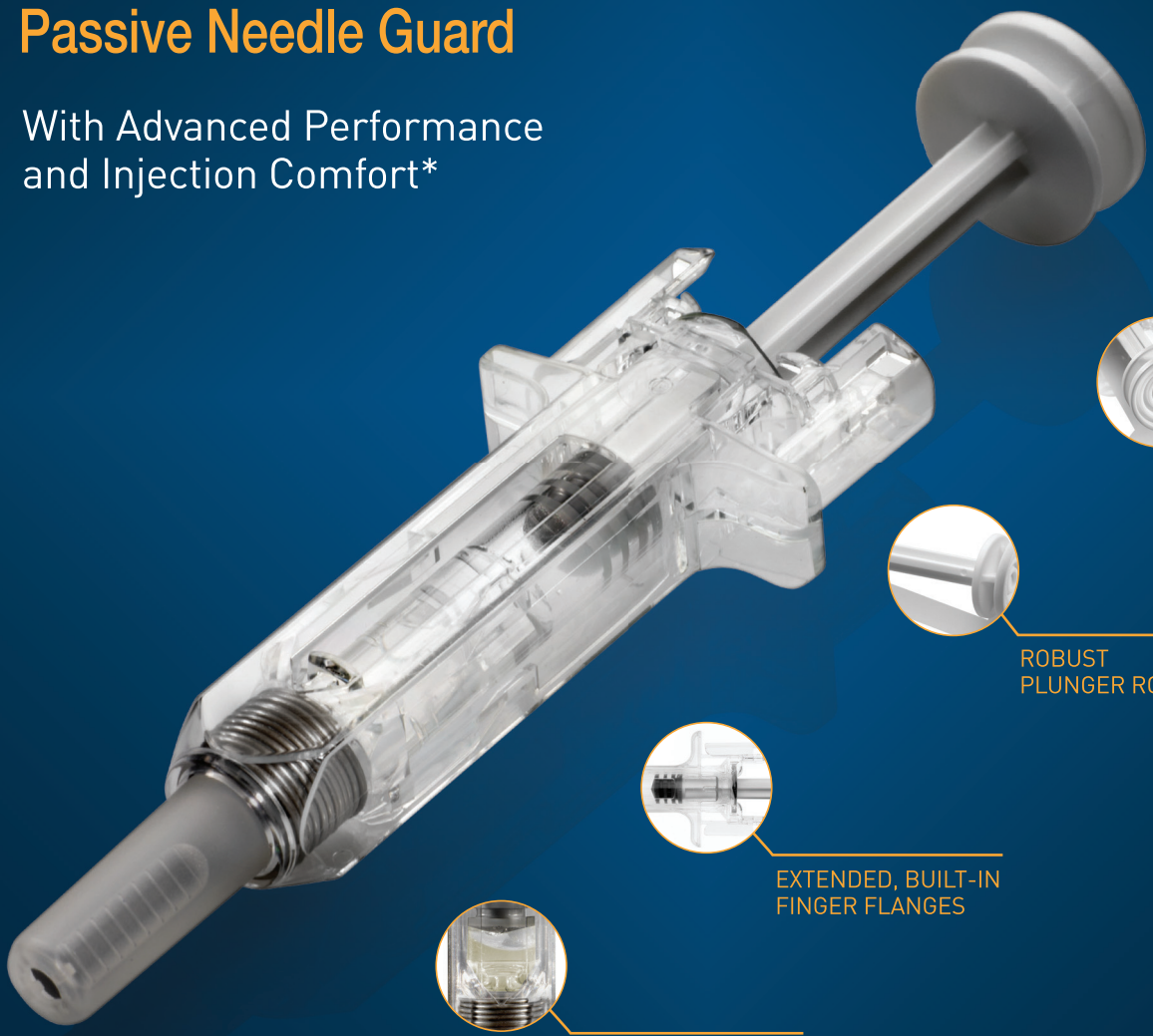

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PRIMEQUAL TALENT™ REVOLUTIONARY OPEN PLATFORM: A NEW GENERATION OF PREFILLED INJECTION SYSTEMS

In this exclusive article for ONdrugDelivery Magazine, Mr David Weill, Chief Executive Officer, Primequal SA, describes the company's Talent™ open platform, an injection technology developed using an entirely novel approach to device design and innovation that Primequal calls the pqtoolbox™.

NEW NEEDS & HIGH PRESSURE

The pharmaceutical market for injections and delivery devices is shifting. Further than just delivering the right amount of drug at the right place, there is increasing interest in how we can deliver it in a more efficient, better, easier, safer and faster way. There is a strong will to go for solutions that are more treatment-centric and more user-centric. Authorities are multiplying, and "guidances" and "human factors" have become central subjects to address presenting challenges to overcome. A device must not only work perfectly but at the same time needs to look and feel perfect too. Expectations on pain management are increasing and pain reduction is mandatory. Marketing is now looking for differentiations that will turn their chosen device into an exclusive solution and a decisive competitive advantage. Pressure on price and timing has never been so high. Creating a device takes a lot of time and is often delayed, engulfs incredible amounts of money with permanent budget calls, generates long and difficult discussions for something that will always remain uncertain and at high risks.

To overcome all these problems and provide an answer to those needs, Primequal™ has created a revolutionary open platform, Talent™ .

TALENT™ OPEN PLATFORM

The Talent™ open platform is a Dispenser – Injector – Doser, which propels a gauged amount of liquid, gel or paste each time you press on the lever. The precision of the dose is defined by the mechanical step size and the number of pressures that are applied on the lever.

"SMOOTHJECT™ IS A MUST-HAVE TECHNOLOGY IN A MODERN INJECTION SYSTEM"

For the first time, a step-by-step doser is available in a single use, disposable device, fully adapted to each field of application thanks to the pqtoolbox™ (see below). As an example, the Talent™ open platform was used to create the legendary Talent BT™ , the world's first botulinum toxin automatic injector (see Figure 1).

Mr David Weill
Chief Executive Officer

T: +41 22 354 05 50
E: dweill@primequal.com

Primequal SA
Rue des Pierres du Niton 17
1207 Geneva
Switzerland

T: +41 22 354 05 50
F: +41 22 354 05 51
E: info@primequal.com

www.primequal.com

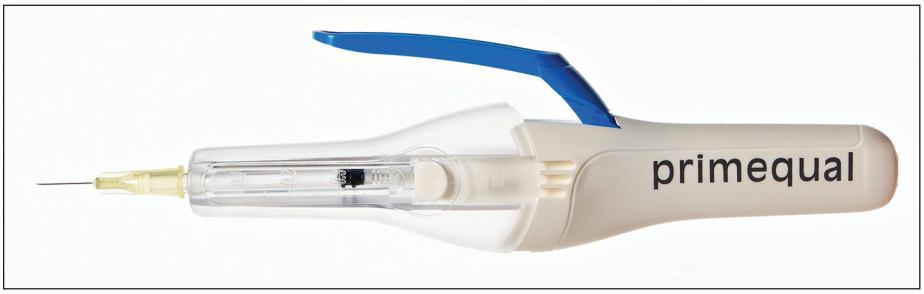

Figure 1: Talent BT™ World's first botulinum toxin automatic injector, an example product from the Talent™ open platform.

NEW APPROACH USING THE PQTOOLBOX™

Primequal's approach is based on an innovative and modern concept named the pqtoolbox™. Instead of adapting the specifications requested for the treatment to an existing device, Primequal creates a totally new device from the beginning, picking each pqtool™ from the pqtoolbox™ (see Figure 2).

Every pqtool™ is specifically designed and mastered, and ready to use. The idea is to assign a dedicated pqtool™ to each design specification, which fully satisfies each need and its requirements. Then, the pqtool™ selection is assembled to create a totally new device that is unique, dedicated to the treatment and matching the full spectrum of specifications.

The advantage of the pqtoolbox™ lies in the fact that each pqtool™ does more than meet a specification, but is designed to take into account all the aspects of a medical device: ergonomics and handling, human factors, international regulations, ISO standards, guidelines, aesthetic appearance, pain management, raw materials, design phase, clinical phase, industrialisation phase, manufacturing, assembly, controlling, testing, reliability, validation, sterilisation, and so on … So by selecting a pqtool™, Primequal already knows the full path to the validation and market release of the device. Timing is shorter and risk is reduced to its minimum.

PQTOOL™ PORTFOLIO

The Talent™ open platform is a mature platform, for which Primequal has been developing and patenting a portfolio of pqtools™ for more than six years. The pqtools™ cover a great number of mastered possibilities such as **Preciquant™** (shown in Figure 3), **AutomInject™, 1 click 1 dose™, SmoothJect™, Nanodroplets™, Primeasepsis™, Sterifullshield™.** These pqtools™ offer a range of solutions including safety against re-use, safety against multiple use, self-locking systems, anti-refill, oxygen full protection, airless propelling, ultimate spray, and from one to 200 clicks, amongst others. The pqtool™ portfolio is completed by having access to a broad range of proprietary technologies and patents from third parties and partners. Needle-safe technologies, COC, COP, liquid PC and silicone-free lubrication are examples of such technologies to which Primequal has access.

SIMPLICITY & RAPID DEVELOPMENTS

The Talent™ open platform's key asset is to be simple. This simplicity in on two levels. On the first level, Primequal has the ready-made, mastered, ready to use pqtool™. On a second level the pqtools™ are designed to be truly simple. Simplicity is the most dif-

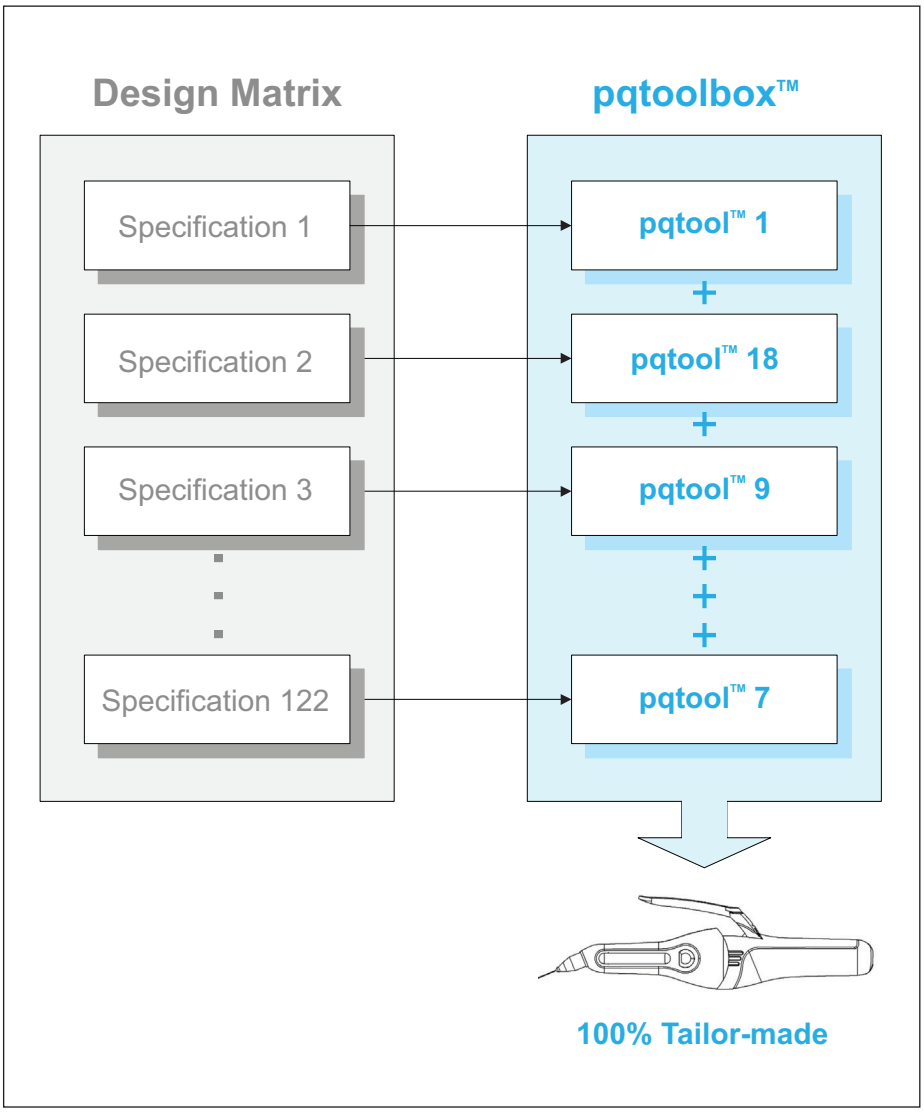

Figure 2: The pqtoolbox™ – instead of adapting the specifications requested for the treatment to an existing device, Primequal creates a totally new device from the beginning, picking each pqtool™.

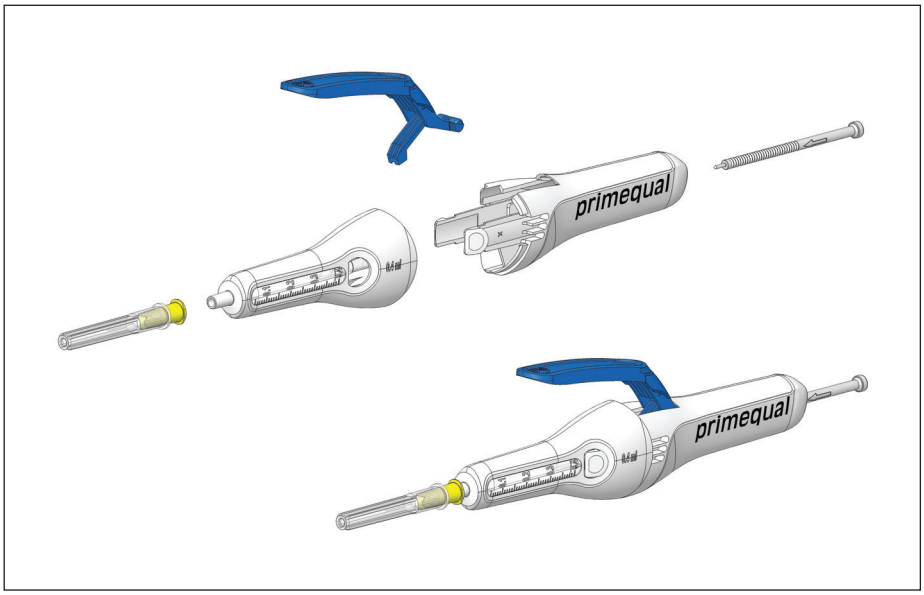

Figure 3: Preciquant™, a mechanical dosing system made out of only three parts, is an example of simple and complete pqtool™.

ficult thing to achieve in engineering and it took Primequal a number of years to build its pqtool™ portfolio. Using pqtools™ that are already designed, ready to use and simple will shorten the time needed for the development of a device. Preciquant™ pqtool™ (Figure 3) is a clear demonstration of this simplicity, it is a mechanical dosing system made out of only three parts. Adaptation of a small number of parts is easier, the number of tools is small, with only a low number of parts to produce and assemble, controlling is reduced, validations and process validations are reduced, reliability is increased (based on Murphy's Law : the more parts, the more problems).

COST EFFECTIVENESS & REDUCED COSTS

Primequal's Talent™ open platform reduces costs in a number of ways. Firstly and most obviously, pqtools™ are already designed so there is no investment or time needed for this first step of design. Secondly, all pqtools™ are simple, and simplicity is a great cost reduction. Thirdly, the timeline is shorter, and time is money.

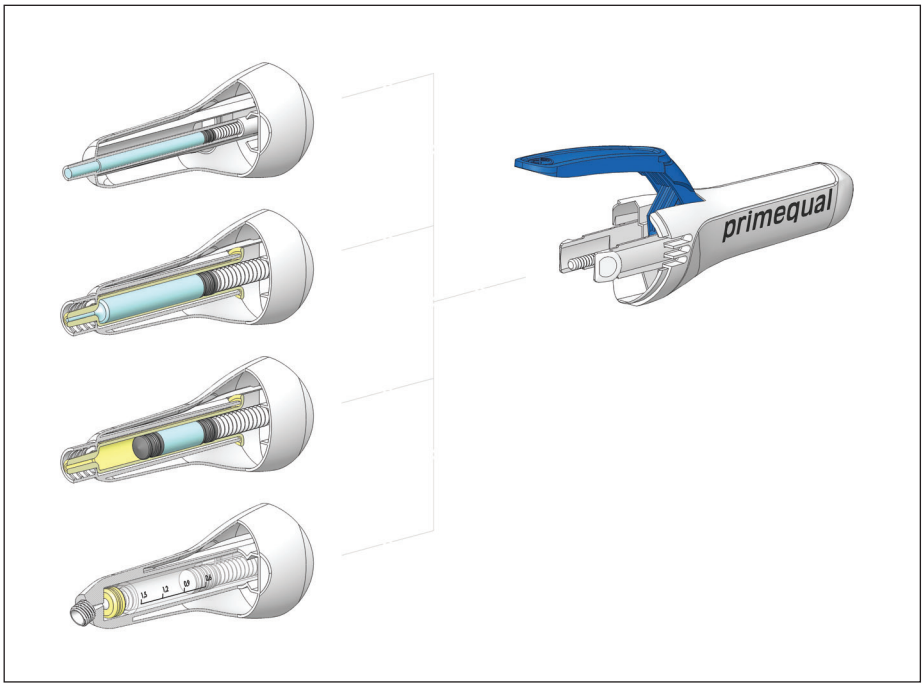

Figure 4. The Talent™ open platform as primary or secondary packaging (glass syringe, dual chamber and cartridge).

FLEXIBLE AND FUTUREPROOF

The Talent™ open platform is one of the most flexible platforms currently available on the market. This allows the device to be rapidly upgraded or personalised. For anyone integrating this technology there is the option easily to adapt the device if the treatment or the market is shifting. This futureproofing aspect is a real asset for sales and marketing. It also allows for the expansion of the range of devices to serve different applications (see Figure 4).

PHASE I, II & III TRIALS

The system's evolution capacity is so high that it is one of the few that can be applied directly during Phase I, II and III clinical trials. With this capacity, pharmaceutical companies can considerably reduce development costs, industrial costs and market delivery time while having set the device for the authorities right from the beginning.

EASIER, SAFER & FASTER

Whether it is a prefilled syringe or a system to filled at the point of use, the number of manipulations for the user to make is minimum, and close to the number required with standard syringes. Talent™ open platform can be used from day one without training, which is particularly appreciated when the need is to have an injection device that can be used globally by everyone.

Preciquant™ innovative patented technology makes it possible to control the precision and repeatability of the dose simply and comfortably. Preciquant™ increases the success rate by removing the risks common to unit dosage and dosage symmetry. Preciquant™ automatic single button operation allows a faster treatment. Needle-based treatments can rarely be described as comfortable for the patient, and at Primequal we think it is important to be able to reduce the overall time of treatment for maximum patient comfort. As dose precision concerns are ensured by the Preciquant™ patented system, this allows the practitioner to concentrate fully on the treatment and to perform his injection skills as never before, taking the treatment to higher performances levels.

TREATMENT & USER-CENTRIC

Each treatment is specific and has its requirements, its environment, its rules, its users, its user's skills, its manipulations, its type of product to inject, its reconstitution,

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its type of patients, its pro and cons, its limits and its subjective aspects. The number of parameters and disciplines involved is extraordinarily high, and this is why at Primequal all devices are 100% dedicated, drug-centric, treatment-centric, user-centric and patient-centric.

For this reason all Talent™ devices are different; tailor-made, and unique. By being fully dedicated to the application, the device performance is of a higher level. This higher level has successfully been demonstrated by the number of awards the technology has received.

PAIN MANAGEMENT

The SmoothJect™ pqtool™ allows an injection with reduced pain, and sometimes even no pain depending on the treatment. SmoothJect™ was designed when Primequal was involved with clinical studies of injections to children and the company now has extensive experience on reducing pain to children, in addition to experience with adults. SmoothJect™ has been granted with professional awards and is regularly pointed out as a strong benefit by patients and practitioners. SmoothJect™ is a must-have technology in a modern injection system.

LOW RISK

Companies that are risk adverse and that are keen to reduce their overall risk on each discipline to the minimum welcome the Talent™ open platform. The use of pqtools™ significantly diminishes risk, as their design is set and mastered. Right from the start we know where we are heading, what will be the device, how it will work, how it will be handled for the treatment and what are the risks. Clinical studies of the "combination product" and homologations are straightforward with no unwanted surprises. Industrialisation is easier and safer due to the low number of parts. This is a comfortable situation, both marketing and engineering teams agree.

SAFETY AGAINST RE-USE & MULTIPLE USE

The Talent™ open platform does not allow refill and is also self-locking after use, preventing a second use. This makes it a secure injection system with an unprecedented level of security. This also avoids multiple patient injections and has been shown to be most welcome for some vaccines and expensive injection applications. This quality sets the technology apart as a reference point in the future of safe drug delivery.

DECISIVE COMPETITIVE ADVANTAGE

Owning a Talent™ based device brings with it the possibility of promoting a clear and powerful differentiation in the market, with a unique value creation. This differentiation will be the key interest for clients and will allow the promotion of decisive benefits. This factor will be highly appreciated by the sales team, sales reps and distributors. Talent™ devices are identified as incredible sales boosters. This is especially true in the US, where Primequal™ has received the highest demand. In that respect there is no doubt that the Talent™ open platform represents a "decisive competitive advantage".

AWARD WINNING TECHNOLOGY

The Talent™ open platform has won an outstanding number of awards such as the Reddot™ Design award for the visual look and the handling, ADF™ innovation of the year for the painless injection system, Top 100 most innovative in Europe, etc … Talent™ open platform also won the coveted Pharmapack™ "Innovation of the Year" Award 2011, where the jury gave to Talent BT™ a particular mention of "ease of use", which was flattering as it is most difficult to obtain with a device. We are pleased that end users will benefit from the ease of use the device offers. Accessing such multi-awarded technology is unique on the pharmaceutical market.

MANUFACTURING FREEDOM TO OPERATE

Through its Talent™ open platform, Primequal has entered into collaborations with most known pharmaceutical device manufacturers, pharmaceutical suppliers and pharmaceutical subcontractors in the world. This allows Primequal to access the most efficient manufacturing structures and therefore allows Primequal's clients to achieve the best quality with the most competitive prices.

In this respect, Primequal represents a surprisingly unique performing solution. Primequal can propose to manufacture based on its network, Swiss Made if requested, but the Talent™ device owners can industrialise the product with their preferred suppliers, sub contractors and also integrate in one of their manufacturing plants. This is part of the unique flexibility and quality of service that Primequal stands for.

CONCLUSION

The Talent™ open platform is a new generation of prefilled injection and delivery systems, designed to offer a superior level of efficiency and safety while reducing timelines and costs.

This technology matches the increasing demand for prefilled injection systems with mastered dosing, easy and safe for both the practitioner and the patient. Talent™ open platform's simplicity is the core factor that has given rise to a truly global acceptance of this technology.

Talent™ open platform is available for pharmaceutical, medical, dental, veterinary, cosmetic and industrial applications, and Primequal is now focused on deploying this technology based on exclusive requests and exclusive licensing. Contact us, and start a game-changing conversation today…

SHL GROUP

STREAMLINING KEY SERVICES YOUR DRUG DELIVERY DEVICE PARTNERS PROVIDE

As the market demand for auto-injectors and pen-injectors continues to grow at a rapid pace, greater emphasis is now being placed on which partners can provide integrated solutions to address the needs of biopharmaceutical companies today and help them bring their combination products to market. Steven Kaufman, Marketing Director of the SHL Group, talks about the importance of streamlining the services required to make a drug delivery device by focusing on the areas of development, capabilities and final assembly.

Extensive project management expertise and logistical control know-how are obviously required when working on a combination product from the concept stage to eventual launch. Cross-functional teams from both the biopharmaceutical company and device supplier must work together for several years to co-ordinate efforts in a collaborative manner, overcome related challenges and ensure the right steps are taken. Taking into account the number of biologics coming to market and the entry of biosimilars, we see an increasing number of biopharmaceutical companies in need of the same services currently provided across various geographic areas by a broad number of suppliers and specialists.

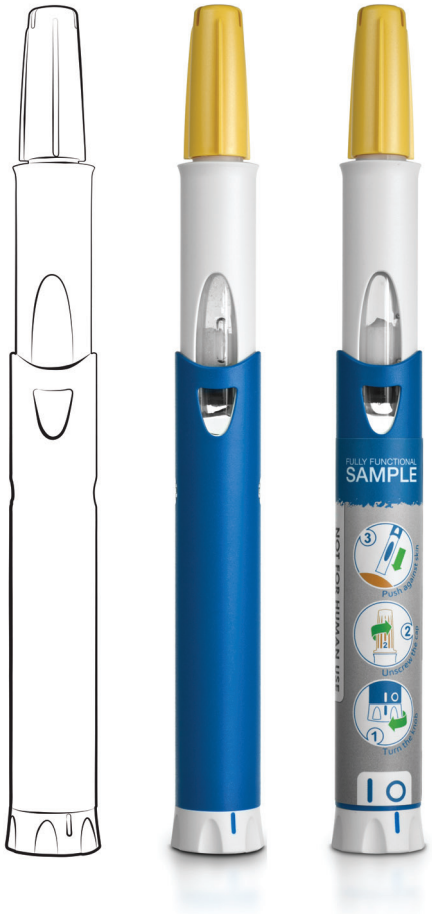

Figure 1: Taking an auto-injector from early design and moving it towards being ready for mass production.

Over the years, a few early-mover biopharmaceutical companies gained valuable experience producing their own devices, working with the suppliers of devices and by establishing a good rapport with companies providing related services. These early-movers have experienced first-hand the extensive number of pieces within the combination product puzzle that need to be put together to move forward with a device such as an auto-injector.

Some of the choices that need to be made by the biopharmaceutical company include selecting a suitable primary container, filling supplier, regulatory consultants, human factors engineering (HFE) experts, final-assembly integrators, and so on – all vital to the successful launch of a device. And the benefits of bringing an innovative device to market clearly make the investments of time, finances, and resources, worthwhile for biopharmaceutical companies.

Of all the choices that need to be made, selecting the right drug delivery device partner should be considered one of the highest priorities. And to support that selection process, visiting potential drug delivery device suppliers, looking at their track record and understanding their company culture are obvi-

Steven R. Kaufman
Marketing Director

T: +886 3 217 0303 (Ext 1400)
F: +886 3 217 4928
E: steven.kaufman@shl-group.com

SHL Group
#136, Kuo Sheng 2nd Street
Taoyuan
Taiwan

www.shl-group.com

ous, but it may also be helpful to focus on the following three areas:

1. DEVELOPMENT

Taking a product, such as an auto-injector, from early design and moving it towards being ready for mass production is a complex process. Development involves several stages (Figure 1) such as planning, design, engineering and process validation. As a project moves forward, having both the design and development teams in the same company is ideal, but not always possible. For example, the mechanical or technical design of the device may come from the device company, but the biopharmaceutical partner may choose to utilise an external industrial design company for appearance of the device. Involving another party may certainly add a new flavour to the uniqueness of the product, but doing so may also slow down the overall development of the device by simply adding to the growing number of voices involved in your project. At the end of the day, there are pros and cons to both approaches.

During the development process a delicate balance exists between providing device design features that fulfill end-user needs and making certain that device design is manufacturable. It is between these two areas that one has to find equilibrium; if they come into conflict with each other, the end-user needs should always have priority over the manufacturing process, so long as it does not affect the safety and effectiveness of the device. Finding a balance is the key. SHL, for example, works closely with customers to develop devices that complement the manufacturing process.

Frank Isaksson, General Manager, SHL Group, commented: "A robust design that truly fulfills end-user needs, which in combination with a reliable and repeatable manufacturing process is of paramount importance. The goal should be to continuously improve."

During the development stage we "cut steel" and start to verify the design of the device by performing extensive physical tests such as proving the mechanical sequence of the prototype devices. We review numerous stereolithography (SLA) models and other prototypes of device variations for the industrial design and work with patient groups to find a shape for our devices that patients like, but also a shape that can be produced and assembled efficiently. Over the course of the development process we ensure that the design of the device is robust and the functionality is there.

Several factors involved in the development process rely heavily on consistent and effective communication between all parties involved in the project. This is one of the reasons why SHL has chosen to pursue the strategy of maintaining all key capabilities, processes and services needed to develop and produce drug delivery devices in-house. By doing so we enhance speed to market and help drive projects forward, especially during the development of any device.

However, it is important to recognise that not all things can or should be brought in-house. At times there is a need to involve experts or consultants for guidance in areas such as: HFE, packaging materials, freedom to operate (FTO) opinions, and so on.

2. CAPABILITIES

Manufacturing advanced drug delivery devices requires an extensive range of capabilities. Tooling, molding, automation, assembly, and metrology are just a few of the many capabilities which are utilised. While maintaining such capabilities in-house is ideal, in some cases, it is just not practical due to the extensive capital investment that a drug delivery device supplier is required to make. In addition to purchasing and maintaining the required machinery, developing the expertise needed to run this equipment at an optimum level is challenging and takes time.

For these reasons, some drug delivery device companies, such as SHL, have followed a staged approach to incorporate key manufacturing capabilities in-house over several years (Figure 2) and many suppliers have been forced to accelerate this expansion in recent years due to an increase in orders and a desire to maintain a sufficient level of capacity.

Ideally, the majority of key capabilities and processes needed to produce a drug delivery device, and the services that support bringing that device to market, should be available in-house from primarily one supplier.

Tooling and automation are two areas that deserve special attention by biopharmaceutical companies as these capabilities are sometimes outsourced by device suppliers. Tooling is a significant expense in any drug delivery device pro-

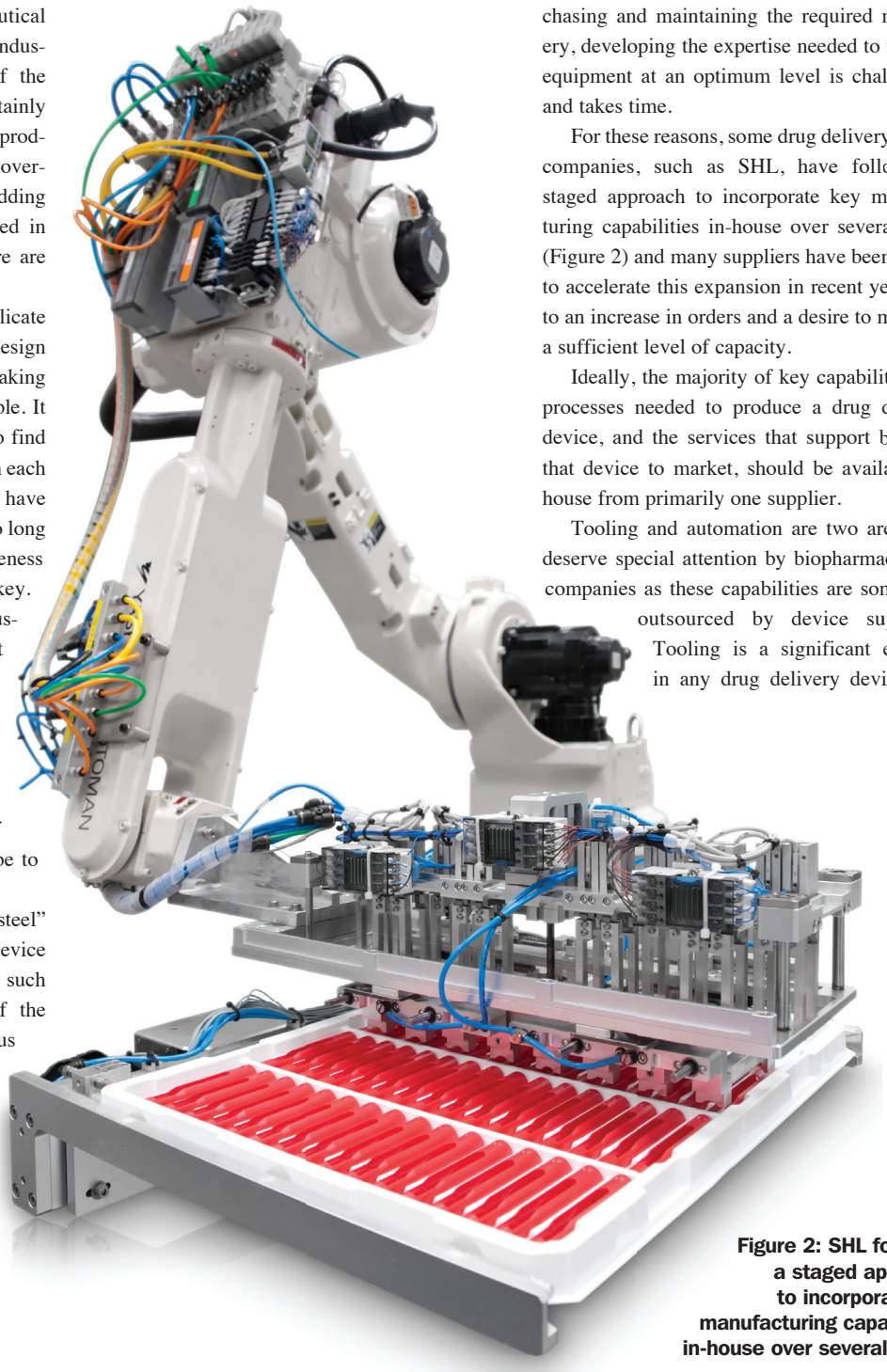

Figure 2: SHL followed a staged approach to incorporate key manufacturing capabilities in-house over several years.

gramme and lead times must be planned for carefully. For high volume projects multiple sets of tooling are needed for production, safety stock and risk mitigation. The intellectual property of new devices must be protected by strictly controlling who has access to these tools and related drawings. Taking tooling in-house is very costly for device suppliers, but can really help control quality and timeline concerns. In addition, having a capability like automation internally means that a device company can quickly build robust and flexible solutions for assembling and testing devices even while the design for the device is still being finalised. Certain tasks can be done in parallel and this will increase response times.

Metrology is another area that is vital to having a successful device project. For example, the dimensional precision of components is critical to ensuring a device can be properly assembled and that it functions as intended. Some devices have as few as three components, while others have more than 45. Metrology study for drug delivery devices is a specialised skill and related training is paramount as it takes years to develop a certain expertise in this field. For high-volume projects where greater metrology utilisation is needed, biopharmaceutical companies should ensure that their suppliers have enough of the right equipment, adequate numbers of well-trained staff and the resources to avoid potential bottle necks in this area.

"A ROBUST DESIGN THAT TRULY FULFILLS END-USER NEEDS IN COMBINATION WITH A RELIABLE AND REPEATABLE MANUFACTURING PROCESS IS OF PARAMOUNT IMPORTANCE. THE GOAL SHOULD BE TO CONTINUOUSLY IMPROVE"

Figure 3: In response to customer requests SHL now offers final assembly.

Spring production may be one of the last capabilities that people would think of ever in-sourcing, but in many ways the spring is the primary driver to successful injections performed by most auto-injectors. Some devices have three springs, each with their own unique requirements and some very specialised. If springs are too powerful they can cause breakage, if not powerful enough injections can stall. Certain springs are ideal for dealing with highly viscous biologics, others are more suited to ensuring that a more consistent force is achieved and that completeness of injection is not an issue because no one focused enough attention on this component. In addition to springs, there are several other metal components crucial to the functionality of a high-end drug delivery device. Ideally, these metal parts should be produced in-house in order to maintain optimum control and quality.

3. FINAL ASSEMBLY

Once the sub-assemblies of a device are produced the next step is integrating them with the biologic-filled primary container to create a completed combination product. Biopharmaceutical companies basically have three options to consider at this stage: do the final assembly themselves; outsource to a third-party; or find a drug delivery device partner that can provide this service.

In response to customer requests to provide final assembly of combination products, many device suppliers, including SHL, offer final assembly (see Figure 3), labelling and packaging services for devices to pharmaceutical and biotechnology companies. In the case of SHL, a specialised company was established as SHL Pharma, streamlining the production and distribution process for SHL Medical products, improving end-product quality and speed-to-market for customers. By integrating an additional piece of the supply chain, SHL can now offer a full one-stop-shop experience, from product design to distribution. Utilising our in-house automation expertise to produce customised assembly and test equipment is a significant advantage that helped SHL when setting up SHL Pharma operations in Florida, US.

"We were asked to vertically integrate final assembly into the range of services we offer our global biopharmaceutical customers. We started in North America, and will do the same in Europe and Asia," said Lucio Giambattista, President of SHL Pharma.

From a quality and regulatory point-of-view, final assembly facilities should be ISO13485 certified and registered with the US FDA as a

Figure 4: SHL's devices include a range of disposable and re-usable injectors with fixed or variable dosing, enhanced precision and the ability to accommodate high viscosities.

"IDEALLY, THE MAJORITY OF KEY CAPABILITIES AND PROCESSES NEEDED TO PRODUCE A DRUG DELIVERY DEVICE, AND THE SERVICES THAT SUPPORT BRINGING THAT DEVICE TO MARKET, SHOULD BE AVAILABLE IN-HOUSE FROM PRIMARILY ONE SUPPLIER"

drug establishment, qualified to handle and distribute pharmaceutical products. Additionally, they should conform to all other regulatory requirements for medical device and pharmaceutical packaging and distribution, as per 21 CFR Parts 820, 210 and 211. The staff involved at this level will have both drug and device expertise to help ensure the safe production of the combination product.

In addition, when a project will soon enter the final assembly stage there are a number of new considerations that also must be addressed, such as types of packaging, labelling, Instructions for Use (IFUs), inserts and more. Protective packaging not only holds the device for shipping, it helps to protect it if designed properly. Clear IFUs will also help to ensure that end-users know how to use a combination product properly. Drug delivery device suppliers should independently, or in co-operation with external experts, be relied upon for guidance in these areas.

ABOUT SHL

SHL is the world's largest privately-owned designer, developer and manufacturer of advanced drug delivery devices. With more than 2,000 staff globally, its primary design centres are located in Sweden and the US, and manufacturing centres are located in Asia. Final assembly, labelling and packaging services for drug delivery devices are offered at our newest facility in the US.

SHL supplies auto-injectors, pen-injectors and inhaler systems to global biopharmaceutical companies. Significant investment in R&D has enhanced our broad pipeline of "next-generation" drug delivery systems. These innovative devices include a range of disposable and re-usable (Figure 4) injectors with fixed or variable dosing, enhanced precision and the ability to accommodate high viscosities.

INSPIRING INTEGRATION

INSPIRING INTEGRATION & THE WAY FORWARD

Enhancing the convenience and ease of administering biologics is a proven strategy for biopharmaceutical companies to augment product differentiation and to compete in an increasingly competitive market. As patients become more familiar with various types of drug delivery devices they will expect suppliers of these devices to continue to innovate and to take their true user needs into consideration. Biopharmaceutical companies that proactively partner with experienced drug delivery device suppliers will be able to ensure that such needs are met and that projects can be completed on time.

The term "inspiring integration" is used internally at SHL to remind our staff of the importance of continually improving, and strengthening the in-house capabilities and services that we can provide to our biopharmaceutical partners. Controlling the number of companies, suppliers and individuals involved in the design, development, production and final assembly of your combination product will result in improved communication, enhanced time to market and stronger control of the supply chain.

INSPIRING TEGRATION

FINAL ASSEMBLY

SHL's final assembly, labeling and packaging services for our drug delivery devices improve end-product quality and speed-to-market for customers.

PDA Parenteral Drug Association

VISIT US AT:
The Universe of Pre-Filled Syringes & Injection Devices
Oct. 15-16th, Las Vegas Booth #103

SHL GROUP

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Aptar Stelmi

AN INTERVIEW WITH MR OLIVIER FOURMENT, PRESIDENT, APTAR PHARMA

In July 2012, Aptargroup acquired Stelmi, which is now part of Aptar Pharma Prescription Division. In this interview with ONdrugDelivery Magazine, Olivier Fourment, President, Aptar Pharma, discusses the acquisition which he says expands the portfolio Aptar provides to the pharma industry and will reinforce Stelmi's strong innovation capabilities and high growth potential in the field of elastomeric closures for parenteral packaging.

Q: What were the aspects of Stelmi that made it a good fit with Aptar Pharma?

Aptar Pharma is the world-leading supplier of nasal spray pumps for allergic rhinitis, nasal decongestants and nasal salines as well as metering valves used in pressurised aerosols for asthma and COPD. Stelmi is a market leader specialised in elastomer primary packaging components for injectable drug delivery.

Our primary driver in the acquisition of Stelmi was the attractiveness of the injectable drug market. As you know, this is a very large market segment with almost 30% of drug sales. It is very dynamic: its growth is twice that of the overall drug market thanks to biotech drugs that represent 50% of all new drugs approved. Aptar Pharma devices are not used very often for biotech drugs, which are mostly based on large molecules. Dispensing these drugs via nasal sprays or pulmonary aerosols is difficult, so they often need to be injected.

So the acquisition of Stelmi gets us into a new market that complements our core market and which we see as growing long-term in the future. In addition we believe Stelmi is an excellent company with strong innovation capabilities and high growth potential.

Q: Can you tell us about the talks leading up to the acquisition, and describe the acquisition process itself? What was your experience? What lessons did you learn?

First of all, let's go back in time a little bit. We had been looking at Stelmi as a potential acquisition for Aptar Pharma for several years because it fitted with our long-term growth strategy. It is a company that we targeted and had conversations with. When the owners of Stelmi (a family-owned company at that time) decided to sell, they contacted several companies including Aptargroup to start discussions, and then moved on to negotiations with a short list. The timing was perfect for us so the whole process took only a few months including mandatory due diligence. The use of specific secured web-based repositories to access and check the various due diligence documents, information and data contributed to speeding up the whole process, to the benefit of both parties who were willing to close the deal. One of the key take-home messages we learnt from this venture is that to proceed successfully and swiftly, you need to get to know all the decision-makers on the sales side, and keep regular and personal contact with them.

Q: How will the combined companies be structured in terms of name/branding, facilities, geography, management, product/service offering, and financials?

Stelmi is in the process of being renamed Aptar Stelmi and we are in the middle of a full rebranding operation. This process will be implemented in steps and include modification of all documents and communication media. As a first step we are going through a transition period with the objective of properly informing our employees, customers, suppliers and partners. Some communication materials such as printed documentation and the website will be modified in a second step.

The organisation of Aptar Stelmi, which has more than 550 employees, remains unchanged although Mr Jean Jacques Rumpler, former CEO, has retired as planned with myself taking over as President [*Mr Olivier Fourment is also President of Aptar Pharma*]. Aptar Stelmi is a specific organisational unit within Aptar Pharma Prescription Division. The R&D and manufacturing sites as well as the product and service offering remain unchanged, though technical synergies and multiple best practice exchange will be explored and leveraged. I think this company has been very well managed and the succession is well in place. We have great confidence in the Aptar Pharma and Aptar Stelmi management teams.

Q: What is Aptar Stelmi's core offering to the industry going to be?

Aptar Stelmi's core offering remains unchanged: elastomer primary packaging components for the pharmaceutical and biotechnology industries worldwide, as well as for parenteral drug delivery device manufacturers and their partners. The product portfolio includes a variety of ready-to-sterilise and sterile vial and infusion stoppers; plungers, needle shields and tip caps for prefilled syringes and cartridges; and a set of closures and other elastomeric primary components. Aptar Stelmi offers a panel of proprietary elastomer formulations and ultra-clean options incorporating specific finishing treatments and cutting-edge in-process visual controls. The latter represents one of the many key differentiating factors of Aptar Stelmi. In addition Aptar Stelmi will enhance its offering to customers

by leveraging Aptar Pharma's strengths in analytical and regulatory sciences. Both companies possess complex drug delivery device technologies and have experience with challenging regulatory environments. Thanks to Aptar Pharma's global presence and capabilities, Aptar Stelmi will expand its technology expertise, offering and geographical reach.

Q: How do you expect to grow Aptar Stelmi's business?

Currently Aptar Stelmi's business is split 70% in Europe / 30% outside of Europe. However, some Aptar Stelmi customers in Europe export their drug products outside of Europe as well (just like Aptar Pharma customers). One strategic axis for growth is certainly expansion out of Europe into geographies which include the US and Asia, where Aptar Pharma has a larger commercial footprint and long experience (we were the first supplier in our category to set up a manufacturing facility in China more than 15 years ago). We will optimise ways to secure the supply of synthetic rubber materials given that both organisations use these materials and part of our supplier base is common.

Q: What are the advantages of the acquisition for the industry (that is, for your existing customers and for new, prospective clients)?

This transaction brings a large, global player with proven abilities and credibility to the market. Aptar Stelmi will have the full support and leverage of the Aptar Pharma organisation which can support future growth, especially in regions outside of Europe. In addition the industry will benefit from our combined strong culture of market-driven technology innovation fostered in both organisations.

Q: What are the commercial/financial advantages for Aptargroup and Stelmi?

First and foremost we plan to leverage the Aptar Pharma brand name to grow the business with existing and prospective customers of Aptar Stelmi on a global basis. Secondly, Aptar Stelmi and Aptar Pharma have complementary customer bases hence we expect the acquisition of Stelmi to help us grow both customer bases and business. We will look carefully at best commercial practices on both sides to align and enhance our service to customers wherever we can.

Q: Is there any crossover from Stelmi with Aptar's existing pulmonary/nasal drug delivery business, and if so what will be the advantages for Aptar clients?

Elastomer components, known as seals, are critical to Aptar Pharma's customers. These have a key role within an aerosol delivery device, with sealing functions and chemical interactions, and particularly in pressurised metered-dose inhalers (pMDIs). Development and manufacturing of elastomer seals are strategic and so Aptar Pharma has historically integrated these activities into the business, while our competitors rely on external suppliers. With Aptar Stelmi being an expert in elastomers, we will leverage technical synergies and cross fertilisation in this area. This is going to be an additional benefit for our clients in terms of elastomer formulation and manufacturing capabilities.

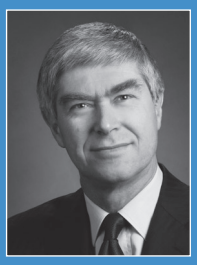
Q: How does this acquisition fit in with general trends in the drug delivery / prefilled syringes sector?

We expect it to be the springboard for further creativity and innovation. Historically, both companies have created a competitive advantage out of innovation. Aptar Pharma is an established expert in complex drug delivery devices and has a track record stretching back for more than 60 years. We hold a portfolio of more than 600 patent families. We expect a number of technical synergies including marrying elastomer, plastic and metal technologies, including novel surface treatments and innovative process technologies. These will help us optimise existing products and create new products for the benefit of our clients and their patients. The issues of extractables/leachables, component lubrication, and optimised user-device interface are a few examples of challenges we understand at Aptar Pharma. We hope that we can turn these challenges into opportunities with Aptar Stelmi. Certainly the prefilled syringe components market, which is one of the faster growing end-markets, is a point of focus in terms of growth. We are excited by Aptar Stelmi's solid pipeline of products and customer projects. In addition we have some very interesting technical ideas that can be used to innovate in this field. These include opportunities nurtured within Aptar Pharma, and some that we have developed with our strategic partner Oval Medical in the area of auto-injectors.

Q: What does the future hold for Aptar Stelmi?

This transaction is not based on cost synergy because it is a growth synergy venture.

The future is bright for our new combined organisation given the profile and dynamics of the market of elastomer primary packaging components for injectable drug delivery and the historical success of both organisations. This is an exciting time for us to define the appropriate strategy and combine the strengths of both organisations to make it a global success. Aptargroup's core values and rules of leadership are certainly a great tool for the management team to create the right spirit and environment for a cohesive integration.



Olivier Fourment
President, Aptar Pharma

Olivier Fourment has been the President of Aptar Pharma since 2008. From 2000 to 2008, he was Co-President of the company's Valois Group and President of the Valois Pharma division. Prior to 2000, Mr Fourment held various sales and marketing positions within the Valois Pharma division. He is a member of the Aptar Executive Committee and a Vice-President of Aptargroup. Between 1982 and 1984, Mr Fourment was Area Sales Manager with Sacilor and, from 1979 to 1981, he was Assistant to the French Trade Commissioner, in Atlanta, GA, US. Mr Fourment is a graduate from ESCP Business School and completed an Insead General Management Course in 1999.

Aptar Stelmi

STELMI

WE'VE CHANGED OUR NAME, BUT NOT OUR COMMITMENT

aptarstelmi.com

Delivering solutions, shaping the future.

CHARTING THE DEVELOPMENT OF A TRUE DIFFERENTIATED PORTFOLIO OF PARENTERAL DELIVERY SYSTEMS

In this article, Alan Shortall, Chief Executive Officer, Unilife Corporation, describes how the company has developed a portfolio of primary drug containers and advanced delivery systems, which it believes is one of the most expansive, market-driven and differentiated in the industry to enable or enhance the administration of injectable therapies.

Unilife Corporation follows a new paradigm for injectable drug delivery. The US based company is dedicated to addressing a series of converging market trends to help pharmaceutical companies optimise patient care, improve therapy compliance and differentiate their drugs against competitors to build or protect market share. Emerging and unmet market needs where Unilife has developed innovative device solutions include needlestick prevention, the efficient reconstitution of lyophilised drugs, the subcutaneous bolus injection of large-volume doses and the intuitive self-administration of injectable therapies outside of healthcare facilities.

Technology platforms now established under the Unilife device portfolio include prefilled syringes with integrated safety features, reusable and disposable auto-injectors, drug reconstitution delivery systems, bolus injectors for large and specialised delivery systems.

Combined with a dynamic business structure, advanced operational capabilities and an open architecture framework for component materials, this broad, highly innovative portfolio represents a compelling opportunity for pharmaceutical companies seeking to enable and enhance the clinical development, regulatory approval and lifecycle management of their injectable therapies.

PREFILLED SYRINGES WITH INTEGRATED NEEDLE RETRACTION

Unilife has developed a comprehensive platform of prefilled syringes for the delivery of a broad range of liquid stable and lyophilised drugs and vaccines. The Unifill® portfolio represents the world's first and only known range of prefilled syringes with automatic needle retraction features fully integrated within the glass barrel. All Unifill syringes are designed for simple, intuitive, one-handed use by either healthcare workers or self-injecting patients, and can be customised to specific customer, drug or patient needs.

Each device draws upon a highly proprietary combination of features including:

- An automatic and fully integrated needle retraction mechanism
- A series of audible, visible, and tactile indicators signal end of dose delivery and the activation of the needle retraction mechanism
- Operator-controlled withdrawal of the needle directly from the body into the barrel of the syringe to virtually eliminate secondary infection risks such as aerosolisation
- Easy and intuitive steps of use to maximise user acceptance and preference
- Seamless integration with drug fill-finish lines
- Pharmacopoeia-compliant materials within the drug-fluid path
- Complete needle containment and automatic lock-out features to prevent re-use or re-exposure of the contaminated needle and encourage compact, convenient disposal.

Unifill syringes offer several significant advantages over conventional, commodity-style prefilled syringe technologies. To comply with needlestick prevention laws in the US, Europe

Alan Shortall
Chief Executive Officer

Unilife Corporation
250 Cross Farm Lane
York
PA 17406
United States

T: +1 717 384 3400
E: info@unilife.com

www.unilife.com

and other regions, pharmaceutical companies have traditionally purchased ancillary safety devices that are attached on to a standard prefilled syringe by means of a secondary assembly operation after filling. In addition to the extra steps and costs associated with their secondary attachment, these devices can lead to an increase in packaging, transport and storage costs by up to 60-70% due to the bulky size and weight of the final product.

Prefilled syringes utilising ancillary safety devices may also require additional steps which can often be non-intuitive to the end user. Unifill syringes eliminate the need to purchase and attach ancillary safety products, to help streamline the fill-finish process and reduce packaging costs. The elegant, unique and highly compact design of the Unifill syringe, compared with prefilled syringes marketed with ancillary safety products, also creates significant opportunities for a pharmaceutical company to differentiate their therapy against brand-name, generic or biosimilar rivals.

Many conventional needlestick prevention technologies also require operators to activate the safety mechanism manually, only after the contaminated needle has been removed from the body of the patient. Many needlestick injuries occur either before or during activation of the safety mechanism, or after disposal when a safety mechanism has not been properly activated.

Needlestick prevention laws, such as those in the US, require every healthcare facility to evaluate, select and purchase devices that can eliminate or minimise the risk of occupational exposures to blood-borne pathogens. With devices utilising automatic (passive) and integrated safety systems commonly preferred for use, Unifill syringes can help pharmaceutical companies turn needlestick compliance into a competitive market advantage.

THE UNIFILL PORTFOLIO CONSISTS OF THE FOLLOWING PRODUCTS:

Unifill Syringe:

The Unifill syringe (see Figure 1) features a staked (fixed) retracting needle, and is designed primarily for use with liquid stable drugs. In independent, user acceptance and preference studies with healthcare workers and target self-injection patient groups, operators reliably administered the full dose, activated the safety mechanism and retracted the needle into the barrel. Participants found the Unifill syringe and associated procedure to be easy to learn and easy to use, even on the first attempt. The device received strong levels of user preference over previously used syringes, with highly positive levels of feedback relating to the syringe design, the retraction mechanism, the audible, tactile click and the overall injection experience.

Figure 1: The Unifill Syringe.

Initial production of the Unifill syringe is underway at Unilife's US FDA-registered manufacturing facilities in York, PA, US. To facilitate the development process with these and other pharmaceutical customers, Unilife has recently completed the development of a comprehensive Extractable Material Data Package (EMDP). This technical package of information enables pharmaceutical customers to qualify the Unifill syringe as a primary container system and shorten the development cycle time for the use of the device with target injectable therapies. The EMDP allows pharmaceutical customers to design their leachables studies rapidly to support drug stability and regulatory activities for the drug-device combination product.

Companies seeking information regarding the Unifill syringe, or to order initial quantities for device evaluations, stability and compatibility studies or fill-finish line validation are encouraged to contact Unilife.

Unifill Select:

The Unifill Select (Figure 2) is the world's first and only known glass prefilled syringe that incorporates an attachable needle with integrated retraction. The device enables the user to choose from a selection of needle gauges or lengths for attachment onto the syringe at the time of injection. The syringe may be filled with either a liquid stable drug or vaccine, or a diluent to reconstitute and deliver a lyophilised drug supplied in a vial. The Unifill Select is available for commercialisation with interested pharmaceutical partners seeking to utilise the device with target injectable drugs and vaccines.

AUTO-INJECTORS

Traditional auto-injector devices are relatively large in size, as they must accommodate various mechanisms to enable the depression of the prefilled syringe for needle insertion into the body, the injection of the dose, and either the withdrawal of the syringe back into the device

Figure 2: Unifill Select – the world's first and only known glass prefilled syringe that incorporates an attachable needle with integrated retraction.

Figure 3: Each device within Unlife's proprietary range of auto-injectors is compact, intuitive to use and can be customised.

or the extension of a sleeve to cover the needle. The large size of some auto-injectors can restrict their portability, obstruct intuitive use and handling with some patients, and increase disposal volumes. They also lack true end-of-dose indicators to alert patients when the full dose has been delivered, potentially causing dose wastage or reducing therapy compliance rates.

Unilife has developed a full platform of auto-injectors (Figure 3) that are designed for use with the Unifill syringe. Each device within this proprietary range of auto-injectors is compact, intuitive to use and can be customised to address specific customer, drug or patient needs. They represent the world's first and only known auto-injectors with true end-of-dose indicators, with an audible, tactile click signaling the delivery of the full dose and the retraction of the needle into the barrel of the Unifill syringe. The potential risk of a needlestick injury occurring after the use of the device is virtually eliminated.

Products developed within this portfolio include:

Rita™ Disposable Auto-Injector:

Rita is a disposable auto-injector that is designed to inject the prefilled dose from a single Unifill syringe. Following the removal of the cap and the placement of the device against the skin, the operator pushes a single button to inject the dose. Rita is more compact in size than many other marketed auto-injectors for improved patient portability, intuitive handling and convenient disposal. In addition to there being no visible springs or mechanisms, the needle is hidden from view until the completion of the injection when it can be viewed in its retracted state through a window on the side of the barrel.

The true end-of-dose indicators (audible, tactile click) associated with the Unifill syringe can also help to minimise potential drug wastage and optimise therapy compliance. The Rita Auto-Injector is available for commercialisation with pharmaceutical partners seeking to utilise the device for use with their target injectable drugs and vaccines.

Lisa™ Reusable Auto-Injector:

Lisa represents arguably the most advanced, fully automated and patient-friendly reusable auto-injector system ever developed. The electro-mechanical device utilises a single activation button for the automatic removal of the needle shield and injection of the dose. Operators can select the speed of dose delivery for their comfort, with LED indicators instantly relaying key information during each stage of use. When used with the Unifill syringe, Lisa is the first and only known reusable auto-injector that can protect patients from the risk of needlestick injury when removing a used syringe from the device.

DRUG RECONSTITUTION DELIVERY SYSTEMS

The supply of an injectable drug in a lyophilised (freeze-dried) state can help to enable or fast-track its commercialisation and approval. Many biologic drugs are also unable to be prefilled into a liquid-stable format due to their molecular complexity. As a result, an increasing number of novel drugs and vaccines are now being approved by regulatory agencies in a lyophilised format for reconstitution at the point of delivery. Some pharmaceutical companies are also developing injectable therapies that require mixing of two liquid-stable drugs at the point of delivery.

Lyophilised drugs and vaccines have traditionally been supplied in a vial or ampoule for reconstitution at the point of delivery. Reconstitution from a vial or ampoule can require more than a dozen steps of use, with the required level of complexity making lyophilised drugs largely unsuitable for patient self-administration.

In recent years, some pharmaceutical companies have begun to develop or market certain drugs for use in a dual-chamber prefilled syringe format. A dual-chamber prefilled syringe can

Figure 4: The EZMix dual or multi-chamber prefilled syringe is a safe, simple and efficient system for the reconstitution and delivery of injectables.

contain either a lyophilised or liquid-stable drug in one pharmacopoeia-compliant container, and another liquid-stable drug or diluent in a second container. Operators are required to undertake several steps to mix or reconstitute the drug combination so that the injectable therapy is ready for administration. The process of reconstitution using some traditional dual-chamber prefilled syringe technologies may also compromise drug sterility or require the use of secondary vent filters.

EZMix™ Dual or Multi-Chamber Prefilled Syringe:

Unilife has developed the EZMix dual or multi-chamber prefilled syringe (Figure 4) to serve as a safe, simple and efficient system for the reconstitution and delivery of injectable therapies. An innovative and proprietary reconstitution technology allows healthcare workers or patients intuitively to mix together a combination of liquid or lyophilised drugs with minimal steps of use. The process of reconstitution can occur without compromising drug sterility or the use of secondary venting.

The EZMix syringe utilises the Unifill platform of fully integrated and automatic needle retraction features to virtually eliminate the risk of needlestick injuries, prevent device re-use and encourage convenient, safer disposal. Companies seeking information on how EZMix can be customised to enable or enhance delivery of injectable therapies requiring reconstitution or mixing at the time of use are asked to contact Unilife.

BOLUS INJECTORS

A significant number of drugs within the clinical pipeline of pharmaceutical companies are biologics, such as monoclonal antibodies, that are being targeted for subcutaneous administration. In many cases, the molecular complexity of these drugs makes them too viscous for formulation in dose volumes of 1mL or less that would typically be used for a prefilled syringe.

Unilife has developed a portfolio of bolus injectors (Figures 5 and 6) to meet the delivery needs of these large dose volume drugs. This family of wearable, disposable devices is suited to the subcutaneous delivery of drugs that require dose volumes between 1mL and 30mL. Unilife's bolus injectors utilise a primary drug container made of standard materials and are designed for integration into standard filling lines.

Every Unilife bolus injector is not only very compact, sleek and elegant in design, but incorporates human factor engineering so that it can be tailored to address the specific needs of the target patient population. External customisation options available to a customer include the contoured shape of the device, the number or position of activation buttons and various colour configurations.

Figure 5: Unilife's family of wearable, disposable bolus injectors for subcutaneous delivery of dosages between 1mL and 30mL.

The steps of use for a Unilife bolus injector are highly intuitive for patient self-administration. After removal of an adhesive liner from the bottom of the device, it is placed onto the body. An on-body interlock mechanism prevents accidental initiation of dose delivery from occurring before the operator is ready. After pushing the button when the patient is ready to start the injection, a soft indwelling cannula is automatically inserted into the subcutaneous layer to administer the dose with minimal pain or irritation. The device is pre-programmed as designated by a pharmaceutical customer to deliver the dose automatically at the preferred rate and duration.

Figure 6: A Unilife disposable bolus injector shown with a US Quarter Dollar coin for scale.

An electronic user interface conveys key information to the patient, with tones and colours indicating the status of the device during each stage of dose delivery. Furthermore, no sharp is exposed during any stage during usage of the device, virtually eliminating the risk of needlestick injury to the patient or those downstream following its compact, convenient disposal.

The Precision-Therapy™ range of bolus injectors is designed for use with bolus-based therapies that require short or long duration injections. The Flex-Therapy™ range of bolus injectors is designed for use with rate-based therapies that require infusion over a longer duration of time where the delivery rate is controlled for hours or days. Unilife has begun to supply its bolus injectors to a number of interested pharmaceutical companies for evaluation with their injectable therapies. Pharmaceutical companies seeking further information on the range of bolus injectors should contact Unilife.

SPECIALISED DELIVERY SYSTEMS

There are many acute and chronic conditions with high prevalence but without effective treatment options. Many pharmaceutical companies have several early-stage yet promising molecules in their clinical pipelines that have the potential to redefine treatment for these conditions. Examples include the localised delivery of injectable therapies targeting specific organs of the human body such as the eye, ear or brain.

However in many cases, due to the novel nature of the therapy, application or procedure, these novel molecules can require a specialised delivery system to enable their commercialisation and approval. There are also many approved drugs utilising conventional device technologies that limit their clinical efficacy and hence provide for sub-optimal clinical outcomes. Such therapies and drugs can significantly benefit from specialised delivery systems.

Proprietary platforms being developed by Unilife include specialised devices for targeted organ delivery, low-dose delivery systems and implant-deployment systems. These devices can be leveraged to enable the localised or targeted delivery of a novel drug to areas such as a targeted organ or the controlled deployment of a drug depot via an intravitreal or intraocular injection. Companies seeking innovative device solutions to help enable or enhance the delivery of their novel injectable therapies should contact Unilife.

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EZ-FILL™ VIALS & CARTRIDGES: A SOLUTION FOR CLEAN & STERILE PHARMA GLASS CONTAINERS READY TO BE FILLED

In this paper, Andrea Cecchetto, PhD, Product Manager, EZ-fill™, and Andrea Salmaso, PhD, QA, Regulatory & Compliance Manager, both of Nuova Ompi – Stevanato Group, describe how the company has extended its EZ-fill™ syringe business to a full range of vials and cartridges.

The first ready-to-fill containers (syringes) were launched with success in the pharmaceutical market in the 1970s, as a solution for clinical phases. During the subsequent decades, nobody thought to develop a different type of ready-to-fill container, such as vials or cartridges, because nobody ever defined a standard to do it. Building on the successful of its EZ-fill™ syringes business, Nuova Ompi (the main company within Stevanato Group's Glass Division), has developed a standard to extend the ready-to-be-filled-containers range to vials and cartridges.

The EZ-fill™ Vials & Cartridges solution (see Figure 1) is a particularly innovative option because it allows pharma companies to benefit from its various advantages: lower time to market, higher quality and safety, total cost of ownership (TCO) reduction, and process standardisation and filling flexibility providing a common filling platform for vials, cartridges and syringes.

The manufacturing development process for new and existing drugs, especially for the emerging biotech needs and small-batch needs such as orphan drugs, is very often in a stand-by phase or it is frequently delayed due

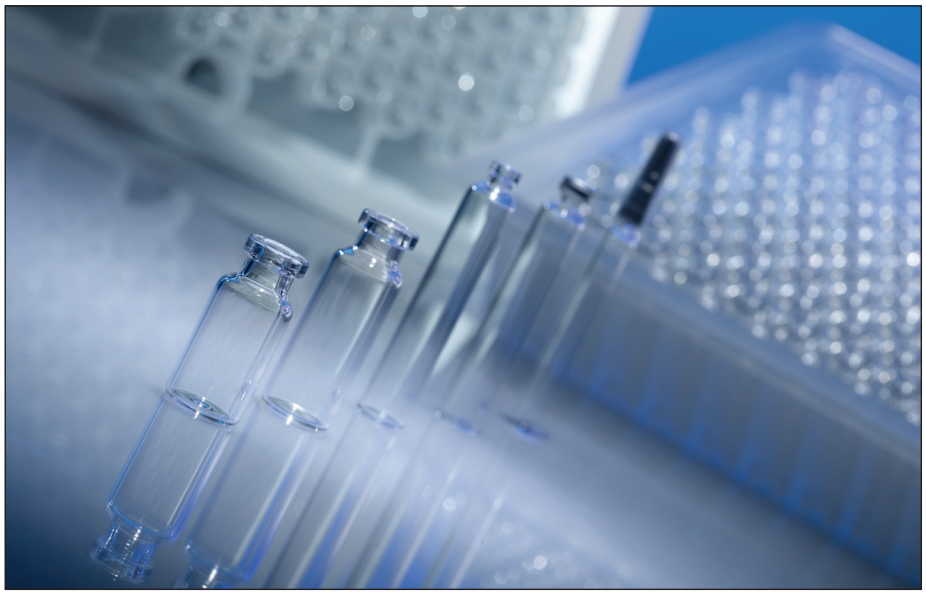

Figure 1: Vials, cartridges and syringes in an EZ-fill™ nest & tub format.

Dr Andrea Cecchetto
Product Manager EZ-fill™

Dr Andrea Salmaso
QA, Regulatory & Compliance Manager

Nuova Ompi – Stevanato Group
Via Molinella, 17
35017 Piombino Dese (PD)
Italy

T: +39 049 9318111
F: +39 049 9366151
E: nuovaompi@stevanatogroup.com

www.nuovaompi.com
www.ez-fill.com

to the limited availability of filling options and formats at existing aseptic lines.

The effective availability of containers for direct filling operations could represent a consistent reduction of the time-to-market, cutting cost related to the manufacturing process.[1]

Until a few years ago, only syringes were available on the market in nest&tub in a steribag: a configuration that ensures a standard machinable format able to keep particle content below limits assuring sterility. The lack of other containers in this format inhibited pharma companies from developing expensive treatments. The lack of different types of sterile containers does not always allow very specific production like clinical trials or orphan products and so it implies a huge investment in capital for the washing and the sterilisation of the container itself, resulting in a consistent TCO and increased time-to-market.

For this reason, for several years, Stevanato Group, among the top leaders in the glass-tubing converter market, has been developing a new standardised production process to extend the existing "ready to be filled" concept (launched in 2007 for the syringes) to a wide range of glass containers for pharmaceutical use, including vials and cartridges: *EZ-fill™ Vials & Cartridges*.

This kind of solution provides clean, sterile, not pyrogenic and ready-to-be-filled glass containers for pharmaceutical use, different from syringes, to be used in injection devices, simplifying and standardising the traditional production process. In fact, with *EZ-fill™ Vials & Cartridges*, pharma companies and CMOs can outsource even more non-core manufacturing, thereby reducing overall costs and concentrating resources on added-value core activities, such as aseptic finish and filling.

The development of the EZ-fill™ project represents a synchronised effort between two of Stevenato Group's divisions, Glass and Engineering, combining glass-forming technology with engineering experience. In fact, the involvement of SPAMI (representing the Group's Engineering Division), specialised in the design, manufacture, installation and after-sales support of high-speed precision machinery for the production

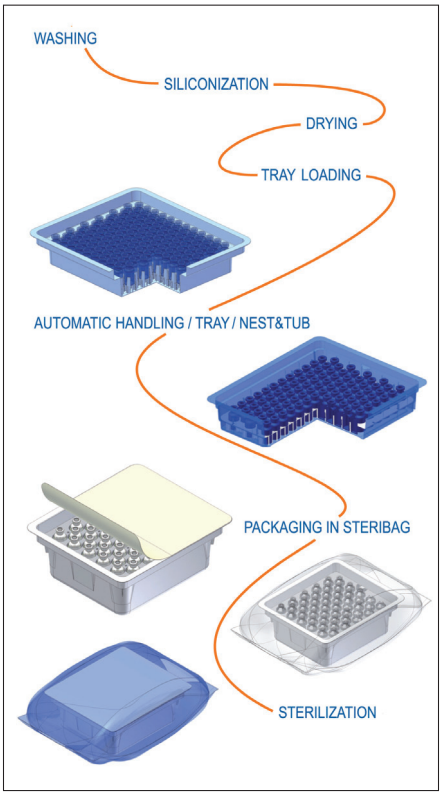

Figure 2: Schematic workflow of the EZ-fill™ process.

and control of glass containers as well as vision inspection systems, provided the technological support during the project. The application of SPAMI technology guarantees the 100% cosmetic control on vials and cartridges and no glass-to-glass contact.

Moreover, a very important point to consider is that the concept has been approved and developed with the main manufacturers of fill/finish machines and it can therefore be easily integrated into the already existing pharmaceutical manufacturing filling lines installed. Every one of them may have format change parts already fully suitable and industrialised for the EZ-fill™ concept.

Machine manufacturers have been involved in the development of the packaging design and concepts for the proper handling and machine-ability with a wide range of fill/finish units. In addition to that, *EZ-fill™ vials and cartridges* can be easily managed in clinical trials and small batch productions thanks to new machines developed by the main filling machine manufacturers, designed to be used in sterile room applications, in accordance with cGMP regulations; changeover to different sizes is carried out quickly, easily and without tools, by exchanging complete sets of format parts.

EZ-FILL™ VIALS & CARTRIDGES PROCESS

The *EZ-fill™ Vials & Cartridges* process can be described in the following phases (see Figure 2):

- ***Incoming materials:*** vials and cartridges are supplied to the EZ-fill™ area (ISO7 and ISO5 under laminar flow)
- ***Washing:*** vials and cartridges are washed into the washing machine with WFI (Water For Injection)
- ***Siliconisation:*** cartridges are optionally siliconised with high-performance layer distribution process
- ***Heating:*** drying and depyrogenation in an oven. The cycle is optimised in order to reduce the timing and assure an optimal drying
- ***Packaging:*** the final steps place the vials and cartridges into one of two final packaging solutions: either the Tray, a one-piece box (Figure 3); or Nest&Tub (Figure 4), which is the same standard nest&tub format as the prefilled syringe.

Both are sealed with a Tyvek® lid, packaged in steribags and case-pack allowing for sterilisation. Key attention is given to the cleanliness of the packaging components as to the production of the glass container itself. Final configuration includes packaging in pallets.

- ***Final sterilisation:*** filled tubs/tray in steribags are sterilised by Ethylene Oxide (EtO). EtO sterilisation is mainly used to sterilise medical and pharmaceutical products that cannot support conventional high-temperature steam sterilisation. This process is completed by aeration. (Further developments/validation of alternative terminal sterilisation methods are ongoing, as requested from most of the top pharmaceutical companies.)
- ***Capping:*** cartridges can optionally (upon customers' requests) be pre-capped with selected rubber formulations.

Nuova Ompi has already launched an EZ-fill™ industrial process, the second step after implementation of pilot process, and expansion of the same area.

The EZ-fill™ process is GMP oriented, already approved by several top global pharmaceutical companies.

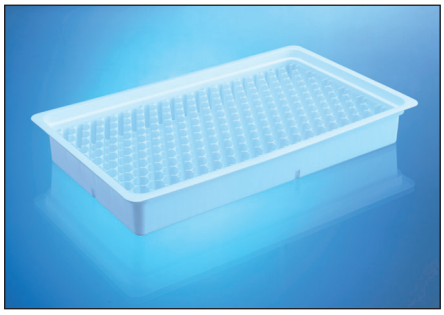

Figure 3: Tray configuration.

Figure 4: Nest & tub configuration.

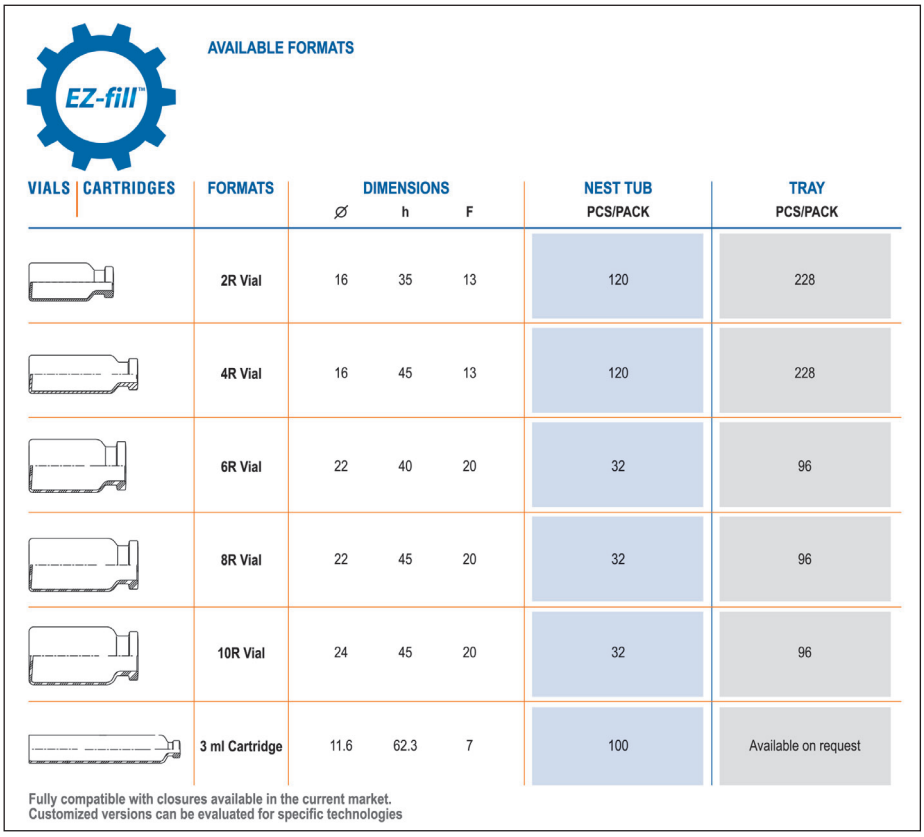

Figure 5: Available EZ-fill™ Vials & Cartridges formats in tray and nest & tub configuration.

TCO REDUCTION FOR PHARMA COMPANIES

In a traditional manufacturing approach using a bulk vial or cartridge, there is the need to wash and depyrogenate them before the filling and closing by capping and crimping. With EZ-fill™, within the pharma environment, there is still the filling and closing but the washing and depyrogenation tunnel are no longer required.

A further strength is keeping compatibility with existing equipment (minimum change) and filling lines but also process simplification at pharmaceutical site and reduced costs for production equipment (washing line, depyrogenation tunnel, etc). Other strengths are a faster validation time, a saving on production area size, a saving on qualification operations and validated state management.

The result is that the EZ-fill™ approach has positive impact on TCO. Specifically this is seen in:

- Cost of Packaging: at industrial quantities, same model of syringes
- Capital Investment: the concept allows a significant reduction of the capital investments because implementing the EZ-fill™ approach means less machines, less space, less clean rooms, less utilities, etc.
- Cost of Operations (for the pharma company): for the same reason this concept lowers costs associated with the acquisition, validation and maintenance of traditional lines (fewer operators, fewer variable costs, less maintenance, etc.)
- Cost of Non Quality: considerable reduction of the breakage rate expected at pharma company and prevention of recall phenomenon in the market.

FLEXIBILITY

Another crucial advantage of the EZ-fill™ model is its flexibility. Fill/finish "combo" machines able to manage vials, cartridges and syringes in a standard nest&tub format (EZ-fill™ platform) are already available on the market.

FILL FINISH FLEXIBILITY

Combo machines carry out the following workflow: automatic steribag opening, surface decontamination, Tyvek® removal and a system to extract the glass container from the nest in order to process them in a segment transport system line in a conventional filling unit. The use of these kinds of machines allows an immediate saving and an optimisation of manufacturing operations and avoids the need to use several machines for each container. Therefore, the EZ-fill™ approach is particularly interesting for CMOs and all pharma companies that need to support customers with different containers from early clinical trials up to the product launch with the additional significant advantage of saving time.

TRAY OR NEST&TUB

The option of two different packaging formats – tray or nest&tub (shown in Figures 3 & 4, respectively) – is also a real advantage. On one hand, the tray sealed with Tyvek® lid and protected by a steribag is the ideal solution for existing linear filling line. On the other hand, the nest placed inside a tub (sealed with Tyvek® lid and protected by a steribag) is suitable for existing x-y syringe filling processes. The nest&tub format is becoming the new industry standard that could be sublicensed or subcontracted to the other pharma primary packaging producers in order to have a unique format solution.

In summarising (and shown in Figure 5) the actual portfolio of *EZ-fill™ Vials & Cartridges* available comprises: the 3 mL cartridge in nest&tub format, and the 2R, 4R, 6R, 8R and 10R vials both in nest&tub and in tray configuration. More options are available upon request.

CONCLUSION

The extension of the EZ-fill™ range to different types of glass containers besides syringes has been permitted thanks to the strong exchange of information that Nuova Ompi had with all the leading machine manufacturers. It represents an example of direct co-development of a project by merging the skills of a manufacturer of glass containers for pharmaceutical use with the experience on aseptic filling with all the best known manufacturers of pharmaceutical equipment, in order to provide a high-quality product.

Thanks to all these synergies and the implementation of innovative approaches, Stevanato Group now offers the market an extended range of clean, sterile, not pyrogenic glass containers, ready to be filled, with the following characteristics:

- WFI-washed glass containers, using a validated washing and drying cycle and a set of utilities and procedures for fast switch between different types of containers and formats
- Glass containers arranged in innovative nest and tub which will prevent, as for the syringes today, the glass-to-glass friction, for the highest cosmetic quality of products
- Packaging operations in Class ISO5/ISO7 environment
- Packaging units subjected to a validated EtO sterilisation process.

REFERENCE

1. *Rybka-Golm R, "Small Batch Filling Requirements of Hospitals". Hospital Pharmacy Department Charité Universitätsmedizin Berlin, 2010.*

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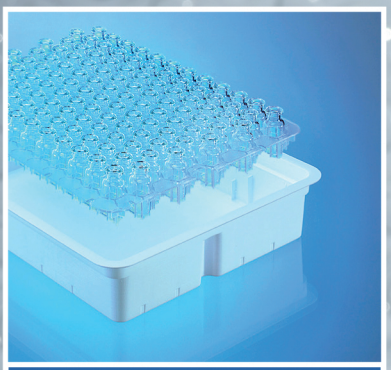
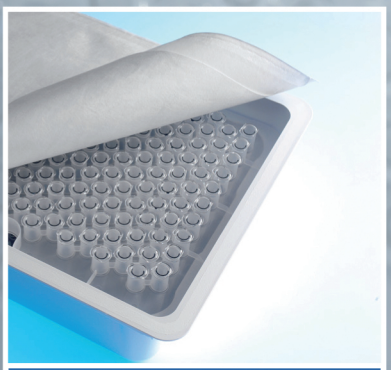
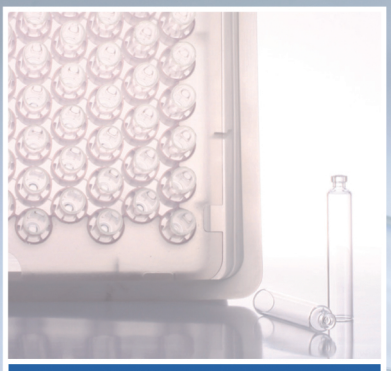


EZ-fill vials



EZ-fill syringes



EZ-fill cartridges

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Publication Month	Issue Topic	Materials Deadline
January 2013	Oral Drug Delivery	December 3rd
February 2013	Prefilled Syringes	January 14th
March 2013	Transdermal Delivery, Microneedles & Needle-Free Injection	February 4th
April 2013	Pulmonary & Nasal Drug Delivery	March 4th
May 2013	Injectable Drug Delivery 2013: Formulations Focus	April 2nd
June 2013	Injectable Drug Delivery 2013: Devices Focus	May 6th
July 2013	Oral Drug Delivery	June 3rd
September 2013	CROs & CMOs Offering Drug Delivery Solutions	August 5th
October 2013	Prefilled Syringes	September 2nd
November 2013	Pulmonary & Nasal Drug Delivery (OINDP)	October 7th
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REALISING THE BENEFITS OF CYCLIC OLEFIN POLYMER PREFILLABLE SYRINGE SYSTEMS

In this excellent article, our regular contributor, Graham Reynolds, Vice-President, Marketing and Innovation, Pharmaceutical Delivery Systems, West Pharmaceutical Services, Inc, describes the role of polymer materials for syringes, and particular how COC polymers have been central in broadening the company's established prefilled syringe offering into a complete injectable drug delivery device and container platform.

Plastic prefillable systems have long been recognised as having considerable advantages over glass in many applications. The evolution of a complete system that is designed, manufactured and provided to West's partners in a format that enables the drug manufacturers to meet increasing quality, manufacturability and performance needs offers an exciting opportunity for the future of drug containment and delivery. West has worked closely with industry-leading partners to provide a lifecycle containment and delivery solution to its customers, and its recent collaboration with Vetter Pharma, a recognised leader in the contract filling of biopharmaceuticals, has extended efforts to ensure that customers not only have a desirable delivery solution for their product, but also an easy and economical way to fill.

In order for West's customers to be successful, West must provide an effective drug delivery system as well as expertise and support throughout the drug development and manufacturing journey. This partnership begins at the early stage of development, incorporates material selection, stability testing, system selection, filling and handling, and ends with commercial introduction. Often the process may be complicated, particularly when a syringe forms part of a combination product and is incorporated within systems such as needle-safety systems or auto-injectors. Many partners require various expertise and advice at different stages of the product lifecycle, and working together we can seek solutions that will enable manufacturers to look forward to successful commercial introductions of many significant products.

> "THE ADVANCE TOWARD POLYMER SYSTEMS AND THE NEED FOR HIGH-QUALITY SOLUTIONS, LED BY WEST'S WELL-ESTABLISHED MARKET PRESENCE WITH THE DAIKYO CRYSTAL ZENITH POLYMER, HAVE LED TO MANY INITIATIVES BY GLASS COMPANIES AND OTHER POLYMER SYRINGE MANUFACTURERS IN AN ATTEMPT TO OFFER IMPROVED PRODUCT OPTIONS"

The advance toward polymer systems and the need for high-quality solutions, led by West's well-established market presence with the Daikyo Crystal Zenith polymer, have led to many initiatives by glass companies and other polymer syringe manufacturers in an attempt to offer improved product options. In

Mr Graham Reynolds
Vice-President, Marketing & Innovation, Pharmaceutical Delivery Systems

T: +1 610 594 2900
E: graham.reynolds@westpharma.com

West Pharmaceutical Services, Inc
101 Gordon Drive
Lionville, PA 19341
United States

T: +1 610 594 2900
F: +1 610 594 3000
E: webmaster@westpharma.com

www.westpharma.com

addition to the well-documented advantages provided by the Crystal Zenith system (including absence of tungsten and adhesive and that no silicone oil is added for lubricity), the fundamental benefits of reduced breakage and lower particulate contamination remain driving forces for the evaluation of polymer systems. Many companies now regard polymer systems as the future of packaging for pharmaceutical and biopharmaceutical products.

One key benefit is the ability to provide container systems with improved dimensional tolerance, and the ability to create customised containers. This becomes even more critical when the container is part of an integrated delivery system. Functionality between a syringe and an auto-injector, for instance, needs to be thoroughly understood and optimised to provide an effective system.

THE DAIKYO CRYSTAL ZENITH 1ML LONG INSERT NEEDLE SYRINGE SYSTEM

West has worked extremely closely with its affiliate, Daikyo Seiko Ltd, of Japan, who developed the Crystal Zenith material. Together, we have been successful in gaining approval for the use of the Crystal Zenith polymer for more than 20 marketed drug products around the world, including approvals in the US, Europe and Japan. The flexibility of the technology makes it ideal for a wide range of containment systems, and these approvals include vials (of differing sizes) and Luer Lock syringes.

Recognising that many biologics are typically contained in a 1 mL long staked-needle format, West initiated a development programme resulting in the commercial availability of the 1mL long insert needle system in 2010. This lengthy process involved collaboration between West and Daikyo, as well as equipment manufacturers and fillers, to ensure an optimum system was available to our customers in a validated, sterile format, compatible with established filling equipment. Although the outer dimensions and tub format were designed to be consistent with current glass syringes, the similarities ended there. A combination of the unique Crystal Zenith and FluroTec® materials with a manufacturing process developed at The Tech Group (a West subsidiary) facility in AZ, US, has resulted in an ideal solution to meet the needs of the next generation of biologic products.

To overcome issues of tungsten and glue interaction, West developed a process to mould the needle into the polymer hub with no need for adhesives. To address issues with silicone oil causing aggregation with certain drug products, West and Daikyo developed a system that does not require any silicone oil to be added for lubricity (with the exception of siliconisation on the outer surface of the needle). This is possible through the improved dimensional tolerances on the inner geometry of the syringe and the patented FluroTec barrier film technology, which enables the outer surface of the plunger to be coated with fluropolymer film to optimise lubricity without the need for silicone oil. Finally, the manufacturing process has been developed within a classified clean room, with robotic handling and multiple camera inspection stages (including 100% X-ray inspection to ensure quality and positioning of the needle) to ensure the final product is of the highest quality. The tub, nest and plungers have also been developed to ensure that the final product can be filled on existing equipment with minimal change parts.

In all, it has been a journey of several years and significant investment, but the result is a containment and delivery system optimised to meet the challenges of today's biopharmaceutical products.

SYRINGE FILLING: AN INTEGRAL OFFERING

Providing an optimum solution to the challenges of packaging and delivering today's sensitive and complex biopharmaceutical products requires not only a unique syringe system, but also the assurance that this system can be filled, handled, validated and approved in accordance with all appropriate cGMPs and pharmaceutical practices. In 2011, West announced a collaboration with Vetter Pharma, a leading global independent specialist in the contract manufacturing of prefilled application systems. While many pharmaceutical manufacturers had expressed an interest in using the Daikyo Crystal Zenith system, they were concerned about the ability to fill the system.

This collaboration has allowed both parties to develop and optimise the manufacture, validation and packaging of the syringe system to ensure it is fully compatible with the filling capabilities and requirements at Vetter. Media fills and equipment validation have been successfully completed for the 1mL long insert needle syringe system, providing customers with an option for filling that could be used instead of, or in addition to, in-house capabilities.

West continues to work closely with other contract fillers, as well as customers with internal filling capabilities, to help ensure a smooth transition toward the use of Crystal Zenith systems.

"THESE FOUR ELEMENTS ARE THE DRUG PRODUCT, THE CONTAINER, THE DELIVERY DEVICE AND THE PATIENT. IF ANY ONE OF THESE ELEMENTS, OR THE INTERFACE BETWEEN THEM, IS NOT FULLY UNDERSTOOD AND MAY NOT PERFORM IN AN OPTIMAL WAY, THE OVERALL TREATMENT MAY BE COMPROMISED"

DESIGN FLEXIBILITY OFFERS SIGNIFICANT POTENTIAL FOR INNOVATIVE DRUG DELIVERY SYSTEMS

In many cases, such as the 1mL long syringe and many of the standard vials, compliance with ISO standards for size has benefits in terms of the interchangeability between glass and polymer, and the ability to use existing equipment, devices and packaging. However, one key benefit of polymers over glass is the ability to design more innotvative containers with high precision.

While this always has to be balanced by the practical considerations of the ability to fill the system and maintain an effective stability of the drug product over time, the market is now considering the potential use of a novel drug container in order to offer design flexibility with devices. As an example, an auto-injector designed around a standard 1mL long syringe will always need to be of a shape and size to accommodate the length of the syringe and the necessary plunger movement. If, however, the same dose could be delivered from a much smaller container, the ability to manufacture devices that are designed more specifically for the needs of the patient may create a desirable market advantage.

In addition, larger dose volumes can be achieved through the development of an alternative syringe system. West is working closely with customers to develop complete systems, using the flexibility of design offered by the Crystal Zenith polymer, our ability to understand patient needs, and the device

Figure 1: The SmartDose®* electronic patch injector technology platform.

development and manufacturing capability existing in an organisation that has effectively developed and commercialised numerous drug delivery systems.

A SOLUTION TO THE CHALLENGES OF DELIVERING HIGHER DOSE VOLUMES

The SmartDose®* electronic patch injector technology platform (Figure 1) uses a Daikyo Crystal Zenith cartridge system. The cartridge system was chosen based on its superior performance with biopharmaceuticals, as well as its improved dimensional tolerance and functional consistency. The use of a Crystal Zenith container also provided the opportunity for a single containment material to be used as part of a lifecycle management program. Many customers also find that a bridging study between a Crystal Zenith syringe and the SmartDose cartridge can be a beneficial approach.

The SmartDose electronic patch injector technology platform offers the opportunity to deliver a dose volume in excess of 1mL subcutaneously, over a longer period of time. For many modern biologics, a dose volume in excess of 1mL may be required to achieve an effective therapeutic effect. In these cases the options may include multiple injections or more frequent injections. Consideration for the needs and preferences of the patient have led to many advances in drug delivery system development. The SmartDose technology platform has been developed specifically to meet the technical challenges of containing and delivering a higher dose volume, but has also taken into account the results of many patient-focused studies, to help optimise the human factors elements of the system and ensure usability.

UNDERSTANDING PATIENT NEEDS IS KEY TO DEVELOPING INTEGRATED DRUG DELIVERY SYSTEMS

West recognises the importance of collaboration in ensuring a successful drug delivery system. A drug therapy or treatment can only be effective if the four key elements of an integrated drug delivery system are understood, and the relationships between them optimised. These four elements are the **drug product**, the **container**, the **delivery device** and the **patient**. If any one of these elements, or the interface between them, is not fully understood and may not perform in an optimal way, the overall treatment may be compromised.

As an example, an effective drug molecule, in a safe container, and within a functioning self-injection system, can only be effective if that patient can effectively use the device and chooses to take the required dose in accordance with an appropriate regimen. In addition, factors such as overall cost, reimbursement, speed to market and competitive positioning will also be key in any success. This is particularly important when considering prefilled drug delivery systems that are based on standard syringes, polymeric syringes or custom containers.

West will continue to work side by side with customers and partners to develop solutions that will meet or exceed the increasing challenges in the market.

**For investigational use only by our pharmaceutical and biotechnology development partners. West markets SmartDose® and ConfiDose® as integrated systems with drug filling and final assembly completed by the pharmaceutical company.*

Daikyo Crystal Zenith® is a registered trademark of Daikyo Seiko, Ltd. Crystal Zenith technology is licensed from Daikyo Seiko Ltd.

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Advance Your Delivery System with Daikyo Crystal Zenith® Insert Needle Syringe Technology

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ZEON

INTRODUCTION

Over the past decade Cyclo Olefin Polymer (COP) and Cyclo Olefin Copolymer (COC) based syringes, cartridges and vials have attracted ever increasing attention from the pharma industry as a valid transparent plastic alternative to glass primary drug containers. The main application focus is with injectable parenteral drugs, especially modern biopharmaceuticals.

Zeon Corporation, headquartered in Tokyo, Japan, is a leading and globally operating, specialty polymer company. As part of its specialty materials operations, Zeon manufactures and sells COPs under the brand names ZEONEX® and ZEONOR®.

Europe:
Reinhard Scheller
Commercial Manager, COP Europe
T: +49 211 52 67 – 0
F: +49 211 52 67 – 160
E: zeinfo@zeon.eu

Zeon Europe GmbH
Hansaallee 249
D-40549 Düsseldorf
Germany

Americas:
Toshiro Katayama
Product Manager, New Business Divison
T: +1 502 775 2000
F: +1 502 775 2025
E: zeonex@zeonchemicals.com

Zeon Chemicals LP
4111 Bells Lane
Louisville KY 40211
United States

Asia:
Mitsugu Ishihara
Manager, Sales and Marketing, Specialty Plastics Divison
T: +81 3 3216 1769
F: +81 3 3216 2334
E: mikkun@zeon.co.jp

Zeon Corporation
1-6-2 Marunouchi, Chiyoda-ku
Tokyo 100-8246
Japan

www.zeonex.com

SPECIALTY MATERIALS BUSINESS STRATEGY

Since the establishment of Zeon Corporation in 1950, the company has consistently taken advantage of its original technologies and created numerous unique products. Based on proprietary C4 and C5 extraction technologies, Zeon developed an integrated production system and is striving to create new products and new business areas by utilising these core technologies. ZEONEX® and ZEONOR® polymers are prominent examples of how Zeon core competencies have established leadership in both major and niche markets around the world.

ZEONEX® AND ZEONOR®

ZEONEX® and ZEONOR® are fully amorphous and highly transparent thermoplastic resins. The balance of outstanding water barrier properties in combination with high purity, excellent chemical resistance, high transparency and no interaction with drugs, position ZEONEX® and ZEONOR® as a perfect alternative to glass or other plastics solutions for vials, syringes and other customer designed drug containers.

REGULATORY STATUS

Zeon has three certified COP grades with medical/pharmaceutical approvals (see Figure 1). Each grade has its own Type III Drug Master File registration, passes actual EU-, US- and JP-Pharmacopoeia requirements and selected chapters of ISO 10993 biocompatibility.

ZEONEX® and ZEONOR® provide the extremely low extractables and leachables levels needed for containers like prefilled syringes or cartridges (carpoules).

KEY ADVANTAGES OF ZEONEX® AND ZEONOR®

Due to the non-polar, hydrophobic and non-reactive surface nature of ZEONEX® and ZEONOR®, there will be no interaction with the pharmaceutical product inside the prefilled container.

Actual Medical COP Grades

ZEONEX® / ZEONOR®

ZEONOR® 1020R	Tg: 102 °C MFI: 20 g/10min	Type III Drug Masterfile Number: 13885
ZEONEX® 690R	Tg: 136 °C MFI: 20 g/10min	Type III Drug Masterfile Number: 14084
ZEONEX® 790R	Tg: 163 °C MFI: 6 g/10min	Type III Drug Masterfile Number: 17236

MFI at 280 ºC ; 2,16 kg

All grades above meet the test requirements for plastic containers in
EU-Pharmacopoeia (7th)
US-Pharmacopoeia (35th)
JP-Pharmacopoeia (16th)
ZEONOR® 1020R and ZEONEX® 790R meet biocompatibility requirements of
ISO 10993-4 and -5
ZEONEX® 690R meets biocompatibility requirements of
ISO 10993-4 , -5 , -6 , -10(a) , -10(b) and -11

Figure 1: Regulatory status of medical grade ZEONEX® and ZEONOR®.

Figure 2: Commercial prefillable ZEONEX® syringes of various sizes (*Images courtesy of Transcoject and Gerresheimer/Taisai Kako*).

Typically the adsorption of proteins or other biomolecules to ZEONEX® and ZEONOR® surface is very small compared with glass. Such adsorption can change the API level in the drug formulation. The trend towards new protein-based pharmaceuticals, produced by modern biopharmaceutical methods, pushes the use of alternative packaging materials like ZEONEX® and ZEONOR® as first choice.

ZEONEX® and ZEONOR® can be sterilised utilising steam autoclave, electron beam, gamma radiation and ethylene-oxide gas. Other handling benefits of ZEONEX® and ZEONOR® versus glass, include their low specific weight and excellent shatter resistance.

A number of leading syringe and vial suppliers offer fully commercial ready-to-use and ready-to-fill standard container designs made from ZEONEX® and ZEONOR® (Figures 2 & 3).

A recent development is the introduction of multilayer vials to market. These constructions combine the excellent water barrier of ZEONEX® and ZEONOR® with high oxygen barrier and additional mechanical strength from other polymers like polyamides.

Another significant benefit of plastics containers versus glass containers is the freedom of design. Therefore ZEONEX® and ZEONOR® is very well suited for the development of fully customised drug cartridges in auto-injectors , pens and other injection devices.

APPLICATIONS IN ANALYTICS & DIAGNOSTICS

High transparency in the UV-wavelength range and very low autofluorescence of ZEONEX® and ZEONOR®, makes them highly desirable for cuvettes, High Throughput Screening (HTS) microplates or biochips in analytical/diagnostics applications. Microfluidic arrays benefit from the excellent mouldability and precise transcription of microscopic structures, achieved with ZEONEX® and ZEONOR®.

ZEON IN THE EU & US

Zeon Europe GmbH in Düsseldorf, Germany, is the European marketing/sales organisation and Zeon Chemicals L.P. in Louisville,KY, US, is the American marketing/sales organisation of Zeon Corporation.

More detailed information about ZEONEX® and ZEONOR®, properties and applications, can be obtained directly from these companies (see contact box).

Alternatively the technical website WWW.ZEONEX.COM offers a variety of information.

Figure 3: Commercial ZEONEX® standard vials (*Image couresy HPT Pharma Packaging*).

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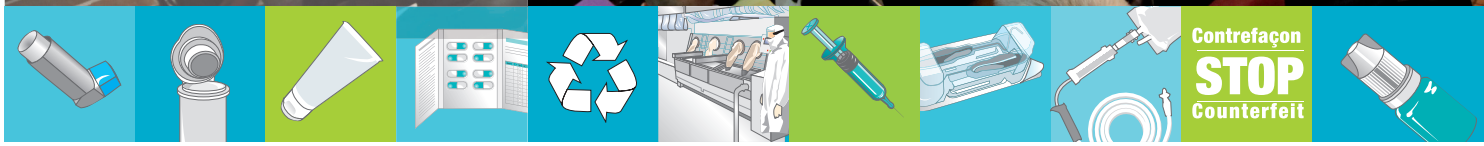

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SPECIALTY COATING SYSTEMS™

CHALLENGES WITH PREFILLED SYRINGES: THE PARYLENE SOLUTION

In this article, Lonny Wolgemuth, Senior Medical Market Specialist, Specialty Coating Systems, Inc, concisely describes the applications and advantages of Parylenes, a series of inert polymeric coatings. In the prefilled syringes sector, Parylenes serve dual purposes being both an effective barrier material and highly lubricious coating.

LOOKING AT THE ISSUES

The chemical nature of modern drugs is becoming highly aggressive and some of these formulas tend to actually attack pharmaceutical container components. When prefilled syringes dwell in storage, two things can happen. First, a phenomenon often referred to as "stiction" occurs and the plunger doesn't slide freely upon first push. Consequently, it takes a larger than desired force to break it free. This can cause an initial uneven delivery of the drug. Second, the rubber used for the plungers may contain unwanted trace elements that can leach out of or be extracted from the stopper and contaminate the contents of the syringe, compromising the effectiveness of the medication or patient safety.

"IT SPONTANEOUSLY POLYMERISES ONTO ALL SURFACES, FORMING THE ULTRA-THIN, UNIFORM & CONFORMAL PARYLENE FILM"

A solution may be to coat syringe components with both a lubricant and a protective shield, without adding significant physical dimension to the syringe components. This, of course, rules out most of the conformal coating materials used in other industries.

The only biocompatible conformal coating that can both protect and lubricate without adding dimension to the surface is Parylene. It provides barrier protection for the syringe barrel, plunger and seals, and for the drug (see Figure 1). It is also highly lubricious, eliminating sticking plungers (see Figure 2). Parylene is widely applied on syringes to make their use easier and more precise.

UNDERSTANDING PARYLENE

Parylene is the generic name for a unique series of chemically-inert polymeric organic coatings. Several types of Parylene exist to suit a variety of applications. All are free of fillers, stabilisers, solvents, catalysts and plasticisers. As a result, the Parylenes present no leaching, outgassing or extraction issues.

Devices to be coated with Parylene are placed in a room-temperature deposition chamber. A powdered raw material, known as dimer, is placed in the vapouriser at the opposite end of the coating system. The double-molecule dimer is heated, sublimating it directly to a vapour, and the dimer vapour is then heated to a very high temperature that cracks it into a monomeric vapour. This vapour is then transferred into an ambient-temperature deposition chamber where it spontaneously polymerises onto all surfaces, forming the ultra-thin, uniform and extremely conformal Parylene film.

The entire Parylene coating process is carried out in a closed system under a controlled vacuum. The deposition chamber and items to be coated remain at room temperature through-

Lonny Wolgemuth
Senior Medical Market Specialist
T: +1 317 244 1200
E: LWolgemuth@scscoatings.com

Specialty Coating Systems, Inc
7645 Woodland Drive
Indianapolis
IN 46278
United States

www.scscoatings.com

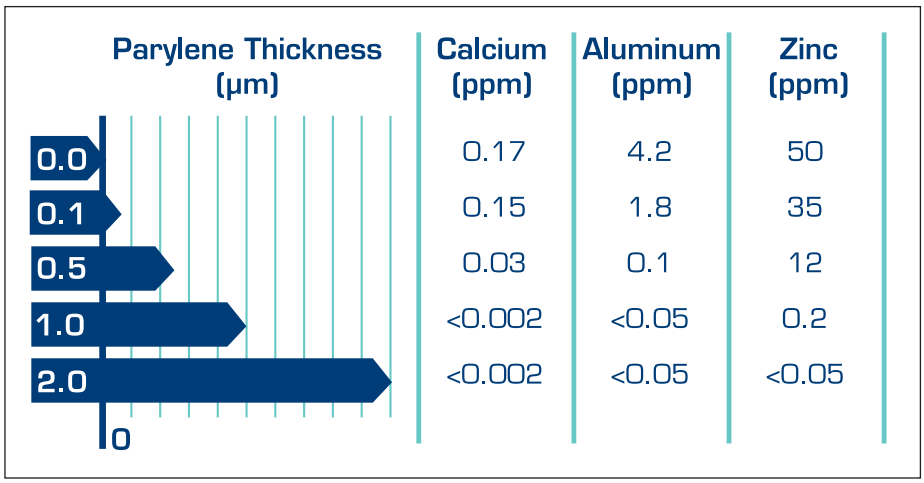


Figure 1: The effect of Parylene C coating thickness on extractable metals in rubber specimens*.

out the process. No additional curing process or steps are required.

The molecular "growth" of Parylene coatings ensures not only a uniform, conformal coating at the thickness specified by the manufacturer yet, because Parylene is formed from a gas, it penetrates into every crevice, regardless of how seemingly inaccessible. This assures complete encapsulation of the substrate without blocking, or bridging, even the smallest openings.

There are three commonly utilised variants of Parylene: C, N and Parylene HT®. Parylene N has particularly high dielectric strength and a dielectric constant that is independent of frequency. Because of its high molecular activity in the monomer vapour state, Parylene N has a greater penetrating power than Parylene C, with the ability to coat deep recesses and blind holes. Because of its lower maximum operating temperature, however, it is not suitable for applications requiring steam sterilisation.

Each Parylene has unique properties that suit it to particular medical coating applications, but Parylene C has a chlorine atom in its molecular structure resulting in modified electrical and physical properties, particularly its low permeability to moisture and corrosive gases. Because of its excellent barrier properties, Parylene C is often the first choice for protection of pharmaceutical containers, syringes and vials.

Parylene HT substitutes fluorine for the hydrogen atoms in the Parylene N molecule, resulting in some very useful attributes. Parylene HT, alone among the Parylenes, is stable in the presence of ultraviolet light, has a very high temperature capability (350°C) and has the best crevice-penetrating capability.

Parylenes N, C and Parylene HT offer similar lubricity capabilities and all are equally biocompatible. Since syringes and all types of pharmaceutical containers are typically manufactured in mass quantity, the manufacturer can have one or all components coated before sending them to the end customer, who fills and packages them for distribution.

"PARYLENES PRESENT NO LEACHING, OUTGASSING OR EXTRACTION ISSUES"

COMPLEMENTARY APPLICATIONS

Shelf-life is important for all medications; prefilled syringes as well as pharmaceuticals in vials or bottles. For these, the more aggressive chemicals tend to attack not only the containers, but can actually cause unwanted chemicals to be extracted from the container material into the drug itself. Parylene can prevent this. It is an excellent barrier coating, protecting the container, including caps and seals, and also protecting the drug from any unwanted leaching or extractions.

Some prefilled syringes have sealing mechanisms to ensure needle sterility and to prevent premature drug dispensing. These seals can occasionally form a very tight bond as it sits on the shelf. The self seal can be difficult to break. Coating these components with Parylene before assembly helps prevent seal bonding. In this case, Parylene acts as a release agent allowing the sealing material to release easily when needed.

The use of prefilled syringes, both by medical professionals and by consumers, is an extremely efficient method for dispensing drugs. Convenience, cost saving and safety aspects drive this market, particularly in the area of patient home use. Adding Parylene as a protective barrier and lubricious coating eliminates issues faced by both prefilled syringes and various pharmaceutical containers.

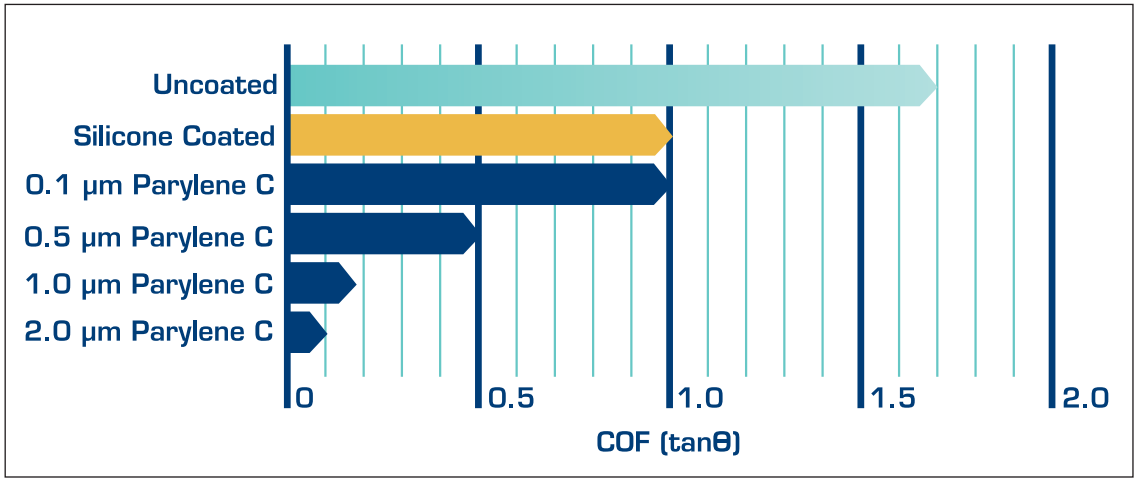


Figure 2: Co-efficient of friction measurements for Parylene-coated rubber specimens*.

* *US Patent No. 4,808,453, February 28, 1989, Romberg VG et al.*

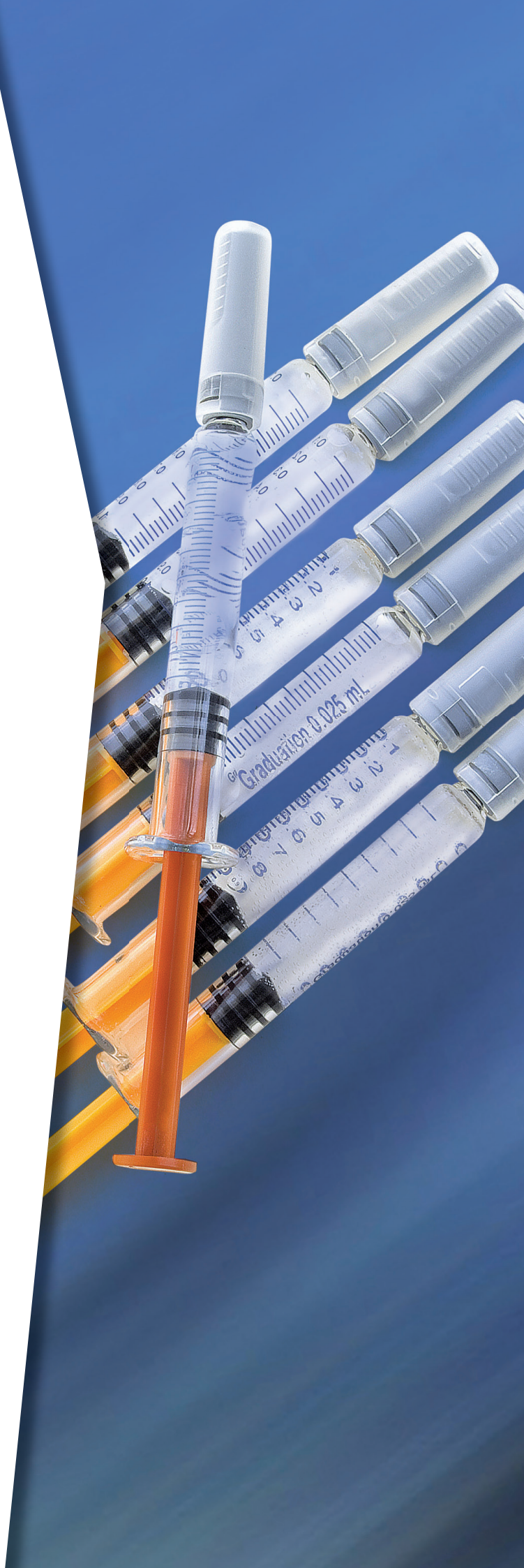
SPECIALTY COATING SYSTEMS™

When it comes to reliability, nothing protects like Parylene.

Parylene is an ideal conformal coating for medical and pharmaceutical delivery devices and components. SCS Parylenes can be applied to virtually any material to provide ultra-thin, pinhole-free coatings with superior extractables/leachables barrier properties and excellent non-liquid, low friction/stiction characteristics. Biocompatible Parylene coatings are USP Class VI certified and ISO 10993 tested.

With 11 locations around the world (6 in the Americas, 3 in Europe, 2 in Asia), Specialty Coating Systems is the leader in Parylene coatings and maintains comprehensive FDA Drug and Device Master Files for customer reference.

Contact SCS today for more information about the ways Parylene coatings can enhance the performance and reliability of your medical or pharmaceutical applications.



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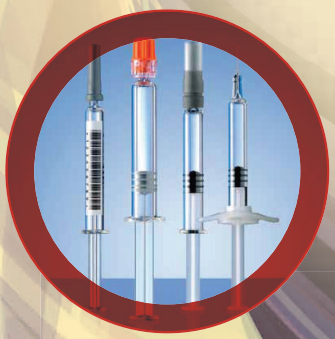

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HASELMEIER

Haselmeier is dedicated to meeting the self-injection needs of pharmaceutical manufacturers and patients.

In 1920, Wilhelm Haselmeier established a medical device company in Stuttgart, Germany. Since that time, Haselmeier has continued to develop and create injection devices designed for patient comfort and ease-of-use.

Today, Haselmeier is one of the leading designers and manufacturers of pen and auto-injector systems. Many of these systems feature Haselmeier's patented hidden needle system, which is designed to help patients overcome the fear of self-injection, provide a more comfortable injection and help increase compliance of the patient's medication.

PRODUCT DESIGN

Our capabilities include design and development from concept to finished device using Haselmeier's strong IP portfolio or tailoring of existing Haselmeier designs to meet customer and therapeutic needs.

All designs undergo comprehensive testing, in addition to risk management, risk analysis and FMEA design review. Three-dimensional CAD designs are utilised for creation of customer-specific concepts or customisation of existing designs.

MANUFACTURING AND QUALITY

As a specialist in the manufacture of complex system assembly, product integrity is assured by Haselmeier's manufacturing processes. All new device concepts are created with an "Integrated Design Approach" which focuses on both, the device and the efficiency of manufacture and assembly.

All manufacturing is within compliance with applied standards EN ISO 13485:2003 and Annex ll, Section 3 of the European Directive 93/42/EEC on medical devices. CE certification is certified by TÜV SÜD Product Service (Munich, Germany).

PLATFORM & PRODUCTS

Axis Pen System: variable-dose injection device

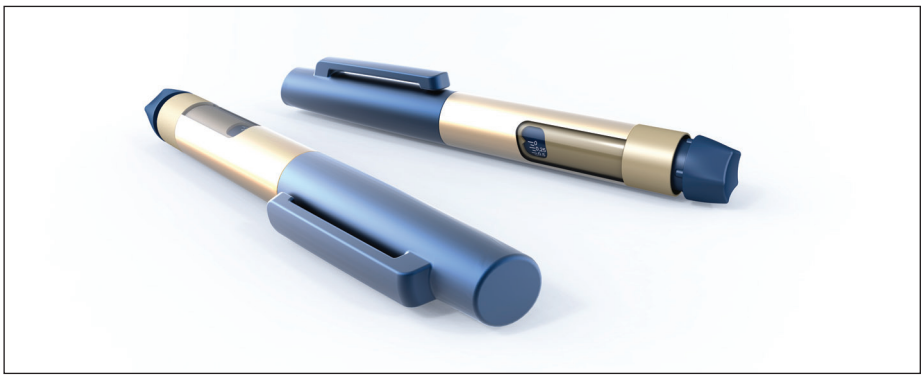

Figure 1: Axis Pen System – variable-dose injection device.

The Axis Pen System is a variable-dose injection device for manual injection. It is available in a disposable or re-usable presentation. The Axis-D and Axis-R Pen Systems (Figure 1) provide a new, unique technical function.

Figure 2: i-pen: re-usable – variable dose injection device.

Figure 3: i-pen²: re-usable – variable dose all-plastic injector device.

The Axis pens feature:
- No or minimal priming
- Accurate dose reading with sliding window
- No rotating outer components
- Protected dose scale

i-pen: re-usable, variable dose injection device

The Haselmeier i-pen is a re-usable, variable-dose injection device for use with a standard 3 ml cartridge. The i-pen (see Figure 2) features an elegant non-medical design which is the result of extensive research and patient testing.

The i-pen is available as a standard Haselmeier design or can be customised to your specific requirements. It features:
- Dose adjustment from 0.01-0.6 ml per injection
- Compact size enables easy handling and portability
- Large, easy-to-read dose indicator
- All metal outer body

i-pen²: re-usable, variable dose all-plastic injector device

The i-pen² (Figure 3) is a reusable, variable dose injection device for use with a standard 3ml cartridge. The i-pen² was specifically created to provide a high-quality pen at economic cost.

The i-pen² is available as a standard Haselmeier design or can be customised to your specific requirements. It features:
- Dose adjustment from 0.01-0.6 ml per injection
- Compact size enables easy handling and portability
- Large, easy-to-read dose indicator
- All plastic components

Softpen – reusable injection device

The Softpen (Figure 4) is a fully automatic, re-usable injection device featuring Haselmeier's patented hidden-needle design. Upon depressing the clip on the pen, the needle automatically enters the subcutaneous tissue followed by delivery of the solution. The Softpen features:
- Fully automatic needle insertion and injection
- Needle is hidden prior to and during injection
- Multiple injections from single 3 ml cartridge

Figure 4: Softpen – a fully automatic, re-usable injection device featuring Haselmeier's patented hidden-needle design.

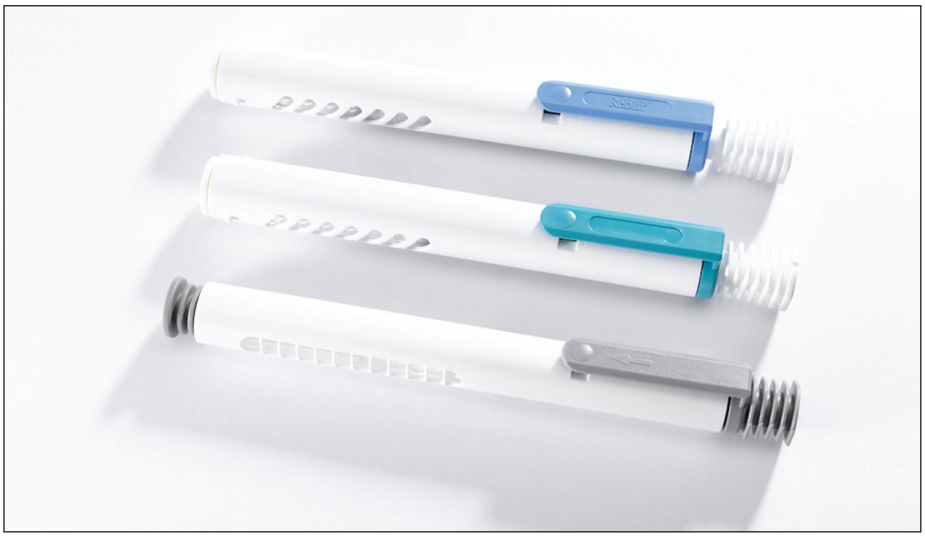

Figure 5: The disposable Penlet is a fully automatic, fixed-dose injection device designed for use with a standard 3 ml cartridge.

Penlet – disposable, fixed-dose injection device

The Haselmeier disposable Penlet is a fully automatic, fixed dose injection device designed for use with a standard 3ml cartridge. Upon depressing the clip on the pen, the needle automatically enters the subcutaneous tissue which is followed by delivery of the solution. The Penlet features:
- Ready for use by the patient and no dose adjustment required
- Fully automatic needle insertion and injection
- Needle is hidden prior to and during injection

Haselmeier USA
517 Benfield Road, Suie 301
Severna Park
MD 21146
United States

Robert J Kilgore
T: +1 410 647 7300
E: r.kilgore@haselmeier.com

Haselmeier GmbH
Dufourstrasse 32
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PRECISION EQUIPMENT & STELLAR SERVICE: SETTING FARGO AUTOMATION APART

Prefilled syringes have emerged as one of the preferred methods for the delivery of parenteral drugs. As the speed and quality requirements for prefilled syringe lines continue to increase, there is a growing need for precision syringe handling & packaging equipment. To meet this need, Fargo Automation, Inc (FAI), has developed a full line of syringe handling equipment to complement its already extensive line of pharmaceutical & medical device packaging equipment.

Fargo Automation started by building custom automation equipment, so its business model is very flexible and quick to respond. FAI has now developed several standard product lines, but still remains as flexible and innovative as ever, capable of tackling challenging automation projects.

ROBOTICS: PRECISION AND SPEED

FAI has designed and developed a full line of Delta and SCARA robots to complement its product lines (Figure 1). Using robotics allows a very flexible configuration, high speed, and minimal change tooling. The robots are fully integrated, even controlled by the same Allen-Bradley programmable logic controller (PLC), so robotic integration is entirely seamless. Because the controls are shared with the base machine, high-speed motion co-ordinated with an adjacent feeder, conveyor, thermoformer, or cartoner is easily accomplished.

PROCESS CONTROL: ENSURING QUALITY FROM THE START

To meet the strict standards of the pharmaceutical industry, FAI has taken an engineering approach to process control. All parameters critical to a process, whether thermoforming blisters, robotically picking & placing a syringe, or loading a blister into a carton, are tracked by the PLC. If any of the parameters for that process are out of range, the product is rejected and the operator is alerted. Timers, temperatures, pressures, and servo positions are closely monitored, and the set points are automatically selected when switching formats at the human-machine interface (HMI). All of this ensures that the machine has control of the process while still remaining flexible.

"FAI HAS DEVELOPED A FULL LINE OF SYRINGE HANDLING EQUIPMENT TO COMPLEMENT ITS ALREADY EXTENSIVE LINE OF PHARMACEUTICAL & MEDICAL DEVICE PACKAGING EQUIPMENT"

ALLEN-BRADLEY CONTROLS: GIVING YOU CONTROL OF YOUR SYSTEM

FAI uses Allen-Bradley ControlLogix PLCs to control its machines. Allen-Bradley ControlLogix gives the operator the tools they need to make process improvements and troubleshoot machine stoppages. The HMI screens are informative and intuitive. Icon-based HMI screens are easy to navigate and user-friendly for any level of operator. The HMI screens are multi-level password protected and 21CFR11 compliant.

Fargo Automation, Inc
969 34th Street N
Fargo
ND 58102
United States

T: +1 701 367 9914
E: info@fargoautomation.com

www.fargoautomation.com

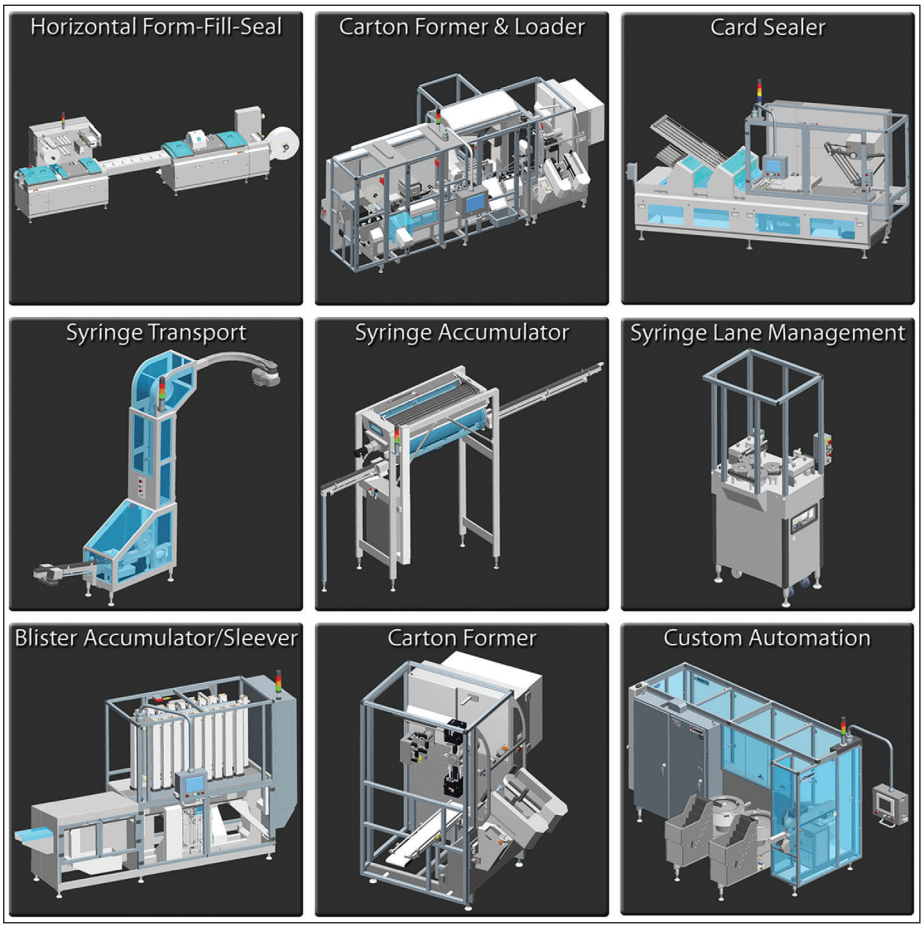


Figure 1: Sample of Fargo Automation's product lines.

ADVANCED INTEGRATION: USER FRIENDLY DESIGN

FAI takes integration seriously and can fully integrate entire lines in their facility, giving the customer peace of mind that the entire line will work together as planned. The company's HMI data can be merged with adjacent machines, allowing operators at any HMI on the line to view alarms or select formats on all machines. FAI also fully-integrates peripheral devices with the HMIs. All printers, labellers, lasers, cameras, check-weighs, and other devices pass signals through the machine's PLC, including format setup, error messages, low ink or label levels, pass/fail reject signals. This simple and intuitive machine interface ensures the operators are comfortable with the equipment, and reduces operator errors. FAI also offers fully-integrated serialisation solutions including printing, inspection, and database communication.

CGMP DESIGN: NOT AN AFTERTHOUGHT

FAI has taken the steps necessary to design and manufacture equipment for cGMP environments. Each machine has been designed and developed specifically for the pharmaceutical and medical device industries, so cGMP is always a top priority. FAI has invested in additional manufacturing equipment to construct machines with all-aluminum CNC machined frames for precision-fit parts, rounded edges, easy-to-clean surfaces, and ergonomic designs. Cables are routed through conduit, and stainless steel covers are used to keep surfaces clean and accessible.

FARGO AUTOMATION PRODUCT LINES

Non-Contact Syringe Conveyor

FAI's non-contact syringe-conveying system (Figure 2) is specifically designed for precise handling and protection of the syringe. Its flexibility allows the system to fit almost any equipment configuration. Syringes are able to be conveyed overhead, increasing usable floor space and creating walkways. Each system is purposely designed and built for a cGMP environment.

Syringe Handling

Fargo Automation prides itself on its ability to develop cost-effective ways to manipulate syringes throughout a packaging line efficiently. Whether in a Syringe Lane Management System (Figure 3) or tooling on a robotic loader, great

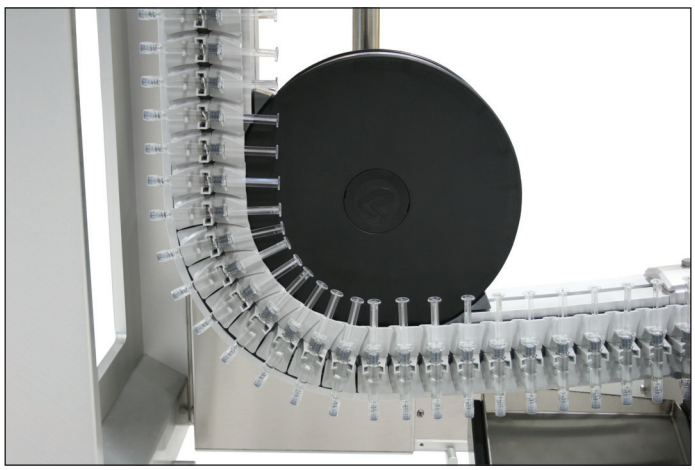


Figure 2: Non-contact conveying.

Figure 3: Lane diverting and merging.

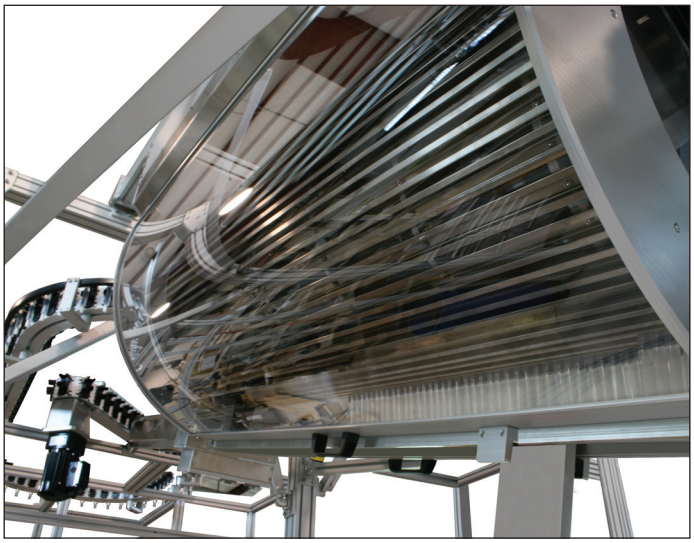


Figure 4: Syringe accumulator.

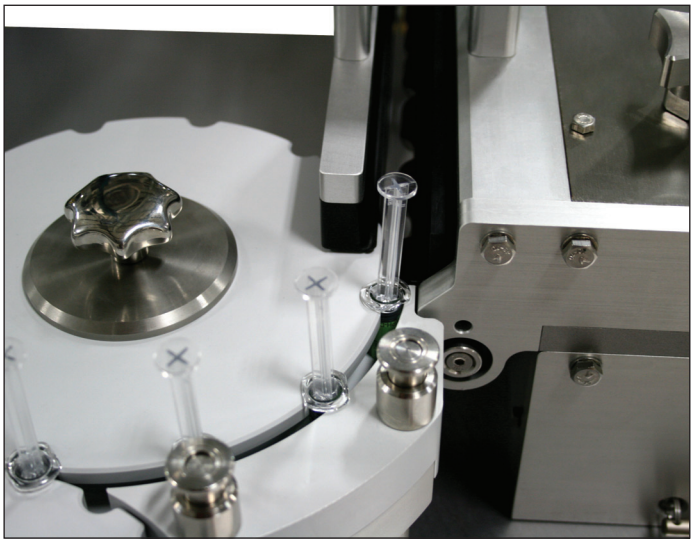


Figure 5: High-speed, precision transitions.

care is taken to ensure transitions are as smooth and as gentle as possible.

Accumulators

Accumulators are a valuable tool to increase Overall Equipment Effectiveness (OEE). FAI offers several methods of accumulation with capacities up to 4,000 syringes and speeds of 600 syringes per minute or more (see Figure 4). Fully non-contact accumulators are also available.

Nesting/De-nesting

Merging FAI's advanced syringe handling and conveying with the Delta robot technology has led to the development of a nesting and de-nesting system. Hypak-style tubs are loaded into the system, the lidding material is removed, and the syringes are robotically picked and placed directly into FAI's non-contact syringe conveyor. Tubs and trays are stacked for easy offload. A modular design allows for incorporation of accumulation or cart loading if needed.

Tray Handling / Sterilisation

Combining FAI's Non-Contact Syringe Conveyor and their advanced syringe handling abilities allows the company to help its customers develop tray handling and sterilisation concepts to fit their needs. Syringes, glass or plastic, are typically brought into the system using the non-contact syringe conveyor where they are picked and place into trays. Trays are automatically loaded into a cart and presented to an operator for sterilisation. Trays are then offloaded after sterilisation using the same non-contact methods.

Horizontal Form Fill Seal

FAI's deep-draw Horizontal Form Fill Seal (HFFS) machine fills a niche in the pharmaceutical and medical device market. Clean, cGMP design and complete process control makes it a perfect fit for sterile-barrier packages. Running on all Allen-Bradley controls, the HFFS machine readily integrates with the

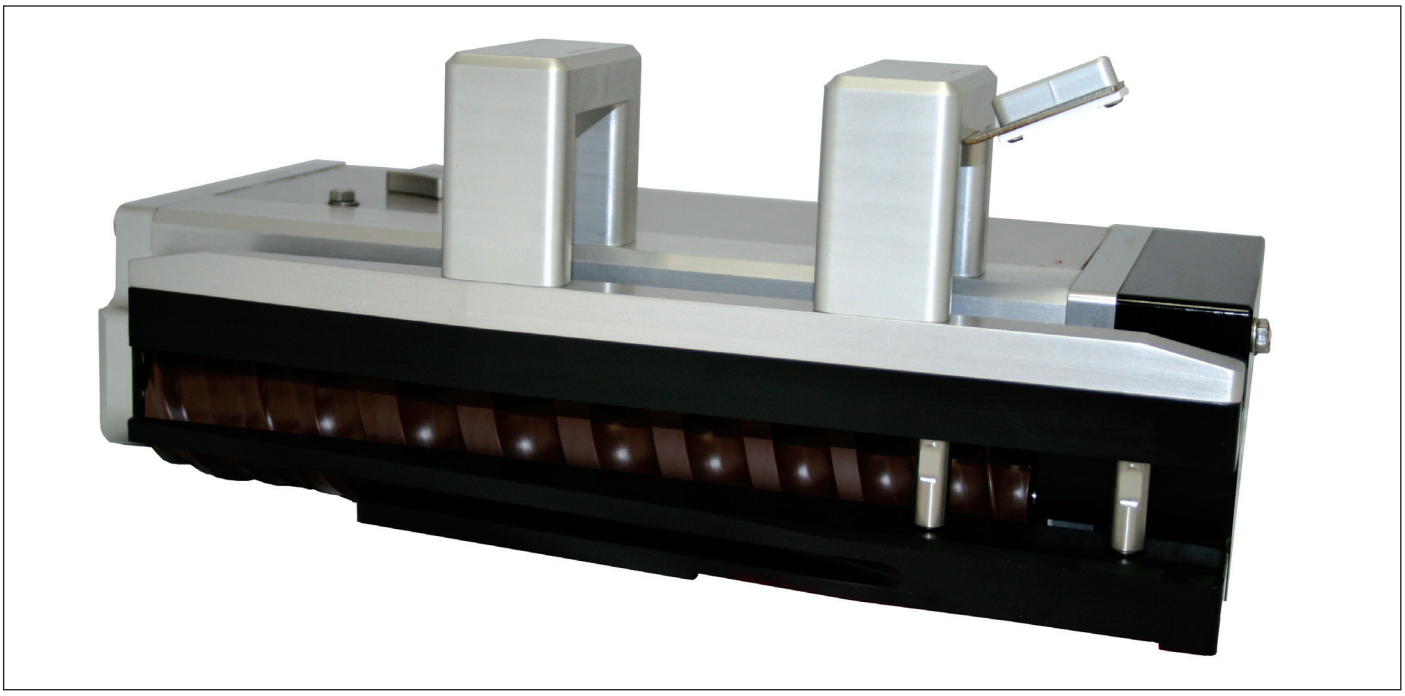


Figure 6: Quick-change tooling for different syringe sizes.

rest of FAI's syringe equipment to offer a fully integrated packaging solution. Customers can supply their own package design or FAI can help develop new and innovative concepts.

Top-load Cartoner

FAI's carton loader integrates syringe-handling abilities with carton former/loader to supply a fully integrated cartoning solution. Top-loading cartons by using a Delta robot allows high-speed cartoning with flexible pick-and-place positions and minimal changeover. Cartons are formed and glued on-line from a flat pattern, saving material costs versus auto-erecting cartons. All printing, labelling, vision inspection and check-weighing is fully integrated into the cartoner.

CONCLUSION

All of FAI's solutions are specifically designed for each customer's needs and thoroughly tested to meet the high demands of the medical device and pharmaceutical industry. All custom developments are completed by experienced engineers with every detail put through testing as if it were one of FAI's standard product lines.

The final question on every pharmaceutical manufacturer's mind is about service. FAI has an amazing track record of providing their customers with rapid and thorough service, which has resulted in building positive long-term business relationships with their customers. Fargo Automation's innovative equipment and stellar service are what set them apart from the competition.

ABOUT FARGO AUTOMATION

Based in Fargo, ND, US, Fargo Automation has been building automation equipment since 1996. The company designs and manufactures automated packaging equipment for the pharmaceutical and medical device industries. FAI's equipment is designed and built specifically to the customer's specifications. All machines are designed with a focus on performance, efficiency, safety, and process control. Additionally, FAI offers advanced integration services, providing a complete packaging line with all of the controls and mechanical components seamlessly tied together. From its inception, FAI has been rapidly developing new and innovative packaging equipment to meet the ever-changing needs of the pharmaceutical and medical device industries.

TOP-FIVE REASONS TO HAVE FARGO AUTOMATION BUILD YOUR NEXT SYRINGE PACKAGING LINE

1. Lane-Management System

FAI's Lane Management System (Figure 3) is designed to combine and redistribute multiple syringe lines at speeds of 600 syringes per minute or more. Its benefits are most realised when placed before a machine requiring two syringe inputs at a matched rate, such as a cartoner or HFFS machine. Typically, if one of these lines stops for any reason, the entire packaging line must also stop. With the Lane Management System, if one of the lanes stops, the other lane can run and divert to both of the packaging machine's inputs, maintaining ongoing production while the other line is repaired or restarted.

Key Features
- Balance flow of multiple syringe lines
- Multiple lines can be merged into a single line or a single line can be diverted to multiple lines
- Speeds of 600+ Syringes per minute

2. Precision Speed-Matched Transitions

Great care is taken to maintain the integrity of each syringe. Transitions (see Figure 5) are made only when the speed and direction is matched to prevent sudden violent accelerations. This eliminates a problem often found in other manufacturers' equipment where a "sawtooth" wheel cleaves syringes perpendicular to the product flow.

Key Features
- Syringe transitions are seamlessly timed and controlled
- Violent accelerations and catch points are eliminated

3. Non-contact Conveyor System

FAI's non-contact conveyor system conveys syringes anywhere they are needed while still allowing access to machines and ample room for walkways. Each syringe is individually contained in its own flight, eliminating problematic transitions between short lengths of conveyors. Repeated contact between syringes is also eliminated during transportation. The flexible conveyor system and the individual containment of the syringes allows the conveyor to be routed anywhere throughout the plant, including over head. This opens up floor space and allows for increased machine accessibility and unobstructed paths for material flow.

Key Features
- Production floor space is decongested, providing increased machine access
- A single conveyor system eliminates multiple problematic transitions between conveyor transitions
- Individual containment eliminates repeated glass-to-glass impacts

4. Accumulation

Accumulation can mean the difference between an average syringe line and an outperforming syringe line. FAI offers several methods of accumulation. A compact gravity rail design can be used for accumulation of up to 1,000 syringes. For accumulation levels of 4,000 or more, a barrel configuration can be used to increase capacity while keeping an efficient footprint. Non-contact accumulation is also available.

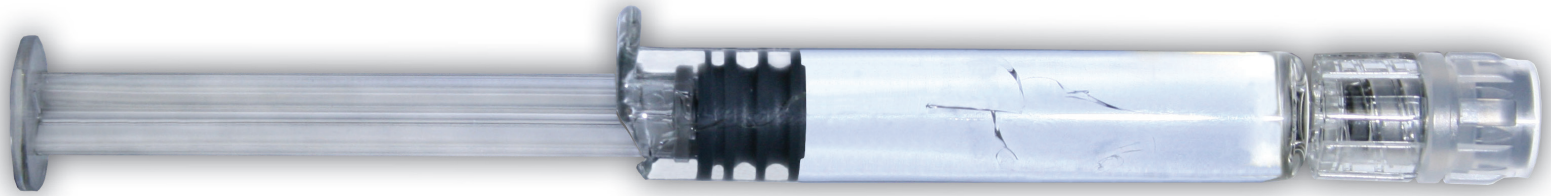
Key Features
- Up to 4,000 syringes can be accumulated in an efficient compact design
- Non-contact accumulation is available

5. Change-Over

Change-over is designed to be as quick and as simple as possible. When changing equipment over to run a different syringe size (Figure 6), colour-coded change parts can be easily changed in the accumulators, non-contact conveyor, and syringe lane-management system. The PLC can also verify that the correct change tooling is installed for the selected syringe format.

Key Features
- Format changes are designed to be as quick and simple as possible
- Change tooling is color coded and verified by the PLC to ensure the correct parts are in place for the desired format

Broken Glass?



Problem Solved.

Non-contact syringe handling by Fargo Automation.

FARGO AUTOMATION INCORPORATED

969 34TH STREET N FARGO, ND 58102

INFO@FARGOAUTOMATION.COM

701.232.1780

WWW.FARGOAUTOMATION.COM