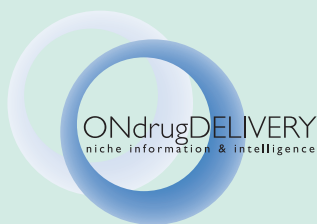


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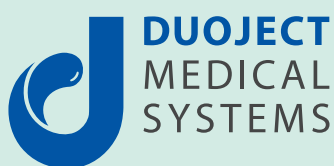
## DEVICES FOCUS



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## "Injectable Drug Delivery 2013: Devices Focus"

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Oct: Prefilled Syringes  
Nov: Pulmonary & Nasal Drug Delivery  
Dec: Delivering Biotherapeutics  
Jan: Ophthalmic Drug Delivery  
Feb: Prefilled Syringes  
Mar: Transdermal Patches, Microneedles & Needle-Free Injectors  
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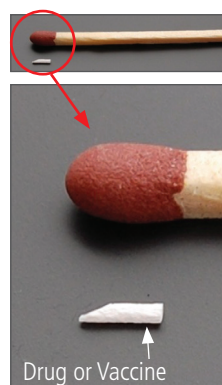
The Glide SDI (Solid Dose Injector) comprises two main components; a single use, disposable cassette which is prefilled with the drug or vaccine and a handheld, reusable, spring-powered actuator used for pushing the drug into the target tissue.

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Features	Potential Benefits
Novel solid dosage	Product differentiation with patented technology Enhanced stability; avoid refrigeration Immediate or tailored pharmacokinetic profile Ideal for wide range of peptides and proteins
Simple delivery device	Suitable for self-administration
Needle-free	No needle stick injuries
Convenience	Preferred by patients, increased compliance
Bioequivalence (if appropriate)	Reduced regulatory pathway
Suitable for vaccine delivery	Enhanced vaccine efficacy



**For further information or to discuss licensing opportunities please contact:**

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## HUMAN FACTORS ENGINEERING OF SELF-INJECTION DEVICES

In this overview, Tobias Nemeth, Business Development Manager, Ypsomed Delivery Systems, provides a useful insight into human factors engineering. The article shows how human factors engineering is implemented in the development process of a combination product and highlights its key aspects.

Today's pharmaceutical market shows a clear trend towards self-injection. Although a few years ago predominantly medical reasons like dose accuracy or needle-stick prevention were the main drivers for this trend, today the patient and his need for convenience and discreteness are more in focus.

Many self-injection devices are combination products, as defined in the US FDA 21 CFR 3.2(e), consisting of a product that comprises two or more regulated components. Some examples that are within this definition are disposable autoinjectors, pen injectors and inhalers. All of them require user interaction for successful delivery of the drug. Incorrect handling of the device by the user may have negative effects on the product efficacy, putting the treatment of the patient at risk. It is therefore absolutely necessary that the device is designed in a way that limits or excludes any risk of user mishandling.

Before taking a look at the relevant guidelines dealing with human factors engineering, a short summary of the most frequently used self-injection systems available in the market may help to choose the correct platform for a certain drug product.

### FREQUENTLY USED INJECTION SYSTEMS

One of the most common combination products is the autoinjector. It facilitates injection from a prefilled syringe that is integrated in the system. This system is suitable for all liquid-stable drugs. The injection volume, i.e. the filled volume, is usually in the range 0.2-1.0 ml. The autoinjector is a very easy-to-use system. In the case of YpsoMate, Ypsomed's 2-step autoinjector platform (see Figure 1), injection is performed in two easy steps. First,

the cap of the autoinjector is removed, the YpsoMate is then pressed against the skin and automatically starts the injection. The end of the injection is visible through the viewing window and audible by a clear end-of-injection click.

When injections are required more often than once a week, or the injection volume needs to be variable or very small, cartridge-based pen injectors are commonly used. They allow flexible dosing in increments as low as 10 µl. In order to facilitate the storage of the liquid drug

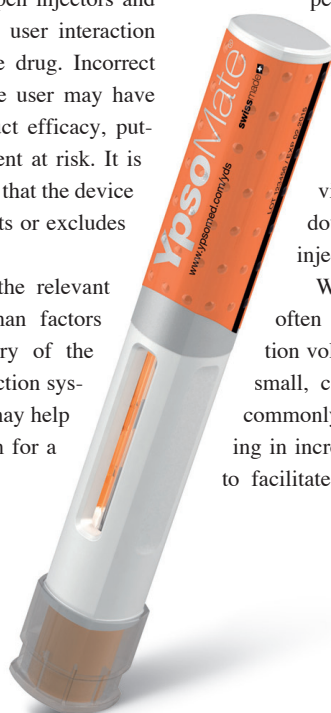


Figure 1: The YpsoMate™ 2-step autoinjector.



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between the injections the drug needs to be preserved. The UnoPen (see Figure 2), Ypsomed's disposable pen platform, is ideal for use with hormone-based therapies such as insulin, human growth hormone (hGh), follicle stimulating hormone (FSH), parathyroid hormone (PTH) and glucagon-like peptide-1 (GLP-1).

In line with customer needs, it is easily customisable according to the customer's individual primary packaging, drug and therapy needs. Other pen injectors, such as the ServoPen or the YpsoPen Twist (also shown in Figure 2), are reusable to lower device cost in use, but require the patient to exchange the cartridge when empty.

Autoinjectors and pen injectors are designed for delivering liquid drugs. However, some drugs are not liquid-stable. They need to be preserved in a freeze-dried state and reconstituted with solvent prior to injection. The procedure the healthcare professional or the patient has to follow in order to prepare such drugs for injection is invariably complex. Very often it includes a vial with lyophilised product, a syringe prefilled with solvent, and a transfer device to connect the syringe with the vial facilitating the reconstitution of the drug – a rather lengthy process with some risk for errors.

The LyoTwist platform (see Figure 3), which facilitates a dual-chamber cartridge, allows the reconstitution and injection of the drug in just one device. It is based on Ypsomed's proven twisting method providing excellent visualisation of the reconstitution, priming and injection steps, reducing handling steps and minimising risk of errors. Moreover, Ypsomed offers different technical solutions covering manual or automatic injection with fixed or variable doses. The customer may choose a ClickFine AutoProtect pen needle in combination with the LyoTwist pen (Figure 3). This needle, which is also produced by Ypsomed, adds passive needle safety to the device.

The LyoTwist platform shows how the preparation and injection may be improved compared with a conventional process thus achieving the key objectives of human factors engineering.

## OBJECTIVES OF HUMAN FACTORS ENGINEERING

The basic objective of human factors engineering is to improve the quality of the device user interface with the aim to avoid non-intuitive or difficult-to-learn handling steps,



**Figure 2: The ServoPen®, YpsoPen® Twist and UnoPen™.**

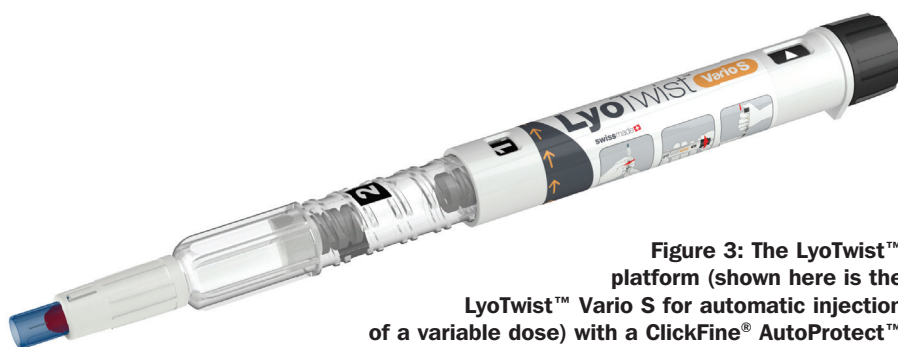
to minimise use-related risks and ultimately to ensure safe and effective use.

In the field of combination products there are multiple risks of mishandling by the user associated with inadequate device design. Considering autoinjectors, some examples of inadequate design are:

- A misleading protective needle cap that misguides the user, who could falsely inject the drug into his finger
- Forces to remove the needle cap or the need to use a push button for activation of the device that might be beyond the physical abilities for some patients. In such cases self-injection of the drug becomes difficult for the patients
- In cases where the device handling concept is too complicated, the user might be unable to operate the device at all

Over the last few years human factors engineering has become increasingly important which is reflected in different guidelines and standards. One of the most recent publications is the 2011 US FDA Draft Guidance “*Applying Human Factors and Usability Engineering to Optimize Medical Device Design*”. Once finalised it will supersede the 2000 guideline “*Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management*”. More information can be found in ANSI/AAMI HE75:2009, “*Human Factors Engineering – Design of Medical Devices*” and within the ISO 62366:2007 “*Application of Usability Engineering to Medical Devices*”.

The development of a medical device is key for its role as user interface. The development process is therefore of major importance, with



**Figure 3: The LyoTwist™ platform (shown here is the LyoTwist™ Vario S for automatic injection of a variable dose) with a ClickFine® AutoProtect™ pen needle that adds needle stick safety to the device.**

human factors engineering being an essential part of it.

## HUMAN FACTORS ENGINEERING IN DEVICE DEVELOPMENT

Human factors engineering starts early in device development and should be an integral part of the development process according to the aforementioned standards. Figure 4 shows the major steps of human factors engineering which are part of the development process. Development starts with a device concept that takes into account the following design inputs:

- User profiles
- The use environment
- Inputs from market research.

The user profile characterises who the users of the device will be and specifies any other special requirements that might have an impact on design decisions. Typically, user abilities that cause limitations due to their state of health are the key part of these user profiles. For example, for diabetics who suffer from limited eye-sight, devices with small markings, labelling or numbers will inevitably cause difficulties.

The aim of medical device development with regards to the user profile should either be to make the device less dependent on the abilities of the user or to make the device fit the disabilities of the user better. Another critical factor is the level of training: A patient, self-injecting for the very first time, might act differently compared with a trained user. A complex device requiring a lengthy training process might be more prone to use errors than a simple device with just a few handling steps.

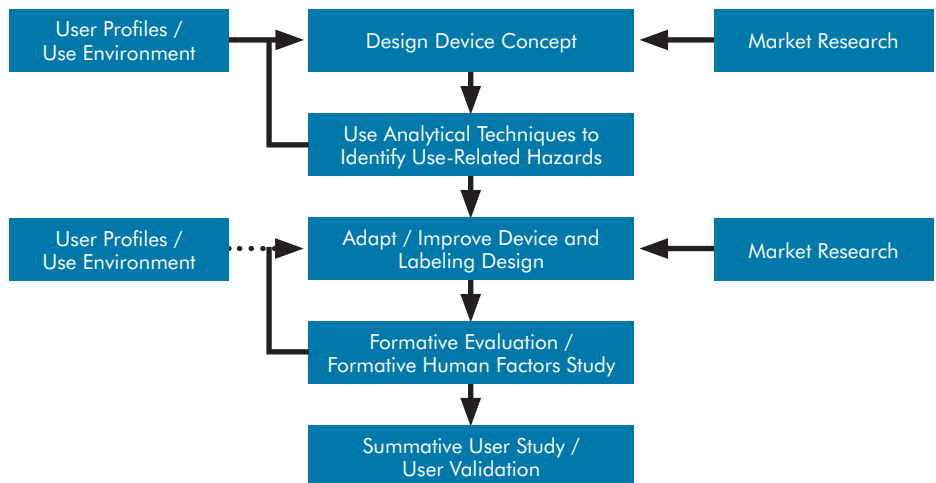
The environment where the device is used is as important as the user profile and training. Traditionally, use environments are separated into:

- Home use
- Hospital use
- Emergency use

Considerations here might include, for example, that loud surroundings would make it hard for the user to receive audible feedback from the device, or if the level of lighting in a room is insufficient, it might be difficult for the user to read displays.

Medical devices for emergency use play a special role. Typical examples are autoinjectors for the emergency treatment of anaphylactic shock. They should be designed in a way that allows them to be carried around for a long period of time and then to be used within seconds, even allowing injection through clothing.

Next to user profile and use environment, market research plays an important role for



**Figure 4: Human Factors Engineering in device development.**

specifying a device concept. Market research not only builds the body of patient-related information regarding user needs and requested features, it also provides data when competitor devices are included and provides indications for future needs. Other than collecting general information, market research may be conducted as a preference study for selection and improvement of the device concept. Within a preference study, two or more devices may be compared with each other in regards to their:

- Handling concept
- Shape, texture and colour
- Labelling concept

Early in the device development, with the device concept taking into account inputs from market research, user profiles and use environment, the device is assessed with analytical techniques. This approach is used to identify specific interactions of user and device that very often include inadvertent use errors.

This helps to identify and also to resolve hazards before physical mock-ups or device samples are available for a user study. Some analytical techniques include:

- Risk analysis
- Application FMEA
- Interviews
- Function and task analysis
- Heuristic / interface reviews
- Expert reviews

The analytical approach has the benefit of discovering use errors and hazards with low probability that might not be identified in simulated use testing.

The results of the analytical techniques as well as market research and further possible clarification of user profiles and use environment will enable to further adapt or improve the device.

## FORMATIVE EVALUATIONS AND SUMMATIVE USER STUDY

Formative evaluations are conducted when product development is still in progress and used to create design inputs to mitigate use errors when changes to the device are still possible and not too costly. Among the different formative techniques suggested by literature and the standards, we focus on the following approaches which Ypsomed usually employs:

- Cognitive walk-through
- Formative human factors study

The cognitive walk-through is a fairly simple approach including a single user or a group of users being guided through the process of using the device by means of a simple mock-up or prototype.

The formative human factors study is more sophisticated, collecting data from users in a simulated or actual use environment with the device. It allows us to record and to analyse the users' actions and errors. With a preliminary version of the instructions for use (IFU) it is possible to test whether the document is well understood and indicates where changes are needed. Furthermore labelling of the device can be tested and assessed by users. Important for a formative human factors study is the possibility to ask follow-up questions if a use error occurs and to include open questions to the users at the end of the trial. This gives valuable input for further modification of the device or label design as well as the content of the IFU.

It is important to include representative end users in the study that match the targeted user profiles. With approximately five to eight participants per user profile and associated cost of approximately US\$1,000 (£650) per user, the benefit of such a formative human factors study clearly outweighs the relatively low costs.



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The summative user study will demonstrate with the final device design and IFU of the future commercial product that the device is safe and effective to use. Crucial for the study is that actual users are recruited. They need to represent the population of the intended users. For statistical reasons at least 15-20 participants per user profile, with a minimum of 30 participants in total, might be indicated. The cost per participant is approx. US\$1,500 when contracted to an external organisation. The study should be performed under actual use conditions. This may include different lighting conditions or noise levels, or other distractions. It is important that for the summative user study the final IFU as well as the final device and label design is used to allow the assessment of precisely the same system as intended for market supply.

During the assessment, the test facilitator should not interact with the participant. Although objective data (such as use-errors during the test) are important, allowing participants to think aloud during the test, interviews after testing, and follow-up questions in case of use errors, may all be a recommended part of a summative test as well. The summative human factors study marks the end of the design process.

In some particularly challenging cases it might be indicated to perform a clinical study under actual conditions of use for validation of the design.

Important for achieving positive feedback from the regulatory agencies – as well as being mandatory in a pharmaceutical background – is an exemplary documentation of all tests, risk management and design optimisations.

## CONCLUSION

Human factors engineering is a complex process. As a pharma company, the selection of a device manufacturer with a proven track record of self-injection devices launched in several countries as well as experience in the field of human factors engineering is beneficial to achieve a high level of success. Ypsomed can support its customers with unique platform products that have been thoroughly engineered to meet the demand of various patient groups. With the possibility to customise these platforms further according to the needs of special user groups, Ypsomed aims to set new standards with regards to maximum design flexibility and minimum project duration.

## YDS – YPSOMED DELIVERY SYSTEMS

Ypsomed is the largest independent developer and manufacturer of injection systems for self administration. Our pens range from simple disposable pens to reusable pens with variable dosing and spring-assisted injection. We develop and manufacture autoinjectors for use with prefilled syringes as well as innovative injection devices for use with dual-chamber cartridges. Unique click-on needles complete our product portfolio.

All products are developed and manufactured in Switzerland, where internal capabilities include R&D, tool-making, injection moulding, cleanroom production and assembly facilities. Ypsomed provides not only marketing, regulatory and technological expertise but also production expertise according to the latest authoritative requirements, for both low and high-volume production. Ypsomed manufactures in US FDA-registered facilities, is inspected regularly by its customers and regulatory authorities and supplies devices approved for all leading markets including US, Europe and Japan.

Ypsomed has well established partnerships of many years with numerous leading pharmaceutical and biotech manufacturers.

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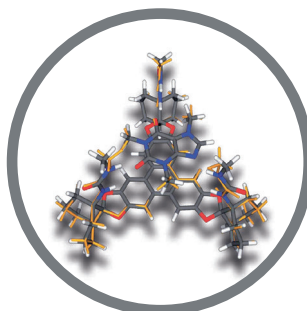


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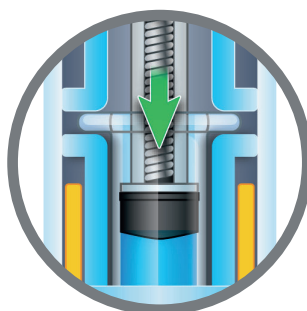
Biotech Syringe Series



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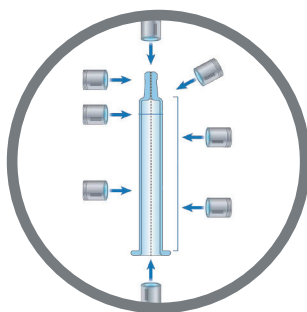
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# HYPODERMIC NEEDLES WITH INTEGRATED PASSIVE & ENCAPSULATING SHARPS-PROTECTION TECHNOLOGY

In this article, William Dierick, Technology Development Manager, Global Pharmaceutical Solutions, Terumo, highlights the product profile and features of K-Pack Surshield™, offering distinct benefits for healthcare professionals and patients, as well as benefits from a manufacturing perspective to the pharmaceutical industry.

For parenteral medication in luer prefilled syringes, pharmaceutical companies often co-package hypodermic needles within the drug package presentation to provide the healthcare professionals and self-injecting patients with the convenience to administer the medication in an efficient manner, enhancing the adoption of the appropriate injection practice for the specific drug and adherence to the therapy by patients.

With decades of expertise and core competences in parenteral drug delivery and injection technology, Terumo strives continuously to research and develop advanced and innovative devices that meet market needs. In 2011, Terumo launched K-Pack Surshield™, a next-generation sharps protection technology (see Figure 1).

With K-Pack Surshield™, Terumo offers the pharmaceutical industry an optimal technological solution to market injectable drugs with injection devices that allow them to be compliant with established regulations and legislation concerning the prevention of sharps injuries, such as the European Council Directive 2010/32/EU.

For the latter, EU Member States had to bring into force the laws, regu-

lations and administrative provisions necessary to comply with this Directive or ensure that the social partners had introduced the necessary measures by agreement by May 11, 2013.

K-Pack Surshield™ is an innovative hypodermic needle with an integrated passive sharps protection feature for use with (pre)-filled syringes. The device geometry is designed to allow for automated manipulations during the packaging process, making it ideal for bundling and inclusion into the secondary packaging of parenteral medication (Figure 2).

Designed in particular for subcutaneous and intramuscular injection applications, a route of administration for many parenteral pharmaceutical and biopharmaceutical drugs,

K-Pack Surshield™ is a hypodermic needle with a passively actuated feature that provides protection against accidental needle stick injury and hence minimises the risk of transmission of blood-borne pathogens from needle-stick injuries.

The encapsulating protection feature is integrated with the needle and therefore the needle is never exposed; neither before, during nor after injection. As a



Figure 1: K-Pack Surshield™, the next-generation sharps protection technology launched by Terumo in 2011.



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truly passive system, the protection mechanism is 'armed' during needle insertion, thus the protection system cannot be bypassed. The needle fits to (pre)-filled syringes with standard 6% luer slip or 6% luer lock conical fittings (see Figure 3).

K-Pack Surshield™ is regulated as a medical device, independently of the pharmaceutical product, meaning the pharmaceutical industry does not have to invest in and validate additional assembly operations. This minimises resource requirements and may assist in limiting regulatory hurdles that would otherwise be encountered when implementing sharps-protection features along with the parenteral drugs that are placed onto the market.

As such, this innovative device offers specific product features and benefits, described below.

#### User criteria and benefits

- Truly passive system; easy to use
- Efficient and permanent cover of the sharps
- Not possible to skip a crucial step to activate
- Needle sharps not exposed, before, during and after injection
- Does not require more time to use
- Clear view of syringe contents and access to syringe label
- Permanent and visual indication of activation
- Ergonomics appropriate for injection technique
- Terumo's needle quality for patient comfort

From a manufacturing perspective, the inclusion/bundling of K-Pack Surshield™ needles into the secondary packaging, together with the injectable medicine also offers the pharmaceutical industry with specific benefits:

#### Features and benefits from manufacturing perspective

- Compact design, individually packed, requiring minimal space
- Product configuration suited for automated manipulations
- Colour coding on tamper-evident label for in-line product detection by vision systems
- Does not require an additional assembly step (less investment compared with add-on systems)
- Less involvement of pharma companies for product and process validation (time-to-market)
- Own regulatory status as a medical device (time-to-market)
- Safety feature activation does not require interaction with the syringe; does not affect the syringe performance (e.g. dose accuracy)
- Provided by a global operating company with core competences in needle manufacturing



**Figure 2: The device geometry of K-Pack Surshield™ allows automated manipulations during packaging, for bundling and inclusion into the secondary packaging of parenteral medication.**

Furthermore, K-Pack Surshield™ needles fulfil the requirements of:

- EN ISO 7864 – Sterile hypodermic needles for single use
- ISO 23908 – Sharps Injury Protection – requirements and test methods: sharps protection features for single-use hypodermic needles, introducers for catheters and needles used for blood sampling

Having obtained regulatory approvals, K-Pack Surshield™ was launched in 2011 with industrial-scale production facilities installed at the manufacturing site in Leuven, Belgium, utilising state-of-art injection moulding technology and fully automated assembling equipment with on-line vision control systems for 100% in-line inspection to ensure optimal quality and functionality of the device.

Upon commercialisation of this new device, Terumo engaged in several negotiations with the pharmaceutical industry and was pleased to announce that a global pharmaceutical company selected its K-Pack Surshield™ needle for purchase and first commercial shipments of the device were started early 2012.

The customer, whose identity remains confidential, market the innovative safety needle together with drugs for applications in fields such as hepatitis and liver transplantation. In particular, patients who self-inject these medications are expected to benefit from this new drug and device solution.

Currently, more applications are being introduced and shipments of products began for such new application.

To service the customers in true partnership spirit, Terumo assists the pharmaceutical companies to prepare for marketing the products by providing training and educational materials, as well as assistance to prepare for regulatory documentation.

The value and benefits of this innovative device were also underscored by receiving the prestigious Pharmapack 2012 Manufacturers



Award in the category "Safety Device", showing recognition to Terumo efforts to innovate in this field of application and contributing to the health and safety of both healthcare professionals and patients.



**Figure 3: K-Pack Surshield™ fits to (pre)-filled syringes with standard 6% luer slip or 6% luer lock conical fittings.**



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## ONdrugDelivery 2013/14 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
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
December 2013	Delivering Biotherapeutics	November 4th
January 2014	Ophthalmic Drug Delivery	December 9th
February 2014	Prefilled Syringes	January 13th
March 2014	Transdermal Patches, Microneedles & Needle-Free Injection	February 10th
April 2014	Pulmonary & Nasal Drug Delivery	March 10th
May 2014	Injectable Drug Delivery 2014: Devices Focus	April 14th

# Next generation of sharps protection technology



- Truly passive system
- Sharps never exposed
- Easy to use
- Compact, individually packed
- Suited for automated manipulations
- Terumo's high quality needle



## K-Pack Surshield™

*Hypodermic needle with integrated passive sharps protection*



# GERRESHEIMER

## THE RIGHT SYRINGE FOR EVERY APPLICATION: PREFILLABLE SYRINGES MEET NEW MARKET CHALLENGES

In this piece, Mr Bernd Zeiss, Manager, Technical Pre-Sales Support, Gerresheimer Bünde, shows how recent innovations and technological advances in prefilled syringe development align with the major drivers for change in today's patient populations and healthcare markets.

Prefillable syringes are fuelling one of the medical device industry's fastest growing and most innovative markets. The key drivers are closely linked.

### ECONOMIC & DEMOGRAPHIC CHANGES

#### Developments in Emerging Markets

The globalisation process has improved the level of healthcare provision in countries around

sions appear to compete with the few and generally expensive innovations. In this scenario, prefilled syringe suppliers are selected according to the criterion of cost-effectiveness, which makes standard solutions necessary.

#### Aging Population

Another trend has emerged as a result of demographic developments. In aging populations, the proportion of people with long-term or chronic health problems such as diabetes, rheumatism or cancer, who often need parenteral drugs, increases. Administering these parenteral drugs at medical centers or clinics puts a great strain on both the healthcare system's budget and the patients' quality of life. Prefilled syringes and auto-injectors which are suitable for home treatment are therefore becoming more significant.

"TOLERANCES WHICH ARE AS NARROW AS POSSIBLE ENSURE THAT THE PRIMARY PACKAGING SITS FIRMLY IN THE INJECTOR WITHOUT BEING AT RISK OF BREAKING"

the world. Patient numbers are growing as a result of the rising incidence of the lifestyle-related diseases that are typical of the western world, such as Type 2 diabetes or high blood pressure, in developing and emerging markets.

#### Healthcare Costs

Rising demand inevitably means greater pressure on costs. Healthcare providers are calling for a cap on the continuously rising costs to prevent what is known as the 'patent cliff'. Once drugs lose patent protection, generic ver-

### NEW DRUGS & TECHNOLOGIES

Medical and technological progress is another prefilled syringe innovation driver. New biotech drugs and a range of new ophthalmic drugs require primary packaging manufactured to exacting standards. The primary packaging for these drugs also has to meet increasingly tough safety and ergonomics requirements, which is driving innovation in drug delivery device development. For example, the legal require-



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**Figure 1: Diving nozzles for silicone application in the RTF® process can considerably improve the evenness of the coating across the entire length of the syringe body.**



**Figure 2: ClearJect™ COP syringes and MultiShell® vials made of COP will be increasingly used for sensitive or aggressive formulations or for pharmaceuticals with special container design/container closure system requirements.**

ment that the packaging has to provide effective protection against needlestick injuries has led to the development of new needle safety systems.

Drug delivery device designs are incorporating more ergonomic features to simplify the administration process for patients and medical personnel. In this context, the traditional vial and ampoule systems are now increasingly being replaced by prefilled syringes, which guarantee precise dosage and save time because there is no need to draw the medications up into the syringe manually or change disposable needles.

#### **Pharma/Syringe Manufacturer Collaborations**

In order to meet the primary packaging requirements of modern pharmaceutical drugs optimally and exploit the limited lifespan of patented products to the full, intensive collaboration between the pharmaceutical industry and prefillable syringe manufacturers is essential. Ideally, they should already be working together when the pharmaceutical product is being developed so that the drug can be matched to the most suitable syringe as soon as possible. If the prefillable syringe is to be part of a drug delivery device, cooperation with the device developer is also necessary so that the fastest and most cost-effective solution can be found and no time is wasted with unnecessary development loops.

#### **PREFILLABLE SYRINGES IN AUTO-INJECTORS**

Auto-injectors reduce the costs of chronic disease treatment and eliminate the need for patients to visit their doctor or a clinic on a daily basis. They ensure the safe and precise dosage of self-administered medications and eliminate psychological barriers surrounding the invasive process of injecting because the needle isn't vis-

ible before the device is used.

The syringe and device have to be tailored to one another to maximise dosage precision. It is obviously important to have a syringe manufacturer with extremely precise production processes. Tolerances which are as narrow as possible ensure that the primary packaging sits firmly in the injector without being at risk of breaking. Above all, the injectors have to guarantee that the entire prescribed dose is administered. Since the auto-injector's spring tension is non-variable, the syringe's break loose and glide forces have to be within the prescribed specifications. The desired mechanical properties of the syringe are achieved by siliconising the syringe barrel in the RTF® process (Figure 1). The silicone coating plays an important role in reducing the forces that are necessary to move the plunger head. On the other hand, the silicone coating cannot be too thick, otherwise there would be too much free silicone oil inside the syringe.

The objective is to match the syringe optimally with the type and viscosity of the medical

use of very low quantities of silicone oil and chemically bonding it to the glass surface.

#### **INNOVATIVE TECHNOLOGIES FOR NEW PHARMACEUTICALS**

Many modern-day pharmaceuticals are bio-engineered. These biotech drugs typically have extremely high molecule size and complexity. Their active ingredients can be effective in the tiniest of quantities and they are often very expensive.

These properties of biotech drugs pose special challenges to pharma manufacturers. Also, they are so expensive that unnecessary overfill has to be avoided at all costs and extremely precise dosage is essential. Prefilled syringes are the answer to both of the above problems.

The silicone coating on these syringes has to meet stringent requirements because it doesn't just have to improve glide properties, but also deliver a hydrophobic effect which impairs adsorption of active ingredients or adjuvants on

**“EVEN A TIME-TESTED MATERIAL SUCH AS GLASS IS PUSHED TO ITS LIMITS BY THESE EXACTING REQUIREMENTS”**

silicone oil used and the plunger head's properties. Diving nozzles for silicone application can considerably improve the evenness of the coating across the entire length of the syringe body. If the active ingredient in the pharmaceutical drug needs a low-silicone primary packaging, the silicone coating can alternatively be baked on (baked-on RTF®). This process involves the

the glass surface. At the same time, it is necessary to minimise the protein aggregation caused by silicone oil micro droplet contamination because these aggregates can potentially trigger undesirable immune reactions.

Even a time-tested material such as glass is pushed to its limits by these exacting requirements. In prefillable glass syringes, tungsten residue

resulting from the cone forming process or residues of the polymer used to glue the needle into the syringe can also cause problems. New technologies make it possible to control these problems in glass syringes and these challenges have additionally driven research into alternative materials.

Cyclic olefin polymer (COP) was discovered to be ideal as a plastic pharmaceutical primary packaging. COP is non-sensitive to a wide range of pH levels, doesn't release alkalis or tungsten and has a far greater break resistance than glass. On the other hand, it is more gas/vapour permeable and expensive than glass. So glass will continue to play an important role in the future as a primary packaging material. However, prefilled syringes and vials made of COP such as ClearJect™ COP syringes and MultiShell® vials (see Figure 2) will be increasingly used for highly sensitive or aggressive formulations or for pharmaceutical drugs with special container design/container closure system requirements.

## ABOUT GERRESHEIMER

Gerresheimer is an internationally leading manufacturer of high-quality specialty products made of glass and plastic for the global pharma and healthcare industry. Its comprehensive port-

## SYSTEMATIC SELECTION OF THE OPTIMUM SYRINGE SYSTEM

There can be no universal solution for the wide range of applications in parenteral drug delivery with prefilled syringes. Pharmaceutical experts therefore demand a comprehensive choice of high quality products that also enable the adaptation of the syringe system to an individual requirements profile.

- This is associated with the question of whether an active ingredient has small molecules or complex bio-engineered substances in it. The field of application is also significant because devices for self-medication in the home have to differ from devices used by medical personnel in a medical practice or clinic. Some medications are also linked to specific legal requirements.
- Once the framework has been clarified, the choice of material can be made. First of all, it has to be ascertained whether glass or COP is the best material, then the optimum syringe format has to be selected. The mechanical properties of prefilled syringes are defined by the selection of the siliconisation method and the plunger head.
- Early liaison between the pharma company and the syringe manufacturer enables the identification of the ideal solution for practically any application and the fastest and most cost-effective way to the optimum product.

folio of products extends from pharmaceutical vials to complex drug delivery systems such as syringe systems, insulin pens and inhalers for safe medication dosage and application. Together with its partners, the company develops solutions which set standards and have role model status in their respective market sectors.

The Group realises revenues of more than €1 billion (£850 million) and has more than 11,000 employees at 47 locations in Europe, North and South America and Asia. It uses first-rate technologies, convincing innovations and targeted investments systematically to consolidate a strong market position.

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## CONFERENCE HIGHLIGHTS

- ✓ Drug delivery, the impact on the future of healthcare
- ✓ How drug delivery is disrupting the diagnostic industry
- ✓ Who is funding drug delivery?
- ✓ The next paradigm on how biologics will be delivered
- ✓ New deal structures and models
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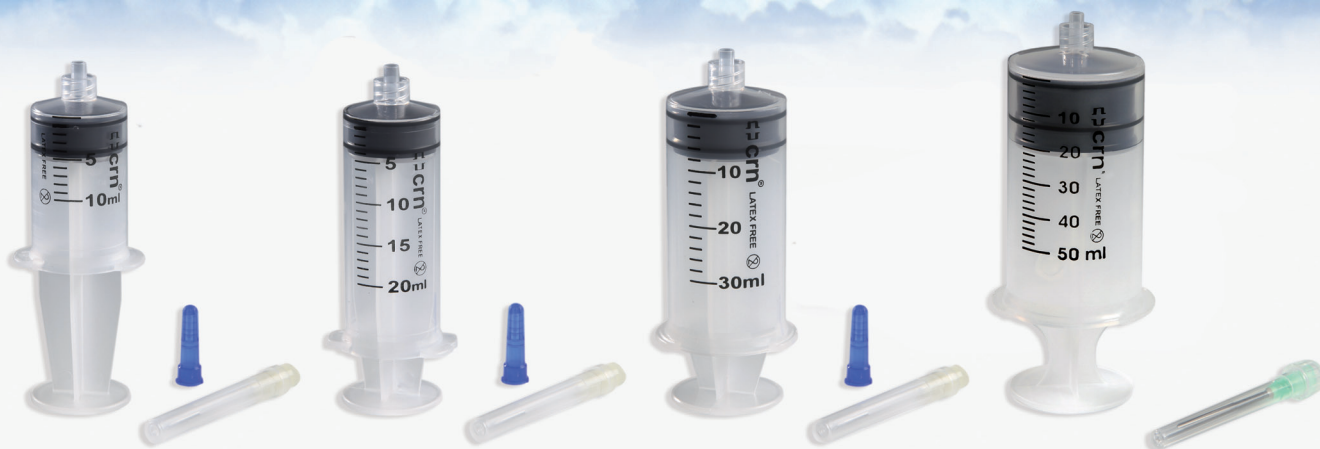


# Crono<sup>®</sup> Ambulatory infusion pumps



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## COMPANY PROFILE – CANÈ S.P.A.



### MEDICAL TECHNOLOGY

Based in north-west Italy, Canè S.p.A. is a leading manufacturer of ambulatory infusion pumps for the administration of pharmaceuticals.

#### HISTORY

Canè was founded in 1978 as a manufacturer of ambulatory infusion pumps for treating thalassaemia. Over the last 35 years it has grown to become the leader in the segment addressing the delivery of drug volumes ranging from 10-50 ml. Starting from the first syringe-drivers, which were relatively bulky, causing patient compliance to suffer, Canè's products have evolved into the Crono line of miniature pumps which may be worn without impacting patients' normal daily routine.

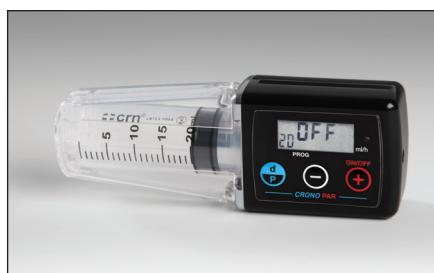
#### THERAPEUTIC AREAS

The Crono series of ambulatory infusion pumps (see Figures 1-5) addresses four main therapeutic areas: primary immunodeficiency, Parkinson's disease, thalassaemia, and pain control. In addition we have models dedicated to pulmonary hypertension and fertility treatment, and we are working with partners in areas as diverse as hormone replacement therapy, radiopharmacology, and skin care.

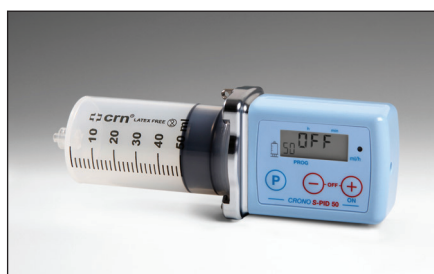
Infusions may be subcutaneous, intravenous, or intrathecal depending upon the pump model. The majority of the pumps are intended for use by patients at home, and are designed to allow them to receive medication almost continuously while maintaining as normal a life as possible.

#### DESIGN & MANUFACTURING

All pump R&D and design work is done in-house, as are final assembly and testing. Our dedicated syringes are designed in-house and are manufactured by an Italian partner. We pride ourselves on the fact that where possible all components are locally sourced, which carries the added advantage of being able to maintain the highest standards of quality.



**Figure 1: The Crono PAR (shown with the protective syringe guard), for the treatment of Parkinson's Disease, has both manual and automatic flow profile operating modes**



**Figure 2: The Crono S-PID 50, for the subcutaneous infusion of immunoglobulins, has a maximum infusion volume of 50 ml which can be administered in just 30 minutes.**



**Figure 3: The Crono Twin uses two 20ml syringes working in tandem to administer immunoglobulins in two or more infusion sites.**

While we have our own series of products, Canè also provides ODM services to pharmaceutical companies who require customised pumps, be it in limited numbers for clinical trials or for mass-produced private labelled devices.

#### PRODUCTS

Canè's Crono series includes the ambulatory infusion pumps and the dedicated syringes which are used with them. Depending upon the therapy, the syringes may have volumes of 10, 20, 30 or 50 ml. Most of the pumps are designed for a specific therapy, so that their features and programmability are tailored to the way in which the drug will be used by the patient. For example, a pump used for infusion of immunoglobulins is generally capable of higher flow rates but has no bolus dose function, whereas pumps used in the treatment of Parkinson's disease are capable of lower flow rates but have the bolus dose function, and some models also have automatic flow profile modes.

All our pumps are characterised by:

- Small size: 7.6 x 4.9 x 2.9 cm (without syringe)
- Light weight: 127g including the battery

Other pump characteristics include (depending upon the model):

- Programmability in terms of flow rate or infusion time
- Flow rates ranging from 0 ml/h (bolus dose only) to 100 ml/h
- Bolus doses up to 10 ml
- Bolus dose interval control
- Partial volume function (for partially filled syringes)
- Selectable occlusion alarm pressure
- Infusion line priming and anti-freeflow systems
- Lockable keyboard, so patients can't change medical practitioners' settings
- Multiple pre-programmed flow rates which are selectable by the patient during an infusion
- Automatic flow-rate profiles through the day
- Bluetooth interface





**Figure 4: The Crono FE is a pump for the treatment of infertility. For this treatment the drug must be delivered as a series of boluses, and the Crono FE may be programmed to administer boluses from 5-1000  $\mu$ l at intervals ranging from 5-300 minutes.**

### CUSTOMISATION

Canè works with pharmaceutical companies and other medical device manufacturers to provide customised solutions where required. In some cases this is for small numbers of pumps, for example for clinical trials of drugs which have particular flow rate or timing requirements. In



**Figure 5: The Crono Basic is a generic pump, with basic functionality, for the subcutaneous infusion of drugs. It has a maximum flow rate of 40 ml/h.**

others we have developed privately labelled models which we manufacture exclusively for the customer. In both cases the customisation can range from small modifications to programming parameters to fully fledged redesigns of mechanics and firmware.

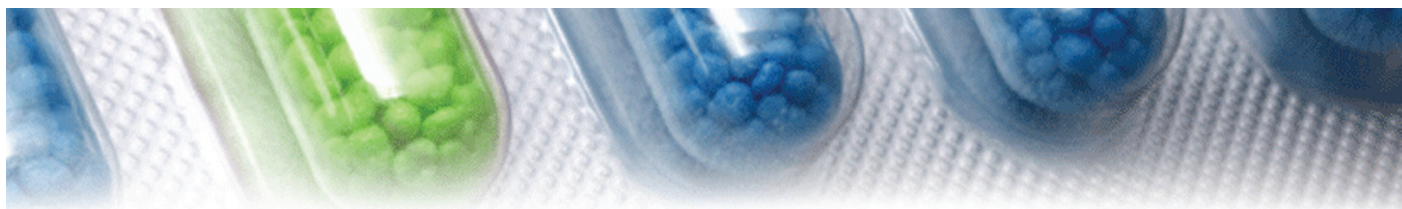
### AVAILABILITY

Availability of Canè's Crono pumps depends upon the geographical area in question, since

not all pumps are yet certified everywhere. In Europe and the US all models have been certified, and work is ongoing to complete the certification process elsewhere.

### QUALITY

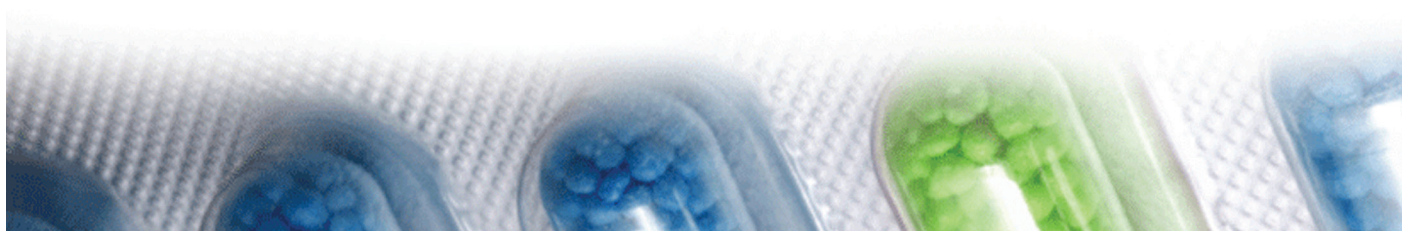
Meeting the highest quality standards is of utmost importance to us. All our operations comply with UNI EN ISO 9001, UNI EN ISO 13485 and European Directive 93/42/EEC on medical devices, modified by Directive 2007/47/CE, and the US FDA's 510k.



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# PREFILLABLE SYRINGE COMPATIBILITY & FUNCTIONALITY: TECHNOLOGIES TO HELP REDUCE RISK & IMPROVE INJECTION

In this article, with an emphasis on biologicals, Amanda Davis, Senior Product Manager, BD Medical-Pharmaceutical Systems, relates some of BD's recent technological advances in the prefilled syringes market to the technical challenges, patient considerations and regulatory requirements that they address.

## INTRODUCTION

When BD launched its first glass prefilled syringe into the market in 1954, the syringes primarily were used for drug delivery by health care workers in a clinical setting. Since then, the dynamics of health care delivery have changed drastically. In particular, biotech drugs (biologics) have revolutionised care for a variety of chronic diseases. By 2018, six of the top 10 leading drugs in the US by sales will be biologics.<sup>1</sup> With the expansion of biologics in chronic disease care, administration of treatment continues to evolve from the traditional model of clinician-administered care to a model based on self-administration by educated and empowered patients. Subsequently, demand has grown for safe, easy-to-use, and convenient delivery devices, such as auto-injectors, pens, and patch injectors.

The biotechnology market and US FDA set very specific requirements for drug delivery of biologics, which have unique properties and consist of large molecules that may be sensitive to interaction with components of the delivery device, such as the syringe lining.<sup>2</sup> Prefilled syringes and auto-injectors, in which biologics are commonly packaged, facilitate patient self-care and are regulated under the FDA's Final Rule on Combination Products, issued in January of this year, that clarifies how earlier requirements are to be applied.<sup>3,4,5</sup> The FDA scrutinises the quality of product components (including sensitivity of drugs to tungsten, silicone, adhesives, and rubber) and the integra-

tion of combination products.<sup>2,4</sup> Pharmaceutical companies also demand a drive to lower total cost of ownership, platform standardisation, and risk-mitigation strategies, such as dual sourcing, to mitigate supply-associated risk for containers and devices.

These changes have transformed the market for delivery devices to meet the demands of clinicians, patients, pharmaceutical companies, and regulatory agencies for simple, efficient, and safe drug administration. In order to meet these increasing demands, drug delivery device suppliers must continue to innovate to address product quality, cost savings, and risk mitigation. BD has a proven commitment to continued innovation in the biotech space.

## INTRODUCTION TO PREFILLED SYRINGES

As many biologics cannot be taken orally, the role of injection devices should grow along with the expansion of biologics in patient care, making the choice of drug delivery system increasingly important. Prefilled syringes offer numerous benefits for patients and treatment administration, including efficiency in terms of time, reduction in medication risk due to dosing errors or cross-contamination, and elimination of the need to measure doses and prepare, fill, and clean syringes.<sup>2,4,5,6</sup> These benefits have led to increased market demand for prefilled syringes to administer a variety of drugs appropriate for patient self-care, including biologics.



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Patients express preference for drug delivery devices that are convenient to use (with strong preferences for auto-injectors), and for more comfortable injections, with less pain and shorter injection times. Another preference, for less frequent injection, while primarily related to the molecule being injected, may be influenced by the capabilities of the delivery device. In their design, prefilled syringes address these patient concerns. In fact, patients prefer prefilled syringes over other options, which have been shown to improve adherence with self-administered treatments.<sup>6</sup>

With increased use of prefilled syringes, regulatory agencies have significantly increased their expectations for the individual components and combined device. Prefilled syringes and auto-injectors generally fall under regulation for combination products and require a system-based approach.<sup>4,6</sup>

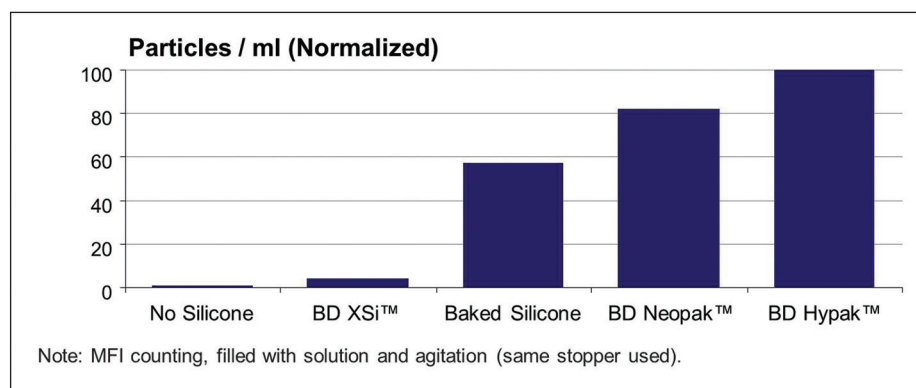
Rigor must be demonstrated in developing and providing data regarding the compatibility of the components of the device as well as compatibility of the drug and container.<sup>5,7</sup> Human factors, such as patient age, visual impairment, or limited dexterity may affect accurate drug delivery, and their assessment is required for all delivery devices.<sup>4,8</sup>

Given these trends, it is increasingly important that drug formulation and delivery strategies be integrated at an early stage in the development of complex biologics. Issues with poor integration of prefilled syringes in auto-injectors have led to recalls and complaints, and can be avoided when compatible design is a priority from inception through delivery.

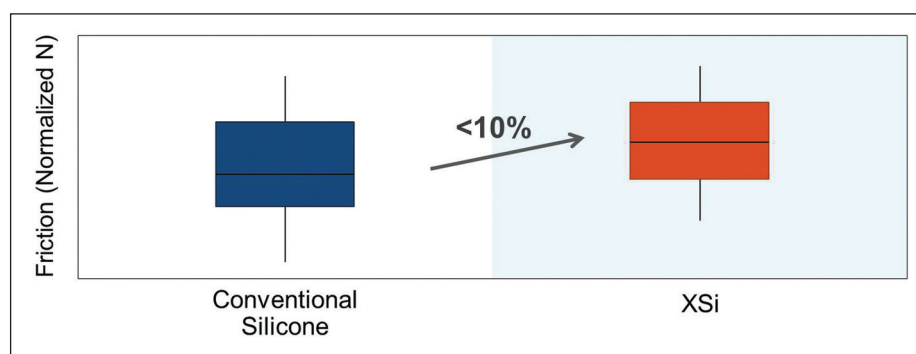
## DRUG-CONTAINER COMPATIBILITY

There is a potential for unwanted interactions between biologics and other substances with which they come into contact, which is an issue with implications for the design of prefilled syringes.<sup>9</sup> Silicone is commonly used to lubricate the inner wall of syringes and facilitate smooth injection. An area of intense interest is the development of subvisible particles (SVPs) of silicone in the range of 0.1 to 10  $\mu\text{m}$  in drug solution.<sup>10</sup> FDA's Container Closure Guidance and SVP Guidance note the potential impact of SVPs and offer strategies for monitoring their presence.<sup>5</sup>

Silicone-induced SVPs arise from interactions between the lubricant and active contents of prefilled syringes. They may be released into the drug (1) immediately or shortly after filling, (2) over time during storage, or (3) only during the injection process itself. The first and second categories are most problematic, as these particles remain in contact with the drug for prolonged periods of time and have the potential



**Figure 1: The Impact of New Technology on Silicone-Induced Sub-Visible Particles.**



**Figure 2: The Impact of New Technology on Glide Force.**

to form silicone-protein complexes or otherwise affect the drug. However, in glass prefilled syringes, a given amount of silicone is needed for injector functionality, limiting the degree to which silicone can be eliminated, and use of plastic syringes without silicone lubrication is not widely accepted.<sup>9</sup>

Recently, surface cross-linking of silicone has been proposed as a solution for silicone-induced SVP reduction without negative effects on performance.<sup>2</sup> BD's XSi™ cross-linked silicone technology has brought this solution to market and been demonstrated to reduce silicone-induced SVPs significantly while ensuring auto-injector functionality with an appropriate glide force (see Figure 1).

Compared with conventional silicone coating, maximum glide force with the XSi™ coating is increased by a minimal 5-10% (Figure 2).<sup>11</sup> While introducing little or no SVPs, syringes using the XSi™ coating provide the expected lubrication and level of glide performance. This latter feature, known as syringeability, has been shown to affect patient's adherence with self-injected therapies.<sup>9</sup>

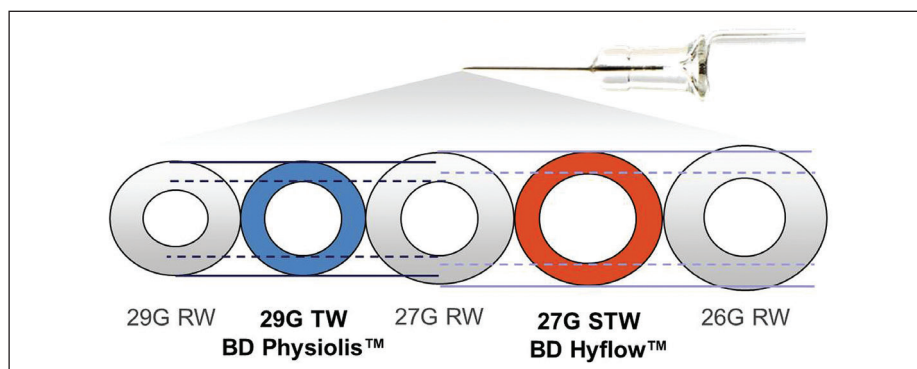
XSi™ technology is inert, resists drug degradation, provides biologic drug stability, produces little or no SVPs, and does not significantly increase glide force. Importantly, in providing these benefits, the XSi™ technology introduces no new chemistry or chemical substrates during the manufacturing process, thus reducing the regulatory hurdle for review and registration.<sup>6</sup>

## PATIENT INTERFACE/ FUNCTIONALITY

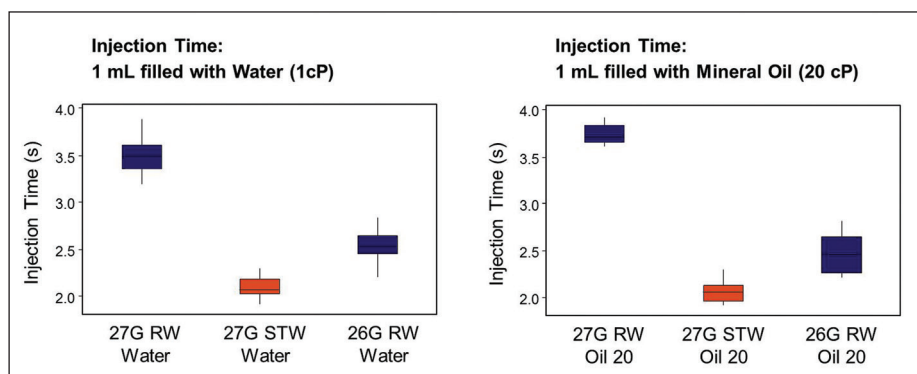
Clinicians factor in ease of administration, convenience, and comfort when making treatment decisions, while patients seek fewer injections and optimised injection comfort (minimised pain and injection time).<sup>6</sup> Designs that integrate prefilled syringes with an auto-injector must take into account components such as spring force, needle gauge, and flange strength, all of which contribute to the patient's injection experience.

Closely linked with innovation in biologics is a trend toward higher-viscosity drug formulations because of the size of the molecules, concentrations needed for effective response, and the practical limitations of subcutaneous injection (for example, volume).<sup>9,12,13</sup>

Molecule size and concentration are relatively fixed qualities, making innovation in delivery necessary. One approach is the use of large-volume solutions, including 2.25 ml syringes and patch injectors, such as the BD Microinfusor™ patch injectors. Once the formulation for a self-injected drug is set, the inner diameter of the needle strongly influences the glide force necessary for injection.<sup>9</sup> New needle technologies present another opportunity for innovation. Good examples are the BD HyFlow™ and BD PhysioliS™ needles. BD HyFlow™ is a 27-gauge needle that uses special thin-wall technology, resulting in a larger inner diameter that allows greater flow of drug without substantially increasing the



**Figure 3: Needle Gauges for Different BD Systems.**



**Figure 4: BD Hyflow™ Allows the Injection of Viscous Drugs up to 20cP in Less Than 15 Seconds.**

outer diameter, which affects patient experience (Figure 3). The BD HyFlow™ needle allows injection of drugs with viscosity up to 20 cP in less than 15 seconds, and decreases the average injection time by 50% versus 27-gauge regular-wall needles; and by 10% versus 26-gauge regular-wall needles (see Figure 4).<sup>14</sup>

## REGULATORY CONSIDERATIONS FOR SILICONE-INDUCED SVPS

The FDA issued specific regulatory guidance to address SVPs and acceptable quality level standards that must be met with regard to assessing the potential for interaction between the product intended for the syringe and the syringe itself.<sup>15</sup> New chemistry introduced to drug containers warrants new FDA submissions, whereas innovations in existing chemistry avoid the need for additional review. Long before the advent of biologics, silicone has been used in prefilled syringes to facilitate smooth gliding of the plunger and stopper. In the biologics era, prefilled syringes represent the current standard for drug administration, but concerns about interactions between silicone syringe linings and silicone-induced SVPs have surfaced. Syringes using XSi™ technology reduce drug-silicone interactions and SVPs to the lowest possible level, are designed to be fully compatible with autoinjectors, and do not introduce new chemicals or chemistry.

## CONCLUSION

Biologic agents continue to revolutionise patient care. Innovation to improve the patient experience of administering biologics will help fulfil the promise of these agents in the treatment of chronic illness. Although prefilled syringes make injection of biologics safer and more efficient, there remain several challenges to be overcome. These include developing technology designed to address the unique characteristics of biologics, such as their higher viscosity and potential to interact with silicone syringe linings. BD has made advances in product engineering and materials that show positive results in meeting and overcoming these challenges with innovative products such as BD XSi™, BD HyFlow™, and BD Neopak™.

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# Dividella

Pharma Technology Solutions

## MACHINE CONSTRUCTORS WITH A FLAIR FOR PACKAGING

The Swiss packaging company Dividella is generally known for its first-class Top-Load cartoning machines. But very few people are aware that pack design plays a key role from the very beginning. Both depend on the specialists at Dividella – the packaging and the machine!

In the production units in Grabs, Switzerland, Dividella manufactures exclusively machines for packaging pharmaceutical products. The focus is totally on the packaging of parenteral pharmaceuticals in Top-Load boxes. These

maceutical products, but also, every now and then, for existing products. In most cases they are parenteral drugs, i.e. liquid pharmaceuticals which are packaged in syringes, flasks, vials, auto-injectors and the like.

**“EVEN THOUGH IN THE CASE OF  
PRESCRIPTION MEDICINES NO  
PURCHASING DECISION IN THE CLASSIC  
SENSE USUALLY TAKES PLACE – PATIENTS  
GET WHAT THE DOCTOR PRESCRIBES  
FOR THEM – THE APPEARANCE AND  
THE PACKAGING ARE NONETHELESS  
OF GREAT IMPORTANCE FOR  
PHARMACEUTICAL MANUFACTURERS”**

sensitive products demand well thought-out packaging solutions. Together with customers, Dividella's specialists develop the ideal packaging for these particular products.

### **THE TOP-LOAD / TOP-OPENING CONCEPT**

A customer from the pharmaceutical industry has a packaging requirement: a packaging solution for one or more products. Usually, packaging has to be developed for new phar-

– patients get what the doctor prescribes for them – the appearance and the packaging are nonetheless of great importance for pharmaceutical manufacturers. The customers' marketing departments generally have a significant impact on the design of the pack. These are the people who work closely from the outset with Dividella's packaging designers.

### **DEVELOPMENT IS TEAMWORK**

The pharmaceutical manufacturer's project team is intimately involved in the entire devel-

On Dividella machines, these products are packaged in Top-Load / Top-Opening boxes. The medicines are inserted from above and can then be removed very easily by the consumer from the top of the pack.

Since Dividella sees itself first and foremost as a provider of solutions, and only as a machine constructor as part of that, packaging design enjoys a very high priority. Because even though in the case of prescription medicines no purchasing decision in the classic sense usually takes place



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opment process right from the start. All products which are to be packaged are therefore defined precisely at the beginning of each project. The aim is to package as many medicines as possible using the same design and therefore on the same machine. To make the packaging process as efficient as possible, Dividella's packaging specialists will on request make proposals on harmonisation of the relevant customer portfolio.

After that, the products for which new packs are required are clarified, and the packaging designers create initial concepts. These may look different: on some projects samples are produced at the very beginning; they are designed and erected manually. On other projects, various possible packaging solutions are put forward in the form of 3D presentations. On the basis of these presentations, the customer indicates a general direction and a sample is then produced. The blanks for the samples are made by Rondo AG (Allschwil, Switzerland), one of Dividella's sister companies. Erection and testing of the samples for correct functioning then takes place, again at Dividella.

The joint production of the samples is logical: Rondo is not just Dividella's sister company but also one of the leading folding-box manufacturers in Europe for the pharmaceutical industry. Involving Rondo in Dividella projects at an early stage ensures that the designs not only meet the customer's needs and can be produced on the machine, but also that they meet the requirements of the folding-box manufacturer. Particular attention is given to the grades of paperboard which are used, the perforations and a number of other stamping details. Dividella's senior management attach great importance to designing packaging solutions from the outset so as to ensure that production subsequently functions smoothly.

## FROM THE SAMPLE TO THE PACK

Once the pharma producer receives the selected samples, they generally carry out various tests before opting for a packaging solution. One of these tests is the so-called handling test: it checks how the end user handles the pack. Does he or she open the pack correctly intuitively? Is any tamper-evident protection which is present handled correctly, for example? In the event that the pack contains products for people with motor disabilities, how easily can they open this pack and remove the drug?

Another test, which is also frequently applied, is the transport test. This verifies that the boxes and packaged products can be transported safely. There are companies which dispatch entire cartons and pallets around the world for this purpose. Others carry out vibration and



**Figure 1: Volume savings of up to 50%: products are packed securely as closely as possible and can be removed individually from the TopLoad pack with its integrated tamper evidence.**

drop tests in the laboratory to check whether the medicines remain undamaged.

## VOLUME SAVINGS OF UP TO 50%

Dividella folding boxes are pure mono-material packaging. That is, the folding box is made from 100% recyclable cardboard material. This distinguishes it from other conventional TopLoad packs. For customers in the pharmaceutical industry, this means that by using only one pack-



**Figure 2: Variable flute concept: syringe, vial and adapter are packaged securely in the shatter-proof combi pack.**

aging material the space required and the transport costs can be significantly reduced. Dividella reports volume savings of 25-50% compared with traditional blister packs (see Figure 1). These space savings are important in that many of these highly sensitive drugs are cold-chain products. In other words, they must be cooled continuously from production until they are used by the patient. The less space these products take up the better. This includes space in the refrigerator in which general practitioners keep temperature-sensitive vaccines, for example.

## THE 'FLUTE' CONCEPT

This space saving is achieved thanks to Dividella's special design concept. Since the whole box is made of cardboard, customised "flutes", specially adapted to the products, can easily be glued inside the box. The product is placed crosswise in relation to these flutes. In the case of a syringe pack, for example, the syringes are inserted in front of and behind the barrel of a syringe in such a way that the product itself virtually "floats" and is connected to the actual box only by the two flutes.

In this way, multiple products can be packaged close to each other without touching. Since the products do not touch the base or the lid of the box, they are highly impact-resistant and the firmly anchored products cannot break even if they are dropped onto the floor. This 'flute' concept is highly versatile, so the layout within a box can easily be adapted to individual customers' needs. In so-called combi packs, not only the syringes but also the accompanying vials and accessories, such as needles, filters and the like can be inserted at fixed points (see Figure 2).

## THE RECIPE FOR SUCCESS: DESIGN PLUS MACHINE

This is what is so special about Dividella: it is a machine constructor in its heart and soul – but with brains. Because – as Dividella's management believe – what good is the most elegant design if the packaging solution does not then work properly in industrial production? The packaging specialists emphasise from the outset that the product is perfectly packaged in accordance with the requirements AND that a solution is provided which can be processed on a machine and which ensures reliable, trouble-free production.

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# Dividella

Pharma Technology Solutions



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# DUOJECT IN PERSPECTIVE: WHERE WE ARE NOW, AND WHERE WE ARE GOING NEXT

In this overview, Simon Williams, Business Development, Duoject Medical Systems, outlines how Duoject Medical Systems has progressed from its origins offering custom medical device engineering services to become a full-capacity manufacturing organisation.

Encouraged by its customers over the last four years, Duoject has been working hard to build on its 25-plus years of successful experience as an engineering-services group offering custom medical device design and development services, to become a full-capability manufacturing organisation. In that time, we have set-up a pre-production prototyping facility (just outside Montreal, Canada) and then, with our long-term partners, C&J Industries (Meadville, PA, US), have established high-volume production capability, with extensive clean moulding capacity and ISO Class 10,000 cleanroom assembly. This US FDA-approved, ISO 13485 facility, in the heart of Pennsylvania, US, has a long history of supplying medical devices to the pharmaceutical industry.



**Figure 1: E-Z-Link vial adapter with safety disc, compatible with 13mm or 20mm drug vial and luer-lock syringe.**

During our many years as a medical device developer, we have built up a significant portfolio of patents in the fields of drug reconstitution and delivery. Building on this patent base, we have identified a number of key products which address many of the common reconstitution and drug delivery issues seen on the market today.

We have faced many challenges and learned many vital lessons during the past four years, and we are proud of where we now stand and are proud of the products we are now offering to the market under the Duoject brand.

Many of our devices will be on the market early next year. We could not have achieved this without the support and belief of a number of loyal customers that have helped us on this journey and selected our devices to enhance the usability and safety of their drugs.

Like you, we truly care about patients and healthcare professionals' safety, and we respect and want to contribute to the efficiency of our precious medical resources. We have conducted many user studies to ensure that our products offer achievable benefits and provide added value and an optimised user experience.

Our **EZ Link** vial adapter (shown in Figure 1) offers some key safety features when compared to the alternative of not using a needle to perform reconstitution as well as when compared to alternative vial adapters available on the market today. Our safety disc ensures that no stick injuries can occur at any time, while also ensuring that the spike cannot be touched and contaminated prior to use. EZ Link even locks if removed from the drug vial to prevent the



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**Figure 2: PenPrep EVO cartridge-based reconstitution device for multi-dose applications.**

possibility of a non-sterile device being reused to reconstitute another drug product.

**PenPrep EVO** (Figure 2) is a unique device allowing the rapid, simple and safe reconstitution of a lyophilised drug vial and diluent contained in a 3ml cartridge. Once reconstituted, the drug cartridge can then be used to deliver multiple injections - using one of the many multi-dose pen injectors widely available on the market. We first described PenPrep EVO in our previous article “*DuoJect Introduces PenPrep EVO*”, which appeared in *ONdrugDelivery Magazine*, 2013, Issue 39, pp 20-21.

**VaccJect** (Figure 3) is our revolutionary alternative to a prefilled syringe, fitted with a needle-safety system, resulting from the challenge we set ourselves in proving that needlestick protection should not cost more than a standard drug delivery system. There is now a growing demand and need to transport and store an ever greater variety of vaccines and drug products, many of which must be transported and stored in temperature-controlled environments. By



**Figure 3: Vaccject delivery device, simple and intuitive, incorporating needle safety technology.**

separating the drug container from the delivery device, we have been able to reduce drug storage space requirements by up to 10 times compared with current single dose systems used today.

Physicians and other healthcare professionals love that our device does not look like a “scary” syringe and that the needle is covered both before and after the injection, ensuring it is never seen by the patient or uncovered to endanger the healthcare professional.

announced as they are ready for the market in the coming months.

At the same time, our Engineering Services Division continues to work hard with key customers to develop unique devices that answer the specific needs of their drug.

We are ready to help you and your customers improve the safety and efficiency of the medical work place and to make life easier and more convenient for the growing number

**“ENCOURAGED BY ITS CUSTOMERS, OVER THE LAST FOUR YEARS, DUOJECT HAS BEEN WORKING HARD TO BUILD ON ITS 25-PLUS YEARS OF SUCCESSFUL EXPERIENCE AS AN ENGINEERING-SERVICES GROUP OFFERING CUSTOM MEDICAL DEVICE DESIGN AND DEVELOPMENT SERVICES, TO BECOME A FULL CAPABILITY MANUFACTURING ORGANISATION”**

We are excited to see these devices on the market and to contribute in improving safety within the health care industry, but we are not sitting still. We are continuing to innovate and produce more cutting-edge devices that are intuitive, user friendly and add value to the healthcare industry. These new devices will be

of patients being treated in the home environment and caregivers providing said treatment. Duoject’s extensive experience in the field of drug reconstitution and delivery has led us to focus on designing products that are “user-driven”, which translates in all of our devices being intuitive, simple and, above all, safe.

# User-driven reconstitution and delivery

Because you care



**PENPrep EVO**



**EZLink**



**VaccJect**