

PREFILLED SYRINGES:

PRIMARY PACKAGING WITH SUBSTANTIAL BENEFITS



ONdrugDELIVERY
niche information & intelligence

www.ondrugdelivery.com

bespak...
Injectables

 HASELMEIER

Helvoet Pharma

Passion for Excellence


Elcam
Medical


STERILE PRODUCTS AG

ONE2ONE®
A Service of Hospira

 Nuova Ompi
glass division

tip-top

UNILIFE 
medical solutions

West 
Delivering Innovative Solutions

“Prefilled Syringes: Primary Packaging with Substantial Benefits”

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.

EDITORIAL CALENDAR 2011:

March: Oral Drug Delivery & Advanced Excipients
April: Pulmonary & Nasal Drug Delivery (OINDP)
May: Injectable Drug Delivery (Devices Focus)
June: Injectable Drug Delivery (Formulations Focus)

September: Prefilled Syringes

October: Oral Drug Delivery

November: Pulmonary & Nasal Drug Delivery (OINDP)

December: Delivering Biologics (Proteins, Peptides & Nucleotides)

SUBSCRIPTIONS:

To arrange your FREE subscription (pdf or print) to ONdrugDelivery, contact:

Guy Furness, Publisher

T: +44 (0) 1273 78 24 24

E: guy.furness@ondrugdelivery.com

SPONSORSHIP/ADVERTISING:

To find out more about how your company can become a participant in ONdrugDelivery, contact:

Guy Furness, Publisher

T: +44 (0) 1273 78 24 24

E: guy.furness@ondrugdelivery.com

MAILING ADDRESS:

Frederick Furness Publishing
48, Albany Villas, Hove, East Sussex, BN3 2RW
United Kingdom

PRODUCTION/DESIGN:

Mark Frost

www.frostmark.co.uk

“Prefilled Syringes: Primary Packaging with Substantial Benefits” is published by Frederick Furness Publishing.

Copyright © 2011 Frederick Furness Publishing.
All rights reserved



The views and opinions expressed in this issue are those of the authors. Due care has been used in producing this publication, but the publisher makes no claim that it is free of error. Nor does the publisher accept liability for the consequences of any decision or action taken (or not taken) as a result of any information contained in this publication.

Front cover image: Unifill syringes. Reproduced with kind permission from Unilife Corporation.

CONTENTS

Company Profile – MG STERILE PRODUCTS AG

5

Elastomeric Components for Prefilled Syringes Patrick Grueninger, Global Marketing & Business Development Manager Helvoet Pharma

6-8

Intuitive, Simple & Reliable Ultra-Low-Cost Needle Safety Devices Barry Liversidge, Managing Director tip-top.com Limited

10-11

Company Profile – Bepak Injectables

12

Differentiation Without Disruption Alan Shortall, Chief Executive Officer Unilife Corporation

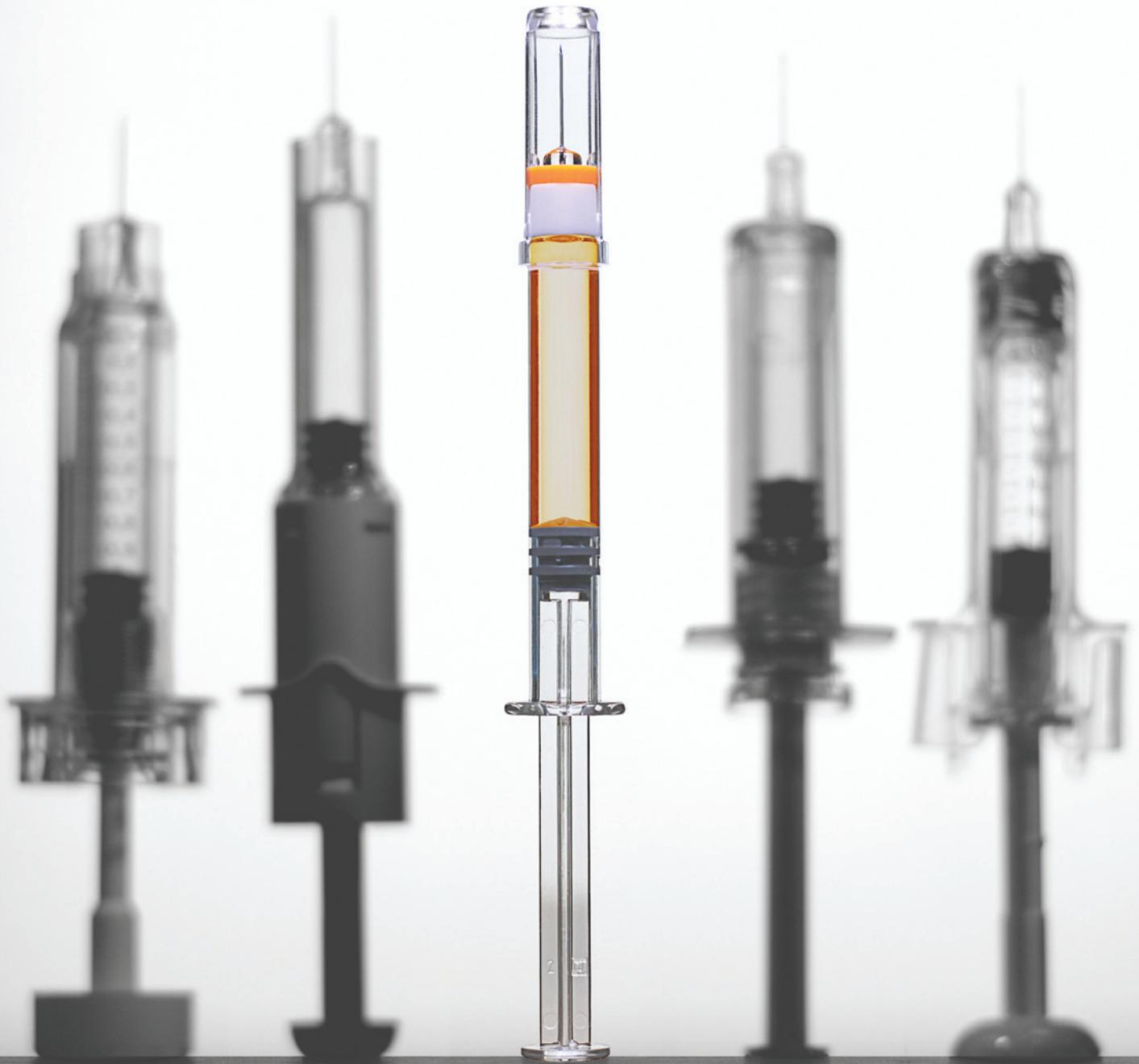
14-17

Quality & Safety Characteristics of Prefilled Syringe Systems: Hazard Concerns & Mitigation Strategies Tibor Hlobik, Associate Director, Marketing for PFS Technologies, Diane Paskiet, Associate Director, Scientific Affairs West Pharmaceutical Services, Inc

22-26

Haselmeier - Dedicated to Meeting the Self-Injection Needs of Pharmaceutical Manufacturers & Patients Robert J. Kilgore, Volker Wirth Haselmeier GmbH

28-29



a passive needle shield that uses 80% less plastic, has no metal spring and integrates with ready-to-fill syringes into trays and tubs

tip-top.com

HOW INNOVATIONS IN PACKAGING AND DRUG DELIVERY PACKAGING ENHANCE HEALTH PRODUCT SAFETY



Pharmapack special 10th edition...15 years of innovation!

The exhibition gathers over **250 exhibitors** coming from **40 countries**, who are leading manufacturers and suppliers of materials, packaging & drug delivery systems, components, design services, contract manufacturing and equipment for packaging and production lines for the pharmaceutical industry.

Even more innovation through the **two-day conference** focusing on the latest international market trends and packaging developments.

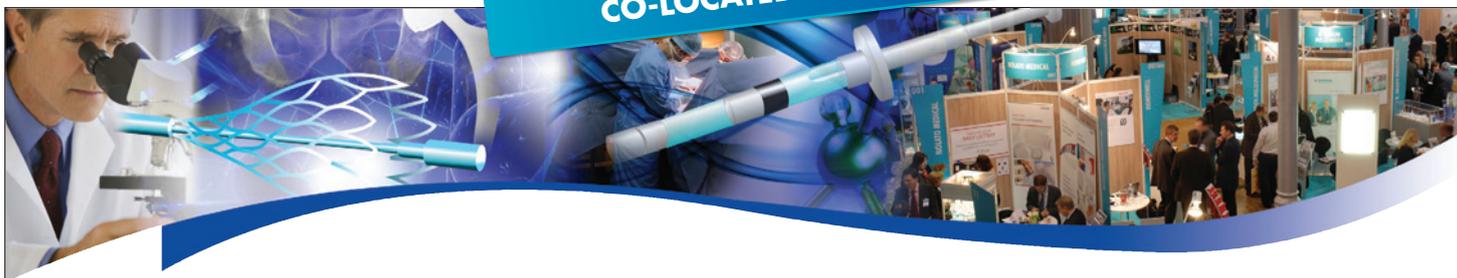
SPECIAL 10th edition—The most significant innovations in packaging and drug delivery systems over the past decade and future expectations from the industry.

Pharmapack Awards 2011—Contact us to find out how to participate

Complete exhibition, conference and awards programmes available on www.pharmapack.fr
For more information, call +33 (0)1 77 48 10 00 or e-mail pharmapack@ubm.com



GRANDE HALLE DE LA VILLETTE
CO-LOCATED EVENT



CONFERENCE



EXHIBITION



BIOMEDevice

The first European convergence conference & exhibition for the biotechnology, medical device and pharmaceutical industries for the development and manufacture of combination devices.

23–24 FEBRUARY 2011 • PARIS

www.biomedevice-europe.com

COMPANY PROFILE MG STERILE PRODUCTS AG



Sterile packaging systems are now supplied by MG STERILE PRODUCTS AG (MGS), established in 2008 as a sister company of MGlaser AG (Münnerstadt, Germany). These two enterprises are partners of the pharmaceutical industry for primary packaging materials made of tubular glass. While MGlaser AG specialises in the manufacture of syringes, vials and ampoules, MG STERILE PRODUCTS AG focuses on processing the bulk goods produced by MGlaser AG into sterile packaging systems.

Today syringes, tomorrow potentially cartridges and vials. Intensive market observations will surely result in further innovations down the line.

HOW ARE STERILE SYRINGES PRODUCED TODAY?

MG STERILE PRODUCTS AG processes the syringes into "D2F® units" (D2F = Direct To Fill).

In a first step, the bulk syringes (non-sterile syringes) are washed inside and outside in a multi-stage washing process. MGS itself produces the WFI (water for injection) in a water-purification system designed in accordance with modern environmental requirements. An integrated heat recovery system offers additional eco-friendly benefits.

After washing, the syringes are dried and siliconised. Silicone oil is applied to the inside of the syringe barrel as well as to the needle in a sensor-controlled process. Depending on the syringe configuration required, the accessories (e.g. needle shield or Luer-Lock adapter) are assembled and the syringes are placed into specially designed containers (nests and tubs).

The entire fully-automated process takes place in a state-of-the-art clean room (shown in Figure 1).



Figure 1: Inside the MGS state-of-the-art clean room. (Inset, a D2F® nest and tub.)

Sterilisation itself is carried out at a renowned business partner. From there, the sterile units (see Figure 2) are shipped to our customers worldwide.



Figure 2: A finished sterile D2F® Unit

A suitable industrial building was thoroughly remodelled and converted into a pharma centre for sterile syringes within 15 months (see Figure 3). Potential future expansions have already been considered in the structural design. On completion of the construction work, the new machinery and processes were validated by the end of 2009. Since the beginning of 2010, sterile syringes are manufactured in serial production.

This development is just a further step on our way to establishing a technological centre for primary packaging materials made of tubular glass for the pharmaceutical industry in Münnerstadt. The process described is merely a logical consequence of the increasing requirements from the market. While bulk goods were commonly purchased in the past, procuring finished sterile containers is

the current trend. There are clear benefits for customers in terms of saving costs and time.

Just like the bulk systems are supplied by MGlaser AG, MG STERILE PRODUCTS AG can now offer syringes and all essential components (plunger stoppers, plunger rods, needle shields, tip caps) in sterile execution.

MG STERILE PRODUCTS AG is a system supplier working closely with the component manufacturers to offer complete sterile packaging solutions to its customers.

MGS will be exhibiting (stand 360) at Pharmapack, Paris, France.



Figure 3: The MGS facility has been manufacturing D2F® Units since 2009

MG STERILE PRODUCTS AG
Otto-Liebmann-Strasse 2
97702 Münnerstadt
Germany

T: +49 9733 8088-0
F: +49 9733 8088-199
E: info@mg-sterile-products.com

www.mg-sterile-products.com

Helvoet Pharma

Passion for Excellence

ELASTOMERIC COMPONENTS FOR PREFILLED SYRINGES

In this article, Patrick Grueninger, Global Marketing & Business Development Manager at Helvoet Pharma, provides prefilled syringe market data and current trends in the sector, highlights the importance of elastomeric components within the development and manufacturing process, and describes how Helvoet Pharma continues to offer elastomeric products and processes ahead of the continually fast-moving innovation curve.

More than 50 injectable drug products, with a total revenues of more than €37 billion (US\$51 billion), are currently available in a prefilled syringe (PFS) format and a rising number of pipeline products are also targeted for marketing in prefilled syringes. The demand from pharmaceutical companies for prefilled syringes currently exceeds 2 billion units per year, in a market continuously growing at around 10% per year, projecting a market volume of close to 4 billion units by 2015. The currently largest field of use for prefilled syringes is believed to be the heparin and vaccine markets, in which prefilled syringes have an estimated market share of 75%.

Nevertheless, due to the economic pressure on these particular products, the heparin and vaccines segments of the PFS market are estimated to contribute to only about 10% of the total revenue of the PFS market, indicating that 25% of the products are making 90% of the revenue.

Prefilled syringes have experienced a strong and continuous growth in the last few years and enjoy a great popularity. Some of the reasons for this are:

- Reduced overfill, which helps to reduce costs and maximise yield
- Enhanced differentiation
- Greater efficiency
- Increased patient compliance
- Ease of use and convenience for healthcare professionals and patients
- Reduced risk of dosage error and contamination

In particular, the staked-needle versions of prefilled syringes have the undeniable advantage

of being the only packaging form which does not need anything else to administer the injection. Neither handling of vials and disposable syringes is required, nor even breaking glass to get to the drug products as is the case with ampoules.

It is estimated, that around 50% of the whole syringe market comprises staked-needle syringes, and that the majority are the 1ml format (either of the “long” or “short” variety). Figure 1 shows a 1 ml “short” staked-needle syringe, with soft needle shield FM27.

With development continuously moving forward, the next step has already been taken by combining the PFS with an auto-injector, which guarantees precise injection depth and excellent dose accuracy for any user, and especially in the growing field of self-medication. Auto-injectors also offer a solution for the increasing number of people with needle phobia. It is estimated that 20% of the US population is suffering from needle phobia.

However, there are also great challenges. For injectables, the prefilled syringe is one of the most complex packaging options a pharmaceutical company can select. Compatibility issues with the drug product and lubricant, the particles created by the lubricant, the permanent contact with the elastomer, the needle glue, the needle itself and traces of metal used for the glass syringe production (often tungsten), and the presence of two different elastomer formulations, are just a few of them. Functional questions have to be addressed like container closure sealing integrity, pull-off forces of tip covers after storage, break-away and gliding forces of plungers, needle sharp-



Patrick Grueninger
Global Marketing & Business
Development Manager

T: +41 (0)79 959 6819
E: patrick.grueninger
@helvoetpharma.com

Helvoet Pharma
Industrieterrein Kolmen 1519
BE-3570 Alken
Belgium

T +32 11 59 08 11
F +32 11 59 08 08

www.helvoetpharma.com



Figure 1: Short 1 ml syringe with staked-needle, shown with soft needle shield FM27

ness and siliconisation level, plunger placement and movement during thermal sterilisation and transport. Also the field of lyophilised products in prefilled syringes is a very delicate one and only a few have learned to manage it well.

These great challenges might be part of the reason why PFS still represents a relative small part of the overall primary packaging market. Another factor might be the elevated packaging cost for a PFS compared with traditional vial and ampoule presentations.

Some estimates indicate that a “vial” packaging is around 8-10 times less expensive than a PFS for the same fill volume and the “ampoule” option even an astonishing 30-40 times cheaper. Nevertheless, the positive aspects of PFS do certainly outweigh the challenges and there is no indication, that the positive trend will come to an end very soon.

ELASTOMERIC COMPONENTS

A PFS requires two elastomeric components, the plunger to seal the back-end and a tip closure (tip cap or needle shield, as shown in Figure 2) to seal the front.

Plunger

The sealing function is the same as for a simple vial stopper but where for the stopper its main purpose ends here, the syringe components have to deliver much more. The plunger is not only supposed to seal the syringe but also be mobile enough to be pushed forward in order to deliver the drug product using a reasonable



Figure 2: Tip cap in FM457 and needle shield in FM27

force and that mobility must remain from the start to the very end of the shelf life.

This force is usually split up in two sections, the break-away force and the gliding force. The break-away force is the initial “push” to overcome the static friction (stiction) between the plunger and the syringe barrel and initiate the movement. Break-away forces might change during storage to higher values since uncoated plungers tend to absorb and/or squeeze away the silicon oil film on the syringe barrel surface over time.

This is usually not an issue if the syringe is used manually by a healthcare professional or patient but it might offer a challenge if the syringe is used in a autoinjector. During manual injection, the individual using the PFS will automatically adjust the pressure of the thumb based on the individual condition of the PFS. As simple as this is for an individual, it is challenging for an auto-injector to achieve. They are usually equipped with a mechanical power system (such as a spring), which is calibrated to a certain fixed force with no means to spontaneously change the setting.

The right plunger design and material as well as the optimal siliconisation level and distribution in the barrel are very important to assure best functionality from the moment of plunger placement to the end of the drug products shelf life.

The gliding force on the other hand is needed to overcome the sliding friction in order to keep the plunger in motion. The gliding force behavior depends very much on the level and uniformity of the silicone oil in the syringe barrel. Similar as with the break-away force, an individual can compensate for irregularities in the gliding force such as fading, spiking or progressive patterns. For all applications, an ideal combination has to be found and especially

using an auto-injector will require a more careful look into all components.

Break-away and gliding forces are important factors for drug delivery since it is the common understanding that they are directly connected with the pain experience by the patient during the injection. A low break-away force, followed by a consistent gliding force is the desired end target. The pain-sensation has a tremendous psychological impact on the acceptance of a product by the patient, especially if the product is treating a chronic disease.

Tip-Cover

The second elastomeric component for syringes, the tip cover (examples shown in Figure 3), also has an important dual function.

It has to be ethylene oxide (EtO) permeable. The syringe producer pre-assembles the tip closure together with the syringe prior to the sterilisation. The whole system will then undergo EtO sterilisation and the tip closure has to be



Figure 3: Soft needle shield and mushroom-style tip cap made out of FM27



Figure 4: Luer cone PFS with FM457 plunger

sufficiently EtO permeable in order to assure the sterility of the PFS in all areas.

The traditional plunger elastomeric formulations are halobutyls, which are not EtO permeable, and therefore a different kind of elastomer has to be employed. This resolves the sterilisation issue but exposes the drug product to another material with its own extractable & leachable profile. Coating is not an option because the usual fluorocarbon layers are not EtO permeable. Sterilisation prior to assembly and assembly in an aseptic area would be an option but financially challenging. Gamma irradiation would work yet provoking a yellowish discoloration of the borosilicate glass due to metal traces in the glass matrix. This aspect could be resolved by switching from glass to advanced polymers like Daikyo's Crystal Zenith



Figure 5: OmniflexCP in 1 ml long form

or cyclic olefin copolymer (COC) but they do not offer the oxygen barrier of glass.

Helvoet Pharma has developed a possible alternative called FM480. Helvoet's FM480 is the only elastomeric formulation in the market, which can be used as both plunger and tip cover and handle the individual requirements. The great advantage is that only one extractable profile has to be taken into account.

EXTRACTABLES & LEACHABLES

Besides the requirement for perfect container-closure integrity and ideal functionality, the direct and permanent exposure of the drug

product to the elastomeric component in a PFS demands special attention be paid to the extractables & leachables profile of the elastomer.

Extractables (E) are commonly defined as chemical entities that can be extracted from components of a material by exertion of an exaggerated force (for example by an organic solvent, extreme temperature, ionic strength, pH, or contact time). Leachables (L) are defined as chemical entities that can migrate from the primary packaging into the drug product. Leachables are considered a subset of extractables.

Evaluation of extractables is usually considered an essential step in the accurate prediction of leachables as well as in the selection of an adequate closure system employed in the production of a given biologic product.

Modern and uncoated elastomeric compounds like FM457 (see Figure 4) are capable of managing this quite well but whenever the small risk of integration with uncoated components is of any concern, coated products offer an elegant risk-mitigation strategy. A fluorocarbon barrier is placed between the elastomer and the drug product, eliminating the direct contact. Helvoet Pharma offers detailed E&L profiles.

OMNIFLEX CP

Omniflex CP (OCP) is Helvoet Pharma's response to the ever-growing requirements on PFS plungers. The base material is FM257, a bromobutyl formulation with many years of successful use and the ideal hardness for a

plunger (~52° ShA). The entire surface is then coated with a fluorocarbon layer which provides a perfect barrier all around the plunger. Figure 5 shows OCP plungers for the 1 ml "long" syringe.

Besides the excellent barrier function, the coating is lubricious and does not require any additional lubricant, eliminating one source of particulate contamination. Syringe plungers with a fluorocarbon barrier coating can help reduce the risk of product loss caused by interaction of the drug and the plunger and the loss of the drug through adsorption and absorption.

OCP can protect the shelf life of packaged drugs, enhance drug/plunger compatibility and have exceptional lubricity for enhanced machi-

neability and processing. OCP coating provides an effective barrier against organic and inorganic extractables to minimise interaction between the drug product and the plunger and maintain the plunger's seal integrity. OCP coating reduces absorption and adsorption of the drug product, an important benefit for maintaining the full strength and shelf life of most drugs.

FIRSTLINE®

Producing elastomeric components had been a very industrial process. Lots of time and efforts had been invested at the end of the process to make sure quality product would be supplied to the pharmaceutical industry. The requirements of the pharmaceutical industry for not only better but also consistent quality led to the point of rethinking the elastomeric production entirely.

The vision of quality by design grew stronger and finally found its manifestation in FirstLine®.

FirstLine® moved the entire production process out of the industrial and into a pharmaceutical environment. Each zone was meticulously designed and constructed with the clear mission to preventing any kind of contamination. Cleanrooms, material airlocks, state-of-the-art pass-through washing equipment with automatic loading from one side and automatic unloading into a higher class clean room. The latest generation in camera inspection techniques has also been integrated to confirm quality.

FirstLine® incorporates rational and ideal production flows in accordance with the Lean Six Sigma methodology.

CONCLUSION

The prefilled syringe market is rapidly growing and prefilled syringes have become the packing option of choice wherever possible.

Nevertheless, prefilled syringes also represent the most sophisticated packaging with many details, characteristics and requirements to be taken into account. Elastomeric components are an essential part of a PFS system and have a great influence on integrity, stability and functionality of the whole system. Risk mitigation is therefore an important topic to be addressed in an early stage of any project independent if it is a new product development or just packaging change.

What might have been sufficient for a vial presentation could jeopardise a successful introduction into a PFS system. Solutions for risk mitigation strategies are available but should not and cannot be generalised. Best practice is the early dialogue between the pharmaceutical manufacturer, the PFS producer and the component supplier. Together, we can make it fly!

omniflexCP

Excellence in Coated Plungers

- Redesigned plunger types
- Improved breakaway and gliding force
- Total barrier coating
- Free from any surface silicone



V9417
0,5 ml



V9416
1 - 3 ml



V9403
1 ml long

Sales Office Belgium
Industrieterrein Kolmen 1519
B-3570 Alken
Belgium (+32 11 590 811)

Sales Office USA
9012 Pennsauken Highway
Pennsauken, NJ 08110
USA (+1 856 663 2202)

Sales Office Italy
Viale dell'Industria 7
20010 Pregnana Milanese
Italy (+39 02 939 651)



tip-top

INTUITIVE, SIMPLE & RELIABLE ULTRA-LOW-COST NEEDLE SAFETY DEVICES

In the previous issue of ONdrugDelivery, tip-top introduced its innovative designs for needle safety devices. Here, Barry Liversidge, Managing Director, tip-top.com Ltd, outlines the latest tip-top developments and describes the benefits of the company's mini-Max and minim devices.

The need for effective needlestick protection is well established and accepted within the pharmaceutical and medical industries. With legislation already passed in the US, Europe is now specifically addressing the healthcare industry's concerns for a harmonised approach to providing effective and affordable needlestick prevention devices. The implementation of this co-ordinated approach will reduce the prevalence of needlestick injuries, and make the delivery of parenteral drugs safer for both the caregiver and the patient.

So, here at tip-top, we are now in the process of inviting pharmaceutical companies to participate in a validation programme that will demonstrate the efficacy of our range of innovative safety-engineered needlestick

protection devices. This process will involve our two flagship products – the mini-Max integrated needlestick protection system for prefilled staked-needle syringes, and minim, a standalone passive safety needle for Luer connection to any syringe. These safety-engineered devices can provide the simplest, safest and most cost effective way to make delivering injectables safer.

mini-Max and **minim** were introduced and described in detail in an earlier article, which was published in the October 2010 issue of ONdrugDelivery. The article, "*tip-top: Truly Passive Integrated Needlestick Protection For Prefilled Syringes*", can be viewed as a PDF at:

www.ondrugdelivery.com/Tip Top.pdf



Figure 1: mini-Max is attached by the syringe manufacturer before the syringes are nested into the 'trays and tubs' used on many of today's filling lines.

Barry Liversidge
Managing Director

T: +44 1206 564 994
F: +44 1206 578 953
E: barry.liversidge@tip-top.com

tip-top.com Limited
2, Moss Road
Stanway
Colchester
Essex
CO3 0LE
United Kingdom

www.tip-top.com



Figure 2: Syringes fitted with mini-Max (shown in their blister pack, left and boxed, centre) are approximately 50% less bulky than those fitted with clip-on needle guards (shown boxed, right).

TIP-TOP'S TECHNOLOGIES PROVIDE CHANGE, WITHOUT DISRUPTION...

tip-top's safety needle systems have been designed to work with any existing syringe manufacturer's products – including those from BD, Gerresheimer, M Glas, Nuova Ompi and Schott form vitrum, amongst others. The mini-Max design therefore maintains the integrity of the standard prefilled syringe as the primary drug container without having to change the internal components of the prefilled syringe

mini-Max is fitted to standard ready-to-fill staked-needle syringes and is fitted by your chosen syringe supplier as a safe and simple alternative to ordinary needle covers. The syringes with mini-Max attached (see Figure 1) are then nested into ordinary trays and tubs that are purchased today, ensuring no changes, and avoiding the need for expensive additional secondary packaging equipment.

mini-Max will be available with all the popular rubber formulations so your existing primary contact materials remain unchanged, eliminating the need for new stability studies.

And mini-Max's sister product minim, a stand-alone fully passive safety needle, can replace unsafe Luer injection needles, (that are bundled

along with a drug offering) with a fully-passive safety needle – that is then fitted to the syringe by the user at the time of administration.

BENEFITS OF MINIM AND MINI-MAX: AT A GLANCE:

1. Works with any standard staked needle or Luer Lock prefilled syringe
2. No change or additions to your current manufacturing process
3. A cost-effective solution, that provides fully-passive needlestick protection to ensure compliance amongst healthcare professionals and self-medicating patients alike.
4. Ultra-compact design minimises storage space and reduces sharps waste, to lessen the burden on the environment.
5. Simple design builds-in reliability.
6. Needle uniquely protected before & after injection
7. Tamper evident & available for most common needle lengths

LOW-COST, COMPACT DESIGN

tip-top has spent years refining and simplifying its designs, and this has resulted in the

most cost-effective devices available. The ultra-compact format of mini-Max means that, (compared with typical clip-on secondary-packaged needle-guards), it would require 500 tonnes less polymer to produce 100 million units. That means 500 tonnes less plastic to be purchased, shipped, warehoused, moulded, stored and transported.

Yet the mini-Max system is not just about low cost effectiveness – the simplicity of the system provides other significant benefits. For example, staked-needle syringes fitted with mini-Max are approximately 50% less bulky than those fitted with clip-on needle guard accessories (as illustrated in Figure 2), and with a weight reduction of around 35%, a reduction in shipping and storage costs is guaranteed. Such a dramatic bulk saving is particularly important if the drug product needs to be maintained in cold-chain storage.

Similarly, because of the considerable space saving advantages of the mini-Max system, hospitals, healthcare providers, and patients will be thankful for the savings mini-Max can provide by reducing both storage costs and sharps waste.

INTUITIVE, SIMPLE, RELIABLE

By constantly challenging conventional thinking, tip-top has after many years managed to miniaturise safe needle shields down to their very essence. Both mini-Max and minim require only a few moulded parts, and have no need for a metal spring. And because these devices activate independently of any user input, they will comply with the demands of the most rigorous safety regulations.

Our devices protect the needle both before and after the injection, they are extremely compact and so do not encumber the healthcare provider or patient during the delicate activity of administering an injection (see Figure 3). These devices are incredibly simple and intuitive to use, require minimal or no training and will promote compliance in the use of safer needles.

tip-top will be exhibiting (stand 566) at the upcoming Pharmapack conference in Paris, France.

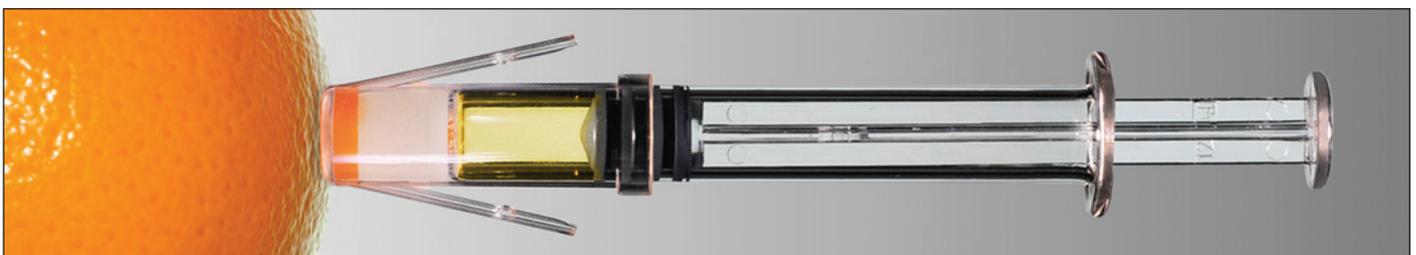


Figure 3: tip-top devices are very compact and so do not encumber the healthcare provider or patient during the delicate activity of administering an injection.



Bespak Injectables specialises in the design, development and manufacture of innovative delivery devices for parenteral drugs. Designed to accommodate prefilled syringes, Bespak’s disposable auto-injectors enable patients and other non-clinicians to easily and safely undertake injections in a comfortable, convenient manner.

OTS™ AUTO-INJECTOR

Based on its patented auto-injector technology platform, which offers a fully automated injection process, Bespak is pleased to introduce the OTS™ auto-injector. Figures 1a and 1b show the device before and after use, respectively.

Incorporating a 1 ml ‘long’ prefilled syringe with staked needle, the OTS™ auto-injector represents not only a standardised, market-ready product, but one which can also be readily adapted according to the needs of particular patient groups and drug formulations, or for brand differentiation.

The innovative design of the OTS™ auto-injector, and its associated manufacturing systems, allows devices to be optimised in relation to:

- Operating system
 - 2-step “Push-actuation”
 - 3-step “Button-actuation”
- External device geometry
- Liquid viscosity
- Injection volume

From established manufacturing facilities, OTS™ auto-injector devices are available within short lead times for clinical studies



Figure 1: The OTS™ auto-injector shown (a) before use and (b) after use.

and commercial supply. By supplying OTS™ auto-injectors in alternative configurations, Bespak can also facilitate early-stage assessment of user preferences, to assist partners in defining the optimal device for their needs.

DEVICE GEOMETRY

The external components of the OTS™ auto-injector can be varied around the device’s underlying structure and operating mechanism, permitting variations in the device’s ergonomic and aesthetic features without the need for embarking on a device customisation programme - which could otherwise be both costly and time-consuming.

VISCOUS DRUG CAPABILITY

Building on Bespak’s considerable experience with delivery of viscous injectable drugs, the OTS™ auto-injector can deliver formulations which may otherwise prove difficult to inject without risk of syringe breakage. Bespak’s patented Compression Pad system protects against the damage that can occur when glass syringes are subjected to elevated forces required to successfully deliver viscous drugs.

OTS™ APPLICATIONS

As a cost-effective and versatile delivery system, incorporating industry-standard

primary containers, the OTS™ auto-injector can support:

- New drug products
- Extensions to therapeutic indications
- Lifecycle management programmes
- Product pipelines

BESPAK INJECTABLES

Bespak Injectables (formerly The Medical House PLC) is a Consort Medical company. Consort Medical group operates state-of-the-art medical device manufacturing facilities in US and UK. Bespak is a leading supplier of drug delivery systems to the global pharmaceutical industry and manufactures over 450 million devices each year.

In addition to its patented drug delivery technologies, Bespak offers comprehensive design, development and manufacturing capabilities taking device projects from early stage development through to commercialisation and long-term supply. Bespak has experience with a wide range of technologies including injectors and inhalers, as well as nasal, ophthalmic and diagnostic systems.

The OTS™ auto-injector is one of a number of injection devices developed by Bespak. For more information on these technologies, or to discuss your particular requirements, please contact Bespak.

Syringe	1ml ‘long’ barrel
Needle	½ inch; staked
Syringe Fill Volume	Up to 1ml
Delivery Volume	Fixed dose; up to 1ml
Drug Viscosity	Up to 40 Cps*
Actuation Mechanism	Push or Button

OTS™ Disposable Auto-Injector Specification

*Bespak Injectables’ ASI™ auto-injector platform can deliver liquid viscosities in excess of 40 Cps. Please contact Bespak Injectables for further information.

David Urquhart
Commercial Director

Bespak Injectables
199 Newhall Road
Sheffield S9 2QJ
United Kingdom

T: +44 114 261 9011
F: +44 114 243 1597
E: david.urquhart@bespak.com

www.bespak.com

Adding Value, Adding Life. Since 1949.
Sustainable and Appraised Growth.
Delivering on Promise.

FROST & SULLIVAN

2010 Europe Product Differentiation
Excellence Award in Prefillable Syringes to
Nuova Ompi (Stevanato Group).

Award Benchmarking Criteria:

- *Unique Features/Functionality*
- *Quality/Complexity*
- *Customization*
- *Matched to Target Markets Needs*
- *Brand Perception of the Uniqueness of the Product*

A Best-in-Class Company/Partner.



Synchronized Solutions, Synchronized Value Chain.



Stevanato
group



Nuova Ompi
glass division

DIFFERENTIATION WITHOUT DISRUPTION

Significant commercial opportunities exist for pharmaceutical companies willing to raise the industry benchmark and supply their drugs and vaccines in innovative devices that can better protect healthcare workers and enhance patient care by making dose administration more intuitive, convenient and safe. Unilife Corporation has developed the Unifill syringe, which it describes as the first and only known ready-to-fill syringe with safety features fully integrated within the glass barrel. Here, company Chief Executive Officer Alan Shortall, explains how, by converging therapeutic drugs and innovative devices into a truly unique combination product, the Unifill syringe offers pharmaceutical manufacturers significant opportunities to optimise lifecycles and generate powerful brand differentiation in competitive market sectors. As a primary drug container with integrated safety, the Unifill syringe may even help to improve claims for the combination product and hence obstruct the entry of competitor products by reducing the likelihood of substitution.

Pharmaceutical manufacturers of therapeutic drugs and vaccines today face competitive challenges across several fronts. Products with annual sales of more than US\$140 billion will face generic competition over the next six years in major developed markets such as the US, according to IMS data. Ten drugs approach-

pressure on pharmaceutical companies to reduce drug costs to help fund healthcare reforms and service the needs of an ageing population.

The need to optimise the lifecycle of therapeutic drugs and vaccines has never been more acute. Pharmaceutical companies are seeking to refine their industrial and marketing strategies

to maximise potential revenue streams for approved drugs in the midstream of their lifecycles, those approaching patent expiration, and new product launches. Building efficiencies across all sectors of the production process and the supply chain has been one natural area of focus. Another area has been to expand and diversify global operations via acquisitions and internal expansion, to enter emerging countries or capture a share of fast-growing generic and biosimilar drug markets.

"IN RECENT YEARS, PHARMACEUTICAL COMPANIES HAVE BEGUN INCREASINGLY TO FOCUS ON THE LIFECYCLE MANAGEMENT BENEFITS THAT CAN BE GENERATED FROM THE LAUNCH OR CONVERSION OF A DRUG WITH A SUPERIOR DELIVERY DEVICE."

ing the patent cliff with total annual sales of \$33 billion are available in a prefilled syringe. Prospects for replacing these ageing prefilled drugs with new blockbusters are scarce however. Regulatory compliance and development costs have increased the cost of bringing a new drug to market tenfold this decade to a current estimate of \$1.3 billion. Meanwhile, the governments of many countries are placing significant

Arguably the simplest and most cost-effective way to enhance the productivity and marketability of drugs is lifecycle management. Lifecycle management strategies have traditionally sought to build revenue streams, increase market share and compete against rival drugs by improving product claims or expanding the number of indications for use. In recent years, pharmaceutical companies have begun increasingly to focus on



Alan Shortall
Chief Executive Officer
T: +1 717 938 9323

250 Cross Farm Lane
York, PA 17406
United States

T: +1 717 384 3400
F: +1 717 384 3401
E: info@unilife.com

www.unilife.com

the lifecycle management benefits that can be generated from the launch or conversion of a drug with a superior delivery device.

The commercial opportunities that can be generated through the effective use of innovative and customer-friendly devices have led to the start of a new 'arms race' amongst pharmaceutical companies. Today, the convergence of therapeutic drugs and delivery devices into unique combination products represents one of the fastest-growing trends and most highly sought-after goals within the pharmaceutical industry.

A unique medical device can add value to the overall drug delivery combination product in many ways. It can help to streamline industrial and supply systems, simplify administration procedures, protect healthcare workers, enhance patient care, make disposal more convenient, or ideally, all of the above.

In the pharmaceutical market for injectable drugs and vaccines, the first-generational shift towards the use of combination products was the transition from vials or ampoules to the prefilled syringe. The relative advantages of prefilled syringes are plentiful, including the elimination of dose wastage during the filling process, and making the administration of an accurate dose more reliable, faster and patient friendly. There are more than 2.5 billion prefilled syringes used a year with annual rates of growth exceeding 12%. More than 20 pharmaceutical companies utilise prefilled syringes, with more than 60 drugs and vaccines available in this primary drug container format and many more in the pipeline awaiting regulatory approval.

The introduction of legislation mandating the use of devices that could protect healthcare workers from needlestick injuries within markets such as the US and Europe prompted many pharmaceutical companies to introduce temporary stop-gap measures that would facilitate legal compliance for drugs supplied in a prefilled syringe format. However there remains at present no prefilled syringe with safety features that are integrated within the glass barrel.

Pharmaceutical companies today utilise ancillary safety products that can be attached onto the primary drug container. For many drugs, particularly those administered via subcutaneous injection, these safety products are clipped over a prefilled syringe after filling and prior to packaging. Others, such as vaccines targeted for intramuscular injection, are supplied in a needleless format to allow healthcare workers to attach a suitable-length safety needle at the point of administration.

There are significant drawbacks to both of these prefilled safety choices. Ancillary clip-on safety products attached by the manufacturer prior to packaging require the installation and opera-

tion of secondary assembly systems inside the cleanroom. These secondary lines not only take up a significant cleanroom footprint, but may also threaten the continuous operation of the primary fill-finish system and impair stock efficiencies through incidents such as product breakage. Their relatively bulky size compared with an equivalent prefilled syringe can also increase packaging, transport and storage volumes by up to 70%.



Figure 1: Unilife's new 165,000 sq-ft state-of-the-art headquarters and production facility in York, PA, US.

In the field, the size and functionality of these clip-on safety products may also require changes to standard injection procedures and create additional infection risks such as aerosolisation (splatter). Independent evaluations conducted by Unilife utilising some current prefilled safety products identified that many healthcare workers either were not actually aware that the device contained a safety feature, or they chose not to activate it prior to disposal. Healthcare workers have also expressed concerns that the relatively bulky size of these products could exacerbate patient unease or discomfort during an injection, and increase waste disposal volumes.

Conversely, needleless prefilled syringes can minimise pharmaceutical costs relating to the attachment, packaging, shipping and storage of an ancillary safety product. However the responsibility for needlestick compliance is simply shifted from the pharmaceutical manufacturer onto the healthcare facility. Typically, healthcare workers using such needle-free prefilled syringes are required to undertake additional steps that may place them and their colleagues at risk of injury.

For example, needle guard products require the operator to select a product of suitable gauge and length for attachment onto the prefilled syringe before an injection. After the injection, the operator must then remove the non-sterile needle from the body of the patient before manually sliding an external plastic guard over the needle. Most reported needlestick injuries in the US involving safety syringes occur after the needle has been removed from the patient and prior to disposal, indicating that healthcare workers are either being harmed during activation of the safety mechanism or because they elect not to do so.

Arguably the greatest marketing challenge to pharmaceutical companies that utilise cur-

rently available ancillary safety prefilled products is that they all virtually look and function in a similar manner. There is relatively little difference between one needle guard product and another, or one external safety sheath and another. As such, opportunities for pharmaceutical manufacturers to utilise the actual safety feature of a prefilled syringe as a brand differentiator within competitive therapeutic mar-

kets are limited. Furthermore, it is difficult to optimise the lifecycle of a drug with a standard commodity product that is equally available to the competition and offers little in the way of a unique selling proposition.

Such ancillary safety products are primarily designed to protect healthcare workers and facilitate compliance with needlestick prevention legislation. However, none serve as a true medical device that has been designed from the ground up to enhance the overall effectiveness of storing and administering an injectable drug.

Many pharmaceutical manufacturers have long aspired to develop a prefilled syringe that could address these industrial and marketing challenges, and herald the start of a new generational era for injectable drug delivery. However, few in the industry considered it was technologically feasible to integrate safety into the primary drug container without causing significant disruption to conventional fill-finish systems, or introducing new materials into the fluid path that would interfere with fundamental biocompatibility requirements.

In 2003, Unilife Corporation was approached by sanofi-aventis with the concept of developing such a next-generation glass barrelled ready-to-fill syringe. In addition to having to incorporate Unilife's proprietary safety features of passive (automatic) and operator-controlled needle retraction to protect those at risk of needlestick injury or splatter, several fundamental design requirements had to be satisfied before the project was to receive a go-ahead. These included:

- The device can be supplied as per standard handling processes
- It can be inserted into fill-finish systems currently used for equivalent prefilled syringes

“THERE ARE MORE THAN 2.5 BILLION PREFILLED SYRINGES USED A YEAR WITH THE ANNUAL GROWTH RATE AT >12%. OVER 20 PHARMACEUTICAL COMPANIES UTILISE PREFILLED SYRINGES, WITH >60 DRUGS AND VACCINES AVAILABLE IN THIS FORMAT AND MANY MORE IN THE PIPELINE.”



Figure 2: Compared with ancillary safety products attached onto prefilled syringes (three on left), the Unifill syringe (right) can reduce packaging, transport and storage volumes by up to 70%. Such device differentiation also creates strong brand marketing opportunities in competitive therapeutic markets.

- Materials in the fluid path would be USP compliant to support a two-year shelf life
- It must be approximately the same size as equivalent standard prefilled syringes to minimise pharmaceutical packaging, shipping and storage costs
- Minimal dead space for the device after dose delivery
- It can be manufactured reliably at commercial volumes
- Freedom to Operate reports supporting the unique proprietary nature of the device.

In July 2008, after five years of R&D, Unilife signed an Exclusivity Agreement with sanofi-aventis for a device that met all these criteria. Today, Unifill® ready-to-fill syringe is branded and marketed by Unilife as described in the boxed text, “*Introducing the Unifill Syringe*” (below).

Sanofi-aventis has committed approximately \$40 million in upfront fees and industrial milestone payments since 2008 to support the commercialisation of the Unifill syringe. In return, sanofi-aventis has secured the exclusive right to negotiate the purchase of the product until June 2014 within select therapeutic classes including antithrombotic agents and vaccines. Unilife has subsequently retained the right to negotiate with other pharmaceutical companies interested in utilising the Unifill syringe for drugs targeted for use within therapeutic drug classes outside of those secured exclusively by sanofi-aventis.

The Unifill syringe is not a commodity safety product, but a unique proprietary medical device with international patents set to expire between 2026 and 2030. Given the unique characteristics of the Unifill syringe as a primary drug container and its competitive strength against ancillary safety products, it is strongly positioned to help pharmaceutical customers

INTRODUCING THE UNIFILL SYRINGE

The Unifill syringe is considered to be the world’s first and only known primary drug container with safety features that are fully integrated within the glass barrel. It is supplied as per standard handling systems to pharmaceutical manufacturers in the three sub-assembly pieces of a glass barrel (up to 160 units per sterile tub and tray with a Tyvek seal and lid and packaged in a Tyvek pouch), a sterile plunger seal and a plunger. As such, it can be fully integrated into current fill-finish systems used by pharmaceutical manufactures for equivalent standard ready-to-fill devices.

The Unifill syringe is thus well positioned to help streamline industrial systems used by pharmaceutical manufacturers for injectable drugs and

vaccines. It is similar in size to equivalent standard prefilled syringes, and significantly smaller than those with an attached ancillary safety product. By eliminating the need to attach an ancillary safety product onto the prefilled syringe in between the steps of dose filling and device packaging, the Unifill syringe can streamline industrial processes and minimise packaging, shipping and storage volumes by up to 70% (see Figure 2).

All components within the fluid path are constructed of US Pharmacopeia (USP)-compliant materials including borosilicate glass (type 1) for the barrel and USP- and European Pharmacopoeia (EP)-compliant rubber enclosure materials for the plunger and needle seals.

Customers may specify preferred suppliers or materials providing they meet required specifications, with Unilife focused on developing a triple-source supply strategy for components wherever possible. The company has so far qualified a dozen suppliers, with more to be added over the coming year. EtO is being used to sterilise the barrel sub-assembly, with this method having already passed testing.

The handling and administration of the Unifill syringe is similar to injections undertaken with an equivalent standard prefilled syringe, making it highly suitable for use either by healthcare workers or patients that self-administer prescription medication. Upon the delivery

optimise, or even extend, product lifecycles.

For drugs and vaccines which are awaiting regulatory clearance, their launch in the Unifill syringe can create immediate and powerful brand differentiation against entrenched competition. Further, should the pharmaceutical company retain from Unilife some level of special access to the device within a designated therapeutic class, sales teams can have at their disposal a unique selling proposition that no competitor could match.

For approved drugs, particularly those in the mid-stream or approaching the natural end of its lifecycle, conversion to the Unifill syringe can also create significant opportunities to build market share, increase average prices per unit and widen opportunities for its use within healthcare facilities or by patients that self-administer prescription medication.

The transition of drugs approaching patent expiration that are currently supplied in either a standard prefilled syringe or an ancillary safety device to the Unifill syringe may create especially compelling lifecycle opportunities. Lifecycle management consultants engaged by Unilife have developed white papers for interested pharmaceutical companies concerning prefilled drugs approaching patent expiration. Models generated for these ageing blockbuster drugs indicate that their conversion to the Unifill syringe, together with a strategic rebranding campaign, could help protect or regain revenues of around 20% that would otherwise be lost to generic competitors.

Furthermore, based upon legal reviews of recent feedback from the US FDA to several citizens' petitions regarding other innovative drug-device combination products, the Unifill syringe could be utilised to generate unique claims that, when backed by exclusive rights to the device within a therapeutic class, could

of a full dose, a passive retraction mechanism is activated, whereupon operators may control the speed of needle withdrawal directly from the body into the barrel of the syringe (see Figure 3) to help minimise infection risks such as needlestick injuries or aerosol (splatter). The plunger is then automatically locked to prevent needle re-exposure, and to facilitate compact, convenient disposal.

Unilife conducted independent market evaluations with 66 US-based healthcare workers across multiple cities during 2010, comparing the Unifill syringe against two leading ancillary safety prefilled products. The Unifill syringe was the clear favourite, with healthcare workers preferring the product in all surveyed areas including safety, functionality, ease-of-use, performance and appearance.



Figure 3: The Unifill syringe allows operators to control the speed of automatic needle retraction directly from the body into the glass barrel to virtually eliminate the risk of infection from potential transmission modes such as needlestick injuries or aerosol.

obstruct generic or biosimilar competition by reducing the likelihood of substitution.

Conversely, a pharmaceutical manufacturer could submit a new abbreviated new drug application (ANDA), or an NDA under section 505(b)(2), for a new product that would consist of a generic version of an already approved drug but marketed in the Unifill syringe. This could see the generic product receive either three years of marketing exclusivity or allow it to be marketed under its own trade name as an independent product. With Unifill being the only ready-to-fill syringe with such unique safety and functionality attributes, such regulatory strategies could create almost unlimited commercial opportuni-

Initial production of the Unifill syringe is targeted to occur during the first quarter of 2011 at Unilife's new state-of-the-art manufacturing facility and global headquarters in York, PA, US (see Figure 1). The 165,000 square-foot (>15,000 m²) facility meets stringent cGMP industry standards for devices and pharmaceuticals, and has been designed by pharmaceutical architects with the intent to exceed typical customer expectations for the production, quality assurance and supply of primary drug containers.

The facility, which has been designed to have the capacity to manufacture up to 400 million syringes per year in its first stage, includes eleven class 7 and 8 clean rooms of total area 21,000 square feet (>1,950 m²). Other production equipment on-site that is used in the production of the Unifill syringe

ties for a pharmaceutical partner of Unilife.

The Unifill syringe is at the forefront of the pharmaceutical convergence between therapeutic drugs and advanced, patient-friendly delivery devices that are intuitive for use and market-differentiating.

It offers an elegant solution to pharmaceutical companies seeking to streamline industrial systems, protect healthcare workers from harm, enhance patient care and prevent disease. For pharmaceutical companies that place a high value on lifecycle management strategies, the Unifill syringe represents a unique proposition to generate powerful brand differentiation with minimal changes to conventional industrial processes.

include a washing and siliconisation system (Groninger, Crailsheim, Germany), and a Water for Injection (WFI) system from Mecro (Sugar Land, TX, US). Additional amenities in the facility include a product development centre, a microbiology laboratory, quality inspection and control rooms, and a fully segregated warehouse for efficient inventory management.

Batch release of the Unifill syringe to pharmaceutical customers so that they may commence initial stability testing, market evaluations and other activities is targeted to occur during the middle of 2011. The first Unifill assembly line will have an optimal capacity of 60 million units per year. Additional lines, to be ordered in line with commercial demand, are targeted to have a 150-million-unit-per-year capacity.



THE AUTHORITY IN
CONFERENCE EXPERIENCES FOR
MEDICAL DEVICE PROFESSIONALS
www.management-forum.co.uk



INJECTABLE DRUG DELIVERY

Devices, Technology & Development
24 & 25 March 2011, London

**** Exhibition Opportunities Available ****

For more information contact:

Andrea James +44 (0)1483 730071

email: andrea.james@management-forum.co.uk

Website: <http://www.management-forum.co.uk/medical>



THE AUTHORITY IN
CONFERENCE EXPERIENCES FOR
MEDICAL DEVICE PROFESSIONALS
www.management-forum.co.uk



PRE-FILLED SYRINGES

And Advanced Injection Technologies
10 & 11 May 2011, London

**** Exhibition Opportunities Available ****

For more information contact:

Andrea James +44 (0)1483 730071

email: andrea.james@management-forum.co.uk

Website: <http://www.management-forum.co.uk/medical>



Ready to Fill *Safety Syringe*

Streamline your Industrial Filling Processes
Turn Compliance into a Unique Marketing Advantage
Protect your Customers and Enhance Patient Care
Deliver Powerful Market Differentiation for your Brand
Optimize the Lifecycle Management of your Products



- + Only known primary container with passive safety
- + Fully compliant with U.S and EU needlestick safety laws
- + Integration into standard fill-finish lines
- + Optimal protection from needlestick injuries and splatter
- + Components in fluid path are USP compliant
- + Intuitive for use by healthcare workers and their patients
- + Up to 70% less packaging and transport volumes
- + Compact size for easy handling and convenient disposal



Working together with pharmaceutical industry leaders to protect healthcare workers, enhance patient care and prevent disease

www.unilife.com

YPSOMED

SELFCARE SOLUTIONS



Ypsomed is the largest independent developer and manufacturer of custom-made injection systems for self administration. Our pens range from simple disposable pens to reusable pens with variable dosing and spring-assisted injection. We also manufacture unique click-on needles function for both our own and all other widely-available pens.



We are constantly expanding our platform portfolio to cover new therapy and patient needs, including disposable auto-injector platforms for the treatment of autoimmune diseases and other indications. A broad-based technology platform and over 250 patent families mean Ypsomed can meet virtually all partner needs in the growing market for self-injection systems.

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

Ypsomed has well-established partnerships of many years with numerous leading pharmaceutical and biotech manufacturers such as Sanofi-Aventis, Pfizer, Genentech, Roche, Merck-Serono and Lilly.



Ypsomed AG
Brunnmattstrasse 6, 3401 Burgdorf
Switzerland
Tel. +41 34 424 41 11
Fax +41 34 424 41 22
www.ypsomed.com

Contact:
Ian Thompson, Head of Business Development
info@ypsomed.com

the power of CONCENTRATION

THE POWER OF A SINGULAR FOCUS

We focus on one thing – and that's the development of self-injection devices.

We have one vision – and that's to be specialists in our field. It is our purpose to use our expertise, dedicated resources, and experience to provide our customers the ultimate device solutions.

Meet us at the following events:

Pharmapack – Stand 379
February 23-24, 2011, Paris, France
Management Forum, Injectable Drug Delivery
March 24-25, 2011, London, UK

YPSOMED
SELFCARE SOLUTIONS

e-mail us at info@ypsomed.com
on the web at www.ypsomed.com

Our comfort zone is **here**:



Whatever your prefilled syringe needs. **Wherever you need to be.**

With One 2 One®, you have access to broad prefilled syringe filling capabilities. Whether your product is administered via IV, IM or subcutaneously, or you need a unique diluent for your lyophilized product, One 2 One® is your comfort zone for contract manufacturing and prefilled syringes.

- **Glass Syringes:** Industry standard prefills, with or without passive needle guards
- **Glass Cartridges:** Compatible with industry leading auto and self-injector devices
- **iSecure™ Cartridge Syringe:** Proprietary design delivers efficiency and simplicity
- **Ansy™ Plastic Syringe:** Ideal for emergency medications and custom diluents

Discover **your** comfort zone at one2onecmo.com

Get your custom report online or contact One 2 One.

Call +1-224-212-2267 or +44 (0) 1926 835 554 or e-mail one2one@hospira.com

QUALITY & SAFETY CHARACTERISTICS OF PREFILLABLE SYRINGE SYSTEMS: HAZARD CONCERNS & MITIGATION STRATEGIES

Advancement of regulatory science, innovation, safety and integrity of the global pharmaceutical environment are among the US FDA's strategic priorities for the 21st century. Drug product manufactures are faced with increased scrutiny by the FDA, which has shown that the high costs of drugs has been related in part to low manufacturing efficiencies that result in rejected drug product. These factors, coupled with the evolving global regulatory concerns over drug quality and safety, have led to greater interest in innovative packaging and delivery systems. Prefillable syringe systems can enhance drug product integrity and delivery by providing convenient, premixed, sterile, fixed dosages to the patient. In this article, Tibor Hlobik, Associate Director, Marketing for PFS Technologies, and Diane Paskiet, Associate Director, Scientific Affairs, both of West Pharmaceutical Services, Inc, explain how the use of high-quality components will facilitate efficient manufacturing processes that can result in a reliable supply of drug products.

21ST CENTURY NEED FOR ASSURING QUALITY PRODUCTS

Delivery of a safe and effective drug product depends on multiple factors. Many complex systems and components must come together to create a product with appropriate safety and quality controls. The drug development,

along with the raw materials for all processes, have an impact on quality and are obtained from multiple sources.

The appropriate knowledge is not always shared in advance, and unexpected issues may occur, which has led to development through lessons learned as opposed to understanding the science and potential hazards to enable

appropriate risk assessments. The multifaceted and numerous variables become even more challenging with the growing global supply chain. There will always be some degree of risk, but the risk should be reduced as much as possible to realise the greatest benefit for the patient.

Balancing upfront investment with desired time to market must be a co-ordinated effort among the stakeholders.

"BY FORMING ALLIANCES EARLY IN THE DRUG PRODUCT'S LIFECYCLE, MANUFACTURERS CAN HELP ENSURE THE DRUG PRODUCT'S INTEGRITY WITHIN THE DELIVERY SYSTEM, WHICH IS VITAL TO THE WELL-BEING OF THE PATIENT."

scale-up, manufacture, filling, packaging, storage and shipping processes require an in-depth understanding of factors affecting product safety and efficacy; the primary, secondary and ancillary packaging components,

By forming alliances early in the drug product's lifecycle, manufacturers can help ensure the drug product's integrity within the delivery system, which is vital to the well-being of the patient.



Tibor Hlobik
 Associate Director,
 Marketing for PFS Technologies
 T: +1 610 594 2900
 F: +1 610 594 3000



Diane Paskiet
 Associate Director,
 Scientific Affairs

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

www.westpharma.com



Figure 1: With the development of novel materials, including cyclic olefin polymers such as Daikyo Crystal Zenith[®], manufacturers can now offer Luer and insert needle syringes made of a high-quality, transparent, break-resistant material that is more inert than glass.

BENEFITS OF PREFILLED SYRINGE

The accurate dosing of the drug product, reliable delivery and ease of use are major advantages to patient therapy and satisfaction. In addition, the control of components is more easily qualified, tracked and managed from a single source. The mutual dependency between the drug product and administration systems throughout the drug product lifecycle should be established early and monitored.

Control of components, as well as the opportunities for improvements, can be recognised and quickly addressed to improve quality or meet growing needs of delivery systems or devices.

Drug product quality indicators are based on uniformity, purity, integrity and stability, and can be strongly influenced by the materials that the drug may contact. The drug product is comprised of multiple raw materials, as are the components of prefilled syringes, and it is ultimately the compatibility of these systems that will qualify the system for its intended use.

Components of prefilled syringe systems typically include pistons, syringe barrels, needles and needle shields, all of which must be compatible as a system and with the drug product. The understanding of potential hazards to be mitigated can be explored and supported based on the combined knowledge of drug manufacturers and component suppliers throughout the drug product lifecycle.

EFFICIENCIES AND COST SAVINGS WITH PREFILLABLE SYRINGES

Some drug products are in short supply, biologics can be very costly, and manufacturers are increasingly seeking new ways to minimise waste. Prefillable syringes, with their premeasured dosage, have the potential to reduce dosing errors and increase patient compliance while potentially saving manufacturers money.

Unlike single- or multi-dose vials that may require drug product overfill by as much as 30% to ensure adequate withdrawal, a prefilled syringe can virtually eliminate the need for excess overfill, thus conserving expensive drug product. This is important where manufacturing and product costs are high and bulk manufacturing capacity is limited.

Additionally, there is some degree of variability when removing a dose from a vial with a conventional disposable needle and syringe. With a prefilled syringe system, the very nature of its design eliminates the withdrawal step and delivers drug product directly to the patient, which results in a more accurate dose of the drug with less exposure to needles.

PREFILLABLE SYRINGE COMPONENT COMPATIBILITY & QUALITY

The prefilled syringe component with the maximum drug product contact area is the syringe barrel, which can have a major influence on drug product quality. The compatibility

of the drug product with the barrel's contact surface is critical to the drug product quality, while the breakloose and glide forces are key to the administration.

Prefillable syringe barrels are manufactured from either glass or plastic materials such as cyclic olefin polymers. Glass requires lubrication to facilitate the breakloose and glide forces; this can be accomplished through a siliconisation process but not without a quality concern. Silicone can have a negative impact to the formulation, especially in the biopharmaceutical arena, where there is risk of protein aggregation. Eliminating the need for silicone oil can be an important advantage.

Problems from siliconisation can arise from uneven application, particularly toward the nose of the syringe, which is less accessible to the siliconisation process. Such issues can create higher breakloose force or glide force variability – particularly at the end stroke of the piston – resulting in incomplete injection. This is especially of concern when the syringe is used in a delivery system such as an auto-injector. In extreme cases, the syringe may stall before the end of the stroke, and the full drug dose may not be delivered.

The use of silicone is necessary for glass syringes but is not the only hazard when considering glass as a barrel material for a prefilled syringe system. Glass is fragile and broken glass syringe barrels can result in patient safety being compromised and drug product being lost.

In addition, glass is not inert and is particularly susceptible to chemical reactions at the



Figure 2: Disposable auto-injectors, such as West's ConfiDose® auto-injector system, can overcome much of the inherent variability associated with glass syringes, including dimensional variability.

surface. The glass formulation and manufacturing processes can influence the potential for glass flakes (delamination). This occurrence of glass flakes is more pronounced as the temperature and alkalinity of the contacting solution increases. While basic solutions favour siliceous flakes, these flakes can also be observed in neutral or slightly acidic solutions that have been stored for some time, particularly if the containers have low chemical durability. These flakes, which have been the subject of several drug product recalls, are elusive and may occur during storage of the drug product and/or shipping.

With the development of novel materials, including cyclic olefin polymers (COP) such as the Daikyo Crystal Zenith® COP material, manufacturers can now offer high-quality, transparent, break-resistant material that is more inert than glass, and, unlike glass, does not flake, which reduces particulate contamination from the syringe container (see Figure 1).

These components also can be stored and shipped at low temperature – a requirement of many biologics.

MITIGATING RISK OF PROTEIN AGGREGATION

Many biotech drugs are particularly sensitive to contact with glass surfaces. Silicone and tungsten are potential hazards associated with

glass prefillable syringes. Silicone is added to ensure the breakloose and glide force movement, but tungsten is a residual from the glass manufacturing process. The inner needle channel is formed in glass by use of a tungsten pin and the high temperature required for glass forming can oxidise tungsten in the presence of air and interact with the glass. The resulting residuals are not easily removed during washing and have the potential to interact with the formulation. Low levels of tungsten in biologics can produce aggregation and rejected product.

Glues and adhesives are also used to hold the needle in place once it has been staked into the glass syringe. These are additional sources for potential leachables and can also contribute to the rejection of contaminated drug product. The use of syringe barrels made from the Crystal Zenith material can minimise exposure to tungsten and other potential leachables, protecting the drug and enabling a reliable product supply.

CYCLIC OLEFIN SYRINGE BARRELS: A DISTINCT ADVANTAGE

Glass prefillable syringe systems still dominate the market despite their limitations with drug compatibility, performance issues and manufacturing operations. Glass syringe barrels can potentially contribute to delayed produc-

tion, reduced supply or even recalls due to quality issues. Switching from a glass prefillable to a cyclic olefin polymer molded prefillable syringe can reduce the variability and breakage issues associated with glass as well as reduce the need for silicone oil.

The injection molding technology used to manufacture plastic syringe barrels maintains tight tolerances to assure consistent functionality (such as breakloose and extrusion) and minimise risk of non-fit with secondary systems such as auto-injectors.

Recognising opportunities to make improvements to drug product quality should not be burdensome and efficiencies can be achieved with the appropriate regulatory support and co-operation between the drug manufacturer and component supplier resulting in an overall patient benefit. Cyclic olefin syringe systems, which have been extensively used in all major markets for some time, continue to gain strong acceptance from pharmaceutical and biotech drug makers thanks to a variety of benefits.

The benefits associated with a Crystal Zenith cyclic olefin polymer syringe include:

- High break-resistance
- Consistent breakloose and glide force
- Silicone-oil free
- Low exposure to extractables and leachables
- Low particulate levels



Evolve to a superior prefillable syringe technology.

Breakage. Functional performance. Aggregation. These issues and more can affect your product and thus your top and bottom line. Glass syringes may be at the heart of the problems.

Made of a proprietary cyclic olefin polymer, the Daikyo Crystal Zenith Insert Needle Syringe System provides an innovative solution to the limitations of glass syringes, especially with sensitive biologic drug formulations.

System advantages include:

- High break-resistance
- Highest quality assured by 100% vision inspection
- Superior functional performance and barrier protection with Flurotec® film
- No silicone oil on the syringe barrel or piston
- No tungsten or adhesive
- Consistent functionality when used in auto-injector systems

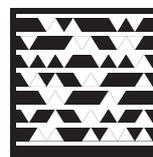
Contact West today.

North America +1 800-345-9800

Europe +49 2403 7960

Asia Pacific +65 6860 5879

www.westpharma.com



Get the free mobile app at:
<http://gettag.mobi>

#5947

- Minimum adsorption and absorption
- Improved drainability
- Excellent low-temperature characteristics
- High transparency

These benefits make cyclic olefins an ideal solution for biopharmaceuticals. As this market continues to grow, cyclic olefin syringes offer clear advantages over traditional glass syringes.

ENHANCING DRUG DELIVERY CAPABILITIES

A significant benefit of a Crystal Zenith COP barrel is that it can be molded around a needle, eliminating the need for tungsten pins, glues and adhesives. This in turn minimises the exposure to leachables and offers manufacturers an option to provide additional protection for the drug formulation.

Ultra-high-quality cyclic olefin plastic syringe systems provide a compelling alternative to existing glass syringe systems. Such systems provide better dosage precision and support for new classes of biopharmaceutical products. At the same time, cyclic olefin prefillable syringe solutions minimise drug product waste that can occur due to excessive overfills or loss due to breakage and provide for silicone-oil-free systems that reduce the risk of protein aggregation.

COP prefillable components together with fluoropolymer film-coated pistons in a ready-to-use format present benefits that are gaining strength industry-wide.

SUPPORT FOR DELIVERY OF INNOVATIVE DRUG THERAPIES

As the industry trends toward the use of prefillable syringes, these same components can be used in devices or delivery systems to aid with the increased need for injection in the home setting. Because of flexibility in molding, these polymers can be used in a variety of drug delivery systems, including custom auto-injectors and cartridges.

When comparing glass with plastic syringe barrels, the limitations are easy to distinguish. Glass is a formed product. To create the component, the glass is heated and mandrels are used to form the syringe's overall length, nose or tip, and flanges. These actions create dimensional variability. When the syringe is used manually, such variability is overcome by the human user, but with delivery devices such as auto-injectors, the device itself must overcome the variability. Since the device cannot judge the pressure required to do so, failures – including incomplete injections or incorrect needle depth upon injection – may occur.

“ULTRA-HIGH-QUALITY CYCLIC OLEFIN PLASTIC SYRINGE SYSTEMS PROVIDE A COMPELLING ALTERNATIVE TO EXISTING GLASS SYRINGE SYSTEMS.”

In contrast, a plastic component is molded. This process creates dimensional tolerances that are consistent and tighter than in a glass product.

As an alternative solution, the West ConfiDose® disposable auto-injector system (shown in Figure 2) has been designed to overcome much of the inherent variability with a variety of glass syringes, including dimensional variability and variable lubrication. Novel design of the force mechanisms and location on the front-end of the syringe allow higher forces to be used, enabling consistent delivery of drugs, even those with higher viscosities.

Accurate delivery as well as safe delivery is a benefit to the patient and healthcare providers. The potential for inadvertent needlestick injuries is a serious concern. To mitigate the risk of needlestick injuries, patients and healthcare workers may choose to use a passive needle safety system, such as West's NovaGuard® safety needle system.

With NovaGuard, a plastic shield surrounds the needle before the injection is given,

leaving only the needle tip exposed for injection-site orientation. The protective shield is activated upon injection and extends forward to cover the needle fully as it is withdrawn. Such systems can help to reduce dangerous injuries from needles during the injection and disposal processes.

FUTURE OUTLOOK

There is a growing demand to ensure the global quality and safety of drug products. By collaborating with component manufacturers early in the drug product's lifecycle, manufac-

turers can develop new solutions for providing quality drug products with manufacturing efficiency that can overcome administration challenges. Innovative drug products and prefillable syringe or auto-injector systems are mutually beneficial to achieving quality standards and patient safety.

Multiple interactions are needed throughout development to identify and mitigate risks to assure integrity of drug products, and for awareness of improvements throughout the drug product lifecycle. The involvement of all stakeholders in the early development stages will lead to successful design and evaluation of delivery systems to meet the needs of patients.

Daikyo Crystal Zenith® and Flurotec® are registered trademarks of Daikyo Seiko, Ltd.

Daikyo Crystal Zenith® and Flurotec® technologies are licensed from Daikyo Seiko, Ltd.

ConfiDose® and NovaGuard® are registered trademarks of West Pharmaceutical Services, Inc., in the United States and other jurisdictions.



IN WHICH EDITION SHOULD YOUR COMPANY APPEAR?

WWW.ONDRUGDELIVERY.COM

The future of innovative pharmaceutical packaging starts with SCHOTT today

SCHOTT forma vitrum is one of the world's leading suppliers of parenteral packaging for the pharmaceutical industry. Our 14 production sites worldwide produce over 7 billion syringes, vials, ampoules, cartridges and special articles of premium SCHOTT Type I borosilicate tubing glass or COC polymer. Continuous research and development enable us to find the best packaging solutions for the healthcare of tomorrow.

To find out more about our forward-looking innovations, visit www.schott.com/pharmaceutical_systems



Vials made of glass and COC Polymer



Glass ampoules with various break systems



Pen cartridges and dental cartridges



Prefillable syringes made of glass and COC Polymer

Visit us at Pharmapack Paris from 23th to 24th February 2011, booth 482.



SCHOTT
glass made of ideas

NEW from Elcam Medical *Flexi-Q PFS and DV*

The only fully disposable auto-injectors for complete life-cycle management for self injectable drugs.

- Product line is designed for administration of biologic drugs - both in liquid and lyophilized forms
- Highly *Flexible* platforms are able to accommodate a wide variety of customization options such as, injection time and force, viscosity, with dosage range of 0.3 mL to 1.0 mL.

Come to see our new Flexi-Q HV platform for Low to HIGH Viscosity Drugs at the Pharmapack, booth #277, Paris, 23-24 Feb.



Improving
Quality of Life



Injectable Drug Delivery Devices

Flexi-Q PFS ▶
Disposable Auto-Injector for Pre-Filled Syringes



Flexi-Q DV ▶
Disposable Auto-Injector for Drugs in Vials



Head Office / Manufacturer
Elcam Medical
BarAm 13860, Israel
Tel: 972-4-698-8120/1/2
Cell: 972-52-831-3890
Fax: 972-4-698-0777
menachem@elcam.co.il

USA
Elcam Medical Inc.
2 University Plaza, Suite 620
07601 Hackensack, NJ
Tel: +1 201 4571120
Fax: +1 201 4571125
info@elcam-medical.com
www.elcam-medical.com

Europe
MedNet GmbH
Borkstrasse 10
48163 Muenster Germany
Tel: +49 (0) 251 32266 0
Fax: +49 (0) 251 32266 22
info@medneteuropa.com
www.medneteuropa.com

China
Elcam China Office
Room 25B, Building B, No. 1118 of Changshou Rd.,
Shanghai 200042, China
上海市长寿路1118号悦达国际大厦B幢25B室, 200042
Tel: +86 2152375561
Fax: +86 2152375562
johnliu02@126.com

www.elcam-medical.com

DEDICATED TO MEETING THE SELF-INJECTION NEEDS OF PHARMACEUTICAL MANUFACTURERS & 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.

Our development approach is summarised in Figure 1.

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

Concept Phase	Development/Construction	Vendor Management	Look and Feel	Rapid Tooling	Serial Production		
<ul style="list-style-type: none"> • Concept proposals and discussion • Feasibility analyses • FTO Research • Project Planning 	<ul style="list-style-type: none"> • Design and product specification development • 3D and 2D drawings and data with CAD • Material choice • Risk analyses: Construction-FMEA Process-FMEA User-FMEA • Production of semi-to full-functional samples in rapid prototyping 	<ul style="list-style-type: none"> • For outsourced services or production supply • Supplier selection and approval • Purchase specifications • Joint Quality management • Setup of Supply chain and logistics 	<ul style="list-style-type: none"> • Solid network of design/engineering partners • From multiple concepts to final design • Analysis of functional feasibility • Construction of non-functional samples 	<ul style="list-style-type: none"> • Solid network of suppliers for plastic components and finishing • Manufacture of metal components • Assembly of first out-of-tool Pens • Validation protocols • Design validation 	<ul style="list-style-type: none"> • Solid network of suppliers for plastic components and assembly equipments • Manufacture of metal components • In-house pre-assembly capacities • Secondary packaging • Stock keeping • Validation protocols, QC, IPC • Documentation preparation: Master Batch record, technical file, etc. • Notified body certification • Customer Service 		
<p>Our quality- and project management accompany the complete cycle.</p> <table border="0"> <tr> <td> Haselmeier's Quality standards <ul style="list-style-type: none"> • DIN EN ISO 13485:2007 • DIN EN ISO 14971:2007 • EC Directive 93/42/EEG Annex II • FDA QSR • 21CFR 820 • CAN/CSA - ISO 13485:03 </td> <td> Project Management at Haselmeier <ul style="list-style-type: none"> • Dedicated project team • Project planning and tracking through MS Project • Budget and resource deployment tracking • Regular Project status report and active risk management • Regular meetings with the customer • Implementation of customer feedback for process improvement </td> </tr> </table>						Haselmeier's Quality standards <ul style="list-style-type: none"> • DIN EN ISO 13485:2007 • DIN EN ISO 14971:2007 • EC Directive 93/42/EEG Annex II • FDA QSR • 21CFR 820 • CAN/CSA - ISO 13485:03 	Project Management at Haselmeier <ul style="list-style-type: none"> • Dedicated project team • Project planning and tracking through MS Project • Budget and resource deployment tracking • Regular Project status report and active risk management • Regular meetings with the customer • Implementation of customer feedback for process improvement
Haselmeier's Quality standards <ul style="list-style-type: none"> • DIN EN ISO 13485:2007 • DIN EN ISO 14971:2007 • EC Directive 93/42/EEG Annex II • FDA QSR • 21CFR 820 • CAN/CSA - ISO 13485:03 	Project Management at Haselmeier <ul style="list-style-type: none"> • Dedicated project team • Project planning and tracking through MS Project • Budget and resource deployment tracking • Regular Project status report and active risk management • Regular meetings with the customer • Implementation of customer feedback for process improvement 						

Figure 1: Summary table showing Haselmeier development approach from product concept to serial production.

applied standards EN ISO 13485:2003 and annex II section 3 of the directive 93/42/EEC on medical devices. CE certification is certified by TÜV product services.

Last year, a new manufacturing facility was opened in Dnesice, Czech Republic. The 3,000 square meter facility provides additional capacity, including a 400 square meter class D cleanroom for sub-assembly of the disposable Penlet and Axis-D pen platforms (see below) and increased capacity for the processing of metal outer bodies for reusable pens.

Haselmeier GmbH
Dufourstrasse 32
8008 Zürich
Switzerland

Volker Wirth
T: +41 44 250 52 40
E: v.wirth@haselmeier.com

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

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

www.haselmeier.com

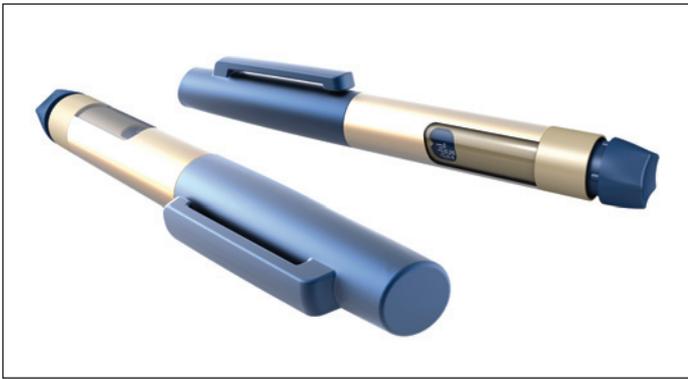


Figure 2: Axis Pen System – variable dose injection device.



Figure 3: i-pen – re-usable, variable dose injection device designed with an intentionally 'non-medical' appearance.

PLATFORM & PRODUCTS

Axis Pen System – variable dose injection device

The Axis Pen System (shown in Figure 2) 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 provide a new, unique technical function.

The Axis-D and Axis-R Pens Systems 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 is designed with an elegant and intentionally 'non-medical' appearance (see Figure 3) 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 specific requirements.

The i-pen features:

- Dose adjustment from 0.01-0.6 ml per injection
- Compact size enabling easy handling and portability
- Large, easy-to-read dose indicator

SOFTPEN – RE-USABLE 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 3ml 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: (figure 4)

- 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

CONCLUSION

Haselmeier's devices feature unique function, design and technology and are marketed by pharmaceutical and biotechnology companies around the world.

The company offers experience, competence and expertise in:

- The development/production of pen- and autoinjectors for self-administration of medicines through subcutaneous injection.
- Custom design and production of medical devices.
- Product design in simultaneous engineering to optimise the development and production processes.
- Quality Management System to guarantee a cost effective, consistent and high quality product.



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



Figure 5: Penlet – fully automatic, fixed-dose injection device

PDA Europe Announcement

The Universe of Pre-filled Syringes and Injection Devices 2011

- Pre-Conference Workshop with ICG
- Conference
- Training Courses
- Exhibition

Don't miss our Interest Group Meeting

Pre-filled Syringes

24 March 2011, Berlin/Germany

7-11 November 2011
Basel, Switzerland

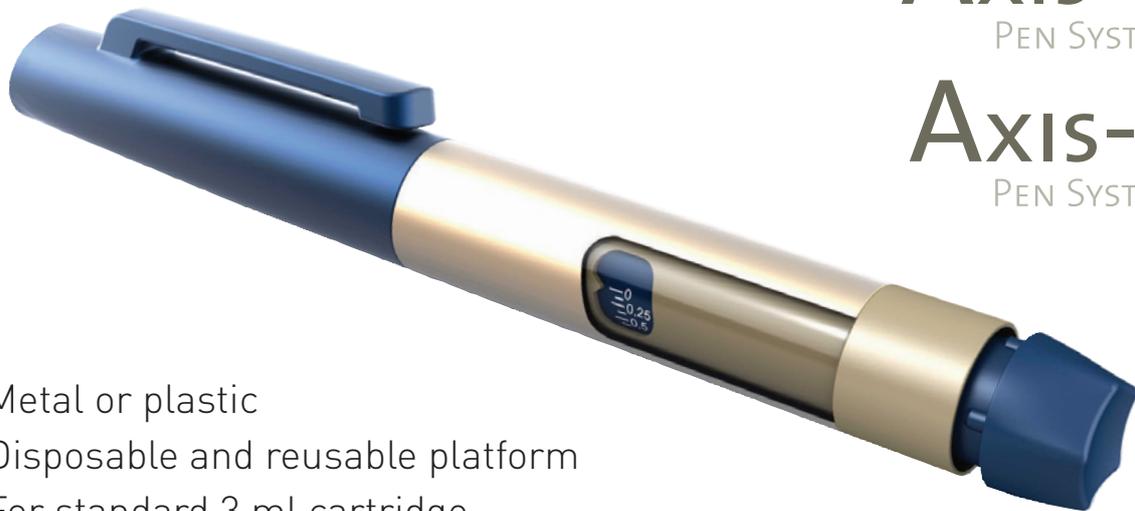
Download the complete program on: <https://europe.pda.org/Prefilled2011>

We Deliver Solutions

Introducing the new Axis Pen System

Axis-D
PEN SYSTEM

Axis-R
PEN SYSTEM



- ☞ Metal or plastic
- ☞ Disposable and reusable platform
- ☞ For standard 3 ml cartridge
- ☞ Dose increments customizable to your needs
- ☞ Distinctive dose indication
- ☞ Easy to use with no or minimal priming

**FOR MORE INFORMATION,
PLEASE CONTACT US OR VISIT US AT
WWW.HASELMEIER.COM**

Haselmeier USA 517 Benfield Road, Suite 301 - Severna Park, MD 21146 - USA
Contact: Robert J. Kilgore - r.kilgore@haselmeier.com - T +1 (410) 647-7300

Haselmeier GmbH Dufourstr. 32 - 8008 Zürich - Switzerland
Contact: Volker Wirth - v.wirth@haselmeier.com - T +41 (0)44 250 52 41

Pharmapack
stand 566



integrated needlestick protection
for ready-to-fill syringes

tip-top.com