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"Injectable Drug Delivery 2010: Devices Focus"

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THE NEXT GENERATION OF AUTO-INJECTORS

In this article, Matthew Young, Founder and CEO of Oval Medical Technologies, describes how, set against the disadvantages and concerns surrounding traditional needles, and the shortcomings of non-needle-based alternative delivery routes, auto-injectors offer the best of all worlds, and how Oval Medical's device represents a new take on auto-injector design.

BACKGROUND – THE CHANGING DRUG DELIVERY ENVIRONMENT

For many years syringes have been the 'Cinderella' of the drug delivery world. The medical device and pharmaceutical industries have been continuously modifying existing technology, which has fundamental constraints, instead of starting from scratch and taking a helicopter view of modern technologies available. Extensive innovation has been applied to inhalers, needle-free injectors, patches and other technologies, but the humble pre-filled syringe remains in many ways similar to the original 'Hypak' launched by Becton Dickinson in 1954. Where improvements have been made (for instance in materials and coatings) these have tended to be incremental and isolated.

The syringe is an extraordinarily efficient way of delivering systemic drugs to the body. Dose accuracy and bioavailability are high, drug wastage is low and the process is gentle on the drug. It could be argued that most other drug delivery device technologies only add one advantage; that they remove the needle, with its associated fear and pain, and which requires a trained person to administer.

Ten years ago, the device industry was seeking technologies to avoid needles by developing inhalation and needle-free delivery systems. However, no blockbuster devices have emerged from these development efforts. Patches and inhalers can give poor and variable bioavailability, and needle-free injectors can impose high shear forces on the drug and tend to be cumbersome and expensive. Inhaled insulin for Type 1 and Type II diabetes (Exubera) is one example of a new drug delivery technology, and was available from September 2006 until October 2007. Sales were not high enough for Pfizer to keep it on the market as the cost was much higher than injecting insulin.

Auto-injectors offer the best of all worlds, giving the benefits of needle-based delivery but with fewer disadvantages compared with other needle-based systems. They are particularly suited to the delivery of biological drugs because of the limitations of other drug delivery technologies.

The benefits of auto-injectors are finally being recognised. In the past five years we have seen a transition as investment has moved increasingly towards auto-injector development from other drug delivery technologies, such as inhalers and needle-free delivery.

OPPORTUNITY FOR OVAL

Oval Medical Technologies was born out of the belief that a novel primary drug containment technology could revolutionise the auto-injector market, and provide radical improvements in the safety, acceptability and reliability of needle-based self-administration. The company started not with a core technology, but with a clear set of aims:

- To resolve known safety and usability issues, and provide a range of user interfaces that would be preferred and accessible to a wider range of patients and carers (including the young, the elderly, those with limited physical or cognitive abilities), and for use in highly stressed environments and by people with minimal training.
- To provide a fundamentally less contaminating environment for the storage of delicate biological drugs.

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Figure 1: Oval Medical's next-generation auto-injector device

- To improve significantly the quality and reliability of auto-injectors both due to manufacturing variation and patient handling.

Even though auto-injectors are relatively simple devices, they have a history of problems and unreliability. Many of the current devices on the market have incurred recalls, and known usability and safety issues exist.

Most of the limitations of existing auto-injectors can be traced back to the glass staked-needle syringes used within them, which were never designed for this application. These limitations are summarised below.

Fragility:
The fragile nature of glass syringes is exacerbated by the difficulty of supporting a syringe anywhere but by the finger flanges, which have low and variable strength. This can make the delivery of viscous drugs difficult, and cause failures in the field.

Biological drugs tend to be more viscous than small-molecule drugs and therefore more difficult to deliver. The higher plunger forces needed to deliver these drugs can cause a glass syringe to shatter. Reducing these delivery forces extends the time needed to deliver a drug to unacceptable levels - there are several published papers documenting that patients remove their injection needles too early, and approximately 10 seconds is considered to be the maximum acceptable delivery time.

Syringe breakage has caused various development projects to be delayed or halted completely and several devices have been recalled post-launch for this reason.

Tolerances:
Staked-needle syringes were never originally designed for use in auto-injectors and dimensional tolerances, which are largely irrelevant for manual injection, can become critical in an auto-injector application. The extended needle length (the penetration distance under the skin) is an example of this.

High and variable friction and stiction:
Regulators require that all devices must produce reliable and reproducible dosing every time. Stiction (static friction) develops over time between the rubber and the glass so that the spring cannot force the plunger down smoothly causing incomplete dosing.

Drug degradation:
Biological drugs can be particularly sensitive to the silicone, rubber, glass and tungsten found in many syringes. There is a history of development delays, product recalls and ongoing concerns about immunogenicity relating to interaction between these materials and biological drugs.

Aspect ratio:
Design flexibility is limited by the narrow diameter of the staked-needle syringes typically used in auto-injectors and the requirements of the driving spring. This is why all marketed auto-injectors have a long, cigar-shaped form, which limits the user interface – a particular issue where patients suffer from debilitating conditions such as rheumatoid arthritis or anaphylaxis. Oval Medical's novel, silicone-free plunger technology overcomes these limitations and allows much greater design freedom and reduced device size.

Needle shield:
The needle shield used on current staked-needle syringes is not ideal for auto-injectors for a variety of reasons:

- It has no inherent tamper-evidence so sterility can be unwittingly compromised
- It can be extremely difficult to remove (sometimes requiring pull-off forces well in excess of 25 newtons)
- If twisted off it can damage the needle and cause rubber particulate to be injected into the patient
- It requires a sizeable hole in any needle safety cover which can compromise a needle safety mechanism.

There are several reasons for using existing syringe technologies within new auto-injectors, most notably due to the regulatory experience and filling equipment that currently exists. However, this approach will always limit the reliability, patient and prescriber acceptance, and economic benefits of auto-injector use.

PATIENT PREFERENCE AND USABILITY

Oval's designs (example shown in Figure 1) are driven by both patient preference (people's feelings about a device) and usability (the safety and compliance with which a device is used). These two factors are often confused with each other, and need to be considered separately if an optimal design is to be achieved.

Patient preference, and the powerful negative aspect of this including fear of pain, needles and the injection process, are affected by many factors. The noise and shock of a device activating can be as significant as the shape, size or colour of the device. Instructions and secondary packaging often appear to have been designed in isolation from the device itself, when they are an intrinsic part of the injection experience for the user. The best way to assure safety and compliance is to consider these factors intrinsic to the design at the earliest possible point in the development process.

A user interface that offers little scope for error tends to be inherently better than one which uses any number of design details to try to prevent users from making possible mistakes. Safety interlocks such as buttons and caps can often confuse as much as they can help. The meanings of colours and embossed icons on devices can seem obvious to the designer but may be interpreted quite differently by users with different backgrounds and experiences.

An independent and rigorous assessment process is essential to allow the variability between users to be considered properly.

PATIENT SAFETY

Patient safety is an ongoing issue, and every year the US FDA receives numerous notifications from patients and carers who have been injured. Several devices on the market have 'false cues' making it difficult for the user to understand which end of the device the needle emerges from, or how the device is activated. Other devices have non-obvious failure modes caused by subtle misuse such as pressing a button out of sequence or holding it down rather than releasing it on activation.

OVAL MEDICAL'S TECHNOLOGY: THE RISE OF CYCLIC OLEFINS

Oval Medical has developed novel technology and IP to overcome all of the problems previously associated with auto-injectors described here. It is important to note that Oval Medical is the first company properly to exploit the opportunities presented by cyclic olefin polymers as an alternative to glass.

Although cyclic olefins are already used successfully in vials and syringes, current applications often simply replicate glass designs without taking advantage of the material in its own right.

This lack of innovation is largely borne out of a reluctance to depart from existing filling technologies. However, Oval's primary drug containers can be filled in tubs on conventional filling lines with simple modifications. The benefits of using this new technology far outweigh the cost of making these modifications, particularly with regards to increased market penetration and competitive advantage in an arena where many marketed drugs are coming off patent and new drugs are proving increasingly difficult to develop.

Cyclic olefin polymers are far from new to the pharmaceutical market; the majority of prefilled syringes in Japan are made from cyclic olefins, so regulatory understanding of this class of polymer is growing. Janssen Cilag's Invega® product is provided in a prefilled syringe made out of cyclic olefin copolymer, as is Aseptic Technologies' novel vial for GSK's forthcoming DNA vaccines.

Oval Medical's technology utilising cyclic olefin completely removes many contamination issues by eliminating rubber, silicone, glue, and tungsten from drug contact. The design also reduces oxygen ingress, which should enhance shelf life of oxygen-susceptible drugs.

In addition to the robustness of cyclic olefin, Oval's low inherent plunger friction and short, wide drug container profile allow delivery of significantly more viscous drugs and higher drug volumes than current technologies. Device size can also be significantly reduced.

This combination of new materials, design advancements and an open-minded approach, has produced an adaptable system for use with many drugs including:

- Fragile biologics – which are often viscous and delivered in larger volumes.
- Biosimilars – which require a competitive advantage to gain market share.
- Generic drugs, for example, growth factor or heparin, which need cost effective delivery systems.
- Crisis drugs such as epinephrine for anaphylaxis and opiates for pain, which need to be portable and easy to use.

BENEFITS OF THIS PROPRIETARY TECHNOLOGY

For pharmaceutical companies:

- Increased market share through better penetration and competitive advantage.
- Improved patient preference due to ease of use compared with competitor devices.
- Extended shelf-life for fragile drugs, for example, silicone and oxygen-sensitive molecules.
- Enhanced lifecycle management by having the option of prefilled syringes, vials and auto-injectors made from common materials and fillable on the same filling lines.
- Cost effective.
- Reliable and robust.

For patients:

- External features are adaptable so can be made for rheumatic hands or can be made small, slim and discrete.
- Usability is intuitive and therefore requires less training.
- Intrinsically safer user interface reduces risk and increases compliance compared with existing technologies.
- Needle mechanism has been developed to achieve maximum patient comfort. Needle length can be modified depending on whether the drug needs to be delivered intramuscularly, intravenously, subcutaneously or intradermally.

CONCLUSION

The drug delivery market is dynamic and growing with 25% of the large pharmaceutical companies' pipeline being novel biologics. At last, the industry is addressing the needs of the healthcare providers to find novel mechanisms of drug delivery and is focusing on auto-injectors.

If you would like to know more about our core technology please contact us directly.

ABOUT THE AUTHOR

Matthew Young's past experience includes work on numerous auto-injectors and many other drug delivery devices for a leading product development consultancy specialising in this area. He founded Oval Medical Technologies, based in Cambridge UK, in February 2009 to develop and commercialise the next generation of auto-injectors.

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COMPANY PROFILE - SENSILE MEDICAL

Sensile Medical AG is an innovative Swiss company with a global business strategy. Its research and development activities are focused on developing tools which help patients control their disease better and improve their quality of life. Its core technologies comprise the development of innovative medical devices which enable micro drug delivery systems.

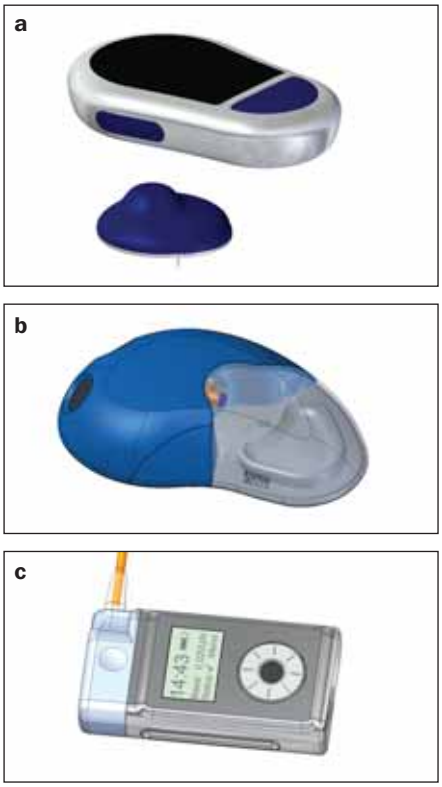

Figure 1: a) The Bolus Patch; b) Patch Pump; and c) the MiniPump.

A sound patent strategy protects the company's intellectual property. The know-how, efficiency and reliability of its employees enable Sensile Medical to ensure patients' interests are well served. As far as research and development are concerned, Sensile Medical collaborates with academic and industrial partners such as the Swiss Federal Institute of Technology in Lausanne. Sensile Medical, located in Hägendorf Switzerland, was founded in 2004 and has solid private financing.

Sensile Medical is developing three drug delivery products for 3 different needs (see Figure 1).

THE BOLUS PATCH

The Bolus Patch (Figure 1a) is an easy-to-use, partially disposable, controlled-delivery technology platform designed to deliver drugs into the subcutaneous tissue.

Sensile Medical's Bolus Patch pump is an innovative product for the subcutaneous delivery of liquid drugs. The patient carries a patch attached to the skin, which contains the medicine. The dose to be delivered is set in a handheld controller and the bolus delivery can be wirelessly activated by positioning the controller over the patch and pressing the buttons.

The infusion set is a separate component, so that it can be changed without throwing the bolus patch containing the remaining drug away.

With this novel technology, it is possible to avoid overdose and to deliver the drug at specific times through integrated reminder functionality. The physician can later check if the patient was compliant and used the adequate amount of medication, as well as the total dose administered into the body of the patient.

Figure 2: The Patch Pump Controller

PATCH PUMP AND MINI PUMP

The Patch Pump (Figure 1b) and the Mini Pump (Figure 1c) are easy-to-use, lightweight, compact, detachable, partially disposable, continuous subcutaneous drug infusion devices. Sensile Medical's accurate and precise Patch Pump and Mini Pump are the next generation of drug delivery pumps.

Patch Pump: Most patients are limited in their daily activities by the long tubing of conventional pumps, and do not want a complicated, cumbersome device. The wireless Patch Pump Controller is shown in Figure 2.

Mini Pump: Most patients only use a few basic functions of their drug delivery pump and do not want a complicated, cumbersome device.

The main characteristics of the three pumps are summarised in Figure 3.

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Bolus Patch	Patch Pump	Mini Pump
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Figure 3: Summary characteristics of the three pumps.

AGUETTANT INTRODUCES A NEW GENERATION OF INFUSION BAG: THE AGUETTANT® SELF-FLUSHING BAG

There are several disadvantages associated with the use of conventional infusion bags. However, their use is ubiquitous in hospitals and is also increasing in the homecare setting. Danielle Labreche, Director, Business Development & Innovation at Laboratoire Aguettant, introduces the company's Self-Flushing Infusion Bag, which overcomes the disadvantages of conventional bags, thus improving safety for patient and healthcare professionals alike, contributing to therapeutic efficacy and reducing reducing hazardous waste and global costs.

Injectable drug delivery via a plastic infusion bag was first introduced to the market in the 1960s. This mode of injection, still predominantly used in hospitals but also increasingly in the homecare market, has associated with it a series of questions and concerns. These concerns, which are a high priority in the hospital sector worldwide, relate to:

- Compliance to drug prescription
- patient safety
- Medical professionals safety
- environmental issues and related costs

"A STUDY CONDUCTED BY THE INTENSIVE CARE & ANAESTHESIA DEPARTMENT OF EDOUARD-HERRIOT HOSPITAL (LYON, FRANCE) REVEALED THAT WITH A BAG CAPACITY OF EITHER 50 ML OR 100 ML, ON AVERAGE, 20% OF THE FORMULATION STAYS IN THE CONNECTING LINE WHEN FLUSHING IS NOT PERFORMED"

For patients, there is concern around the use of infusion bags and their potential contribution to nosocomial contamination risk. For healthcare workers, in addition to the risk of infection that patients face, there is the **risk of exposure to toxic or allergenic drugs when connecting and disconnecting the line**. Another concern is the environmental impact of the waste drugs and medical supplies generated by infusion bags, and the associated financial cost of managing that waste.

There is also a crucial question hanging over the actual dose that is administered to the patient from an infusion bag and compliance to the prescription. In June 2008, an important study conducted by the Intensive Care & Anaesthesia Department of Edouard-Herriot Hospital (Lyon, France) revealed that, with a bag capacity of either 50ml or 100ml, on average, 20% of the formulation stays in the connecting line when flushing is not performed.[1] This may clearly have the effect of underdosing the patient, and result in suboptimal treatment efficacy or even ineffective treatment, with the inevitable serious adverse effects.

At its facilities in Lyon, France, **Laboratoire Aguettant has designed a new infusion bag system that provides far safer drug delivery, and improves compliance by automatically flushing the connecting line without any medical staff intervention**.

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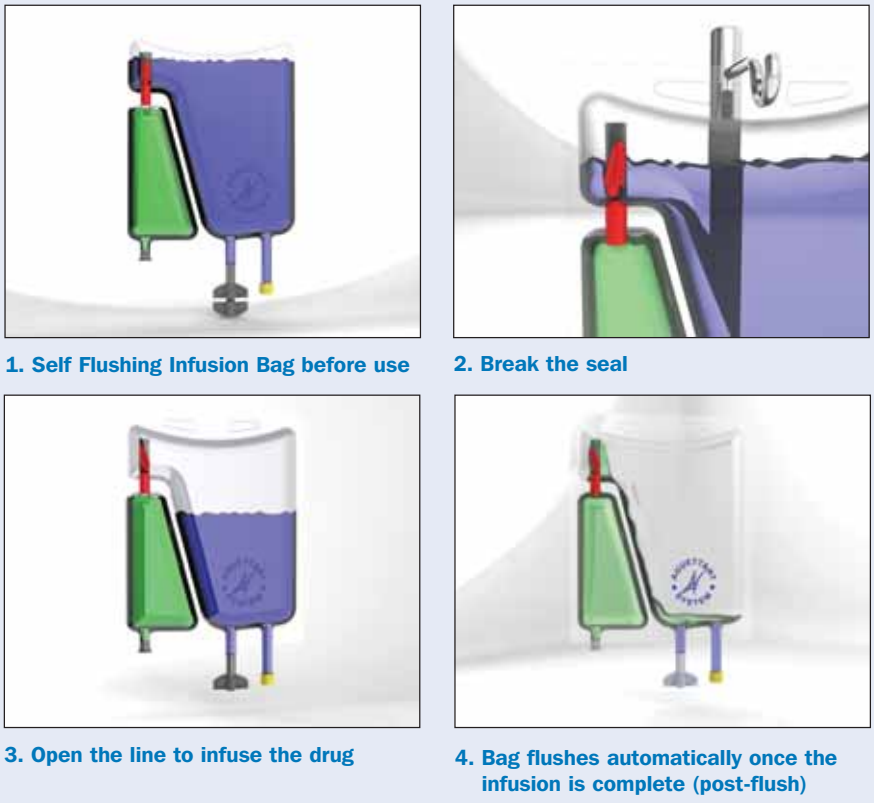
The AGUETTANT® Self-Flushing Infusion Bag, which was patented worldwide in 2005, transforms the flushing procedure from an active process to a passive process.

This infusion bag system can be adapted to fit different drug- and flushing-volume requirements and will accept several types of connections, including but not limited to the standard Luer Lock connector, which enables a needle-free system.

THE KEY BENEFITS ARE:

- Protect staff against drug exposure
- Improve compliance to the prescribed dose by delivering the whole drug quantity to the patient with no loss in the connecting line
- Reduce the risk of nosocomial infections by eliminating the manipulations for flushing preparation and performance
- Reduce waste drugs and medical supplies and consequent cost and environmental impact compared with manual flushing a traditional infusion bag
- Save time of preparation for the medical staff with its intuitive use



1. Self Flushing Infusion Bag before use
2. Break the seal
3. Open the line to infuse the drug
4. Bag flushes automatically once the infusion is complete (post-flush)

Figure 1: Step-wise depiction of the AGUETTANT® Self Flushing Infusion Bag use (dual chamber)

1. Self Flushing Infusion Bag PLUS before use

2. Purge the line (pre-flush)

3. Break the seal

4. Open the line to infuse the drug

5. Bag flushes automatically once the infusion is complete (post-flush)

Figure 2: Step-wise depiction of the AGUETTANT® Self Flushing Infusion Bag PLUS use (triple chamber)

"THE TRIPLE CHAMBER VERSION OF THE INFUSION BAG PROVIDES AN ADDITIONAL KEY FEATURE, WHICH IS TO GUARANTEE PROTECTION OF MEDICAL STAFF AGAINST ANY DRUG EXPOSURE RISKS BY SYTEMATICALLY PRE- AND POST-FLUSHING, AND BY VIRTUE OF IT BEING A CLOSED SYSTEM"

AGUETTANT® SELF FLUSHING INFUSION BAG (DUAL CHAMBER):

Two versions of the self-flushing soft bag are available. The first version – Aguettant® Self Flushing Infusion Bag – with a dual chamber performs a POST flushing. The instructions for use are shown in Figure 1.

AGUETTANT® SELF-FLUSHING INFUSION BAG PLUS (TRIPLE CHAMBER):

The second version – Aguettant® Self Flushing Infusion Bag PLUS – has a triple chamber for a PRE and a POST flushing. This is outlined in Figure 2.

The triple chamber version of the infusion bag provides an additional key feature, which is **to guarantee protection of medical staff against any drug exposure risks by systematically pre- and post-flushing, and by virtue of it being a closed system**. Exposure to toxic drug products is a real issue for heathcare workers, especially, as an example, in the area of oncology. It can also be relevant to high-value biological products such as cell therapy and blood components to limit drug loss in the line.

Laboratoire Aguettant has already entered into an exclusive licensing agreement with one of the largest US pharmaceutical companies to market the Self-Flushing Infusion Bag in association with a range of products in Europe. This collaboration could be soon extended to the United States and the rest of the world.

Aguettant is looking to establish partnerships with clients that want to offer more safety, security and compliance with the prescribed doses through this innovative delivery system, a device that can fit well into the lifecycle management of existing drugs products.

The AGUETTANT® Self-Flushing Infusion Bag, is part of the Aguettant SYSTEM® portfolio, a new label providing a guarantee of quality design and innovative technology.

REFERENCE:

1. Science Direct, Annales Françaises d'Anesthésie et de Réanimation 27 (2008) 514-519.

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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.

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LIFECYCLE MANAGEMENT AND DIFFERENTIATION THROUGH INJECTABLE DELIVERY SYSTEMS

In a pharmaceutical and biotech landscape that is increasingly generating products that require injection, and which is increasingly competitive, the early consideration of packaging and delivery systems is critical. Graham Reynolds, Vice-President, Marketing and Innovation, Delivery Systems, at West Pharmaceutical Services, explains.

When pharmaceutical and biotech companies begin to develop a drug, the delivery system is often far from top of mind. Ideally, drugs will be stored first in bulk containers, then moved to a standard system of vial, stopper and seal during clinical testing. As the drug moves to market, additional containment and delivery systems may be developed. Some drugs, including biologics, may require a delivery device or injection system.

For each new containment system, testing is required and can often be time consuming and costly. However, the development of novel materials, such as cyclic olefin polymers, can provide ideal lifecycle management solutions. Such materials – which are typically break-resistant and inert – can be used in a variety of containers, devices and systems thanks to flexibility in molding.

As the industry tends towards the use of devices and delivery systems to aid with the increased need for injection in the healthcare and home settings, the links between packaging and delivery system manufacturers, and pharmaceutical manufacturers, must be strong. These links should also be made early. The interdependence of the packaging and delivery system needs to be carefully considered at an early stage, and a thorough understanding of both is key to ensuring a successful drug/delivery system combination.

AN ENVIRONMENT FOR INJECTABLE GROWTH

Growth in injectable therapies, driven by increased incidence of diseases such as diabetes and auto-immune diseases (including multiple sclerosis and rheumatoid arthritis), has resulted in the development and launch of an increasing number of new biologics designed to treat these conditions. Most of these products require regular injectable delivery, often by the patient or caregiver.

Evidence shows that there is continued growth in the number of biological products, and that most of these require delivery by injection. An analysis of the top 20 biologics on the market by revenue demonstrates that most if not all of these products are delivered through injection. These trends are driving the need for prefillable syringe systems and drug delivery devices and systems that can be used in either a clinical or home care setting.

Because biologic products are often large molecules that do not transport well through non-injectable routes, delivery devices such as auto-injectors are often the best choice for administration. While different technologies, such as inhalation and transdermal patches, have been attempted, in many therapeutic areas injection has proven to be the most effective method of delivery.

Device requirements are driven either as a means of product lifecycle management or by companies entering an established market area where devices are commonly used (such as in the treatment of various auto-immune diseases). In the latter case, it is often necessary to enter the market directly with a competitive delivery system to ensure competitive parity or additional patient benefits. Such differentiation is key to competing with established products, and partnering with a manufacturer to provide

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novel technology should be an important part of the product's launch plan.

A specific example could be the planned launch of a drug for the treatment of auto-immune disease, where the selection of a system comprised of a prefillable syringe and an auto-injector (usually disposable) requires careful consideration of the primary container and the delivery system, and the performance of the two in combination with the specific drug product.

THE NEED FOR EARLY PARTNERSHIPS

Recent US FDA issues relating to potential risks with glass prefilled syringes in auto-injectors highlight the need for vigilance when considering the interaction between device and container in the development process. Early decisions regarding containment materials and delivery systems may help ensure compliance and increase safety once the product reaches the market.

In some cases, the earliest entry of a drug to the market may be facilitated by the use of a traditional container closure system such as a vial, with some form of reconstitution system if the product is lyophilised. This system is used for the manufacturer's convenience and may not be the final or best delivery system for the product.

Many drugs move to prefilled syringe systems that may later be used within a device such as an auto-injector. The drug molecule is the same, but the delivery system has changed, which may require costly testing to ensure that the new container closure system does not react with the drug. There are many examples of this type of lifecycle management with established products, as well as examples of newer drugs whereby the company may choose to launch in a more sophisticated system, rather than in a vial format.

In some cases – and particularly when large-molecule biologics are concerned – the prefilled syringe system may not be an adequate match for the delivery device, which can lead to safety issues such as breakage when using glass syringes, or incomplete delivery of highly viscous products. Here, early planning and a stronger focus on the lifecycle management of the containment system can be key to ensuring the earliest product launch with lower risk, no matter what format is selected by the drug company. By ensuring a good fit early in the development process, pharmaceutical companies can essentially build in increased compliance and ease of transition to devices and systems once the product hits the market.

Working closely together, pharmaceutical and packaging manufacturers can look for ways to differentiate a product through the packaging and delivery systems. There are several reasons the relationship should start early. First is to ensure that packaging is right for the drug product. Packaging can be a huge factor in the success of a drug product getting through the regulatory approval process smoothly and to the market quickly. How the product is going to be delivered should be determined based on the clinical application. This will help the company to understand what type of primary packaging is needed, and how that packaging will fit with the delivery system. Ideally, the same material should be used for containment from research through to commercialisation.

Figure 1: Devices and delivery systems meet increasing needs for injectable drug delivery in the healthcare and home settings. West offers a variety of delivery systems, including (from top to bottom): West's ConfiDose® Auto-Injector System; Daikyo Crystal Zenith® syringe system and the West NovaGuard™ Safety Needle; and the eris™ safety syringe system.

Proper packaging can have an effect on successful development and registration. While the focus of the regulatory bodies may be on the drug itself, the reality is that when that drug hits the market, it arrives inside a container closure system. Selecting the right system early in the process can help manufacturers not only differentiate their product in a crowded market, but also increase the chances of a successful move to market.

In many cases, the goal is to move from a vial/stopper system to a prefilled syringe system. Here again, early consideration of container closure and drug delivery systems can mitigate risk. Use of a consistent material throughout the drug's lifecycle can minimise risk.

For example, cyclic olefin polymers, such as Daikyo Crystal Zenith® (CZ) resin, provide a break-resistant, silicone-free solution that can be molded in a variety of shapes and sizes. Having the same material for bulk storage, vials and prefillable syringe systems provides consistent functionality and minimises the material contamination risk as the drug moves from research to clinical trials to commercialisation. This is especially important for biopharmaceuticals, which may react with particulates from silicone-oil and tungsten contamination.

DESIGNED FOR INCREASED PATIENT COMPLIANCE AND SAFETY

Many pharmaceutical companies have advanced devices capable of increasing patient compliance. Treatment for diseases such as diabetes and multiple sclerosis are prime for device use. In many cases, a range of device options is available to support a single drug.

For example, a single drug used to treat multiple sclerosis may be available in a ready-

to-use, pre-measured, prefilled syringe. In addition, an auto-injector may be available for those with dexterity issues. Such devices may have both sight and sound signals to aid end users who may have trouble determining when the dose has been given fully, thus aiding in compliance. Recent innovations in devices have also incorporated electronics as a means of providing instant user instructions, in cases of rarely-used emergency treatments, or as a means of aiding compliance.

Diabetic insulin is available in multiple formats, including syringes, pens and pumps. As these devices become more complex, many utilise electronic feedback to ensure patient compliance. Information about the medication can be downloaded from the pen or pump directly to the caregiver. A physician can then determine quickly and easily if the patient has been following his or her medication schedule. Linking diagnosis to treatment, in conditions such as diabetes, is also becoming a more active area in terms of device development.

SAFER FOR CAREGIVERS AND END USERS

Devices can be designed to aid not only in patient compliance, but also patient and provider safety. In recent years, there has been an increased focus on needlestick safety. According to the US National Institute for Occupational Safety and Health (NIOSH), approximately 600,000 to 800,000 needlestick injuries occur annually in the US. These injuries carry the risk of serious infection from diseases such as HIV and hepatitis.

New technologies include passive systems, such as West's NovaGuard™ safety needle and the eris™ safety syringe system (see Figure 1), which allow for safer injection without altering the caregiver's administration technique in the hospital and clinical setting.

In the home care setting, although needlestick prevention has not been a significant issue for self-injecting patients, it can be an area of concern for caregivers, family members, and downstream disposal and safety. Much of the focus for self-injection devices has been on reducing anxiety for the patient through improved needle technology, and injection devices that can reduce needle phobia by hiding the needle both before and after injection. For example, West's ConfiDose® auto-injector system is shown in Figure 1.

Other areas of treatment require needle-free systems. When treating haemophilia, for instance, needle-free systems and devices have been used extensively to eliminate needles during the reconstitution process. Use of vial adapters, needleless transfer devices and diluent-filled Luer lock syringes have helped to eliminate dangerous needles from the reconstitution process and create a safer environment for those suffering from haemophilia.

SOLUTIONS THROUGH NEW TECHNOLOGY

New technologies and novel materials such as CZ resin are helping to make delivery system decisions easier and more effective for both the pharmaceutical manufacturer and the end user. By developing a thorough understanding of the drug's intended use and the patient's needs, packaging manufacturers can lend their expertise to pharmaceutical manufacturers, ultimately developing a package that differentiates the drug in the market and helps to ensure that the patient's needs are met. The key goal remains the safety and effectiveness of the drug product, and a thorough knowledge of potential interactions with packaging, combined with an intimate knowledge of the regulatory and quality environment is key in this area.

When designing a delivery solution, pharmaceutical companies must consider the end user. This is increasingly important since devices are designed to be safe and effective, but also easy to use for those patients who may have limited dexterity, and who may not be medically trained.

West has created an internal group that focuses on early-stage concept development that works closely with outside partner Insight Product Development, a group of industrial designers who help to determine a product's external look and feel and fully understand the needs of the patient and administrator (often the same person).

Creative concepts can be impractical if they are not combined with a fundamental knowledge of how a device can be engineered, produced, assembled and linked to the primary container. West provides a fully integrated process from initial patient needs through to manufacture, always with a thorough knowledge of the requirements of the drug product, which we believe is critical to ensuring that drug products can be launched effectively with an optimum packaging and delivery system.

A range of new technologies is now available to meet the many challenges of the pharmaceutical market. In the area of prefillable syringe systems, West offers the first silicone-oil free product on the market – the ready-to-use CZ prefillable syringe system.

One of the reasons customers choose the CZ syringe system is because it offers much less variability in functionality than traditional glass systems.

Coupled with a plunger with West FluroTec® barrier film, the CZ syringe system does not require siliconisation, which leads to variability that can affect the gliding performance of the plunger. With a prefillable syringe system, gliding performance can have a major impact when you place the system into a device such as an auto-injector, which relies on the complete delivery of a drug from a syringe. Gliding force, drug viscosity and siliconisation consistency can be factors in ensuring reliable dosing from an auto-injector or other device.

The insert-needle version also is produced without the use of adhesives or tungsten, and a high level of built-in quality through novel manufacturing techniques supported by multiple in-line inspections, thereby assuring the optimum container for sensitive biologic products, particularly when used with an injection device such as an auto-injector.

In addition, cyclic olefin polymers such as CZ resin offer customers the benefits of low extractables, break resistance and high quality in a vial or syringe system. CZ resin can be molded into complex shapes, an advantage over glass.

Pharmaceutical companies can select a CZ resin containment solution for the lifecycle of their drug – from development through to commercialisation. When coupled with an auto-injector such as West's ConfiDose® auto-injector system, which works well with all syringes and high-viscosity drugs, pharmaceutical companies have a unique, easy-to-use product that is safe for patients.

By working with an experienced partner, such as West, from an early stage of development, pharmaceutical and biotech companies will have the best opportunity to ensure that both the primary packaging and delivery system are appropriate. This will help ensure optimal drug integrity and efficacy, user experience, regulatory compliance and market differentiation.

Providing Solutions for Injectable Drug Delivery from Concept to Commercialization

Self-injection and needle safety systems

Drug administration systems

Whether you're seeking a life-cycle management solution, a self-injection system, a needle-stick prevention device or some other means to administer your drug product, West offers a solution. More than that, we can help you create the optimum custom solution for your product by fully understanding the end-users' needs. West applies a range of innovative technologies to provide a complete service, from concept through development, scale-up and commercialization.

West has the experience and the expertise to help ensure that your product moves quickly to market, by providing safe, effective and user-friendly drug packaging and delivery systems.

West™

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Daikyo Crystal Zenith® resin solutions

The next generation of autoinjectors

- ✓ Increase competitive advantage
- ✓ Enhance versatility through design
- ✓ Improve patient preference and safety
- ✓ Fill volumes 0.1 to 10 ml
- ✓ Deliver viscous and non-viscous drugs
- ✓ Eliminate rubber, silicone, glue and tungsten

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