A DIFFERENTIATED, CUSTOMISABLE PORTFOLIO TO LEAD A NEW ERA OF INDUSTRY GROWTH

In this article, Alan Shortall, Chief Executive Officer, Unilife, describes the company’s portfolio of injectable delivery devices in the context of a number of specific current pharmaceutical industry trends.

A series of trends are converging to redefine the injectable drug delivery industry. Device manufacturers who are able to provide pharmaceutical companies with a broad, flexible and differentiated portfolio of prefilled syringes and injectable drug delivery systems that can address market needs will lead the industry into this new era of growth.

Pharmaceutical companies utilising prefilled syringes for their injectable drugs and vaccines have traditionally been restricted to sourcing glass barrels, elastomers and associated materials from device manufacturers specialising in the production of commoditised products at high unit-volumes under a one-size-fits-all model. This traditional approach to the production and supply of prefilled syringes has created many challenges for pharmaceutical companies, including:

1. **Differentiation:** When conventional devices sourced from different manufacturers all share the same functionality and visual look, the pharmaceutical company has minimal scope to differentiate their injectable product from brand-name, generic or biosimilar competition.

2. **Customisation:** Where device manufactures are unable or unwilling to customise a product to address specific formulation, marketing or user requirements, a pharmaceutical company is hindered from providing its customers with patient-centric product that can optimise preference and therapy compliance rates.

3. **Materials:** When a device manufacturer is seeking only to market their own proprietary products or materials for use with a prefilled product, the ability of a pharmaceutical company to select their preferred material, lubricant or coating is constrained.

4. **Platform Integration:** Where there is fragmentation between suppliers of prefilled syringes, auto-injectors and ancillary safety products, pharmaceutical customers must bear ultimate responsibility for the integration of these devices, which may not be designed.

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5. Safety: When pharmaceutical companies are required to comply with needlestick prevention laws, they must purchase and attach ancillary safety products onto a standard pre-filled syringe, creating extra steps in manufacturing and adding up to 70% in shipping, transport and storage volumes. The bulkier size of pre-filled syringes with ancillary safety products and need for additional non-intuitive steps for use may also contribute to a sub-optimal rate of non-adherence to prescribed injection techniques.

Because of these and other unmet market needs and emerging market trends, this traditional model is fast becoming obsolete. In its place, pharmaceutical companies are quickly embracing a new paradigm for injectable drug delivery that encourages close, long-term collaborations between drug and device manufacturers. With such long-term partnerships seeking to enable and enhance the delivery of an injectable therapy, these collaborations may originate early in the clinical development process and then extend through the regulatory approval and lifecycle management of the combination product.

There are many factors behind this redefinition of the market for injectable drug delivery systems.

REGULATORY EMPHASIS ON HUMAN FACTORS

The US FDA and other regulatory agencies are placing increased emphasis on human factors during their review of drug applications, with user studies required to show that products are safe, simple and reliable for administration to the target patient population. Human factor studies can seek to confirm patient acceptability across factors such as initiation force, glide force, activation force for a safety mechanism, finger-flange design, ease-of-use, and convenience of disposal. The data generated by these user studies can add significant value to the regulatory approval and commercial success of the combination product. In particular, drugs which are supplied pre-packaged and pre-assembled ready for injection and require minimal steps of use are likely to generate strong rates of user preference and be encouraged for prescription.

SHIFT TO PATIENT SELF-INJECTION

As reported by Ernst and Young in their Progressions 2012 report: “Healthcare Everywhere”, more than 50% of all healthcare within a decade will no longer be administered in hospitals and doctors offices but in the “third place”, or in essence wherever the patient is during their normal daily life. Pharmaceutical companies are responding to this trend towards patient self-administration with the provision of biologics and other injectable therapies in devices that are customised to address the specific needs of the target patient population. From pre-filled syringes with extended finger flanges, soft rubberised grips and extended thumb pads on the plunger to support user dexterity challenges, to auto-injectors that are ultra-portable and convenient for disposal, drug delivery systems are becoming more ergonomic and tailored to the needs and lifestyle of the target patient.

PLATFORM APPROACH TO DEVICE COMPATIBILITY

To accommodate the needs of an entire patient population fully, from mild to severe cases, some pharmaceutical companies are seeking to market an injectable therapy in multiple device configurations including a standard pre-filled syringe as well as a disposable or reusable auto-injector. For such therapies, there is a growing preference amongst pharmaceutical companies to ensure that the pre-filled syringe and auto-injector will be fully compatible and not create challenges during assembly, packaging or use. When device manufacturers have an integrated portfolio of products and are open to building close collaborations with the pharmaceutical customer, the risk of production problems or downstream user issues can be minimised.

OPEN ARCHITECTURE SUPPLY CHAIN MODEL

With biologics now comprising a large and growing proportion of a pharmaceutical company’s clinical pipeline, the flexibility to select a preferred material or elastomer coating is becoming increasingly important. This is giving rise to an open architecture model amongst some device manufacturers, where they will work with each pharmaceutical company to therapy lyophilised in a vial, then transition a few years later into a liquid-stable format with a standard pre-filled syringe, and then perhaps later add an auto-injector. Today, however, the initial launch of an injectable therapy in a pre-filled format is considered to be the absolute bare minimum required to compete. Many pharmaceutical companies are seeking first-launch of their injectable therapies in, for example, a pre-filled syringe with needlestick prevention features, or an auto-injector or, in the case of drug reconstitution, a dual-chamber system.

MAKING SAFETY A COMPETITIVE ADVANTAGE

Needlestick prevention represents a particular area of need for pharmaceutical companies, healthcare workers and their patients. Europe and other international healthcare markets are now following the US toward the mandatory use of devices with needlestick prevention features. These laws require the frontline staff of healthcare facilities to play a role in the evaluation, selection, and use of devices including pre-filled drugs that can eliminate or minimise the risk of occupational exposure to the lowest possible extent. For pharmaceutical companies that must comply with these needlestick prevention laws, the selection of a pre-filled syringe that optimises levels of protection to healthcare workers can represent a significant competitive edge.

Traditionally, pharmaceutical companies have had two options for needlestick compliance. In the case of drugs and vaccines targeted for intramuscular injection, they can
utilise a prefilled syringe in a needleless format. Such devices require healthcare workers to attach a safety mechanism, such as a needle guard onto the prefilled syringe, immediately before injection. However, data suggests that such manual safety products are frequently not activated by the healthcare worker, or associated with needlestick injuries either during use or after disposal.

A more common approach has been to attach an ancillary safety product onto the prefilled syringe after it has been filled with the drug and prior to packaging. The process of attaching an ancillary safety product can require the purchase, installation, and operation of additional assembly systems within the pharmaceutical cleanroom. Any problems associated with the breakdown of these assembly systems or the subsequent breakage of the prefilled syringe can impact the financial efficiency of the entire fill-finish process. The bulky size of these ancillary safety products compared with a standard prefilled syringe also increases packaging, transport, and storage volumes by up to 60-70%.

The US Occupational Safety and Health Administration (OSHA), the FDA, and many healthcare associations cite a preference amongst healthcare workers for the selection and use of devices with automatic (passive) and integrated safety features that can minimise the risk of harm and best comply with routine injection procedures. Pharmaceutical companies that select such prefilled devices with automatic, integrated safety features will be in a strong position to leverage these protective and functionality benefits to build user preference rates and optimise market share.

**LEVERAGING DEVICES TO BEAT THE COMPETITION**

Devices that are differentiated and provide true benefits to the user can be leveraged by pharmaceutical companies to optimise the commercial value of their injectable therapies. In particular, devices which are visually elegant during all stages of use, devoid of unsightly springs or mechanisms and compact in size for convenient handling and disposal can generate powerful brand differentiation for a drug product. When these devices can then be further customised to address the specific needs of a therapy and create the safest, simplest possible injection experience for the target user population, the pharmaceutical company will be ideally positioned to build or protect market share by driving patient, payer and prescriber preference towards their product.
UNILIFE’S INNOVATIVE, DIFFERENTIATED AND CUSTOMISABLE PORTFOLIO

Unilife, a US-based global leader for injectable drug delivery systems is collaborating with many pharmaceutical and biotechnology companies to enable and enhance their injectable therapies. The mission of Unilife is to serve customers fully under long-term partnerships so they can leverage the company’s high-quality, differentiated products to improve patient care, maximise revenues and out-perform the competition.

Six proprietary product platforms have been developed by Unilife for the safe, intuitive delivery and convenient disposal of injectable drugs and vaccines. These platforms, which include prefilled syringes, dual-chamber syringes, auto-injectors, wearable injectors, ocular delivery systems and novel devices, represent arguably the most extensive array of differentiated injectable devices in the industry (see Boxed Text).

Unilife’s platform-based approach to product design means that all base technologies are fully established, with the company able to rapidly customise each product to address specific customer, drug and patient requirements.

SINGLE CHAMBER PREFILLED SYRINGES

Unilife has developed a full platform of ready-to-fill syringes under its Unifill® brand for use with all prefilled biologics, drugs and vaccines (see Figure 1). Unifill syringes are designed with USP-compliant materials in the primary drug container, and can be integrated with standard packaging and filling processes. They are designed for intuitive use and compact, convenient disposal by healthcare workers or patients. Human factor studies continue to highlight strong rates of acceptability and preference amongst a range of target user groups.

A common preference cited in these user studies is the audible click and tactile feel that is registered upon full dose delivery and the automatic activation of an integrated needle retraction mechanism. The user can control the speed of needle retraction directly from the body into the barrel to prevent exposure to a non-sterile needle. Automatic re-use prevention further eliminates the risk of device reuse or needle re-exposure.

Unifill syringes are highly customisable to address specific customer, drug and patient requirements with a selection of product configurations including the:

- **Unifill Syringe:** Featuring a staked (fixed) retracting needle and designed for use with liquid stable drugs.
- **Unifill Select:** Allows the user to attach retracting needles of various sizes at the point of delivery. Designed for use with either a liquid-stable drug or vaccine, or a diluent to reconstitute and deliver a lyophilised drug supplied in a vial.
- **Unifill Assure:** Featuring an extended, easy-to-grip finger flange and a widened thumb press for the intuitive self-injection of biologics by patients with reduced dexterity (shown in 2).

**DUAL-CHAMBER RECONSTITUTION SYSTEMS**

Unilife has developed the EZMix platform of dual-chamber syringes (Figure 3) to serve as a safe, simple and efficient system for the reconstitution and delivery of liquid or dry drug combination therapies. An innovative and proprietary reconstitution technology allows healthcare workers or patients to mix together a combination of liquid or lyophilised drugs intuitively with minimal steps. The process of reconstitution is ventless and orientation-free to maintain sterility and minimise the risk of drug wastage. EZMix syringes utilise the Unifill platform of fully integrated and automatic safety features to virtually eliminate the risk of needlestick injuries, prevent device reuse and encourage convenient, safer disposal. Product configurations include the EZMix syringe with a staked retracting needle, and the EZMix Select with attachable retracting needles.

**HANDHELD INJECTORS**

Unilife has developed a broad platform of auto-injectors that are designed for exclusive use with the Unifill syringe. This proprietary range of auto-injectors are compact in size, intuitive to use and can be customised to address specific customer, drug or patient needs. Unilife considers itself not only to be the first company to offer both disposable and smart reusable auto-injectors, but also the only company with devices that feature true end-of-dose indicators.

RITA™ is a disposable auto-injector designed to inject the prefilled dose from a single Unifill syringe. RITA is more compact in size than many other marketed auto-injectors for improved patient portability, intuitive handling and convenient disposal. In addition to there being no visible springs or mechanisms, the needle is hidden from view until the completion of the injection when it can be viewed in its retracted state through a window on the side of the barrel. The true end-of-dose indicators (audible click and tactile feel) associated with the Unifill syringe can also help to minimise potential drug wastage and optimise therapy compliance.

Figure 4: **LISA™**, an electromechanical reusable auto-injector.

**“OSHA, THE FDA, AND MANY HEALTHCARE ASSOCIATIONS CITE A PREFERENCE AMONGST HEALTHCARE WORKERS FOR THE SELECTION AND USE OF DEVICES WITH AUTOMATIC (PASSIVE) AND INTEGRATED SAFETY FEATURES”**

LISA™ (see Figure 4) is an electromechanical reusable auto-injector that completely automates the removal of the needle shield and the speed of needle insertion and retraction. In addition to enabling a user to select the speed and depth of dose delivery to help minimise pain and discomfort during an injection, the device features a single activation button, LED indicators and a push-on skin sensor. To Unilife’s knowledge, LISA is the first and only known reusable auto-injector that protects the patient from the risk of needlestick injury when removing a used syringe from the device.
WEARABLE INJECTORS

Unilife has developed a scalable, flexible portfolio of wearable injectors (Figure 5) to meet the delivery needs of large dose volume or long duration therapies that are unsuitable for use with handheld devices. Unilife’s portfolio of ReadyToGo™ wearable injectors utilises standard materials in the primary drug container, and is compatible with standard filling processes and equipment. They are programmable to deliver the measured dose over seconds, minutes or hours at a constant or variable rate based upon the specific requirements of the pharmaceutical customer, their drug and the target patient.

Importantly, the system maintains sterility of all drug contacting and fluid-path components without requiring full terminal device sterilisation. Other proprietary features include an on-body safety lock to avoid premature activation, and the automatic insertion of a flexible catheter for patient comfort. Multiple customisation options are available to pharmaceutical companies.

SUMMARY

All these factors uniquely position Unilife to serve as a long-term partner to pharmaceutical companies seeking to enable and enhance the delivery and commercial success of their injectable biologics, drugs and vaccines.

Figure 5: Unilife’s scalable, flexible portfolio of wearable injectors for large dose-volumes or long duration therapies.

Figure 6: Unilife’s broad, innovative portfolio of injectable drug delivery systems.

TEN POINTS OF DIFFERENTIATION FOR UNILIFE

1. A Broad, Differentiated Portfolio
   We have a broad, innovative portfolio of injectable drug delivery systems that customers can leverage to differentiate their injectable therapies and out-perform the competition (Figure 6).

2. Platform-Based, Customisable Technologies
   Our platform approach allows us to leverage an array of established base technologies to customise each product rapidly to specific customer, therapy and patient needs.

3. Enhancing and Extending Product Lifecycles
   The safety, simplicity and elegance of our products have the potential to build therapy compliance and drive preference amongst patients, payers and prescribers to enhance or extend commercial lifecycles.

4. Dedicated, High-Performance Teams
   We select and organise the best industry leaders with deep scientific and technical expertise into vertically integrated, cross-functional teams that can respond to customer needs with unparalleled speed and agility.

5. Compatible with Standard Fill-Finish Processes
   Our products are designed for compatibility with standard pharmaceutical industrialisation processes and equipment to help streamline the filling, packaging and shipment of our pharmaceutical customers’ products to end-users.

6. Modular Design and Manufacturing Approach
   All products are engineered for modular manufacturing to enable efficient customisation and the fast, efficient scale-up of production to support a customers’ pathway from clinical trials to commercial launch.

7. Advanced US-Based Production Facilities
   Our FDA-registered facility has advanced development and commercialisation capabilities including highly automated precision manufacturing to facilitate the supply of high-quality products in accelerated timeframes.

8. Best-in-Class Quality Management System
   So that our products meet the highest quality standards, our Quality Management System is in compliance with, and certified to, ISO 13485 to design, develop, produce and sell ready-to-fill syringes and active and non-active drug injection systems.

9. Flexible Supply Chain Framework
   We have the flexibility to identify and select preferred materials and coatings for components, including those within the primary drug container, from an extensive network of established industry suppliers.

10. A Fast-Growing, Protected Patent Portfolio
    We aggressively protect our novel intellectual property. Our extensive, fast-growing patent portfolio covers all device platforms and associated technologies to provide unrestricted freedom to operate.
Auto-Injectors

Wearable Injectors

Prefilled Syringes

Reconstitution Systems

Ocular Delivery

Novel Devices

Game-Changers

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