INTRODUCTION
PHARMA PERSPECTIVE

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Pharmaceutical industry pipeline trends reflect a significant increase in biologicals, namely monoclonal antibodies (mAbs), in clinical development with most being in Phase II clinical trials. The majority of these mAbs in the drug pipeline are highly viscous and need to be administered subcutaneously with drug delivery systems in volumes that exceed the standard fill of a 1.0 ml prefilled syringe. The emergence of biosimilar and interchangeable mAbs may actually be differentiated based on these delivery device offerings.

The evolution of subcutaneous drug delivery devices includes: syringes, pen injectors, autoinjectors, infusion pumps and, most recently, also so-called large volume delivery (LVD) devices (see Figure 1). The group of this emerging device class is still heterogeneous but it seems that LVD devices are typically electromechanical with low complexity and use standard primary packaging (containers). On the other hand, over the last few years, infusion pump technology has evolved to being tubeless, integrated systems reflecting the migration toward bolus injectors and patch technologies.

Currently, the acceptable volume of subcutaneous injections as a bolus is defined as injections of 1.0-2.5 ml.[1] When reviewing the PDR Nurse's Drug Handbook [2] and nurse guidelines in different institutes and hospitals, injection volumes up to 1.0 ml appear to be considered standard and volumes >1.0 ml up to 2.5 ml are acceptable in special patient populations, such as palliative care.

The current status of LVD includes a plethora of emerging technologies focused on delivering >1.0 ml volumes of viscous drugs/biologics with lower complexity and lower cost as compared with conventional infusion pumps. The primary packaging of some of these technologies are being developed with novel materials and containers.

It is important to remember that primary packaging is an essential interface between drug/biologic formulation and a delivery device. Meanwhile, the International Organization for Standardization (ISO) has taken the initiative to create a new standard on such bolus injectors as an extension to their standard series 11608 ("Needle-based injection systems for medical use – Requirements and test methods") to provide guidance in technical terms.

Industry is competing aggressively for access to LVD technology that can be industrialised for a variety of platform and drug-specific options. While this is an exciting horizon for subcutaneous delivery of mAbs, it is not without risk with regard to potential issues with Intellectual Property (IP). For example, LVD automatic needle/cannula insertion can be a minefield of IP challenges.

Regulatory evolution includes drug/biologic development requirements such as "to-be-marketed" devices to be used in clinical studies as well as in Phase III. For example, US FDA Center for Devices and Radiological Health (CDRH) requirements of usability/human factors validation studies have increased as the FDA focuses on addressing safe use of medical devices for home or self use. This, combined with regulatory feedback will determine specific usability and safety requirements for LVD.

LVD may provide significant advantages and options to patients with regard to home use based upon usability and safety as well as the integration of wireless connectivity for monitoring and information capture and exchanges which will ultimately improve drug adherence, healthcare outcomes and the lives of people living with chronic disease.

The market will sort out proven and acceptable delivery mechanisms which may differ based on patient group drug requirements, based upon patient group (e.g. rheumatoid arthritis as compared with asthma). Patient acceptance is based on the adoption of wearable injectors due to form factor, complexity and duration of drug delivery. The journey has just begun….

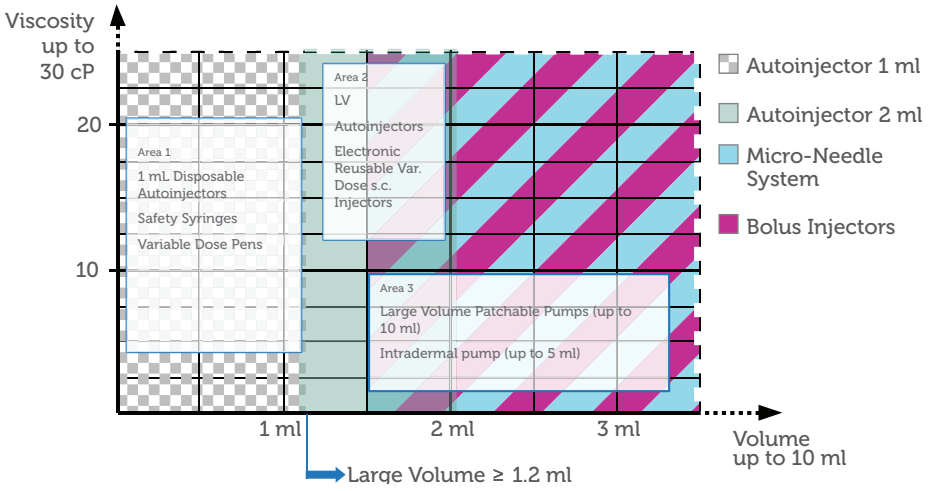

Figure 1: LVD Landscape: Subcutaneous Large Volume Delivery Devices are becoming more diverse.

> "The emergence of biosimilar and interchangeable mAbs may actually be differentiated based on these delivery device offerings"

REFERENCES:

1. *Parenteral Drug Association (PDA); Monograph on Parenteral Administration Policies, Section 2.1.*
2. *Spratto GR, Woods AL, "PDR Nurse's Drug Handbook", 2000.*

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