



PREFILLED WEARABLE DRUG DELIVERY: HARNESSING TECHNOLOGY FOR PATIENT & PARTNER CENTRICITY

In this article, Mindy Katz, Director of Product at Sorrel Medical, describes in detail the company's journey from identifying a clear market need to development and commercialisation of Sorrel's prefilled and preloaded wearable injection device.

INTRODUCTION

For many medical device manufacturers, the development process is a delicate balance between the different needs of two distinct parties: the patient and the pharmaceutical partner. This is especially true when looking to design a device that is both cost effective and intuitive, easy to use and compliant with established pharma practices. To achieve this, technology must be harnessed accurately, with a profound understanding of what constitutes a truly patient- and partner-centric product.

This article outlines Sorrel Medical's insights on today's market needs and

challenges, and points at how these are tackled by Sorrel's prefilled wearable drug delivery platform, bringing both patient-centric design and partner-focused strategy to the spotlight.

WEARABLE DRUG DELIVERY MARKET

Initially, wearable injectors may have been considered a fad, just a buzzword mentioned briefly in guessing what the future holds for drug delivery. Today however, the market indicates a great need for these wearable drug delivery devices. With the growth of biotech research and the increased number of biologics in pharmaceutical companies' pipelines, injectable medications expected to launch in the upcoming years have no solution for administration with today's commercially available hand-held injection devices. Moreover, pharma companies are putting more emphasis on devices, as a way of differentiating their product and providing their customers with a patient-

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centric system. Accordingly, Sorrel sees an increased interest and great potential in the world of wearable drug delivery devices.

Over the years, several leading medical device companies have ventured into this field, coming from various industries and backgrounds, each with their own unique expertise and interpretation of the ideal wearable device. Nevertheless, only a few such products have been launched to date, and devices currently in development vary significantly in terms of user interface and technology.

While there are considerable barriers for entering this market, including complex technology, strict regulations, human factors and financial longevity, wearable drug delivery devices hold vast potential. The changes that this innovation brings to the healthcare market, in terms of enhanced user experience, administration of large volume and high viscosity medications, decreased dosing frequency, connectivity and more,¹ have set Sorrel on the path to perfecting a true platform solution.

SORREL'S BACKGROUND

Sorrel is a medical device company based in Israel, a hotbed of healthcare innovation.² It is one of three privately held companies in the world of drug delivery devices, including Q Core Medical, Avoset Health and Sorrel Medical, all operating under the Eitan Group. The joint experience amongst these three companies includes commercialisation of drug delivery devices across the continuum of care, multiple US FDA approvals, market presence in over 20 countries worldwide and a team of R&D innovators that are experts in parenteral drug delivery, flow control, human factors, software for medical devices, cybersecurity, and more.

After almost a decade on the market with the Sapphire infusion pump system, used in hospitals and healthcare facilities around the world, with over 15 million litres of medication already infused to patients, Sorrel is looking to the horizon to address the next big challenge in drug delivery. While researching the wearable drug delivery market, Sorrel has found the broad experience and multidisciplinary expertise accumulated across its R&D, regulatory, quality and manufacturing teams is an excellent fit to take on the challenges which lie ahead. With this, Sorrel turned to identifying the unique needs and challenges of the wearable drug delivery market.

IDENTIFYING KEY MARKET NEEDS AND CHALLENGES

As a first step, Sorrel characterised the two primary customers for its wearable platform. The end-user was anticipated to be a patient receiving injectable medication, most likely in the home environment without the presence of a healthcare professional. The partner would be a pharmaceutical or biotech company, partnering with Sorrel to bring a drug/biologic-device product to market together. Solving the challenges identified in the research and development process proved to be a delicate tango, which balanced between the distinct need sets of both of these customers, the patients and the partners.

Platform

Sorrel's goal was defined as designing, developing, and manufacturing a wearable drug delivery platform. The term "platform" carries significant weight, impacting design decisions throughout the development process. A device platform means a pre-determined strategy, applied from the initial design input stage to ensure that the device answers to the needs of multiple pharmaceutical partners across a variety of medications, indications and patient populations. A platform approach allows the device manufacturer and pharma partner to leverage marketed devices in terms of supply chain and regulatory approvals, requiring only slight customisation to adapt from one molecule to another.

Reliable, Controlled, Accurate Delivery

Based on Sorrel's experience in the world of infusion pumps, it identified its first challenge to be the development of a reliable, controlled and accurate delivery system. Reliability is the key, because, as a starting point, the system must deliver. Moreover, there is a wide variety of injectable medications out there, some requiring a controlled, variable and accurate dosing regimen, whereas others need a fast bolus injection. Led by the decision to take a platform approach, Sorrel wanted to ensure its technology held the capacity to adapt to the full range of medications.

By forgoing exotic technologies and selecting only proven, reliable components for its pumping mechanism, Sorrel was able to secure the reliability that it targeted. In addition, the electromechanical pumping

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Figure 1: Sorrel Medical's wearable drug delivery devices are available in 2, 3, 5, 10 and 20 mL versions (2, 3 and 10 mL shown here).

mechanism was designed to allow a 2 µL dose per step, at $\pm 5\%$ accuracy, giving the platform inherent accuracy and the crucial adaptability required for medications requiring lower rates and accurate deliveries, as well as those requiring bolus injections.

Primary Container Agnostic

Primary containers are a world of their own. A variety of parameters affect the choice of volume, material and manufacturer of a primary container for a specific medication, which is generally the choice of the pharmaceutical company. Formulation, chemical interactions, business partnerships and cost are all in the mix when it comes to choosing an ideal container closure system.³ Accordingly, Sorrel's goal was to allow pharma partners the freedom to use a variety of drug reservoirs, and the technology was designed to have the flexibility needed to integrate the primary container of their choice. In addition, by being able to accommodate a broad range of volumes, the device platform can be easily customised to fit multiple products in a pharma partners' pipeline.

Decoupling the pumping mechanism from the primary container allowed for the flexibility that was required. Sorrel's platform can be customised to suit the different dimensions of any primary container, with only minor design changes. Currently, 2, 3, 5, 10 and 20 mL wearable injectors are available for customisation, all based on the same technology platform (the 2, 3, and 10 mL versions are shown in Figure 1).

Prefilled and Preloaded

For a self-administering patient, Sorrel wanted to ensure the best experience possible. A simple user interface offers a positive experience that reduces use errors, promoting adherence to therapy. Therefore, Sorrel decided to design a device that is intuitive and easy to use, with no compromises. Ideally, the drug-device system would come as one single unit, preloaded with a prefilled primary container (Figure 2). In this use case, the user would remove the device from its packaging, peel the adhesive liner, adhere to the body and

initiate treatment. A critical challenge in the development of a prefilled and preloaded device is the process of integrating the aseptic drug filling process and the device assembly, in a way that ensures a disinfected fluid path, for a cost-effective device with no user intervention and minimal disruption to established pharma processes.

The industry's current standard practice, of manually swabbing the cartridge crimp with ethanol prior to loading into the wearable injector, does not allow for the preloaded solution that Sorrel desired, as it requires user intervention. On the other hand, creating a micro-organism-free fluid path for a preloaded solution necessitates alterations to be made to the established pharma processes, for accommodating proprietary cartridges that contain the entire fluid path, or loading the cartridge under aseptic conditions. The ideal solution that Sorrel envisioned could have the prefilled cartridge assembled into the device either at the pharma company, a contract manufacturer or at Sorrel's own facilities, with disinfection occurring at the point of care. The theoretical, ideal, solution would be a "Honey, We Shrunk Ourselves" scenario, in which someone may be placed inside the device, swabbing the cartridge septum prior to the engagement between the fluid path and cartridge. As Sorrel searched for an adequate technology that allowed this disinfection at point of care, it found UV technology to be ideal.

UV-CLED technology⁴ enables a prefilled and preloaded device configuration, utilising standard cartridges, without disruption to existing drug filling lines. This method results in automatic, verified and controlled local disinfection at point of care. As with all components within the system, it is widely available, time- and scale-tested, and cost-effective. This is the ultimate prefilled solution, which permits Sorrel to deliver an ideal product configuration for the end-user, while also conforming to pharma practices, all in a cost-effective device. A scientific poster detailing experimental results of the UV technology will be presented at PDA's Universe of Pre-filled Syringes and Injection Devices, October 8-9, 2018 (Orlando, FL, US).

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Smart Sensing

Due to the nature of a patient's dependency on their wearable device, assuming they are prescribed self-administration at home without the aid of a healthcare professional, it is crucial that the device, via its technology, supports their user experience, notifies the patient of any issues, prompts desired actions and gives them the confidence they need to complete the treatment successfully. Sorrel achieved this with a blend of integrated sensors, as well as visual and audio indicators, clearly communicating the device status to the user. The sensors detect air and occlusion, and deliver alerts according to pre-defined parameters. A dedicated sensor ensures that the delivery will not initiate until the device has been firmly adhered to the skin. Additional sensors inside the device detect needle position, cartridge placement and run a range of internal system checks, ensuring that the device is functioning properly. It is not a trivial task to include smart sensing technology in a fully disposable and cost-effective device. In Sorrel's case, this is enabled by integrating sensors with smart algorithms, often using one sensor for more than one purpose.

Connectivity

Over the past several years, there has been significant focus on digital health and connectivity in medical devices. The power of connectivity can be harnessed in a variety of ways, primarily to promote patient engagement and adherence to therapy. Looking at the insulin delivery



Figure 2: Importance of a patient-centric, prefilled and preloaded device.



Figure 3: Bluetooth low energy and NFC connectivity.

market segment, it can be seen how connectivity has begun to sprout seeds that empower the diabetic patient population. While recognising the importance of connectivity, and the increased value it can bring to a drug delivery system, Sorrel believes that the connectivity conversation is one to be had with pharma partners, prior to the commercial release and per-patient population use case. Accordingly, Sorrel has both Bluetooth and near field communication (NFC) already integrated into its device, enabling connectivity in two widely accepted and

secure routes of communication. For the purpose of clinical trials, Sorrel has developed a smartphone application that enables sharing of treatment reports during investigational use (Figure 3).

DEVELOPMENT METHODOLOGY AND PROGRESS

Sorrel is utilising a structured project management method built of phases and milestones, each with a set of predetermined requirements. Quality, regulations, operations and R&D all have

responsibilities and sign-offs for each of the design stages, ensuring efficient co-operation across the board. In addition, Sorrel's pharma partners' participation has been built into this framework, ensuring that input is received and approval is given at relevant junctures throughout the development process. This operational methodology has been proven successful in the commercialisation of infusion pumps, and has been audited numerous times by regulatory authorities in Europe and the US. It also ensures full and automated traceability, starting from user needs, all the way to each device specification and every line of software code.

Sorrel has now completed the development of the technology platform on which the wearable devices are based (Table 1), and is currently setting up manufacturing lines for its first product line. The first configuration expected to be ready for clinical trial use is a 3 mL cartridge-based wearable injector that can be either preloaded or loaded by user, per the pharma partner's choice. The 3 mL device is expected to be ready for clinical trials in Q1 2019, post verification and validation. Working prototypes are available for feasibility testing.

Sorrel is actively pursuing partnerships with pharmaceutical companies, interested in bringing innovative drug-device combination products to market.

General Description	On body and fully disposable, delivering injectable medication to the subcutaneous tissue				
Duration of Use	Up to 3 days	Minutes - several hours			
Fill Form	Filled at point of care	Prefilled and preloaded			
Drug Reservoir	2 mL internal reservoir	3 mL cartridge	5 mL cartridge	10 mL cartridge	20 mL cartridge
Flow Range	0.01-60 mL/hr				
Connectivity	Bluetooth and NFC				
Indicators and Buttons	Audio and visual indicators, SW-controlled hard key for delivery initiation and/or bolus (optional)				
Viscosity	Up to 120 cP				
Customisability	Labelling, branding and software customisation available				

Table 1: Sorrel Medical's platform specification.

SUMMARY

With the wearable device market expected to provide a smart and straightforward drug delivery experience to patient populations worldwide, Sorrel is excited to be harnessing innovative technology that benefits both patients and pharma partners.

ABOUT THE COMPANY

Sorrel Medical is a medical device company focused on prefilled wearable injectors. Sorrel is one of three privately held companies operating under the Eitan Group, all in drug delivery devices, including Q Core Medical, Avoset Health and Sorrel Medical. Q Core Medical develops and manufactures the Sapphire infusion system, on the market in both hospital and homecare environments. Avoset Health is developing a connected homecare infusion pump, available for pharmaceutical companies in a dedicated application configuration. The joint experience shared amongst the Eitan Group's three companies, includes commercialisation of drug delivery products

across the continuum of care, multiple US FDA approvals, market presence in over 20 countries worldwide, and a team of R&D innovators that are experts in parenteral drug delivery, accuracy, flow control, human factors, cybersecurity and more.

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ABOUT THE AUTHOR

Mindy Katz is the Director of Product at Sorrel Medical, responsible for product management, marketing and business development. Her involvement in the company's early days influenced Sorrel's decision to pursue the wearable drug delivery market, and she has been heading the product and business activities ever since.

Ms Katz previously served as Program Manager at Q Core Medical, where she worked across multidisciplinary teams to build structured and collaborative partnerships between companies in the world of drug delivery. She holds a BSc in Biomedical Engineering from the Technion - Israel Institute of Technology.

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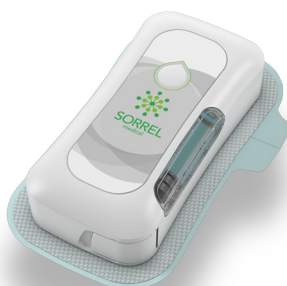
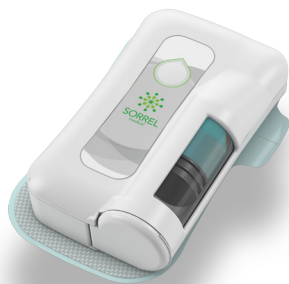
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Introducing Sorrel Medical - your wearable drug delivery platform.

Simplified and efficient administration of large volume and high viscosity medications can now be delivered with Sorrel, the next generation of wearable drug delivery devices.

A true platform solution, Sorrel brings intuitive adherence to therapy for patients and maximized value for pharma companies' full range of indications.

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