REUSABLE WEARABLE INJECTORS: LESSONS FROM *IN VITRO* DIAGNOSTICS

In this Expert View, Thomas James, Lead Mechanical Engineer at Key Tech, explores how insights from the development of successful *in vitro* diagnostic instruments can help guide the evolution of wearable injectors.

Self-administered injectable therapies have been improving patient autonomy and reducing the required frequency of clinic visits for years. These therapies, delivered via the subcutaneous route, have historically been delivered in autoinjector, pen injector or accessorised prefilled syringe presentations, with volumes in the 0.2–2.25 mL range. Modern autoinjector platforms are even beginning to boast larger volumes in the region of 5 mL, which can be expected to push the envelope of what is viewed as "possible" in handheld, self-administered drug-device presentations.

As high-dose, high-volume formulations begin to make their way to the forefront of chronic disease management, wearable injectors – or on-body delivery systems (OBDSs) – are increasingly drawing attention as intriguing devices for administering volumes ranging from 10–50 mL. To handle these larger volumes, these OBDSs naturally become larger and more complex than traditional disposable injectors, often with the inclusion of electromechanical elements, such as motors or pumps. As these devices are presented to drug manufacturers, patients and healthcare professionals (HCPs), a natural question arises, "Why do I have to throw this whole thing out?" And, in response, more and more wearable injector development programmes are taking that question to heart, exploring the potential of reusable, durable-and-consumable device architectures.

REUSABLE DEVICE ARCHITECTURES

Long before the patient's treatment came their diagnosis. The diagnosis process itself was likely performed in a central lab, by an exceedingly complex instrument that took the patient's sample, mixed it with buffers and reagents, performed controlled thermal steps and agitation processes, and optically, electrochemically or ultrasonically interrogated the resultant analyte to make the test measurement. And after that patient's sample came another, and another and another. The complexity of *in vitro* diagnostic (IVD) instruments requires development of a reusable instrument architecture. And since each diagnostic assay is unique in its workflows and sensitivities, each IVD instrument is a bespoke device. Each requires a robust architecture development process spanning needs assessments and technology feasibility activities through late-stage design, verification and transfer to manufacturing.

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As manufacturers explore reusable architectures in OBDSs, insights from successful instruments in the IVD industry can help guide these platforms. Just as with IVD instruments, wearable injector evolution demands thoughtful consideration of usability, complexity, sustainability and functionality to handle high-volume drug administration.

CLARITY OF VISION IS ESSENTIAL

Whether designing IVD devices or OBDS platforms, a clear product definition is an essential prerequisite. That vision comes by way of thorough stakeholder needs assessments – no small undertaking. Although it requires a large upfront investment, having a rigorous understanding of the varied and (almost certainly) conflicting needs of all the system's stakeholders is truly a luxury once development is underway and allows for efficient decision making and analysis of trade-offs.

Thomas James
Lead Mechanical Engineer
T: +1 410 385 0200
E: tjames@keytechinc.com

Key Tech
40 East Cross Street
Baltimore
MD 21230
United States

www.keytechinc.com

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It may be tempting to think that a tightly defined, marketable vision only helps to capture the attention of programme sponsors or early supplier partnerships, but it is far more consequential than that. Particularly in reusable architectures, acute points of tension emerge between dispositioning "features" across the durable and the consumable. For example, shifting a subassembly from the durable to consumable may add cost to the consumable but reduce implementation complexity or manufacturing risk in the durable. Alternatively, consider that the durable may have a battery and the computational overhead to support a more complex user interface – but is that part of the vision for the system? Is a more verbose interface a need from patients, HCPs, commercial strategy experts or the regulatory team – or is it simply a case of the design team being "so preoccupied with if they could…"?

Understand the Reusable Value Proposition

In the IVD instrument market, the rationale for reusability is evident, given the significant cost disparity between instruments and cartridges; a classic example of the razor-razorblade costing model. Once IVD chooses reusability, added features like electronic health records integration and a user-friendly interface become a matter of cost and development effort.

The OBDS perspective differs due to the high drug costs, especially in biologics. Given the cost built into consumables by the drug product, the case for a reusable being more cost efficient is diluted. Moreover, therapies with infrequent doses might not generate enough revenue to support a reusable system's cost.

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Sustainability in and of itself may be a compelling justification. However, the dosing frequency again comes into play – a therapy anticipated to be administered only 10 times to a given patient will result in the disposal of one durable item per every 10 doses, on the whole, in the absence of a robust takeback programme. This complicates the sustainability justification when considering the impact of electronics waste streams if material waste is the primary metric. Alternatively, consider the environmental burden of the sterilisation process and the cold chain, both of which are relieved from the burden of carrying the durable element of the OBDS in reusable architectures.

Because of the immense variability in therapeutic regimens, the value proposition of reusable OBDS platforms may lie not in their eventual "break-even" point as IVD systems frequently do, but in value added to patient outcomes. One such value-add may come through the benefits that data collection and transmission could provide; to the HCPs observing compliance, clinical trial facilitators collecting more robust administration data, and manufacturers performing enhanced post-market surveillance. Patient outcomes might also be improved via more accurate dose delivery, reducing injection variability in pharmacokinetics and pharmacodynamics to drive efficacy or by reducing injection duration uncertainty and, thus, improving patient satisfaction and compliance.

Another value-add may lie in the patient's actual ability to use the device and the acceptability of integrating it into their world. For example, entirely independent of a sustainability lifecycle analysis, a patient's perception of the device waste could play a significant role in the device preference of that patient between an otherwise equivalent single-use OBDS, driving differentiation in the market.

Navigating Feature Creep

As touched on above, as the durable of a reusable system increases in complexity and its cost of goods sold sensitivity is relaxed (relative to disposable systems), it can be tempting to add peripheral features that are not central to the product vision. This is enticing in IVD system development just as it is in reusable OBDS development.

Adding textual displays may seem like a great place to spend the device's excess processing power, but is it worth the localisation cost of translating each of those screens to the patient's native language? In a similar vein, Bluetooth or Wi-Fi connection to an optional companion app is often pitched as a mechanism to provide improved product training and troubleshooting resources, without appreciating the wide disparity in digital fluency within the patient population and the additional security and risk management burden associated with digital offerings.

Peripheral automated functions, such as automatic needle insertion and cartridge ejection, should also be considered very carefully – and can often avoid the expense of an additional actuator. There are on-market examples of manually actuated needle insertion mechanisms cleverly hidden in the OBDS's workflow design. When in doubt, avoid adding additional subsystems and actuation steps, each of which carry their own risk profiles and development burden.

DEVICE CONSTRUCTION AND PLATFORM PLANNING

Any OBDS, reusable or single use, must contain a source container, fluid path and fluid motivation subsystem. The source container and fluid path arrangement will almost invariably dictate candidate fluid motivation methods. These, in turn, will be central to the interface specification. As the development programme considers the possibility of an OBDS "platform" to leverage across several product offerings, typically the container and fluid motivation approach must be held constant. In IVD programmes, a next-generation device might have different connectivity features, usability improvements and speed of results, but rarely, if ever, will accept a different sample container or use an alternative fluid motivation method. Similarly, a reusable OBDS platform may have products with different injection speed capability, in-process feedback indicators or volume range, but the type of pump and container are typically set in stone within the platform. It's worth noting that the fluid motivation portion of the device is typically where most technical risk lives; changing the motivation approach incurs significant new technical risks.

Consumable Development

As soon as the container approach is known, de-risking activities can begin. Container access approach (e.g. with a pierce assembly) is certainly going to be a development challenge, considering workflow and sterility requirements. And among the "standard" containers, such as syringes, cartridges and bags, there are completely different challenges to be tackled. In the cases where the delivery container is patient- or pharmacist-filled, the container filling and installation workflow is going to take a considerable amount of thoughtful design and user feedback. It goes without saying that typical container de-risking activities, such as drug stability, extractables and leachables, biocompatibility, ageing and sterilisation trials, should begin as soon as the container is known. A late-stage container change can be fatal to an otherwise successful development programme.

OBDSs often use an adhesive patch for attachment to areas such as the abdomen or thigh. In reusable designs, this adhesive is single use and part of the consumable. Choosing and assessing its performance can be tricky, so it is important to prioritise an early investigation.

Last, the fluid path and needle assembly typically live in the consumable as they are wetted elements. Depending on the nature of the durable-consumable interface, it may be possible to decouple the fluid path and needle insertion assembly from the durable interface workflow, allowing for focused de-risking of the necessary mechanisms and materials. The fluid path and needle assembly should be reassessed as the product sterilisation plan develops, as it is not uncommon for elastomeric elements to behave in unexpected ways following sterilisation.

Durable Development

Just as an automated pipette or precision syringe pump is the heart of an IVD instrument, so is the fluid motivation subsystem in a reusable OBDS. While there is no shortage of integration and interface definition activities to do in the development programme, the drive mechanism should be assessed extremely early for its ability to achieve any required accuracy targets. The full set of foreseeable delivery conditions (such as the perennially challenging case of viscous drug product delivered while still cold) must be considered.

During these investigations, power consumption should be monitored to aid in building a system power budget and begin battery-scoping activities. Different pump methods will exhibit different sensitivities, but also different strengths. The simplicity of a constant-force actuator is quite attractive, but managing the resultant viscosity-based injection durations tempers its allure. On the other hand, the precise, viscosity agnostic and configurable dosing of an electromechanical syringe pump is compelling, but along with it comes a host of control, power and packaging complexities.

The durable is also where the controller lives – which means that the durable is where the connectivity challenges get solved. Early selection of a wireless communication protocol for data transmission (if applicable to the device) pays dividends down the road. Aside from the wireless communication, the durable typically carries the onus of primary user interface and feedback elements. Early in development, it can be productive to isolate those feedback elements and iterate on them with dedicated, limited functionality prototypes to understand patient expectations around device usage and behaviours.

Interface Definition

Finally, a well-formed interface specification is the glue that holds the reusable architecture together. Identifying the functional requirements and constituent connections that must be made (e.g. mechanical, electrical, pneumatic, optical) between the durable and the consumable is essential for ensuring seamless integration and robust performance. A comprehensive interface specification not only details the physical and operational characteristics of each connection but also provides insight into the tolerances, environmental conditions and potential failure modes. Regularly validating and refining this specification throughout the product development lifecycle can pre-empt many design challenges, thereby ensuring that the durable and consumable components operate in harmony, guaranteeing both safety and reliability for the end user. Proper, thorough documentation, along with iterative testing and feedback, will further ensure that the interface remains adaptive to evolving product requirements and implementations.

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CONCLUSION

The drive towards reusable architectures for appropriate therapies in the OBDS realm mirrors the strides taken by the IVD industry, although with more specific underpinnings of improved sustainability and patient outcomes. The lessons derived from one sector serve as guideposts for another, emphasising the importance of a clear product vision and understanding of the value it aims to deliver, all while addressing the nuanced complexities and challenges inherent in integrating durable and consumable components.

ABOUT THE COMPANY

Key Tech is an end-to-end product development firm specialising in the design of complex electromechanical devices and systems for medical applications. The company is 100% employee owned and located in downtown Baltimore (MA, US). It employs 75 engineers and designers focused on transforming complex technologies into simple, intuitive solutions.

ABOUT THE AUTHOR

Thomas James is a Lead Mechanical Engineer at Key Tech, where he is responsible for both the innovation and development of novel drug preparation and delivery devices. Over his tenure at Key Tech, he has contributed to several in-clinic and in-home infusion and injection systems, from emergency-use, low-cost disposables to highly accurate and flexible advanced-functionality delivery systems. Aside in-the-weeds engineering, Mr James also serves on Key Tech's business development team, focusing on the pharmaceutical and drug delivery industry. He holds a BS in Mechanical Engineering from the University of Maryland (US).