



## SAFE AND AUTOMATIC DEVICE TO IMPROVE DRUG PREPARATION FROM MULTIDOSE VIALS

In this article, Benjamin Morel, Intellectual Property Manager, and Claire Authesserre, PhD, R&D Fluidics Manager, both of EVEON, discuss the challenges and opportunities presented by multidose vials.

The use of multidose vials (MDVs) versus single-dose vials (SDVs) has been the subject of a 40-year debate. Yet the industry has been slow to implement alternative formats to SDVs, even though alternatives are being developed and can challenge existing practices.<sup>1,2</sup>

In 1983, it was already outlined by Sheth *et al*<sup>3</sup> that MDVs could be used with relatively low risk of bacterial contamination. More recent studies demonstrate that using MDVs as packaging presentation for vaccines does not affect immunogenicity.<sup>4,5</sup>

However, this type of packaging is associated with some clinical outbreaks.<sup>6,7,8</sup> The resulting manual handling can induce dosing mistakes and increase the risks of drug contamination and needle-stick injury. Therefore, MDVs require more training and more stringent practices to ensure patient safety.<sup>9,10</sup>

Furthermore, this type of packaging presentation has often been questioned from an economical point of view. The use of MDVs brings an additional challenge of increased dose wastage if opened with lack of planification during a vaccination campaign,<sup>9,11</sup> and is inevitable, according to experts.<sup>12</sup> In addition, studies have revealed that, during the H1N1 pandemic, MDVs were not as economic as expected due to the additional cost of time spent on manual handling and administrative processes.<sup>13</sup>

Today, more than 10 years after the H1N1 pandemic, MDVs are at the centre of the global strategic plan to overcome the current global crisis. Since the beginning

of the covid-19 vaccination race, MDVs have been at the forefront. Worldwide demand for glass vials, as well as the glass technicity required for vaccine stability, and the low number of vials providers, led to the situation of potential shortage if only SDVs were used.<sup>12</sup> To illustrate this point, a few weeks ago the US FDA approved two new MDVs, enabling a shift from six to 11-dose and 15-dose vials to overcome this situation.<sup>14</sup> This measure is another step toward avoiding a vial shortage, but also a proven efficient measure to reduce what is considered “inevitable waste”.<sup>15</sup>

Indeed, the covid-19 crisis pushes forward the use of MDVs – but it is important to consider the beneficial aspect observed on the vaccination value chain and our ecosystem and to use them for more general purposes. We learnt from vaccination campaigns in low- and middle-income countries that MDVs enable a 40% packaging waste reduction<sup>16</sup> and a 47% storage volume reduction in vaccination centres and storage rooms.<sup>16</sup> Those benefits are key when you consider the waste management crisis, which has already started on a global scale.

That is why it would be of interest to see how to improve the use of MDVs and to challenge the current paradigm of SDVs. This global vaccination campaign is the right time to think out of the box, push innovations and overcome the drawbacks of MDVs. Identifying key learnings helps to further improve practices and bring new solutions for future local, regional or global vaccination campaigns.



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“EVEON’s technologies dedicated to automated drug preparation and injection demonstrate key advantages to overcome cost efficiency, healthcare worker usability and patient safety challenges.”

One way to improve is to standardise the manual work performed by healthcare workers (HCWs) to get a repeatable, consistent, secure and cost-efficient vaccination process for each injection. This can be achieved through HCW training in best practice. Since manual work still remains user dependent, a medical device approach would enable the standardisation of preparation and injection steps by getting rid of inter-user variability and greatly limiting the number of manipulations.

One of EVEON’s goals is to address the challenge raised by drug preparation and injection. How can medical devices bring answers to questions raised around patient safety and cost efficiency? How can medical devices be part of the solution for reducing product wastage and improving usability for physicians?

EVEON’s technologies dedicated to automated drug preparation and injection demonstrate key advantages to overcome cost efficiency, HCW usability and patient safety challenges.

By developing electromechanical devices, EVEON enables the automation of drug preparation and/or delivery. All parameters – such as the injected dose, the injection flow rate and the process time – are highly controlled, leading to a very reproducible preparation or delivery and a standard process, thus avoiding user-dependent variability, manipulation risks and dosing mistakes.



Figure 1: The Intuity® Ject device.

Dose (mL)	Expelled dose standard deviation (mL)	Dose accuracy (%)	n
3	0.1	3	n=6
1	0.01	1	n=6
0.3	0.005	2	n=30
0.02	0.0005	3	n=5

Table 1: Examples of doses expelled from EVEON devices for several targeted injected doses (3 mL, 1 mL, 300  $\mu$ L and 20  $\mu$ L). Errors bars correspond to standard deviations; n is the number of expelled doses used for standard deviation calculations.

EVEON devices, using the company’s proprietary micropump, can deliver doses from 20  $\mu$ L up to several millilitres with a high accuracy (<3%). The Intuity® Ject device has been used for several applications with different targeted injected doses. Table 1 shows the dose accuracy for four expelled doses. For example, a 1 mL bolus has been injected with  $\pm$  0.01 mL, leading to 1% accuracy (n=6), and a 300  $\mu$ L dose has been injected with  $\pm$  5  $\mu$ L, leading to <2% accuracy (n=30).

Such levels of dose accuracy with highly reproducible results allow optimisation of the filling of the drug container. In the case of MDVs, the extraction and delivery of an accurate dose allows for the same number of doses to be delivered every time, without requiring precise handling or losing time during the process. In the context of vaccine dose shortages, it also avoids the possibility of an HCW wasting a dose because of a wrong move.

The use of medical devices also enables control and reduction of dead volumes to maximise drug retrieval within the vial. EVEON devices are developed to be adapted to standard pharmaceutical containers. The design of the fluid path and the fluidic process is optimised to reduce dead volume and drug loss in both the containers and the device fluid path. EVEON’s development within its Intuity® Mix platform (Figure 1) demonstrates a 56–66% reduction in drug wastage within the vial, compared with other products on the market.

As HCW time is precious, especially in the context of a pandemic, EVEON devices are also designed to minimise the number of manipulations and the process time required for use. For example, the Intuity® Ject device (Figure 2) is capable of injecting a 300  $\mu$ L dose in less than three seconds.



Figure 2: The Intuity® Mix platform.

“An appropriate medical device, coupled with best-practice training, can fill the economic and patient-safety gap between MDCs and SDVs.”

Usability is also an important factor for time efficiency and device acceptability on the part of the user. That is why EVEON works in close collaboration with HCWs to understand users’ needs and the environment and use conditions of the device. EVEON is used to working with ergonomists and designers to take human factors into account, right from the first steps of device design, to be sure to design an appropriate and easy-to-use device.

An appropriate medical device, coupled with best-practice training, can fill the economic and patient-safety gap between MDVs and SDVs. EVEON can bring easy-to-use and robust medical innovation to standardise dose preparation (dilution) and injection – and turn MDVs into an attractive and competitive solution.

## ABOUT THE COMPANY

EVEON is an ISO 13485-certified company that designs and manufactures safe, connected, automatic medical devices for the preparation and delivery of therapeutic treatments to improve patient quality of life. EVEON places the needs of patients and care professionals at the heart of its development by designing simple, intuitive devices to improve therapeutic performance, compliance and the conditions of at-home care. The company’s expertise has been recognised by Forbes magazine, which ranked EVEON as the third most inventive company in France in the category of medical technology in 2019.

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## ABOUT THE AUTHORS

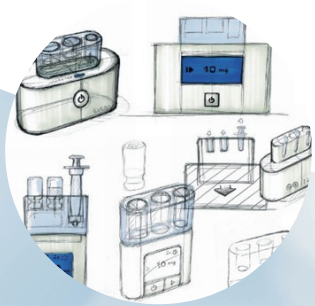
**Benjamin Morel** holds a master’s degree in Bioengineering, specialised in applied molecular and cellular biology, and an advanced master’s degree in Biotechnology Management from Grenoble Ecole de Management (France). After working as a consultant in intellectual property strategy and business intelligence for the life science industry, he joined EVEON as Intellectual Property Manager in 2019. Part of his mission is to assist the R&D team by using tangible information to stimulate the process of innovation. This interdisciplinary role involves integrating multiple business-related aspects from the early stage of product development to generate solutions with strong potential to answer technical needs.

**Claire Authesserre**, PhD, is an engineer who graduated from ESPCI Paris, a major French institution of higher education that combines multidisciplinary scientific courses in physics, chemistry and biology. She is also a graduate of Imperial College London (UK), where she obtained an MSc degree in Biomedical Engineering in 2013. She then completed a PhD in Microfluidics at CEA Leti Grenoble (France). Since 2017, Dr Authesserre has been R&D Fluidics Manager at EVEON, leading a team of fluidics engineers and technician. Placed at the heart of EVEON’s development, the R&D fluidics team works very closely with both the mechanical & plastics and digital teams to design medical devices with optimised performance to fit with customer and patient needs.





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