DE-RISKING DEVICE SELECTION – WHY CHOOSE UNISPRAY FOR NALOXONE RESCUE APPLICATIONS

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Elsie Thomas of **Nemera** explains why UniSpray is a robust nasal platform for generic naloxone, based on an evidence-driven approach that combines usability studies, threshold analyses and interchangeability assessments, and how it ensures safe and reliable performance, intuitive use, and regulatory acceptability in real-world opioid overdose rescue situations.

Naloxone nasal sprays, such as Narcan® (Emergent, Gaithersburg, MA, US), are lifesaving over-the-counter products designed for the rapid reversal of opioid overdoses, including those caused by heroin, fentanyl and prescription pain medications. They act within minutes to restore breathing and their widespread public availability has expanded dramatically in recent years as part of public health overdose-prevention strategies.

Developing generic versions of naloxone nasal sprays is essential to ensure broader accessibility at a lower cost (Figure 1). However, as Narcan is a complex drug-device combination product, manufacturers must demonstrate far more than just pharmaceutical equivalence; they must also prove that the intended users – often in

Figure 1: Patient using UniSpray.

"UNISPRAY CAN ENABLE INTUITIVE, RELIABLE, ERROR-FREE USE ACROSS A REPRESENTATIVE POPULATION – A FUNDAMENTAL REQUIREMENT FOR COMBINATION PRODUCTS PRESCRIBED FOR EMERGENCY AND RESCUE SITUATIONS."

high-stress emergency situations – can use the device safely and intuitively, without additional training compared with the reference listed drug (RLD), in this case Narcan.

Generic developers frequently rely on platform unit-dose devices offered by nasal device manufacturers. Originally, these platforms may have been designed for other molecules or indications and therefore may exhibit structural differences compared with the RLD. Determining whether such differences introduce use-related risks requires a rigorous, evidence-based methodology combining usability evaluations, threshold analyses and interchangeability assessments.

Nemera has applied these approaches with UniSpray to de-risk device selection and support regulatory readiness for generic naloxone applications.

USABILITY STUDIES – CAN USERS OPERATE THE DEVICE SAFELY AND INTUITIVELY?

Usability studies determine whether intended users can perform all critical steps correctly – without prior training – under simulated real-world conditions. In a study using UniSpray:

- 20 participants aged 26–75 years completed six administrations each (three on a dummy, three self-administered)
- A total of 100% of participants successfully activated the device and completed all essential steps
- Users could not or did not attempt to remove the plunger after activation, confirming the robustness of the integrated safety mechanism.

These results demonstrate that UniSpray can enable intuitive, reliable, error-free use across a representative population – a fundamental requirement for combination products prescribed for emergency and rescue situations, such as naloxone nasal sprays for opioid overdoses.

THRESHOLD ANALYSIS – DO DESIGN DIFFERENCES INTRODUCE NEW USER RISKS?

Threshold analysis is a structured, comparative assessment used by generic drug manufacturers to determine whether any differences between a platform device and the RLD introduce use-related risks; it includes:

- **Physical Comparison:** Nozzle geometry, plunger design, finger flange, materials, shape and contours

Figure 2: UniSpray by Nemera.

- **Task Analysis:** Mapping each user action to identify any step potentially impacted by design variations
- **Instructions for Use and Label Comparison:** Ensuring that no ambiguity or additional instructions are required.

While assessing UniSpray as a suitable platform for generic naloxone, the threshold analysis identified one visible difference: the absence of the "arch" that frames the Narcan RLD device plunger, removed to reduce the quantity of single-use plastic in the device (Figure 2).

This feature was evaluated comprehensively, and Nemera demonstrated that it provided no critical user benefit for gripping, positioning, activation or dosing. The analysis confirmed that users can operate a device without the arch at the same performance level.

INTERCHANGEABILITY ASSESSMENT – CAN RLD USERS SWITCH WITHOUT ADDITIONAL TRAINING?

Interchangeability evaluations determine whether someone familiar with the RLD can transition safely to the platform device without further training – a key regulatory expectation for naloxone generics. These assessments typically include:

- Comparison of user interface elements (hand posture, actuation gesture and nozzle placement)
- Alignment of primary container and functional performance, ensuring dose delivery consistency
- Evaluation of potential confusion points, especially when visible differences exist
- Regulatory review of threshold analysis outcomes.

For UniSpray, US regulatory authorities concluded that the identified differences between each device did not affect essential design attributes nor introduce risk. As a result, no comparative use

human factors study was deemed necessary, confirming UniSpray as a functionally suitable candidate platform for naloxone generics. This significantly reduces development burden, cost and timelines for generic applicants.

AN EVIDENCE-BASED PATHWAY SUPPORTING GENERIC NALOXONE DEVELOPERS

When implemented together, usability studies, threshold analyses and interchangeability assessments provide a comprehensive, science-driven foundation ensuring that a nasal unit-dose device is:

- Safe
- Intuitive
- Robust and consistent during real-world handling
- Functionally equivalent to the RLD
- Acceptable for regulators.

For naloxone rescue applications – where seconds matter and users may be untrained, stressed or panicked – this integrated approach helps developers to de-risk platform selection and regulatory submissions, avoid unnecessary human factors studies and accelerate time-to-market for affordable, lifesaving generics.

The integration of usability insights, threshold analysis and interchangeability assessments enables a precise understanding of how design differences translate into real-world performance – ensuring that devices remain safe and reliable even when visible structural variations exist.

"THE INTEGRATION OF USABILITY INSIGHTS, THRESHOLD ANALYSIS AND INTERCHANGEABILITY ASSESSMENTS ENABLES A PRECISE UNDERSTANDING OF HOW DESIGN DIFFERENCES TRANSLATE INTO REAL-WORLD PERFORMANCE."

Beyond naloxone rescue applications, this evidence-based methodology also supports the broader portfolio of ear, nose and throat solutions offered by Nemera. Nasal platforms, from multidose sprays to unit-dose rescue devices, are developed with the same scientific rigour, ensuring robust performance, patient-centric usability and compatibility with bioequivalence pathways across a wide range of molecules. For NDA or ANDA programmes, Nemera supports pharma partners by providing end-to-end services in human factors, analytical testing, device selection and regulatory support, while reducing development risks and accelerating approval timelines.

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Elsie Thomas is Marketing Category Manager for the Ear, Nose and Throat (ENT) Franchise at Nemera. Based in Lyon, she leads strategic marketing initiatives for nasal drug delivery systems, supporting both established products and new combination product developments. Her experience spans pharmaceutical devices, bioequivalence-driven generic programmes and global go-to-market strategies, working closely with R&D, regulatory and commercial teams. In her role, Ms Thomas contributes to portfolio positioning, customer-centric value propositions and the launch of innovative nasal delivery solutions for international markets.

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