AUTOINJECTORS: CREATING A DEVICE-COMPARABLE TRAINER TO ADDRESS INDUSTRY CHALLENGES

Autoinjectors have become the main drug delivery devices of choice due to their ability to simplify the number of steps required for injection. However, many patients make mistakes using the devices such as not holding the device correctly or not keeping it in place for long enough. Mike Siemer, Director of Design and Engineering at Noble reports on the development of training devices that replicate the design and operation of the autoinjectors so patients can better understand how to use them.

Since its inception for emergency medical use in the 1980s, the autoinjector has grown to be the predominate drug delivery device for single-use, fixed-dose self-administration of biologic and biosimilar drugs requiring less frequent administration regimens.[1]

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The autoinjector was developed to be a self-contained, easy-to-use injection device for clinical and home administration applications. It was designed to simplify administration by reducing the complexity of user steps required for injection, taking into account human-factors including psychological considerations as well as dexterity and mobility impairments. Other integrations included tactile feedback such as auditory and visual signals indicating the beginning and conclusion of administration.[1]

While the number of biologic and biosimilar drug launches continues to rise in in the market so does the use of autoinjectors as a preferred drug delivery device. The Pharmaceutical Research and Manufacturers of America (PhRMA) estimates more than 907 biologic medications and vaccines are currently in development across more than 100 disease states.[2] As more patients are being diagnosed with chronic conditions and being prescribed biologic and biosimilar medicaments delivered via autoinjector, training and education will remain essential success components for determining a patient's ability to adhere to therapy safely and effectively.

A study conducted by the University of Texas Medical Branch at Galveston (UTMB), found 84% of patients failed to demonstrate correct autoinjector administration technique, with more than half of users missing three or four steps. Common errors made by patients included failing to hold the device correctly, not choosing a suitable injection site and not pressing the device hard enough to trigger release of the drug. The study also found the most prevalent error to be the failure of 76% of patients to hold the device in place for the required amount of time to receive the full dose, sometimes referred to as a wet injection.[3]

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According to one of the authors of the 2015 UTMB study, *Misuse of medical devices: a persistent problem in self-management of asthma and allergic disease*, Dr Rana Bonds: "Despite the redesign of the autoinjector for easier use, most patients continued to make at least one mistake with the device. Most patients made multiple mistakes and would not have benefitted from self-administration of the potentially life-saving treatment if the need arose."[3,4]

Additional findings reveal other factors contributing to the inability of patients to correctly use autoinjectors. As part of being diagnosed and prescribed a drug delivery device, most patients receive training within a healthcare provider's (HCP's) office. Studies suggest 76% of HCPs fail to review device use with patients and 68% of HCPs fail to correctly demonstrate administration technique.[5]

Furthermore, for the 14% of providers who do demonstrate correct administration technique to a patient, other findings suggest 40-80% of medical information provided by HCPs to patients is forgotten immediately.[6]

ADDRESSING USER CHALLENGES THROUGH A DEVICE-COMPARABLE AUTOINJECTOR TRAINER

To reduce user errors and anxiety, and to build patient confidence, medical device training tools have been developed to support patients in learning how to use their drug delivery devices properly.

In an excerpt from the UTMB study mentioned previously, researchers Bonds, Asawa and Ghazi state: "There is room for improvement in ensuring that patients are able to correctly self-administer medications. Repeated verbal instruction and, perhaps even more effective, repeated visual education, including demonstration using training devices, are highly recommended. Novel methods of providing this repetitive training for patients are needed."[3]

EXTERNAL CHARACTERISTICS: DESIGN AND DEVELOPMENT

In order to set patient expectations and increase familiarity with a drug delivery device, device trainers must mimic the actual device in form and in operational and sequential function. The basic assembly of an autoinjector consists of a prefilled syringe integrated into a barrel housing with a viewing window, springs, activation button, locking safety mechanisms and needle shield.

When creating an accurate representation of a brand's commercial device, such as an autoinjector, designing an analogue device begins with matching the shape and design and external characteristics including barrel dimensions, viewing window, size and shape of actuation button, needle shield and end cap.

INTERNAL MECHANISM: DESIGN AND DEVELOPMENT

Designing and developing an autoinjector trainer can be quite challenging with considerations that do not appear at the surface. The device needs to contain almost all of the elements of the brand device, and also include the ability to completely reset the mechanism back to the original state, while keeping the overall size as close to a 1:1 scale as possible. Not only

Figure 1: Example of a trainer exhibiting typical autoinjector characteristics including the ability for device customisation.

does the training device need to function within the operational requirements of the brand device, but it also needs to perform repeatedly for up to hundreds of cycles depending on the customer requirements.

Although a trainer may mirror an actual autoinjector's exterior, a trainer's internal components do not contain a needle-based prefilled syringe or the same internal mechanisms. Developing the internal mechanisms to represent an existing device's functionality, administration and sequencing attributes accurately, including plunger drop speed, breakout and glide forces, sound replication and actuation forces, requires engineers to modify the internal portion of the barrel housing design to accommodate a plunger.

Additional design considerations must be made for the inclusion of custom and/or proprietary technologies including activation, plunger-drop, reset and safety lock-out mechanisms, or battery-powered electronic smart technologies such as sensors, audio and visual feedback components, and error-correcting platforms.

During the design and development phase, human factors are also taken into consideration with regard to visual and/or auditory cues, which signal beginning and completion of administration – matching the actual device signals – and the Newtonian forces involved in unlock, actuation and reset mechanisms, which allow the trainer to be reusable for multiple training sessions.

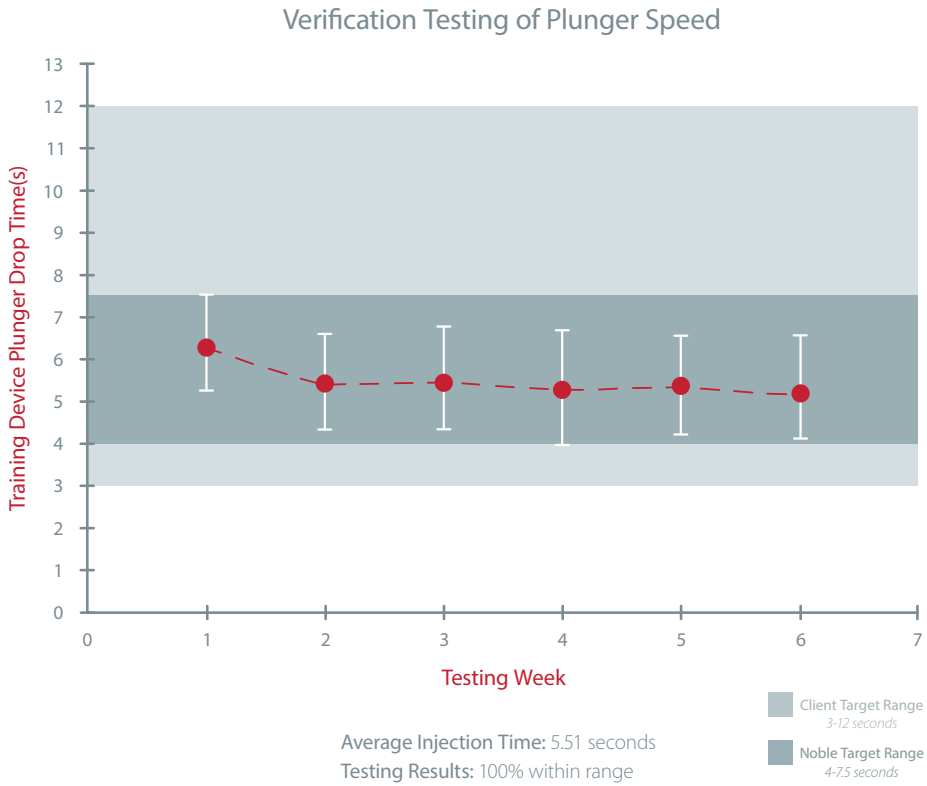

Figure 2: Results showing the average training device plunger drop speed for 35 randomly sampled units tested over six consecutive weeks.

The referenced UTMB study findings suggest most patients do not hold their autoinjector in place for the proper amount of time to receive the full dose, resulting in a "wet injection". Therefore, accurate simulation of plunger speed is very important to effective training.

Preparing patients' expectations for actual device usage and injection times – to prevent a "wet injection" and ensure the user receives the full dose – requires trainer characteristics to replicate a brand's formulation viscosity without actually containing any liquid. Based upon brand specs, autoinjector trainers are developed within a specified delivery time target range to duplicate plunger speed. Similar to the actual device, the training device allows a patient to experience the amount of time an injection takes realistically and enables patients to track the progress of the plunger through the end-of-dose indicator viewing window.

> "In the patient-centric era, companies providing reusable, device-comparable training products will be well positioned for competitive differentiation through improved patient satisfaction, adherence and outcomes."

To develop a training device which accurately represents the administration characteristics of an actual autoinjector, devices are designed to mimic viscosities and volumes, breakout and glide forces and plunger drop speed. Varying viscosities of biologic and biosimilar medications increase the complexities of incorporating a prefilled syringe into an autoinjector platform. Higher-viscosity formulations may require higher injection forces and longer injection times during administration.[7]

VERIFICATION TESTING FOR ACCURACY AND CONSISTENCY

To ensure brand specifications are fulfilled, and an accurate representation of an autoinjector is produced, a systematic methodology process is followed to guarantee consistent optimised manufacturability. Noble conducts rigorous testing, based upon brand specifications and strict internal auditing criteria, spanning from prototype to mass production stage in order to ensure that finished products meet the quality standards necessary for effective training.

One of the keys to success is utilising optimised standard operating procedures (SOPs) and standard inspection procedures (SIPs) during the trainer assembly process throughout both pilot and full production runs, continuously improving critical variables. As sub-assemblies are constructed, various tests are integrated throughout the process to verify targets will be met at the end of the assembly line. For example, plunger speed is measured through semi-automated testing at three different levels throughout the assembly line. A large benefit of making a resettable, multi-use trainer as compared to a single-use device, is that 100% inspection of all defined operational parameters can be

verified before the product is completed and okay-to-ship.

In addition to complete product inline verification, AQL sampling is also performed to test all required critical, major and minor parameters. For example, to validate the consistency in auto injection times of recently developed training devices, a random sample of 35 units was pulled directly from the final production line and was tested over a six-week period. All of the tests showed that the training devices, not only fell within target range of 3-12 seconds requested by the client, but also consistently remained within Noble's specified target range of 4-7.5 seconds and averaged approximately 5.51 seconds per week throughout injection time testing.

CONCLUSION

As patients are becoming more active participants in their own healthcare, the number of patients required to self-administer injectable medications will continue to grow. For these patients, anxiety, confidence, familiarity with the injection device and understanding correct administration technique will be factors affecting adherence.

The development of training devices that replicate the design and operation of the brand device improves patients' ability to anticipate the steps needed to administer the drug, be more familiar with the ergonomics and device interaction, as well as anticipate a device's expected injection time.

By providing patients a better understanding of their device, with the ability to practise administration technique frequently, autoinjector trainers help promote positive onboarding experiences and empower patients to lead healthier lives. In the patient-centric era, companies providing reusable, device-comparable training products will be well positioned for competitive differentiation through improved patient satisfaction, adherence and outcomes.

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Reference: 1. Bonds, R. S., Asawa, A., & Ghazi, A. I. (2015). Misuse of medical devices: a persistent problem in self-management of asthma and allergic disease. Annals of Allergy, Asthma & Immunology, 114(1), 74-76.e2. doi:10.1016/j.anai.2014.10.016