INJECTING HUMAN FACTORS ENGINEERING/USABILITY ENGINEERING INTO INJECTABLE DEVICE DESIGN

In this, the fourth in a series of articles covering quality system requirements for medical devices used to deliver drugs and biologics and combination/borderline products, Marc Egeth, PhD, Director of Research; Patricia McGahern, Associate; and Sarah Johnstone, Research Associate, all of Core Human Factors, discuss use errors associated with marketed and in-development injection systems.

In the US, any medical product that contains a medical device is subject to FDA Quality System Regulation (QSR) 21CFR820. The design control requirements of the QSR (21CFR820.30) require that the design of a medical device be validated (i.e. ensure that devices conform to defined user needs and intended users). Human factors engineering / usability engineering (HFE/UE) is a methodology used to assure that the ultimate design of a medical device is "safe and effective for the intended users, uses and use environments".[1]

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A component of HFE/UE is human factors (HF) testing in which representative users are observed interacting with developmental products to learn about use errors that could occur in real life.

Initially, formative HF testing is conducted to observe use errors and identify their root causes. Representative users interact with one or more aspects of the user interface, which includes the device itself, instructions for use (IFU), packaging, and intended training. Mitigations, based on the root causes of use errors identified during HF evaluations, are implemented during medical device design development to redesign the user interface to assure safety and usability.

A goal of HFE/UE is to have minimised use errors by the end of the iterative design development process. The final HF evaluation, known as the human factors validation (also known as a summative human factors evaluation), is used to demonstrate the validity of the device design. A HFE/UE report contains a summary of the HFE/UE process used to develop a medical device design and is an essential part of the design history file, required by FDA.

In the simplest case of an injection system, a disposable syringe may be used to deliver the wrong dose or the wrong drug unintentionally. To minimise these use errors and improve injection convenience, a variety of prefilled injection systems are available for professional and self-administration, including prefilled syringes, autoinjectors, injection pens and jet injectors. However, while effectively addressing some of the use errors associated with disposable syringes, the use of prefilled injectors presents a new set of use errors.

Prefilled drug delivery devices and kits that combine a drug product and a medical device, which are combination products, are subject to combination product good manufacturing practices (GMP) codified in 21CFR4, and by extension are subject to the QSR, and are therefore required to have validated designs. This article describes some of the challenges manufacturers have encountered in the process of validating the design of injection devices.

USE ERRORS SEEN IN HUMAN FACTORS TESTING

In a study conducted at Core Human Factors, only 2/31 (6%) participants succeed in delivering a full dose from a

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currently-marketed rescue injection kit that included a prefilled diluent syringe.[2] Some participants injected the diluent only, not realising they needed to reconstitute the drug powder in the vial that was included in the kit. This included participants who had previously received training, and those who had the IFU available. Had the diluent syringe not come prefilled, it is unlikely that participants would have injected with an empty syringe, rather the fluid visible in the syringe provided a misleading cue that the syringe was ready for injection into the body. In the same study, other participants bent the needle attempting to insert the needle through the vial cap, not realising that the vial needed to be uncapped before use. Because there was only one needle included, the entire system was then unusable and there was no way for users to recover.

Some manufacturers produce syringes that include unit markings on their barrel that are specific for a particular drug and that are intended to simplify drug administration. However, users may not realise that the graduation markings on the syringe barrel are specific to that drug. This can lead to drug overdoses. With insulin for example, users may draw highly potent U-500 insulin into a syringe with markings intended for use with U-100 insulin.[3] This can lead to a five-fold overdose of insulin because if filled to the "50 units" line on the syringe, there would actually be 250 units of insulin in the syringe. Similarly, users believing they are using syringes with scales printed for insulin units have given ten-fold overdoses of insulin when they accidentally used similarly-packaged and -coloured syringes for the diagnostic tuberculin[4] (see Figure 1).

The insulin syringe confusion was caused by two products that were in some ways too similar to each other. At the same time, if a new technology is too different, users might not know how to use it or might not be confident in its use. For example, in our usability labs at Core, we have seen that using a prefilled autoinjector can lead to overdoses when users are unsure if the first dose was successfully injected and thus repeat the injection. What a user expects a device to do is intimately linked to how the user will interact with the device. When user expectations do not match the reality of the device design, use errors may occur.

Novel device mechanisms implemented to improve the safety and usability of the injection experience can introduce a completely different set of use errors. Issues seen with early device designs include the following:

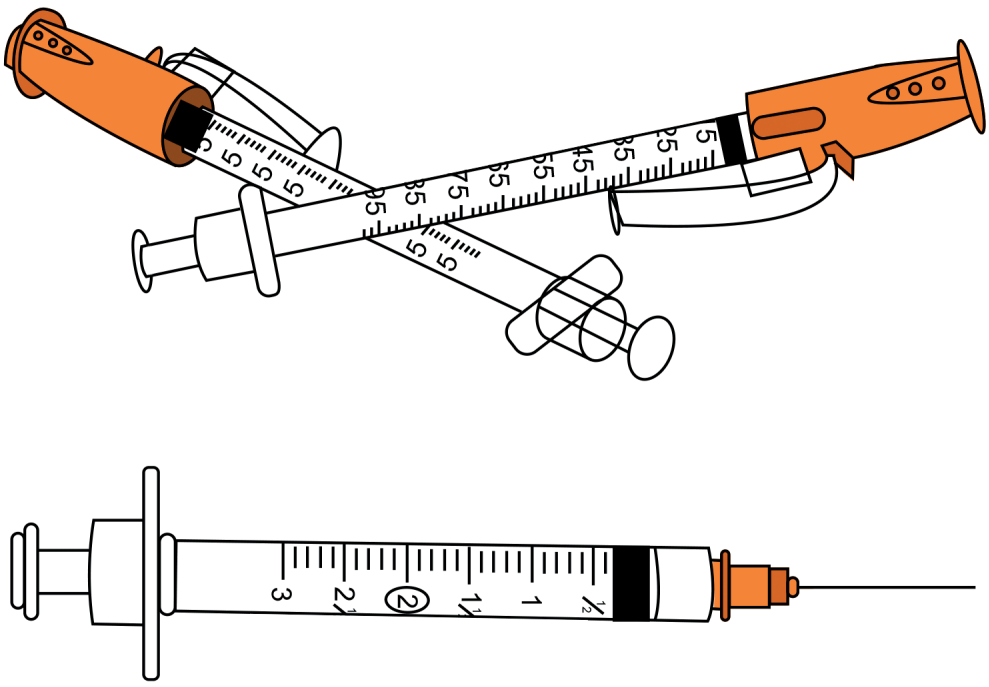

Figure 1: U-100 insulin-specific syringes (top), and generic syringe with 25-gauge needle for e.g. tuberculin (bottom). (Images created by Amanda Shames, BFA)

> "Explaining how products work in the IFU can mitigate some usability issues. However, some users have poor literacy, some do not bother reading the instructions, and others forget what they read after a short period of time. Some users only look at the pictures, others only read the words."

- Auto-injectors do not make the expected "click" sound leading to uncertainty over injection success
- Auto-injectors "click" twice, leading users to assume mistakenly the first click signalled that the injection was complete
- Labelling text too small, leading participant to not notice crucial warnings
- Printed dosing scale does not match user needs for dosing, users are not used to new units of measure, or users need gradations for dosing smaller than are marked and have difficulty with fractional doses
- Users confuse training devices for injection devices
- Users are not sure how hard to press injection device buttons, leading to wasted medication, by pressing too hard too early
- Users are not sure which end of an autoinjector has the needle, leading to injections into thumbs when trying to push a button on the opposite end
- Tactile or auditory feedback from the device is too strong leading users to be startled and drop the device.

INSTRUCTIONS FOR USE

Explaining how products work in the IFU can mitigate some usability issues. However, some users have poor literacy, some do not bother reading the instructions, and others forget what they read after a short period of time. Some users only look at the pictures, others only read the words. Because of this, IFU are considered the least effective strategy for mitigating use errors. Nevertheless, IFU are an important part of the user interface. As part of the user interface, IFU must be validated.

Consider the figures and instructions shown in Figure 2, which are based on actual product figures and instructions (note that each has been re-drawn to avoid disclosing the particular product depicted).

Which side should be twisted according to Figure 2a, and which way? Unintentionally, the arrow is an ambiguous optical illusion. Is the light grey part in front of the black part so the twist is away from the reader, or is the black part in front so the twist is towards the reader? Does it matter, or is it just a minor inconvenience to twist the wrong way at first? Some devices can have internal mechanisms that can be disrupted if turned in the wrong direction, such that afterwards, re-screwing in the correct direction does not undo the damage. This can lead to incorrect dosing completely undetected by the users.

Figure 2b does not show Step "1" (number one, the first). This is step "I" (not the roman numeral but the letter, the ninth), which happened to be placed on the upper-left corner of page two, the backside of the instructions. Some participants in human factors evaluations start on the second page, thinking Step "I" was Step "1", and proceed to inject, thereby skipping key preparation steps A-H. This is the kind of usability issue that can be hard to detect without user testing. A graphic designer looking at images on a computer screen might not realise that down the line the size of the printed page could push this particular step to the start of the next page and appear as a "1" – when working with an alphabet, it might be hard for a graphic designer to see the "I" as anything but a letter. A key benefit of including user testing in the design process is detecting use errors that would otherwise be hard for designers to predict. Applying BF Skinner's maxim on the role of test subjects in experiments, "the rat is always right," designers need to address the use errors that participants encounter, however improbable they might seem a priori, because they point to real ways in which real people might hurt themselves in real life.

The part of the body is also unclear in Figure 2b. We have seen ambiguous

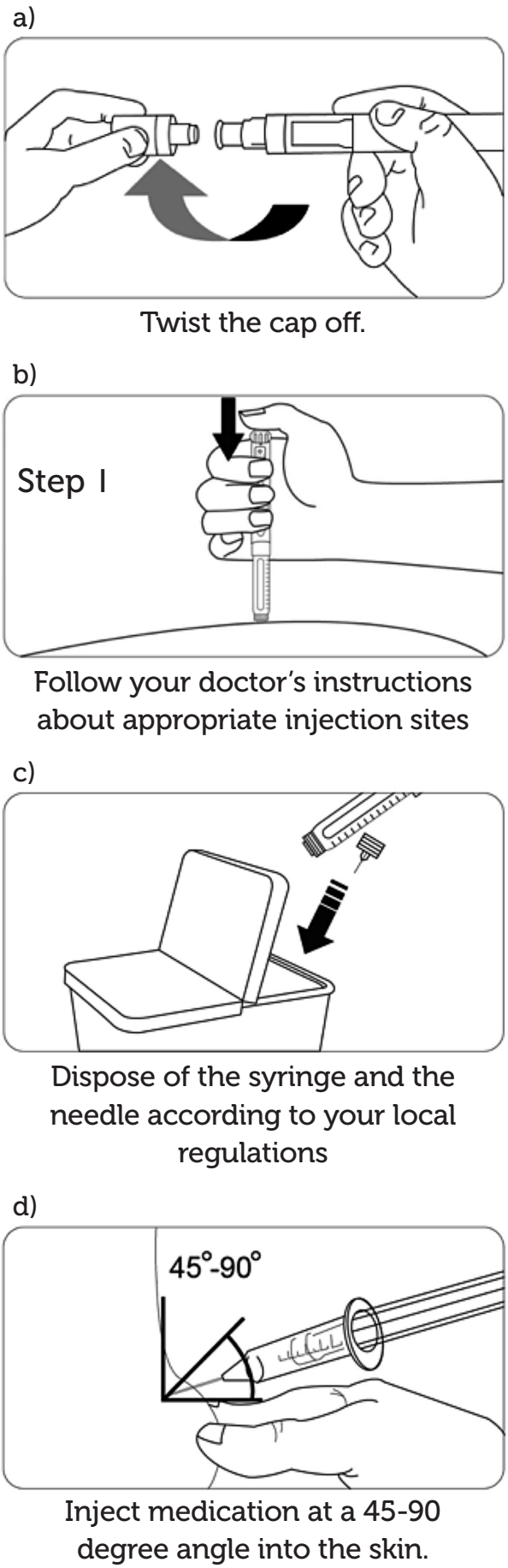

Figure 2: Example figures and instructions based on actual product figures and instructions. (Images created by Amanda Shames, BFA)

illustrations lead participants to inject in locations not intended by the manufacturer.

In Figure 2c, some participants in user testing assumed the black and white line drawing was a standard trash can, whereas the intention of the diagram was to depict a sharps container.

It can be hard for some users to grasp what Figure 2d is trying to convey. The graphic of the angle is superimposed on skin, but it is not lined up with the skin because the skin is pinched. The syringe looks like it is going in to something at greater than a 45° angle because of the orientation of the bold lines. However, looking closely at the fainter lines, the syringe truly is going into the skin at a 45° angle relative to the surface of the skin.

SUMMARY AND CONCLUSION

The HFE/UE process aids medical device developers in improving their designs to meet the needs of users better and to satisfy crucial design control requirements. The method of observing representative users handle prototype products under conditions simulating real-life conditions has the proven ability to predict real-life user difficulties. The process is iterative and focused on the user perspective, such that every aspect of the user interface is tested and validated for safety and usability by the people who would use the device in their daily lives.

It is a common result in HFE/UE testing that designs that seem reasonable to engineers and designers (like a superimposed diagram explaining what angles are) turn out to have flaws that are first exposed only upon user testing. Indeed, it is for finding these "surprise" issues that FDA requires HFE/UE testing to support submissions. HFE/UE encourages early user testing of prototype devices, so manufacturers know early on in product development the sort of errors users are prone to experience. In this way, design safeguards can be introduced in advance of validation testing.

REFERENCES

1. *"Applying Human Factors and Usability Engineering to Medical Devices". FDA Guidance for Industry and FDA Staff, February 3, 2016.*
2. *Yale J, Piche C, Lafontaine M, Margolies R, Dissinger E, Shames A, Fink N, Egeth M, Dulude H, "Needle-free nasal delivery of glucagon is superior to injectable delivery in simulated hypoglycaemia rescue", Diabetalogia, 2015, Vol 58, pp S417-S418.*
3. *"As U-500 Insulin Safety Concerns Mount, It's Time To Rethink Safe Use Of Strengths Above U-100". Institute for Safe Medication Practices, October 2013. Retrieved from https://www.ismp.org/newsletters/acutecare/showarticle.aspx?id=62*
4. *Pennsylvania Patient Safety Authority, "Overdoses Caused by Confusion between Insulin and Tuberculin Syringes". Patient Safety Advisory, 2014, Vol 1, Sup 1, pp 1-2.*

ABOUT THE AUTHORS

Marc Egeth received a PhD in experimental psychology from the University of Pennsylvania (Philadelphia, PA, US) in 2007. His academic publications cover evolution, perception and attention, child development, cognitive neuroimaging (EEG, MEG, fMRI), consciousness, experimental philosophy, medical hypotheses, and human factors in healthcare. Marc's experience in quantitative and qualitative methods includes neuroimaging, eye tracking, ethnographic research, audience/visitor studies, and moderating usability studies. His medical device research and design experience includes iPhone / Android apps, instructional material, and work/office environments including shared healthcare spaces.

Sarah Johnstone holds an MA in Experimental Psychology from the University of Pennsylvania. In her graduate work she received formal training in human perception, language processing, and decision making; her research focused on why people misunderstand or misperceive certain kinds of written, spoken, and visual information, and how they recover from those mistakes. Previously she studied linguistics and sociology, and has experience interviewing diverse groups of people, putting them at ease, and encouraging them to speak and act naturally. She is passionate about discovering what makes an instruction or interface ambiguous, and applying that data to design improvements.

Patricia McGahern holds an MSE in Bioengineering from the University of Pennsylvania. While at the University of Pennsylvania she was involved in neuroscience research on epilepsy and completed her Master's thesis on a project related to this research. She has a passion and fascination with medical devices, and joined Core Human Factors, Inc. to be a part of the medical device field.