Breaking Out of the Human Factors Study Loop, For the Benefit of Patients

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Introduction

Human factors engineering (HFE) is a critical component of life cycle management for medical and combinational drug products. The associated studies required to determine the product is safe and effective for use can be costly. Many companies manufacturing products which require Human Factors (HF) validation often find themselves conducting many usability tests before establishing their respective product is safe and effective for use and all residual risks have been mitigated. This is compounded further by companies manufacturing legacy products, already on market which require HF testing due to evolving and new regulatory guidance. Human factors data are never perfect and for legacy products even less so due to design and/or manufacturing constraints. An appropriate analysis of risk/benefits of the product become essential for it remaining on the market.

Aim

Evaluate select findings from autoinjector HF studies, demonstrating best practices of working within pre-existing design constraints, not so 'perfect' HF results, and provide sound justification to regulatory bodies that risk has been effectively mitigated for the continued use of the manufactured product.

Methodology

- Simulated use study representative where patients were pre-assessed and a determination was made of medical need.
- 50 percent of the participants were trained on the use of the product by a qualified EMS trainer and the remaining 50 percent were untrained-received no instruction on administration prior to treating potential patients.
- Post simulation interview — address unanticipated use issues; explore use issues that were observed by the study moderator or reported by the participant, and to evaluate through knowledge task questions and safety-critical aspects of product use that could not be simulated.

Figure 1 — Table With Devices, Medic Bag, and Bucket of Soapy Water

Figure 2 — EMT Capturing a Study Participant's Vitals and Assisting in Donning Level A PPE

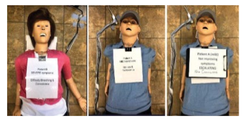

Figure 3 — Patients are Represented as Manikins

Figure 4 — Participant Preparing to Administer the Product

Results and Discussion

In both studies, all critical tasks were evaluated. Critical tasks are tasks which, "…if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user, where harm is defined to include compromised medical care."[4] They can include both performance tasks (tasks users must do) and knowledge tasks (things users must know to use the product safely). For each critical task identified, it was ensured that control measures were in place to mitigate the risks associated with those tasks.

Of the critical tasks identified, there was a high frequency of occurrence observed for dosing and hold time.

In Study 1,[5] use errors were observed while performing the four critical tasks:

Observed Use Error	Frequency of Occurrence
1. Failing to remove the safety release on one or more autoinjectors.	1/31
2. Administering one or more autoinjectors at a site other than the thigh.	3/31
3. Failing to hold one or more autoinjectors in place for 10 or more seconds after device activation.	26/31
4. Under dosing or overdosing based on symptoms.	20/31

Table 1 — Summary of Observed Use Errors on Critical Tasks for the Product

Preceding Study 1, a risk-benefit analysis was performed to assess potential harm and severity to the overall risk-benefit of medication to the patient. Critical use errors were traced through the Use Failure Mode Effects Analysis (uFMEA).

Figure 5: The upper limit of the Dispense Time release specification is no more than seven seconds, which is less than the instructions for use (IFU) hold time of ten seconds. This specification reduces the risk of not delivering a full dose if the autoinjector is removed from the injection site before ten seconds have elapsed. Historical analysis of 133 product lots show a mean Dispense Time of 3.13 seconds with an overall standard deviation of 0.33 seconds. This information suggests that the autoinjector is capable of delivering the required dose provided the user holds the autoinjector in place for at least four seconds — less than half the time specified in the IFU.

Figure 6: All participants were expected to administer multiple autoinjectors during the use scenario. Forty-six injections (31.9%) were held for ten seconds or more, 102 injections (70.8%) were held for seven seconds or more, and 121 injections (84.0%) were held for four seconds or greater. The four second point was chosen to include the successful dispense of the drug based on the historical data of an average of 3.13 seconds with a standard deviation of 0.33 seconds.

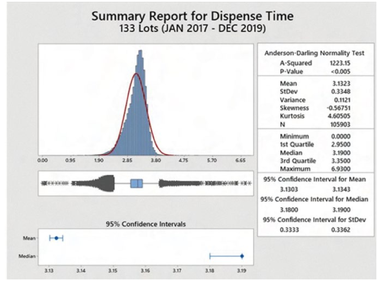

Figure 5 — Dispense Time Summary Statistic for DuoDote® AI

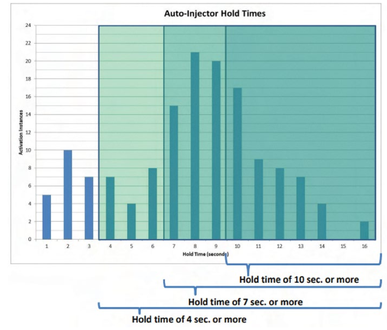

Figure 6 — Histogram of Hold Times for All Instances of Injection

In Study 2,[5] all trained participants (15 total) demonstrated successful task completion and administered the correct number of doses based on severity of symptoms. Only three of fifteen untrained participants demonstrated successful task completion and administration of the correct number of doses based on severity of symptoms.

Figure 7: Trained participants held a total of 90 devices in place for a range of 5.5 seconds-14.96 seconds (avg. 9.2 seconds). Six of the 90 devices were held in place for less than seven seconds but longer than four seconds.

Figure 8: Untrained participants held a total of 93 devices in place for a range of 1.38 seconds-12.72 seconds (avg. 7.6 seconds).

Table 2: For patients exhibiting mild symptoms the user was required to administer one dose, for escalation of symptoms from mild to severe the user was required to administer an additional two doses, and for patients exhibiting severe symptoms the user was required to administer three doses. Eight participants, all untrained, experienced one or more dosing issues during the primary simulation. Five of these eight participants self-resolved their dosing issue in the follow-on simulation, after reviewing/further reviewing the labeling. However, three of eight had residual dosing issues in the follow-on simulation (U05, U11, U13).

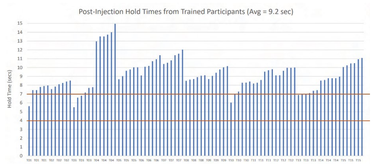

Figure 7 — Hold Times – 90 Devices – Trained Participants T01-T15 – Sorted by Shortest to Longest Hold Time per User

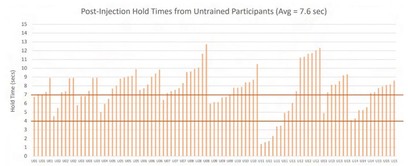

Figure 8 — Hold Times – 93 Devices – Untrained Participants U01-U15 – Sorted by Shortest to Longest Hold Time per User

	Primary Simulation				As needed: Follow-on Simulation after Forced IFU Review		
ID	Opted to review labeling before the simulation?	Patient 1: Severe	Patient 2: Mild	Patient 2: Escalation to Severe	Patient 3: Mild	Patient 3: Escalation to Severe	Forced review of IFU resolved the issue?
U01	No	1 dose	1 dose	0 doses	1 dose	2 doses	Yes
U02	No	1 dose	1 dose	1 dose	1 dose	2 doses	Yes
U03	Yes	1 dose	1 dose	1 dose	1 dose	2 doses	Yes
U04	Yes	1 attempted	1 attempted	1 attempted	1 dose	2 doses	Yes
U05	Yes	2 doses	2 doses	0 doses	2 doses	0 doses	No
U10	Yes	1 dose	1 dose	2 doses	Treated a Severe victim and correctly gave 3 doses	n/a	Yes
U11	Yes	2 doses	2 doses	2 doses	1 dose	3 doses	No
U13	Yes	2 doses	1 dose	1 dose	2 doses	1 dose	No

Table 2 — Participants With Dosing Issues

Implementation of the URRA

After an evaluation of the HF studies, a Use Related Risk Analysis (URRA) was created. The URRA leveraged the end user and use environment analysis. It clearly defined all use cases, tasks, and subtasks related to the user interface, potential use errors, the potential harm to the patient or user that results from potential use errors, and the severity of that harm.

Following creation of the URRA, it became apparent that risk control measures were not appropriately evaluated for critical tasks related to dosing and hold time.

Unlike its counterpart, the uFMEA, the URRA is the process of which risks are identified thereby providing opportunities to design or redesign a product.

Creation of a URAA enabled our team to explore design opportunities not previously considered across the user interface, including but not limited to: packaging, packing labels, outer cartons, and instructions for use.

Irrespective of the not so 'perfect' human factors results, creation and implementation of the URRA in the HFE process provides the real time evidence that all potential risk to the patient or end user has been identified and appropriately mitigated. It also signifies to regulatory bodies that your product is safe and effective for use.

Conclusions

The URRA implemented early in the HFE process, lays the foundation for a systematic, streamlined approach to iteratively improve the design of the user interface and implement appropriate risk control measures. When these measures are implemented and assessed during human factors evaluation(s) and product development we can ensure that risks are reduced/and or eliminated to the extent possible. Risk-based HFE activities incorporated early in product development present minimal cost and effort to design changes compared to late-stage revisions. An integrated, iterative approach to HFE using the URRA as a developmental tool is the most effective way to reduce potential of deficiencies in a pre-market submission to domestic and global regulatory bodies.

Acknowledgement

We would like to thank Human Factors MD for working with us to conduct our studies at their site.

References

1. Kumoluyi, R., and Khanolkar, A. Risk Management in Drug-Device Combination Product Development. Ther Innov Regul Sci. 2022 Sep;56(5):685-688. doi: 10.1007/s43441-022-00425-w. Epub 2022 Jun 26. PMID: 35753035; PMCID: PMC9356918.
2. Reason, J. Human error: models and management. BMJ. 2000;320(7237):768–70.
3. Association for the Advancement of Medical Instrumentation. Risk management guidance for combination products. AAMI TIR105:2020.
4. FDA Guidance, Applying Human Factors and Usability Engineering to Medical Devices, Section 3, page 3.
5. Study 1 and Study 2 reference one of two studies presented; it does not denote the number of HF evaluations that were performed/evaluated.