HUMAN FACTORS CONSIDERATIONS FOR COMBINATION PRODUCTS

Summary of Recent FDA Guidance

Background

On September 7th, 2023, a long-awaited final guidance was issued by the Food and Drug Administration (FDA) - *Application of Human Factors Engineering Principles for Combination Products: Questions and Answers*. The document is intended to be used in conjunction with other human factors related guidance and available national and international standards, such as AAMI HE75 and IEC 62366. In this latest guidance, the agency provides its view on best practices for conducting human factors activities for combination products either comprised of a device and a drug or a device and biologic.

Human Factors is the application of knowledge about human behaviors, abilities, limitations, and other characteristics of the users to the design of products to help ensure safe and effective use of the product[1]. For combination products, this application is applied individually to the respective device and drug/biologic constituents but also to the combination product as a whole. Therefore, it is critical for Drug/Biologic and device manufacturers to work in collaboration on holistic evaluations of use related risk, critical tasks, user interfaces, and study design of the final finished combination product.

Use Related Risk Analysis (URRA)

A comprehensive risk analysis is required for medical devices and for drug or biologic products, respectively. For use related risk, the existing individual risk analyses that exist for the drug/biologic and device should be reviewed to determine if any risks exist for the combination product as a whole that may not exist for each individual constituent. The URRA should focus on the potential hazards associated with the intended use of the final finished combination product, but also consider reasonably foreseeable misuse, users, use environment and user interface. For example, a higher viscosity drug combined with a smaller gauge needle on the device could cause more pain during injection, which could cause user's to prematurely remove the device and lead to an underdose. This user related risk would be specific to this combination of drug/device but may not be present with a different drug and/or a different device. Therefore, evaluation should be conducted on all of the tasks involved with using the bespoke combination product, identifying the potential use errors or failures that could occur and potential clinical consequences of those errors and/or failures. The resulting output is then used to define critical tasks.

Critical Task Determination

As defined in the guidance, a combination product critical task is a user task which, if performed incorrectly or not performed at all, would or could cause harm to the patient or user, where harm is defined to include compromised medical care. Critical tasks should be determined by the URRA and ensure that the evaluation considers the determined tasks for the device and drug/biologic independently, but most importantly for the combination product as a whole. The agency is especially interested in tasks that can impact dosing, administration or have the potential to result in patient harm. Special attention is paid to products which are used in emergency settings or time sensitive therapeutics as tasks for these combination products can have a more significant clinical impact if not done correctly. Once the critical tasks are determined, they are then used as an input to the user interface and further evaluated as part of human factors activities.

User Interface

The user interface for a combination product includes any interaction between the combination product and the user(s). This interface can include displays, controls, packaging, labels, instructions for use, and training, if applicable. The initial user interface should be based on cross-functional input with drug/biologic and device team members and various inputs such as the user information, use environment, URRA and Task (and Critical Task) analysis. Special attention should be made to training requirements as part of the user interface to determine if training is both an effective and viable risk-mitigation strategy based on the intended user group. Once the initial interface is drafted, it can then be evaluated through the human factors formative evaluations to refine based on user feedback. Once finalized, it can then be validated.

Human Factors Evaluation

Consistent with existing guidance and standards, the evaluation of the user needs and the user interface consists of two main phases - initial formative studies and subsequent summative (validation) studies. The resulting effort of these two phases should support that the final combination product can be safely and effectively used by the intended users and in the expected use environment. Due to the unpredictable nature of human beings and the multiple variables present with users and use environment, it is not possible to design a final combination product that is free of errors and risk. However, the amount of risk and potential errors should be quantified against the overall benefit to determine a resulting benefit-risk assessment and supporting rationale. The agency will use this information to determine whether the combination product user interface has been optimized to a point where the use-related risks have been significantly reduced and the overall risk/benefit ratio is acceptable.

Lifecycle Management

Changes to the final combination product and/or user interface can occur based on a number of reasons including, but not limited to, post-market surveillance, supplier changes, and regulatory updates. Evaluation of changes should include a review of the URRA. If the review of the URRA results in a new or changed risk profile, downstream impact to the user interface, critical tasks and existing human factors studies should be determined. Based on the evaluation, additional or supplemental Human Factors evaluation may be needed to support the change and a revised risk/benefit ratio.

Summary

Combination products that include a device and drug/biologic need a holistic human factors evaluation, driven by risk and user considerations, to take the respective considerations of each constituent and add any additional unique considerations for the final product as a whole. Therefore, strong partnerships between the drug/biologic and device manufacturers are needed to ensure the various perspectives and expertise from each side are considered in that holistic evaluation.

Reference:

[1] *Applying Human Factors and Usability Engineering to Medical Devices, FDA Guidance, February 3, 2016*