

Human Factors Considerations for Combination Products



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FDA recently released a draft guidance for the Industry and FDA staff regarding Human Factors and Related Clinical Study Considerations in Combination Product Design and Development (February, 2016). This guidance underlines principles of human factors (HF) studies during the development of combination products, which are comprised of a drug or biological product and a device, for investigational or marketing applications. The guidance clarifies the different types of HF studies, the recommended timing and sequencing of HF studies, and how HF studies are part of the process to maximize the likelihood that the combination product user interface is safe and effective for use by the intended users, uses, and environments.

Risk Based Approach

For medical devices, the use of human factors and usability engineering (e.g., applying the knowledge of human behavior, abilities, and limitations to the design of a medical device) plays a key role. A risk based approach should be used by the device manufacturers to identify and analyze potential use-related hazards, including lessons learned from reported errors with similar products, and as appropriate, incorporate and validate design features that mitigate or eliminate these hazards. This assessment informs the device design development to eliminate or minimize use errors that could cause harm or compromise medical treatment.



Critical Tasks

The use-related risk analysis should identify critical tasks. Critical tasks are user tasks that, 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. The FDA expects the risk analysis for the combination product to include an identification of all the critical tasks required for using the combination product, the consequences for failing to perform each critical task correctly, and the strategies that have been applied in the design of the user interface to eliminate or reduce risks to acceptable levels.

Human Factor Studies

The HF study should be conducted with representative users to assess the adequacy of the combination product user interface design to eliminate or mitigate potential use-related hazards. The study evaluates the ability of the user to:

- Perform critical tasks, and
- Understand the information in the packaging and labeling, such as product labels or instructions for use.

HF studies on a combination product are conducted as part of the product design controls process.

Types of HF Studies

HF Formative Studies: HF formative studies are designed to evaluate early combination product prototypes, taking into consideration the identified use-related hazards. HF Formative study results guide prototype design changes to eliminate or mitigate use-related hazards identified during the product development process. The use of iterative HF Formative studies optimizes the design of the combination product user interface for safety, and minimizes the risk of first discovering use problems during later stages of development.

Human Factors Validation Studies: HF Validation studies demonstrate that the final finished combination product user interface would maximize the likelihood that the product will be safely and effectively used by the intended population, for its intended uses and environments. There are two types of HF Validation studies:

Human Factors Simulated-Use Validation Studies:

Simulation methods for these studies vary and may include the use of a manikin, injection pads, placebo, and other elements intended to simulate the patient, the procedure, or the environment of use.

Human Factors Actual-Use Validation Studies: There are rare circumstances when it is difficult to simulate the conditions of use, physical characteristics of the product, or environment of use. Thus, a HF Actual-Use Validation study may be needed to confirm the adequacy of the user interface design.

For most combination products, FDA expects that a HF Simulated-Use Validation study will be sufficient to assess the adequacy of the user interface.

Changes to the Design After HF Validation FDA recognizes that combination product design changes may occur premarket or postmarket after HF Validation studies have been completed. Design changes made after HF Validation that relate to identified critical tasks or may result in new use-related errors or hazards that could lead to harm should have new HF Validation study assessments.

Relationship of HF and Major Clinical Studies The HF Validation study is not sufficient to establish the safety and

effectiveness of the combination product for the proposed indication. Specifically, data from the major clinical study(ies) establish the combination product's safety and effectiveness for the proposed indication and the complete labeling summarizes the essential scientific information needed for the safe and effective use of the product.

Therefore, ideally, before initiation of major clinical study(ies), the HF Validation study should be conducted on the final finished combination product, including the user interface (e.g., instructions for use, training materials, and any other user labeling, if applicable). It should be noted that in some cases it may be appropriate to conduct human factors studies in parallel with major clinical studies or after your clinical studies to address modifications to your product.

FDA encourages applicants to request early discussions with them regarding the HF program and the type of HF studies that might be appropriate or necessary in the planned submission.

Reference: Draft guidance for the Industry and FDA staff regarding Human Factors and Related Clinical Study Considerations in Combination Product Design and Development (February, 2016). <http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm484345.pdf>

Comparative Use Human Factor Studies for Drug-Device Combination Products

The US Food and Drug Administration (FDA) recently issued a draft guidance: Comparative analyses and related comparative use human factor studies for a drug-device combination product submitted in an ANDA, January 2017. This guidance is intended to assist potential applicants who plan to develop and submit an abbreviated new drug application (ANDA) to seek approval of a proposed combination product, that include a drug and a delivery device intended to administer a drug product.

A generic combination product classified as therapeutically equivalent to the reference listed drug (RLD) can be expected to produce the same clinical effect and safety profile as the RLD under the conditions specified in labeling. FDA recognizes that an identical device design may not always be feasible and, FDA may

accept such design differences if they are adequately analyzed, scientifically justified, and do not preclude approval in an ANDA. In general, FDA expects that end-users of generic combination products, including but not limited to lay-persons, such as patients, and/or caregivers, can use the generic combination product when it is substituted for the RLD without the intervention of the health care provider and/or without additional training prior to use of the generic combination product.



Analysis of the User Interface of a Generic Combination Product

The following three types of analyses are recommended as part of the threshold analyses to compare the user interface of the proposed generic combination product to the user interface of its RLD:

Labeling comparison: a side-by-side, line-by-line comparison of the full prescribing information, instructions for use, and descriptions of the delivery device constituent parts of the generic combination product and its RLD.

Comparative task analysis: potential applicants should conduct a comparative task analysis between the RLD and the proposed generic combination product.

Physical comparison of the delivery device constituent part: potential applicants should acquire the RLD to examine (e.g., visual and tactile examination) the physical features of the RLD and compare them to those of the delivery device constituent part for the proposed generic combination product.

If the threshold analyses determine that design differences may not be minor, the differences in the user interface of the proposed generic combination product, in comparison to the user interface of the RLD, do affect an external critical design attribute, potential applicants should first consider modifying the design of the user interface (e.g., delivery device constituent part) for the proposed generic combination product to minimize differences from the RLD. Alternatively, FDA may request data to support that the user interface design difference(s) will not preclude approval of the generic combination product in an ANDA. Such data

may be gathered in a comparative use human factors study that evaluates user performance of the critical tasks related to the external critical design attributes that are found to be different.

Comparative Use Human Factors Studies

A comparative use human factors study should be designed to provide sufficient data to confirm that the use error rate, for the critical task(s) as impacted by the differing external critical design attribute of the delivery device constituent part for the proposed generic combination product, is not worse than the corresponding use error rate for the RLD when used by patients and caregivers in representative use scenarios and use environments consistent with the labeled conditions of use.

A risk assessment should be done to identify the external critical design attributes and their impact to critical task performance for each end-user group, use scenario, and use environment consistent with the approved conditions of use for the RLD. The comparative use human factors studies would generally be simulated-use studies where the participants, who are representative of the intended patient and caregiver populations, are asked to simulate the use of the proposed generic combination product without actually administering the product.

FDA expects that data and information comparing the user interface of the proposed generic combination product to the RLD's user interface will be submitted to support an ANDA application

About West

West Pharmaceutical Services, Inc. is a leading manufacturer of packaging components and delivery systems for injectable drugs and healthcare products. Working by the side of its customers from concept to patient, West creates products that promote the efficiency, reliability and safety of the world's pharmaceutical drug supply. West is headquartered in Exton, Pennsylvania, and supports its customers from locations in North and South America, Europe, Asia and Australia. West's 2016 net sales of \$1.5 billion reflect the daily use of approximately 112 million of its components and devices, which are designed to improve the delivery of healthcare to patients around the world.

