



Chimera Consulting: Combination Product Training Institute^o

FDA ISSUES FINAL GUIDANCE ON MEDICAL DEVICE HUMAN FACTORS STUDIES

In this, the third in their series of articles for ONdrugDelivery Magazine covering quality system requirements for medical devices used to deliver drugs and biologics, and combination/borderline products, Michael Gross, PhD, RAC, Principal Consultant, Chimera Consulting, and Adam Shames, MBA, Chief Executive Officer, Core Human Factors, discuss US FDA draft recommendations on human factors validation which are part of the design validation requirement of device design controls.

INTRODUCTION

In the first article in this series,¹ the authors summarised quality systems, design control and design validation regulations^{2,3} and draft guidance⁴ for combination products and borderline products. In February 2016, the US FDA issued three guidance documents^{4, 5, 6} that recommend approaches and methods for the identification, assessment and mitigation of hazards related to the use of medical products that utilise a medical device. In the second article in this series⁷, the authors summarised the draft guidance, “Human Factors (HF) Studies & Related Clinical Study Considerations in Combination Product Design & Development”. In this third article in the series, the authors summarise the other two recently released guidance documents. One is a final guidance, “Applying Human Factors & Usability Engineering to Medical Devices”, and the other is a draft guidance, “List of Highest Priority Devices for Human Factors Review”.⁸

SIMULATED-USE & ACTUAL-USE HF EVALUATIONS

HF evaluations should facilitate the analysis of use error and identification of their

root cause. They are often conducted under simulated-use conditions but when simulated-use test methods are inadequate to evaluate the user-device interface, in addition to design validation testing, actual-use evaluations may be conducted under actual-use conditions, or as part of a clinical study as an addition to simulated-use studies.

However, in a clinical study, participants are generally trained differently and/or are more closely supervised than users would be in real-world use, so HF observations and interviews obtained during a clinical study should be viewed in this context. For clinical studies involving self-administration in the home, patient reported HF data should be supplemented with observational data.

FORMATIVE HF EVALUATIONS

Formative HF evaluations are used to refine the results of preliminary empirical/ analytical analyses, and are used to identify and determine the nature of any required design modifications. They are conducted as the device design evolves on mock-ups and prototypes following implementation of risk- mitigation strategies intended to address use-related hazards.

Formative HF evaluations can be conducted with varying degrees of formality



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and sample sizes. The critical task list used in formative evaluations may change as the device design and risk analyses evolve. If formative HF evaluations are not conducted during device development, and design flaws are discovered during HF validation, then the HF validation becomes a formative evaluation.

RISK MITIGATION

When considering implementing risk mitigation strategies, risk severity is more important than risk probability. Hazards may be mitigated through design changes, incorporating protective safety features/mechanisms, or by providing information or training. Design modifications are generally the most effective means for mitigating use-related hazards.

If design modifications are not possible or not practical, it may be possible to implement protective measures. Labelling and training, are important hazard mitigation strategies, but are least preferred because they rely on memory and reference to information and labelling that may be unavailable during real world use; and knowledge gained through training can decay over time.

HUMAN FACTORS VALIDATION

Human factors validation is conducted to demonstrate that the evolved device can be used by its intended users for its intended uses, under expected conditions of use, without serious use errors or problems that could produce serious harm that could be eliminated or further reduced through modification of the design of the user-interface.

The final critical task list is tested in the human factors validation. Test participants should reside in the country or geographical region where the device will be commercially available. The labelling and, if applicable, training materials to be evaluated should also correspond with those to be used in the country or geographical region where the device will be commercially available. Protocols should describe the number of times participants will use the device and its extent of use, identify critical tasks to be evaluated and describe data collection methods and evaluation methods.

Observational and knowledge assessment data collected during testing should, starting with the overall device and

later focusing on each critical task or use scenario, be supplemented with data collected in interviews with participants after use scenarios are completed. Questions should be open-ended and neutrally-worded.

Participants should provide their subjective assessments of use difficulties. All use errors identified in the interview should be discussed determine how and why participants believe the use error occurred. FDA encourages manufacturers to submit for feed-back a draft of the human factors validation protocol before it is implemented.

“Insight into FDA’s thinking about risk assessment, risk mitigation and the design and conduct of human factors evaluations during engineering development of drug delivery devices and systems that include a medical device can be gained from recommendations contained in three recently published human factors guidance documents.”

USER GROUPS IN HF TESTING

Human factors validation testing should involve at least 15 representative participants in each user group. Participants should represent the range of characteristics within their user group. Participant characteristics (e.g. age, occupation, education, literacy level, and sensory or physical impairment) are likely to affect device-user interactions.

Based on task characteristics, certain users may use the device in ways that may be expected to produce responses that are different from those expected of other users. If the device is intended to treat patients with medical condition(s) that cause functional limitations, users with a representative range of these limitations should be included as a distinct user group. Different user groups may perform tasks differently or have different knowledge,

experience or expertise that could affect their interactions with the device interface, or have different potential for use error. These users should be separated into a distinct user group.

Healthcare providers and intended lay device users should be treated as distinct user groups. All of these characteristics should be considered when establishing user groups. The labelling to be evaluated in a human factors validation should explain user capabilities needed for safe and effective device use.

USER TRAINING IN HF TESTING

The test protocol should describe the content, mode(s) of training delivery and dwell time between training and testing. To simulate learning decay, testing should not occur immediately after training. The design and extent of training needed for safe device use that will be evaluated in a human factors validation should reflect real world training that will be used commercially. If intended users will receive little or no training before using the device, then the participants in the human factors validation should not be trained. If training is used to mitigate identified risks, then data should be provided in the HF/Usability Report that demonstrates its effectiveness in reducing risks to acceptable levels.

HF DATA ANALYSIS

Analysis of use-related risk should be used to determine how use errors occurred, if design modifications are needed, or are possible, and how they may be effective at further reducing risks to an acceptable level. The results of human factors validation testing should be analysed qualitatively to determine if the device design, labelling and, if applicable, training, should be modified to reduce use-related risks to acceptable levels. The root causes of all use errors and problems should be considered to determine their potential to produce harm and to determine their priority for implementing additional risk management measures. If human factors validation testing results indicate that serious use errors persist, this is not acceptable unless it can be demonstrated that further reduction of the residual risk is not possible, or practical, and that the benefits of device use outweigh its residual risks. True residual risk is beyond practicable means of elimination or reduction through modifications of the user

interface, labelling, or training. Residual use errors or problems associated with high levels of residual risk should be described, including their relationship to the device design, and justified in the HF/Usability Report.

HF/USABILITY REPORT

The results of the overall HF evaluation program, including results and methods of risk management and HF/usability testing, and design optimisation should be summarised and documented in an HF/Usability Report, which may be included in pre-market applications.

The report should discuss safety-related HF engineering and usability engineering issues, materials, processes, risk analyses focusing on the device-user interface, resolutions, results and conclusions.

The report does not need to include test data. Its level of detail should be sufficient to communicate to marketing application reviewers how all serious use-related hazards were identified, evaluated and mitigated. FDA recommends the following order and

content for a HF/Usability Report:

1. Conclusion
2. Description of intended device users, uses, use environments, and training
3. Description of user interface
4. Summary of known use problems
5. Analysis of hazards and risks associated with use of the device
6. Preliminary analysis/evaluations summary
7. Description/categorisation of critical tasks
8. Details of HF evaluations testing.

HIGH-PRIORITY MEDICAL DEVICES

The draft guidance that provides a list of devices for which FDA believes it is important to conduct and report HF evaluations to marketing applications, is based on Medical Device Reports (MDR) and product recall data. The devices listed in the draft guidance were selected on the basis of their potential to cause serious harm resulting from use error. The following drug delivery device general types are the only ones identified in this list:

- Auto injectors
- Implanted infusion pumps
- Infusion pumps
- Insulin delivery systems.

CONCLUSION

Well-designed HF usability evaluations have become an essential part of the device engineering development process used in part to demonstrate the safe and effective use of devices intended to deliver pharmaceuticals. Insight into FDA's thinking about risk assessment, risk mitigation and the design and conduct of HF evaluations during engineering development of drug delivery devices and systems that include a medical device can be gained from recommendations contained in three recently published human factors guidance documents. One is a final guidance on medical devices, one is a draft guidance on combination products that contain a medical device constituent part, and one is draft guidance that identifies the drug delivery devices for which FDA is most concerned about hazards associated with use-errors.



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REFERENCES

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THE COMBINATION PRODUCT TRAINING INSTITUTE

In 2016, the Combination Product Training Institute® is conducting two identical three-day training programs that address quality system and design controls requirements for combination and borderline products in the US and EU, and the conduct of human factors studies. These programs cover requirements for both newly developed and legacy products as well as quality system obligations of device constituent part

manufacturers. The first of the two training programs took place on March 29-31, 2016 in Philadelphia, PA, US. The second program will take place on June 14-16, 2016 at the NH Barbizon Palace (Amsterdam, The Netherlands). Throughout the year, the Combination Product Training Institute will offer other venue-based training programs on various combination product topics. In-house training programs are also available. For additional details please visit the Combination Product Training Institute website at: www.CombinationProductTrainingInstitute.com.

ABOUT THE AUTHORS

Michael Gross is the Principal Consultant of Chimera Consulting®, specialising in quality assurance, regulatory affairs and technical development of drugs, biologics, medical devices and combination products. He also heads the Combination Product Training Institute®, which provides professional training programs on combination product topics. Michael holds a PhD in Organic Chemistry and conducted post-doctoral research in biochemistry at the National Institutes of Health. He is a former FDA reviewer and inspector. Michael worked for 30 years in senior quality, compliance and regulatory affairs roles for a number of large and small pharmaceutical and medical device companies. Today, he provides an influential industrial perspective on the regulation of combination products and is a frequent speaker on combination products topics and has published numerous articles in regulatory and scientific publications.

Adam Shames is a recognised human factors expert and consultant and is the Founder and Chief Executive Officer of Core Human Factors, Inc, a leader in human factors and usability engineering consulting services with over 12 full-time employees. Adam holds an MBA in international business and a BS in human factors engineering and psychology. He received the De-Florez Prize in Human Engineering and holds a Certificate in Applied Ergonomics Training from the United States Army Center for Health Promotion and Preventive Medicine. Adam has over 15 years of human factors research experience and has served as the Principal Investigator on hundreds of IRB reviewed usability studies involving thousands of participants in cities around the world.



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