FDA CDER Perspective on The Role of Human Factors in Inhalational Products Design and Development

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What is a Medication Error?

A medication error is any **preventable** event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.

Figure 1: Relationship between medication errors and ADEs

1Adapted from Figure 1 in Qual Saf Health Care 2004;13:306–314. doi: 10.1136/qshc.2004.010611

www.fda.gov

Definition of Human Factors (HF)

Ergonomics (or human factors) is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data and methods to design in order to optimize human well-being and overall system performance.

- International Ergonomics Association (IEA)
Medication Error Prevention and HF

Appropriate Medication Use/
Optimize Human Well Being

Medication Error Prevention

Human Factors

www.fda.gov
Who Looks at Medication Errors?

Division of Medication Error Prevention and Analysis (DMEPA)

- Created in 1999
- Scientists and healthcare professionals with varied backgrounds
- 53 employees
- Aligned by therapeutic areas
- Leads CDER review pertaining to medication error prevention and analysis for drug and therapeutic biologics
Center for Drug Evaluation and Research (CDER)

Office of Surveillance and Epidemiology (OSE)

Office of Pharmacovigilance and Epidemiology (OPE)
  - Division of Pharmacovigilance I, II (DPV I, II)

Office of Medication Error Prevention and Risk Management (OMEPRM)
  - Division of Medication Error Prevention and Analysis (DMEPA)
  - Division of Risk Management (DRISK)
DMEPA Mission

To increase the safe use of drug products by minimizing use error that is related to the naming, labeling, packaging, or design of drug products
“I’m Not an Idiot”

https://www.youtube.com/watch?v=nvwR74XpKUM
Proactive vs. Reactive

• Reactive: Historically, some design issues with drug products were not identified and remedied until post-marketing
  – In some cases, the issues were only resolved after medication errors had reached and harmed patients

• Proactive: Today, design issues are identified proactively and addressed prior to marketing to prevent some medication errors from occurring
Combination Products

• Formal Definition in 21 CFR 3.2:
  – Therapeutic and diagnostic products
  – Combine >1: drugs, devices, biological products

• They can be:
  – Physically or chemically combined (21 CFR 3.2(e)(1))
  – Co-packaged in a kit (21 CFR 3.2(e)(2))
  – Separate, cross-labeled products (21 CFR 3.2(e)(3) or (4))
Combination Product Examples

- Prefilled Syringes
- Pen Injectors, Autoinjectors
- Pharmaceutical Aerosol Delivery Devices/Inhalation Products
- Transdermal Delivery Systems/Patches
- Drug Infusion Devices
- Kits containing drug and administration devices
Regulatory Authority

Device:
21 CFR 820.30
Requirement of device

Drug:
• Kefauver-Harris Amendment to the 1938 Food, Drug and Cosmetic Act

HF studies may be needed to demonstrate elimination/minimization of use-related hazards and medication errors

effective use

improved product design including packaging, nomenclature, and labeling

• PDUFA IV development goal: ensure drug safety by prospectively designing a drug that minimizes the risk for errors made by intended end users.
Removal of Use Errors through HF

- Optimized design
- Original design

Risk Level

Low

High
Define intended users, use environments & UI

Identify use-related hazards

Identify and categorize critical tasks

Develop and implement risk mitigation/control measures

Validate use safety and effectiveness

Use-related risks acceptable?

New use-related risks introduced?

Document HFE/UE process

Product Users, Use Environments and User Interface

Preliminary Analyses and Evaluations

Elimination or Reduction of Use-Related Hazards

Human Factors Validation Testing

Documentation
Simulated-Use Human Factors Validation Testing

- Simulated-use should be **sufficiently realistic** so that the results of the testing are **generalizable to actual use**
- Test participants should be given an opportunity to use the device as independently and naturally as possible. Use of the “think aloud” technique is not acceptable in this summative test
- If users would have access to the labeling in actual use, it should be available in the test; however, the participants should be allowed to use it as they choose and should not be instructed to use it
Drug Development Process & Human Factors Considerations for Commercial (to-be-marketed) Product

<table>
<thead>
<tr>
<th>Preclinical Testing</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
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<tbody>
<tr>
<td></td>
<td><strong>FILE IND</strong></td>
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<td><strong>FILE NDA/BLA</strong> for FDA review</td>
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***DMEPA involvement (can be as early as pre-IND phase)***

- Human factors (HF) product design, preliminary analyses, formative work, and HF validation testing
- Continual updates to the Use-Related Risk Analysis (URRA)
<table>
<thead>
<tr>
<th>Regulatory Pathway(s)</th>
<th>New Drug</th>
<th>Generic</th>
<th>Biosimilar</th>
<th>Interchangeable</th>
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<tbody>
<tr>
<td>505(b)(1), 505(b)(2), 351(a)</td>
<td>505(j)</td>
<td>351(k)</td>
<td>351(k)(4)</td>
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<tr>
<th>Application Type(s)</th>
<th>NDAs, and BLAs</th>
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<tbody>
<tr>
<td>Released February 2016</td>
<td>Released January 2017</td>
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# FDA Guidance Timeline

<table>
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<th>Year</th>
<th>Title</th>
<th>Description</th>
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| 2000 | Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management | • First HF guidance from FDA  
• Focused on applying Human Factors Engineering as an **essential component of risk management**  
• Introduced use error as a source of risk largely separate from device reliability |
| 2011 | Draft Guidance: Applying Human Factors and Usability Engineering to Optimize Medical Device Design | • Provides a structure for the manufacturer’s HF reporting  
• Evaluation focused on risk priority of user tasks  
• Continues to treat use error as separate risk from device failure risks |
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| 2012 | Draft Guidance for Industry: Safety Considerations for Product Design To Minimize Medication Errors | • Provides a set of principles for consideration in the development of drug products, using a systems approach, to minimize medication errors relating to product design and container closure design  
• Underscores importance of evaluating the product design using proactive risk assessments before finalizing the design  
• Recommendations based on postmarket safety information  
• Discusses concepts of simulated use testing |
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| 2013 | **Draft Guidance for Industry:** Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors | • Focused on safety aspects of the container label and carton labeling design  
• Provides a set of principles to promote safe dispensing, administration, and use of products  
• Reinforces importance of evaluating design using proactive risk assessments before finalizing the design  
• Recommendations based on postmarket safety information |
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| 2016 | Draft Guidance for Industry and FDA Staff: Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development | • First HF guidance from FDA focused on combination product development  
• Provides recommendations regarding HF data needs in investigational and marketing applications  
• Describes how HF studies relate to other clinical studies |
| 2016 | Applying Human Factors and Usability Engineering to Medical Devices   | • Finalized the June 2011 draft guidance  
• Supersedes “Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management” issued in 2000 |
| 2016 | Safety Considerations for Product Design To Minimize Medication Errors | • Finalized the December 2012 draft guidance |
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<td>2017</td>
<td>Draft Guidance for Industry: Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA</td>
<td>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 includes both a drug constituent part and a delivery device constituent part</td>
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<td>2017</td>
<td>Draft Guidance for Industry: Considerations in Demonstrating Interchangeability With a Reference Product</td>
<td>Intended to assist sponsors in demonstrating that a proposed therapeutic protein product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k))</td>
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Partnership

FDA

Industry

Better Outcomes for Patients
Questions

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