ISAM/IPAC-RS Joint Workshop
New Frontiers in Inhalation Technology

In conjunction with ISAM congress

Saturday, June 3, 2017
Santa Fe, NM
FDA CDER perspective on User Interface Considerations for New Technologies in Inhalational Products

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2017 IPAC-RS/ISAM Joint Workshop
New Frontiers in Inhalation Technology
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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
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
Division of Medication Error Prevention and Analysis (DMEPA)

- Created in 1999
- Scientists and healthcare professionals with varied backgrounds
- 47 FTE’s
- Aligned by therapeutic areas
- Leads CDER review pertaining to medication error prevention and analysis and human factors 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)
  - Division of Epidemiology I, II (DPE I, II)

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

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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
Proprietary Names
Guidance/ Work Groups/AC/ etc.
Post-market Surveillance/ signals
DMEPA
Labels/ Labeling/ Packaging/ Product Design
Human Factors
“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
Removal of Use Errors through HF

- Optimized design
- Original design
- Reduce risk through Human Factors

Risk Level:
- Low risk product
- High risk product

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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
Evolving Technologies for Inhalers

https://www.caretrx.com/
Evolving Technology

Wireless syncing with smartphone

Mobile medical application

Reminder emails/texts

Real time use instructions

Inspiration data capture

Provider dashboards

LCD display
Evolving Indications

...monitor adherence to therapy...

...treatment or prevention of bronchospasm in patients...

...improve adherence...
Evaluating New Technologies

• Do differences in technology change how human factors engineering processes are applied to development of the user interface?

• What are regulatory challenges with evaluating new technologies?
Do differences in technology change how human factors engineering processes are applied to development of the user interface?
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?

YES

New use-related risks introduced?

YES

NO

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
Human Factors Validation Testing

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Evaluation of Use-Related Risk

• Consider intended users, uses, and use environments
• Foundation for product design and HF study designs
• Crucial step in identifying use-related hazards
• Identify all critical tasks required for using the combination product
• Explain consequences of failing a critical task
• Describe risk mitigation strategies implemented
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
  – harm is defined to include compromised medical care

• Examples might include*:
  – Removing the cap of a product used for emergency anaphylaxis treatment
  – Selecting the correct injection site on the body
  – Dialing to the correct dose

*Not specified in guidance
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Training as Part of User Interface

• Does not replace eliminating risks inherent to product design
• May not be needed for all combination products
• Often proposed to mitigate or control risks
  – Is there opportunity for training in actual use?
  – Will training occur routinely and consistently?
    • If no, HF study expected to evaluate the absence of training
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?

Yes

New use-related risks introduced?

Yes

NO

Document HFE/UE process

NO

YES

YES

NO

Product Users, Use Environments and User Interface

Preliminary Analyses and Evaluations

Elimination or Reduction of Use-Related Hazards

Human Factors Validation Testing

Documentation (Section 9)
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
What are regulatory challenges with evaluating new technologies?
Regulatory Challenge Examples

• Rapid pace of technology
  – e.g., software updates
• Cybersecurity
• Meaningful clinical outcomes
• Lifecycle
Draft Guidance

- Focuses on the analysis of the proposed user interface for the generic drug-device combination product (generic combination product) when compared to the user interface for the reference listed drug (RLD)
  - Issued January 2017
Answering A Different Question

• Traditional HF Validation Studies
  – Question 1: Does the proposed user interface support the safe and effective use of the product by intended users for intended uses and environments of use?

• Comparative HF Studies
  – Question 2: Do user interface design difference(s) between a generic and the RLD impact the clinical effect or safety profile of the proposed generic product
Scope of Draft Guidance

• Focus on analysis of the proposed user interface, but not intended to address all information necessary to support approval of a generic combination product

• Provide clarity on FDA’s expectations for the user interface of a generic drug-device combination product when compared to its RLD

• Provide clarity as to when additional information and/or data, such as data from comparative use human factors studies, may be warranted to support differences in design between a proposed generic drug-device combination product and its RLD
Abbreviated New Drug Application (ANDA)

• Drug products that are approved in ANDAs are generally considered by FDA to be therapeutically equivalent (TE) to their RLD.
  – A generic combination product classified as therapeutically equivalent to the RLD can be expected to produce the same clinical effect and safety profile as the RLD under conditions specified in labeling
    • Proposed generic combination product and its RLD do NOT need to be IDENTICAL in all respects
      – Sponsors should generally seek approval of a presentation approved for the RLD

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Substitution of ANDA for RLD

• In general, the FDA expects that the end-users* of generic combination products can use the generic combination product when it is substituted for the RLD
  – Without intervention of the health care provider and/or
  – Without additional training prior to the use of the generic combination product

*Including but not limited to lay-patients, such as patients, and/or caregivers
Summary of Key Messages in Draft Guidance

• Emphasizes that FDA does not expect that the design of a generic drug-device combination product be identical to the design of its RLD
• Focuses on the early development phases of the proposed generic drug-device combination product and encourages early collaboration with FDA
• Recommends that potential applicants minimize design differences between a proposed generic drug-device combination product and its RLD
• Allows for flexibility in the types of information and/or data that may be necessary to support differences in design between the user interface of the proposed generic drug-device combination product and its RLD
• Clarifies that the draft guidance is not intended to cover all information (e.g., CMC) that may be necessary to support the user interface of the proposed generic drug-device combination product
# FDA Guidance Timeline

<table>
<thead>
<tr>
<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 |
## FDA Guidance Timeline

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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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<tr>
<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

Better Outcomes for Patients

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Industry

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Questions

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