

# Human Factors Considerations for Inhaled Antifungal Drug Development

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**Virtual Public Workshop: Addressing Challenges in Inhaled Antifungal Drug Development**  
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# Definition of Human Factors/Ergonomics (HF/E)

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)

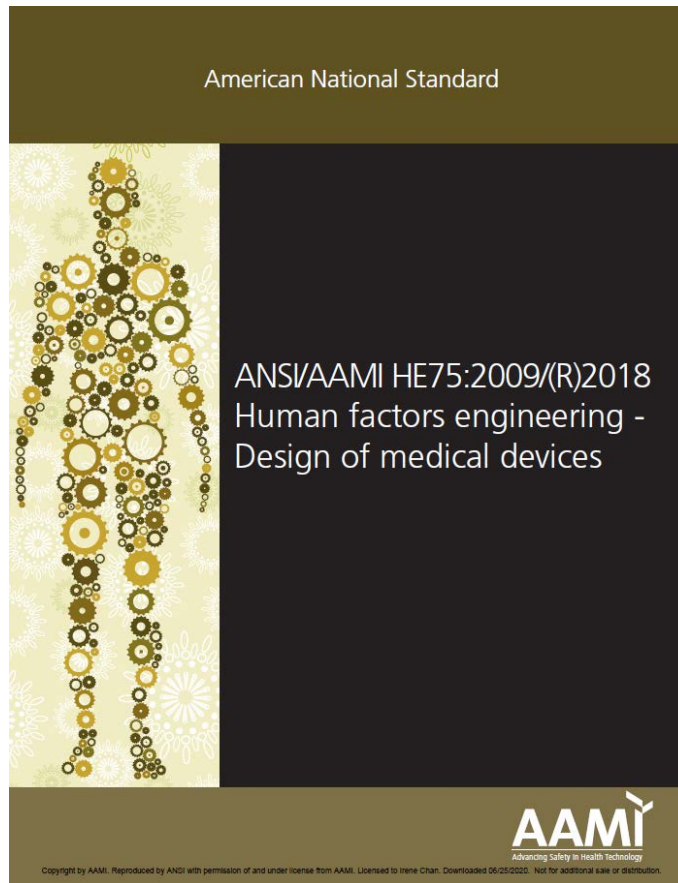
[www.fda.gov](http://www.fda.gov)



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# Are there other definitions for Human Factors?

Human factors: “...the application of knowledge about human capabilities (physical, sensory, emotional, and intellectual) and limitations to the design and development of tools, devices, systems, environments, and organizations....” (ANSI/AAMI HE75:2009, Introduction)



# So just to keep things simple, HF is really about understanding...

Compatibility of systems with people's

- Needs
- Abilities
- Limitations



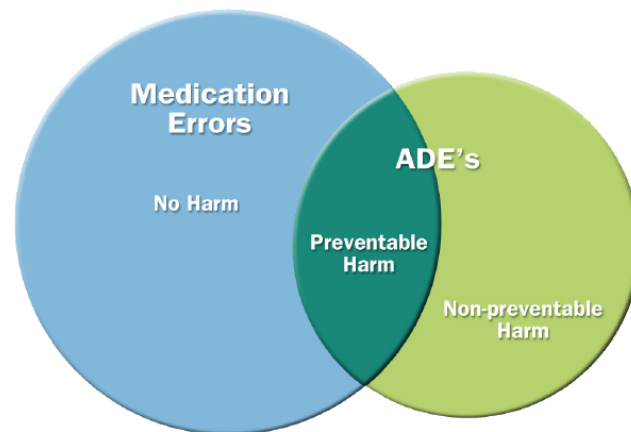
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\*Use environment can influence people's needs, abilities, or limitations

# What is a Medication Error?

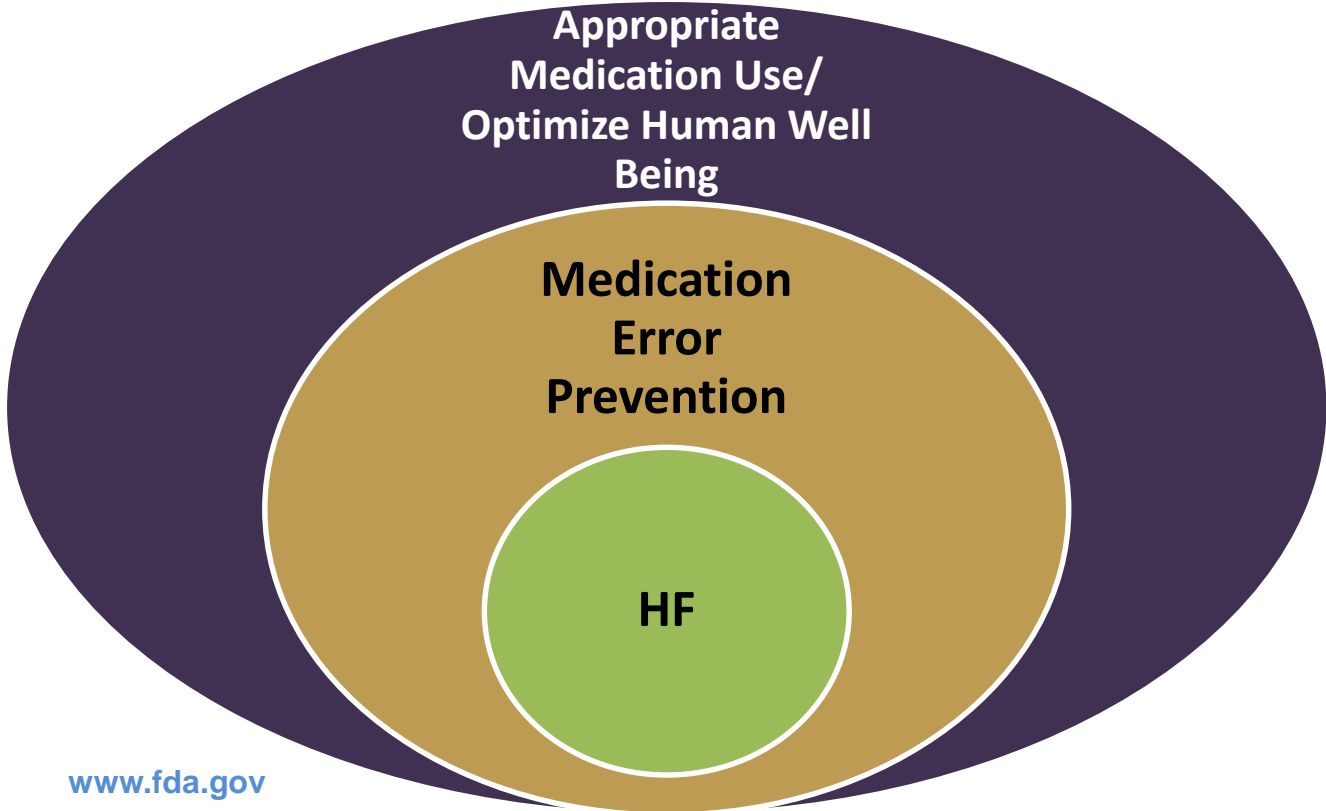
A medication error is any preventable event that may cause or lead to **inappropriate medication use or patient harm** while the medication is in the control of the health care professional, patient, or consumer

Figure 1: Relationship between medication errors and ADEs



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

# Medication Error Prevention and Human Factors – A Natural Fit!





# Who Looks at Medication Errors?

## Division of Medication Error Prevention and Analysis (DMEPA)

- Created in 1999
- Scientists and healthcare professionals with varied backgrounds
- > 60 employees
- Aligned by therapeutic areas
- Leads CDER review pertaining to **medication error prevention and analysis and human factors** for drug and therapeutic biologics



# 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

# Why does CDER care about HF? We want you to optimize the user interface design of your medical product

A user interface includes all components of a product with which a user interacts

E.g.,

- Labels and labeling
- Packaging
- Delivery device constituent part, and any associated controls and displays



# Why optimize the user interface design? Minimize errors



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March 3, 2008

## FDA Warns on Mistaken Ingestion of Inhaled Spiriva and Foradil Capsules

Many patients mistakenly swallow tiotropium bromide (Spiriva) and formoterol fumarate (Foradil) inhalation powder capsules, rather than using them in inhaler devices, the FDA warns.

The agency issued a public health advisory recommending that doctors, nurses, and pharmacists tell patients how to use the Spiriva HandiHaler and Foradil Aerolizer for treatment of asthma and COPD. If patients' breathing fails to improve, providers should ask them whether they are swallowing the tablets.

Although mistaken ingestion of the tablets is apparently common, the agency said few patients have experienced side effects.

LINK(S):

[FDA public health advisory](#) (Free)

Article accessed 9/17/2020 at:

<https://www.jwatch.org/fw200803030000001/2008/03/03/fda-warns-mistaken-ingestion-inhaled-spiriva-and>



- Step 1: Put the SPIRIVA capsule into the HandiHaler device.
- Step 2: Inhale the medicine through your mouth.



Do NOT swallow SPIRIVA capsules.



# Recognize that your inhaled antifungal product may be a combination product

- 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

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



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# What's the Regulatory Basis for Evaluating HF information at FDA?

## Device:

21 CFR 820.30

Requirement of device manufacturers to identify and investigate use-related hazards, and **validate the device user interface** to ensure safe and effective use

## Drug:

- Food, Drug and Cosmetic Act ensures prescription drug effectiveness and safety. As part of drug safety, FDA seeks to reduce risk from medication errors through **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.**

**Medical Devices; Current Good Manufacturing Practice (cGMP); Quality System Regulation Preamble to Final Rule 21 CFR Parts 808, 812, and 820 (61 FR 52502)**

**i.72.** ...”when designing a device, the manufacturer should conduct appropriate human factors studies, analyses, and tests from the early stages of the design process until that point in development at which the interfaces with the medical professional and the patient are fixed..”

**i.159.** ... “FDA emphasizes that any death, even if the manufacturer attributes it to user error, will be considered relevant by FDA and will have a high risk potentially associated with it. User error is still considered to be a nonconformity because human factors and other similar tools should have been considered during the design phase of the device.”

What’s the  
Regulatory Basis  
for Evaluating  
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at FDA?

# Designing a medical product is **NOT** like following a recipe

- Simply following design standards is not enough
- Sponsors shouldn't just be doing a box checking exercise
- Sponsors should be following a **human factors engineering process**



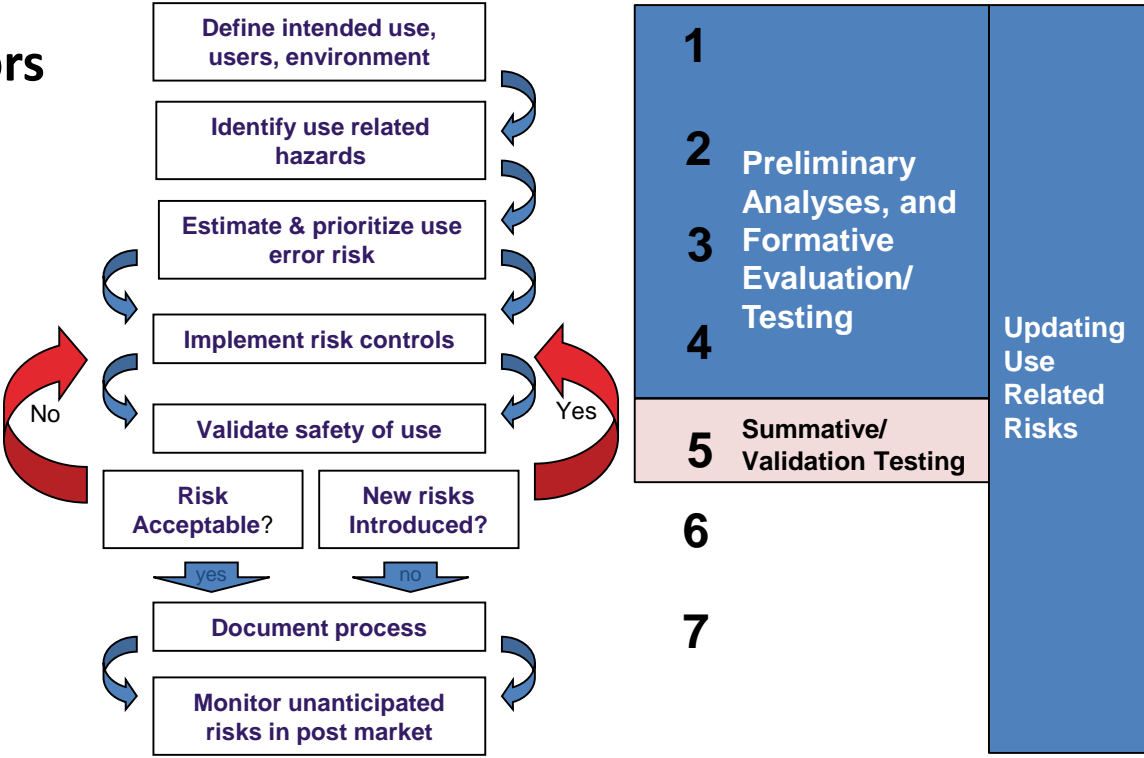
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## Important key point!

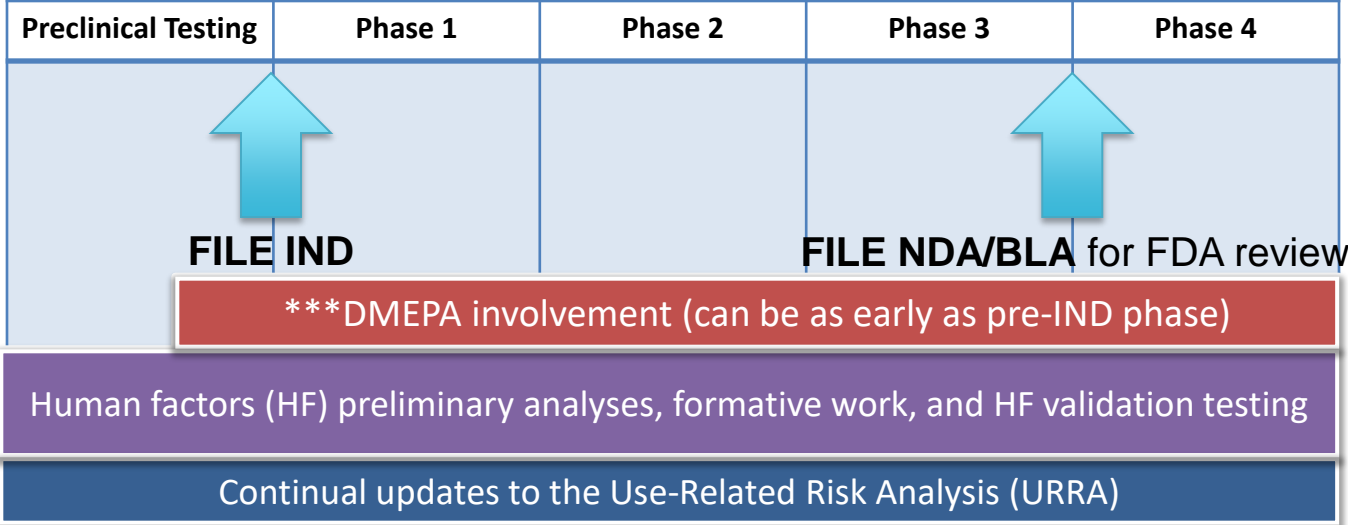
- Human factors engineering (HFE) is **not** just about conducting a human factors validation study
  - We want sponsors to follow a human factors engineering **PROCESS** when they design and develop the medical product

# Human factors engineering process for medical devices

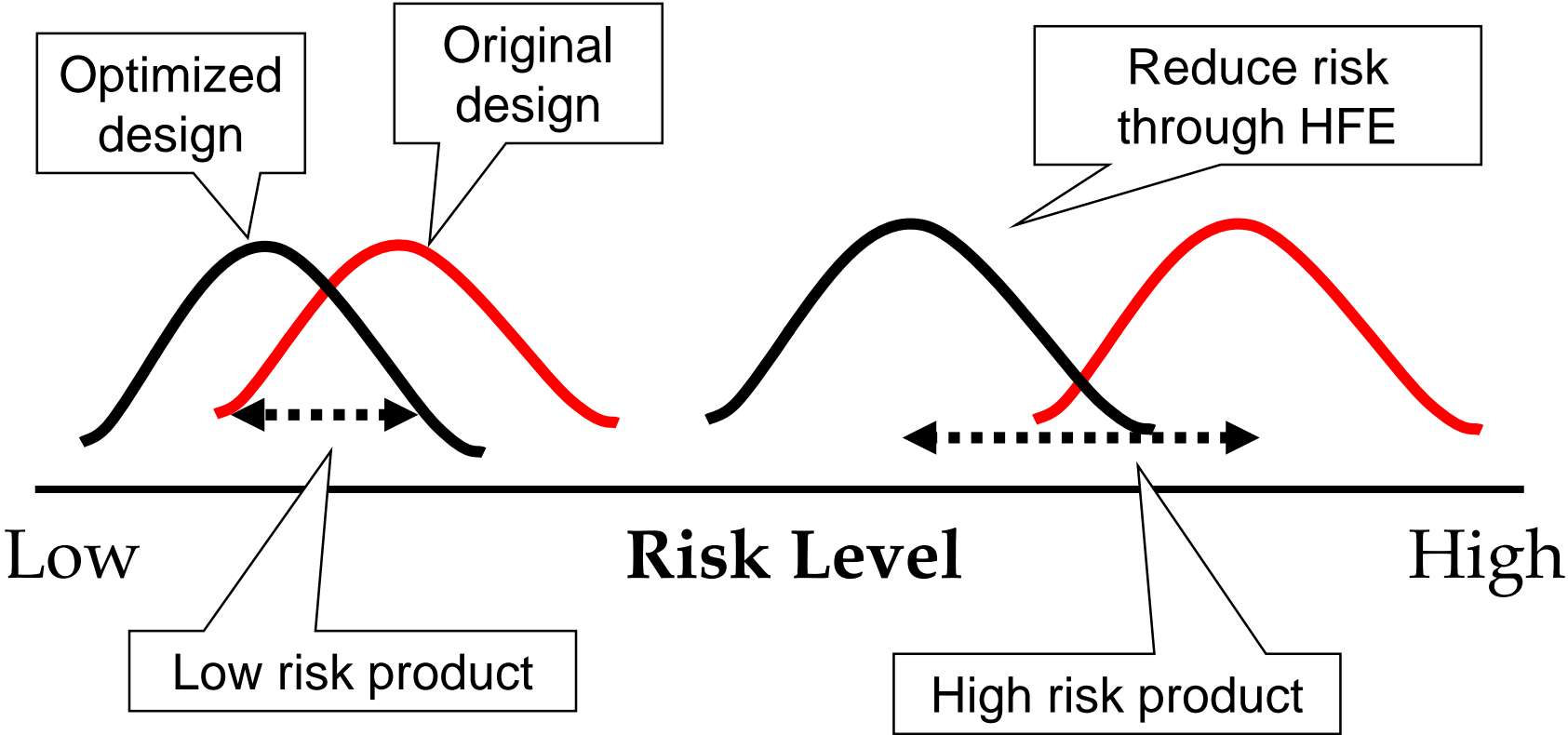


Source:  
ANSI/AAMI  
HE75:2009

# Drug Development Process & Human Factors Considerations for Commercial (to-be-marketed) Product



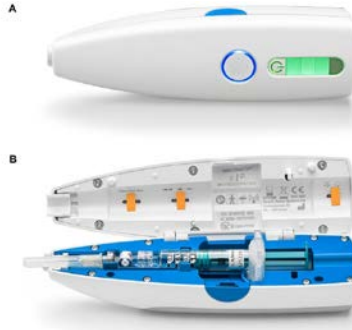
# Reduce Risk Through HFE Process



# Healthcare is Increasingly Complex



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When errors occur, the consequences can be devastating. We want to eliminate hazards (if possible) in the design of medical products to prevent hazardous situations that may lead to harm. In some cases, we may not be able to eliminate the hazard, in which case we try to minimize risk.

# Special Considerations When Designing Antifungal Inhalational Products

- Likely comorbidities (e.g., COPD, CF) should be carefully considered since they can impact your understanding of user needs, capabilities and limitations
- High doses that may be needed may restrict some existing inhalational delivery device platforms (e.g., MDI's may not be able to deliver the high doses necessary)
- Some current delivery device platforms are optimized to deliver to the central lung region, and may not reach other regions of lungs
- Formulation challenges (e.g., due to solubility) may require additional tasks from users and should be considered in overall complexity of product design



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