

# **Role of Human Factors Engineering in Medical Products Regulatory Reviews and Research**

**FDA Small Business  
Regulatory Education for Industry (REdI)  
Burlingame, CA  
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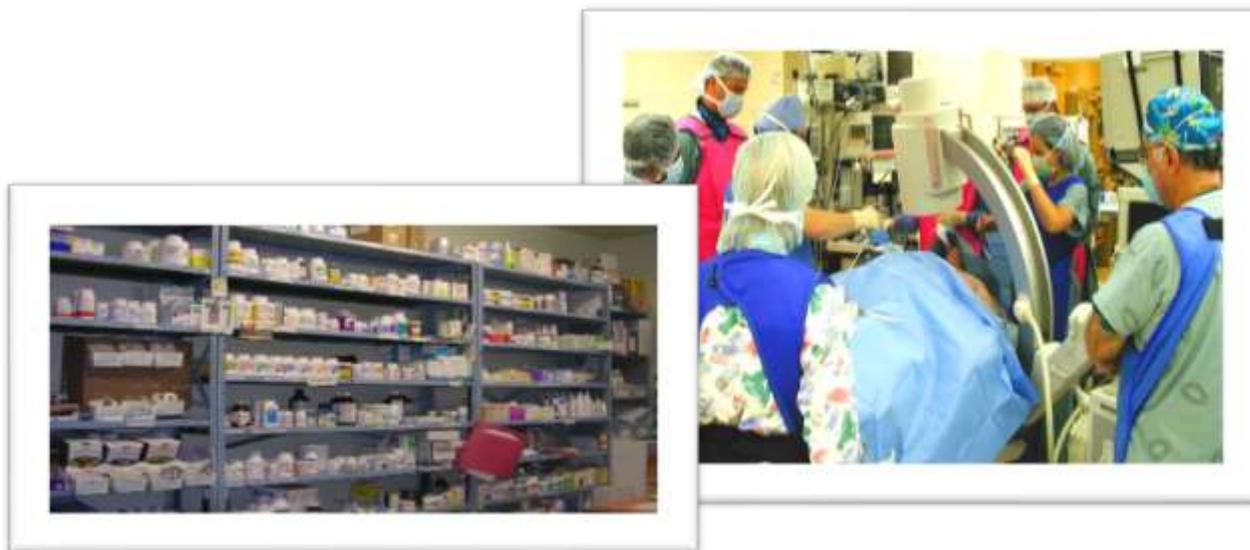
Commander, U.S. Public Health Service  
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Division of Medication Error Prevention and Analysis  
Office of Medication Error Prevention and Risk Management  
Center for Drug Evaluation and Research



# Outline

- Introduction to Human Factors in medical product development and evaluation
- Human Factors Research at the FDA
- Human Factors and Usability Engineering in CDRH
- Combination Products Development and Human Factors Considerations – CDER Perspective

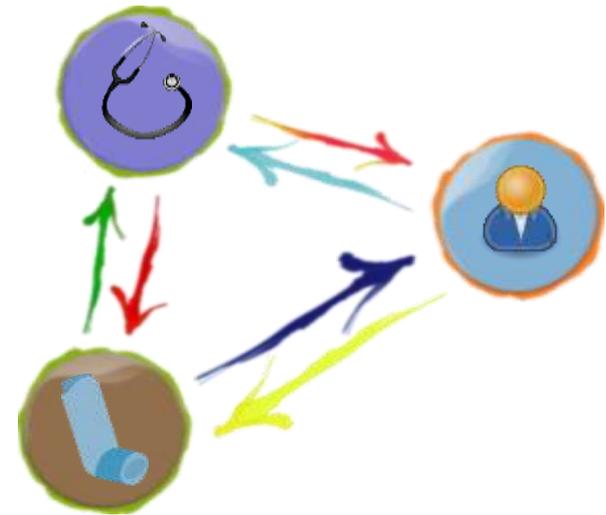
# Increasing Complexity



Humans are exceptionally good at dealing with complexity,  
*HOWEVER,*  
 sometimes the rational action in the moment can have  
 unintended consequences

# What is 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**.



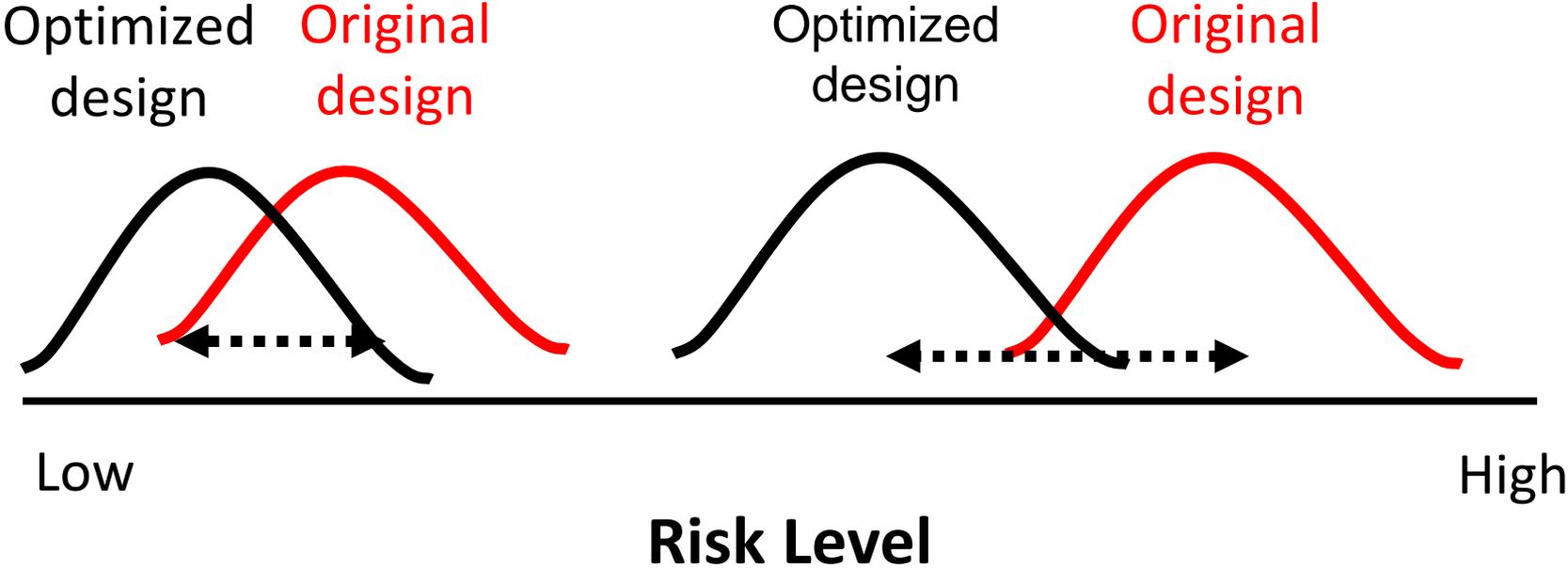
International Ergonomics Association (IEA)

# Goals of incorporating HF

- Provide the best possible user experience
- Combat the medical error problem<sup>1</sup>
- Reduce risk of use errors resulting in harm or compromised medical care

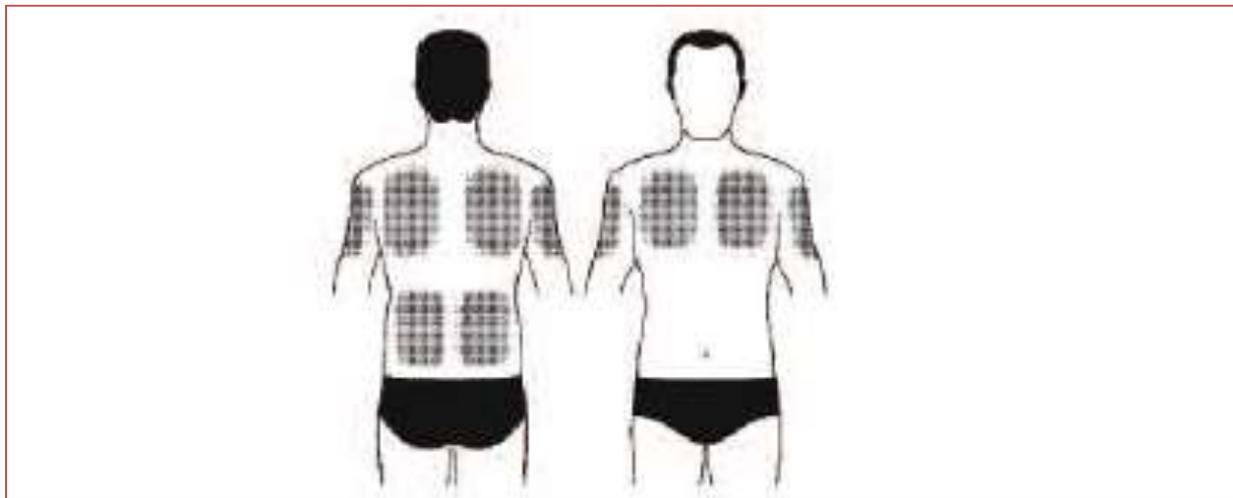
<sup>1</sup>[www.ncbi.nlm.nih.gov/books/NBK225187](http://www.ncbi.nlm.nih.gov/books/NBK225187)

# Removal of Use Errors through HF

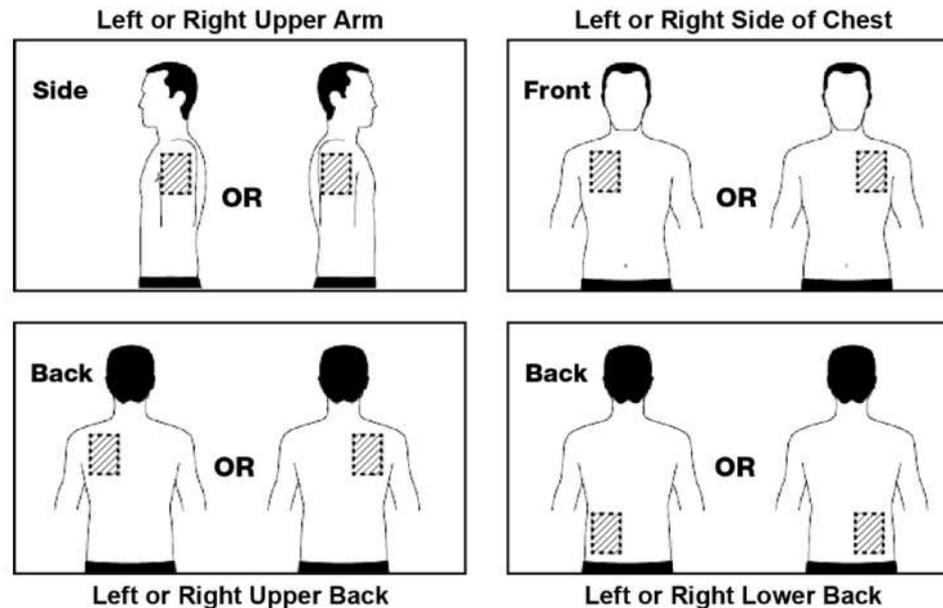


**Example: Illustration in the user manual for transdermal patch.**

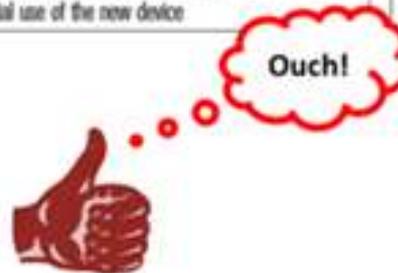
**Where would you apply patch?**



# Revised user instructions: where to apply patch



# Auto-injector example



## EpiPen



## Insulin Pen



**FDA does  
research?**



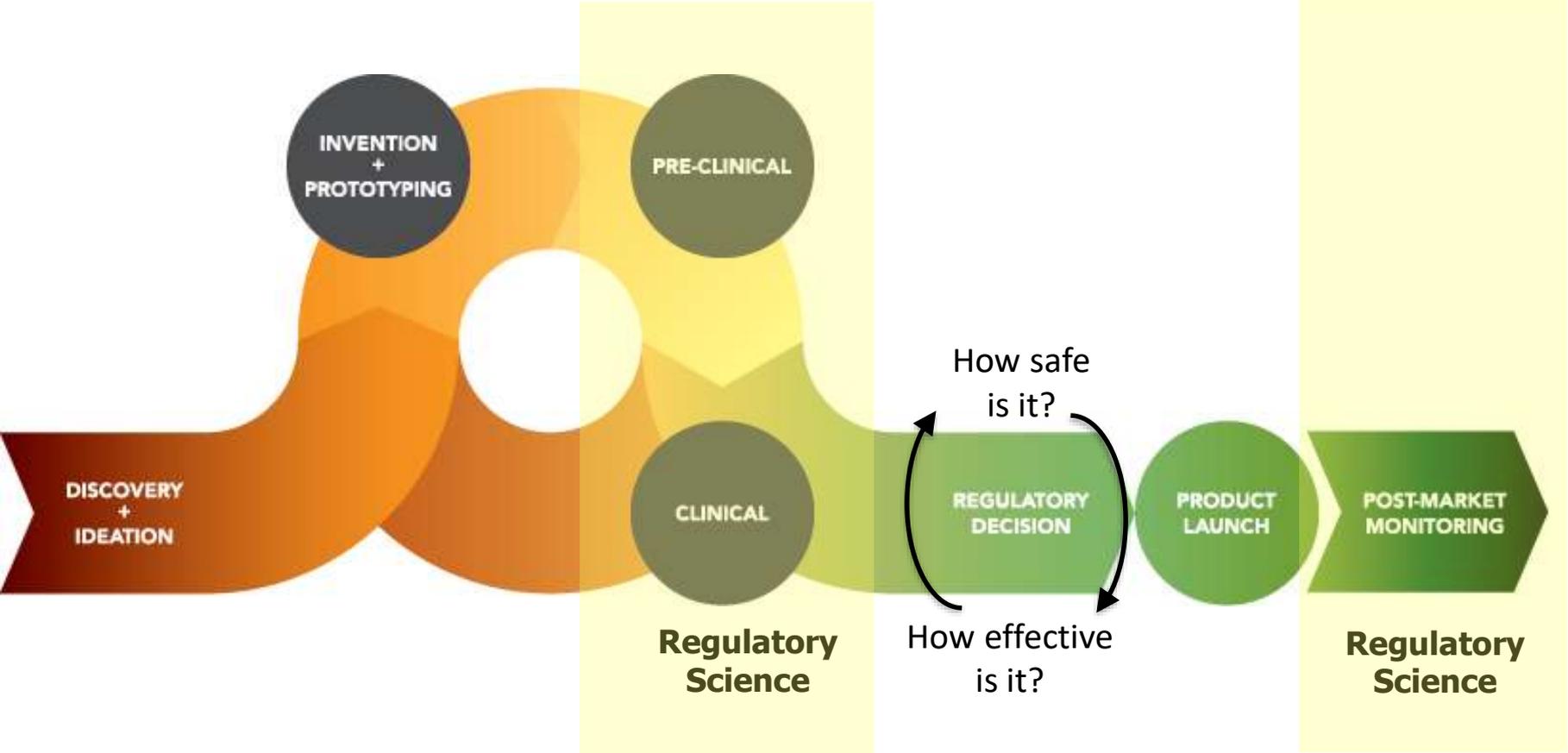


# CDRH Office of Science and Engineering Laboratories Mission

- Ensure readiness for emerging and innovative medical technologies
- Develop appropriate evaluation strategies and testing standards
- Create accessible and understandable public health information
- Deliver timely and accurate decisions for products across their life cycle

# Regulatory Science

consists of the development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA regulated products



# Human Factors Research

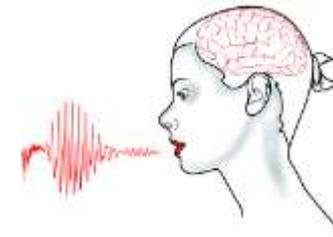
Development of test methods to assess attention and focus during medical product use



Eye tracking



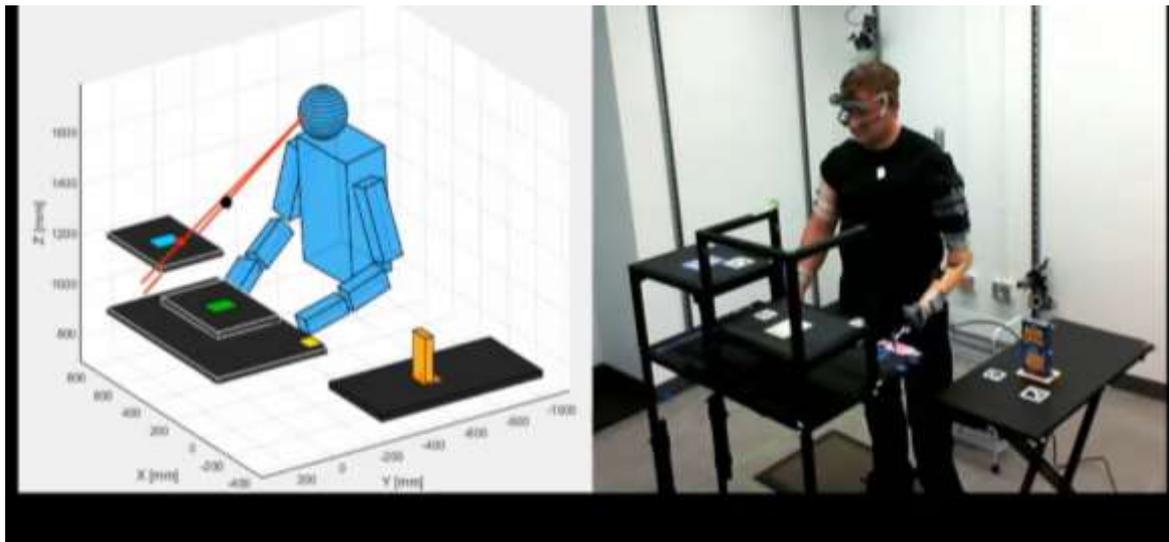
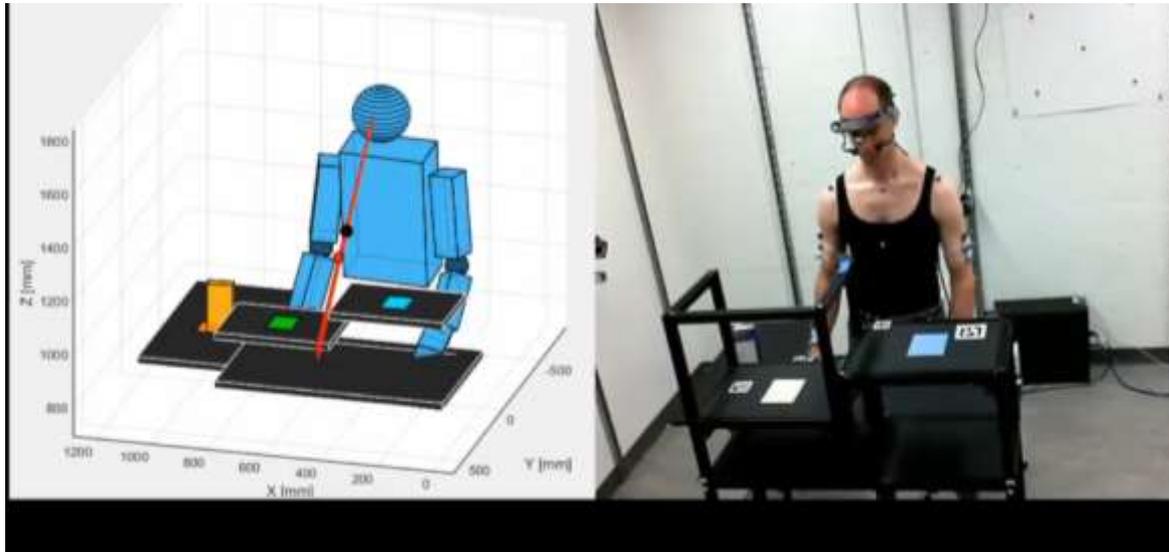
Micro expression facial analysis



Speech analysis

- Which physiological biomarkers are best for the evaluation of focus and attention for a given medical product?
- What aspects of the device UI are confusing?
- Where do users focus their attention during product interaction?

# Human Factors Research



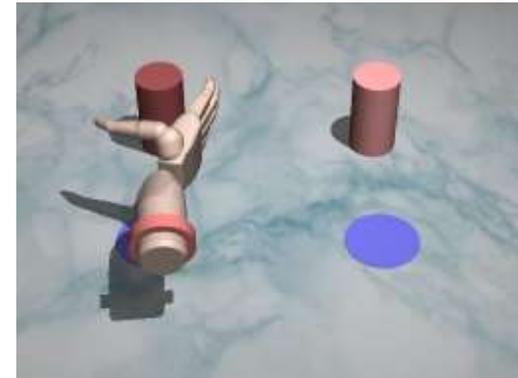
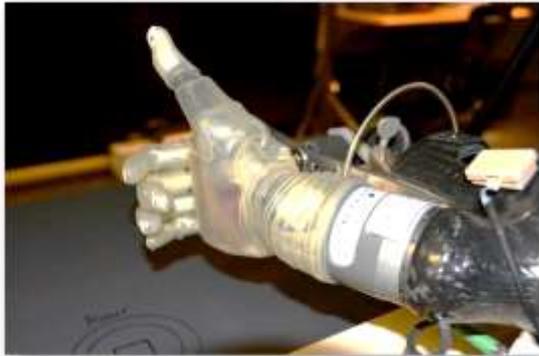
## Eye metrics

- Percent (%) fixation
- Number of fixations (glance rate)
- Fixation on hand and target

# Human Factors Research



Use of virtual reality environments (VREs)  
for product evaluation



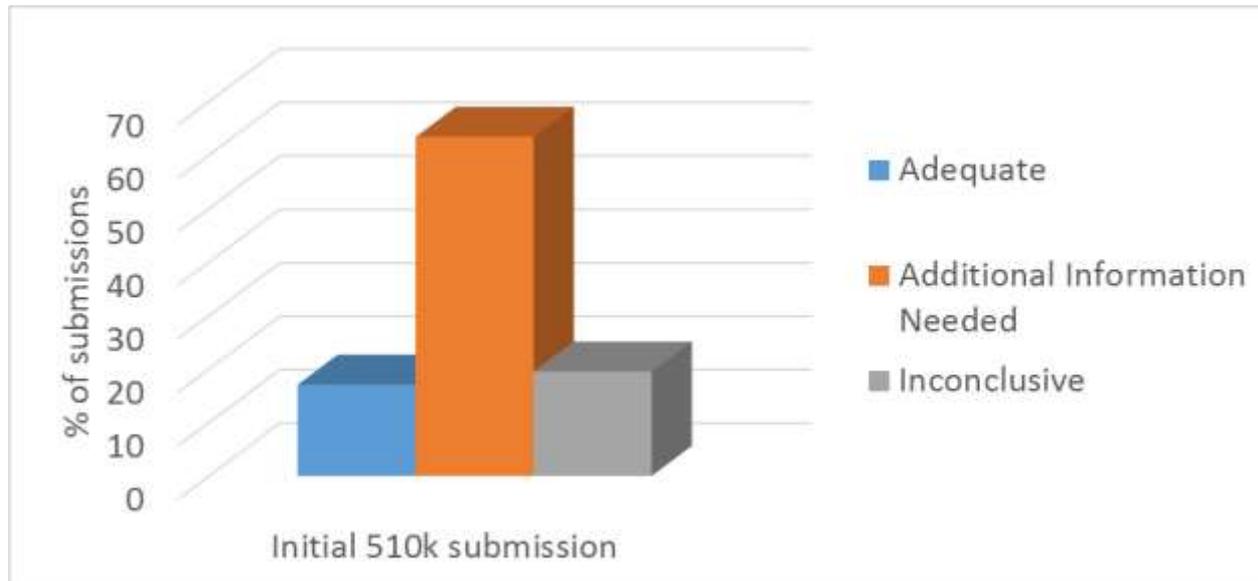
- Are there differences in how patients interact with objects in VRE vs. real-world?
- Where are those differences and how are they impacting product use?

# Human Factors Research



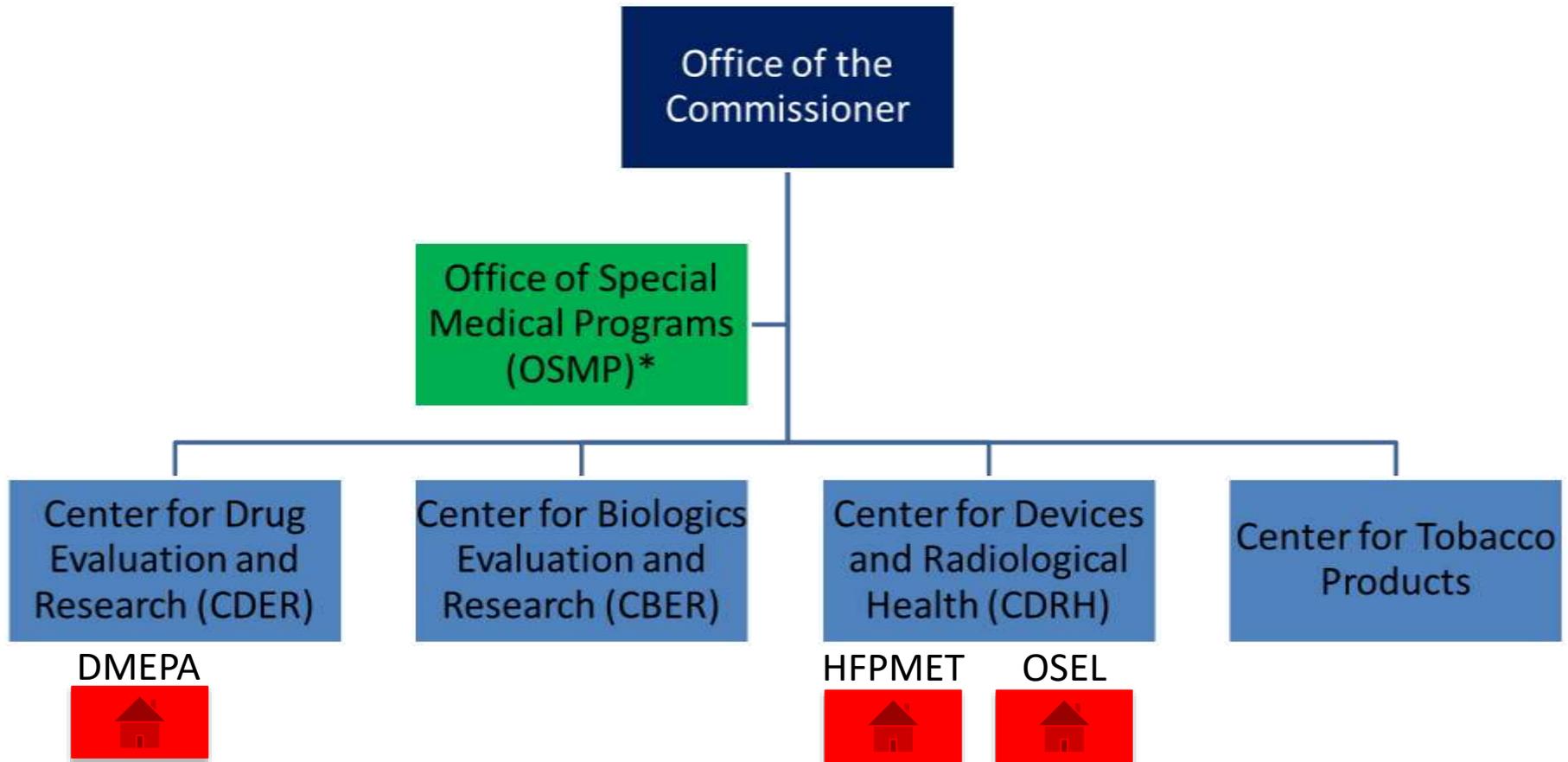
## ‘Big Data’ analytics of HF review material

- How often are submissions with HF data adequate “as-is”?
- What are the common deficiencies found in medical product submissions? How are these deficiencies stratified by product type?



# **Human Factors and Usability Engineering in Premarket Device Evaluation**

# FDA Organizational Structure



\*Office of Combination Products (OCP) housed under OSMP

# Human Factors Team in CDRH



- Scope of work:
  - Premarket submission reviews & combination products (CBER & CDER)
  - Post-market signals: Adverse Events (OSB), Recalls (OC)
  - Guidance development, national and international standards development
  - Panel discussions, outreach & education

# Regulatory Basis for Human Factors in Medical Devices



## 21 CFR 820.30 Design controls

### Design input

Address intended use of the device, including needs of user/patient

### Design verification

Confirm design output meets design input requirements

### Design validation

Ensure device conforms to user needs...and includes testing of production units under actual or simulated use testing

Product development



# Regulatory Basis for Human Factors in Medical Devices



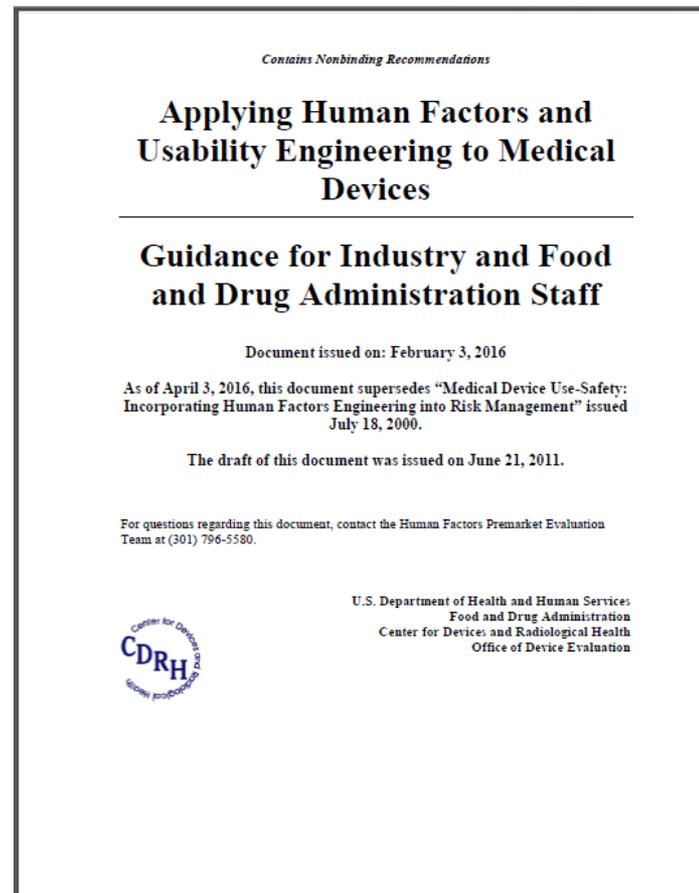
**Medical Devices; Current Good Manufacturing Practice (cGMP);  
Quality System Regulation Preamble to Final Rule 21 CFR Parts  
808, 812, and 820 (61 FR 52502)**

# 2016 FDA CDRH HF Device Guidance



## Aims to clarify expectations around:

1. applying HFE to medical device development and
2. when to submit a HF report for a premarket submission and
3. the content of the HF report



# 2016 FDA CDRH HF Device Guidance



- “CDRH recommends that manufacturers consider human factors testing for medical devices as a part of a robust design control subsystem”.
- “CDRH believes that for those devices where an analysis of risk indicates that users performing tasks incorrectly or failing to perform tasks could result in serious harm, manufacturers should submit human factors data in premarket submissions (i.e., PMA, 510(k), De Novo).”

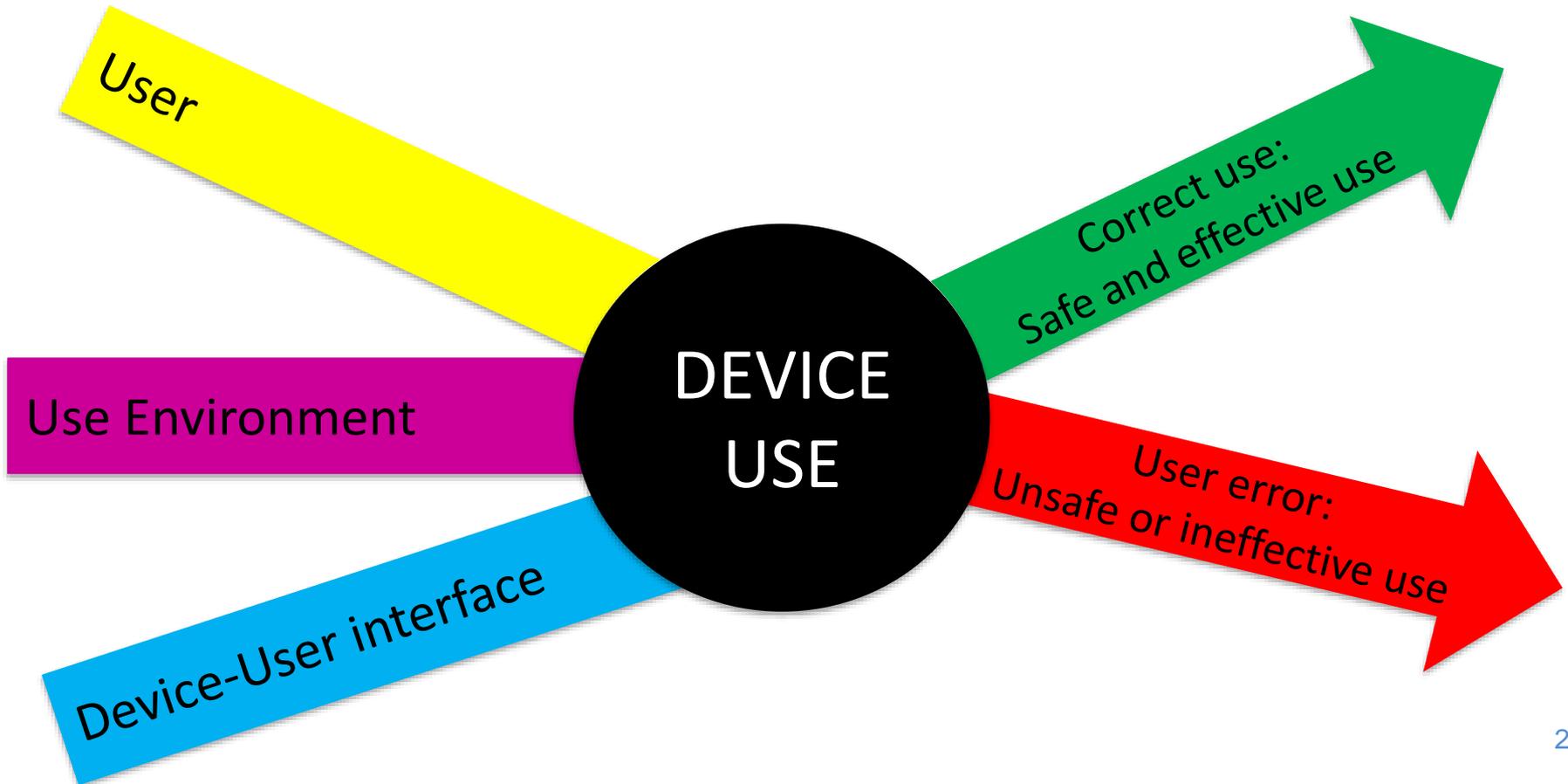
# Human Factors Process Flowchart



Define intended users, use environments & UI

Human Factors Considerations

Outcomes

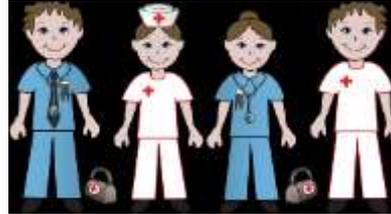


# Human Factors Process Flowchart



Define intended users, use environments & UI

## Who is the intended user?



- Physical considerations
- Sensory abilities
- Knowledge of similar devices
- Level of education related to the medical condition

## Where will the device be used?



## What constitutes the device user-interface?

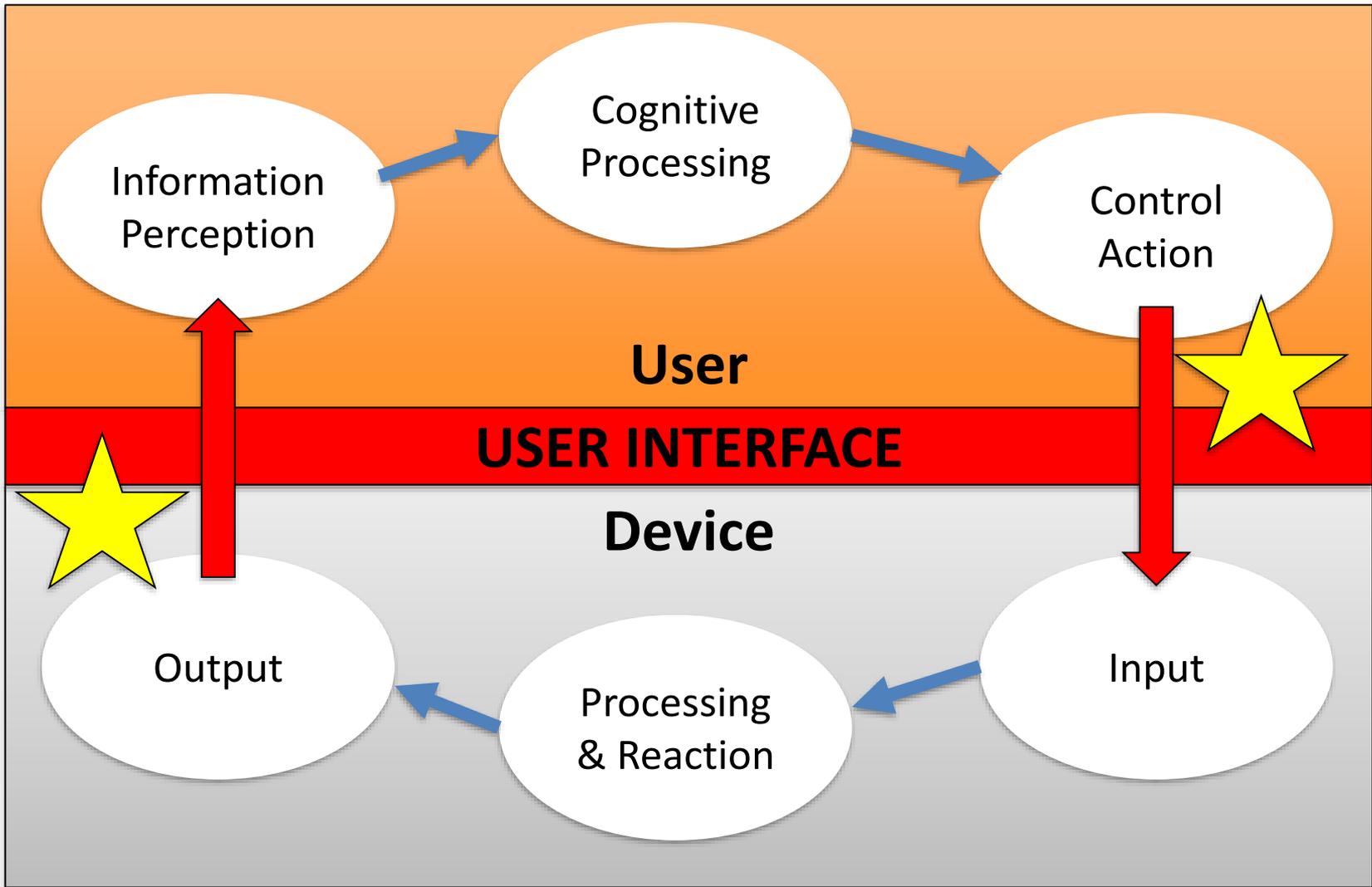
# Human Factors Process Flowchart



Define intended users, use environments & UI



Identify use-related hazards;  
identify and categorize  
critical tasks



**Critical task:** A user task which, if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user, where harm is defined to include compromised medical care.

# Human Factors Process Flowchart



Define intended users, use environments & UI



Identify use-related hazards; identify and categorize critical tasks

- Risk analysis approaches
  - Failure Mode Effects Analysis
  - Fault Tree Analysis
- Identify known use-related problems
  - FDA resources
  - ECRI Medical Device Safety Reports
  - Institute of Safe Medical Practice Alerts
- Analytical approaches
  - Task analysis
  - Heuristic analysis
  - Expert review
- Empirical approaches
  - Contextual inquiry
  - Interviews
  - Formative evaluations

# Human Factors Process Flowchart



Define intended users, use environments & UI



Identify use-related hazards; identify and categorize critical tasks



Develop and implement risk mitigation/control measures

## Risk management options:

- Safety by design



- Protective measures



- Information for safety



# Human Factors Process Flowchart



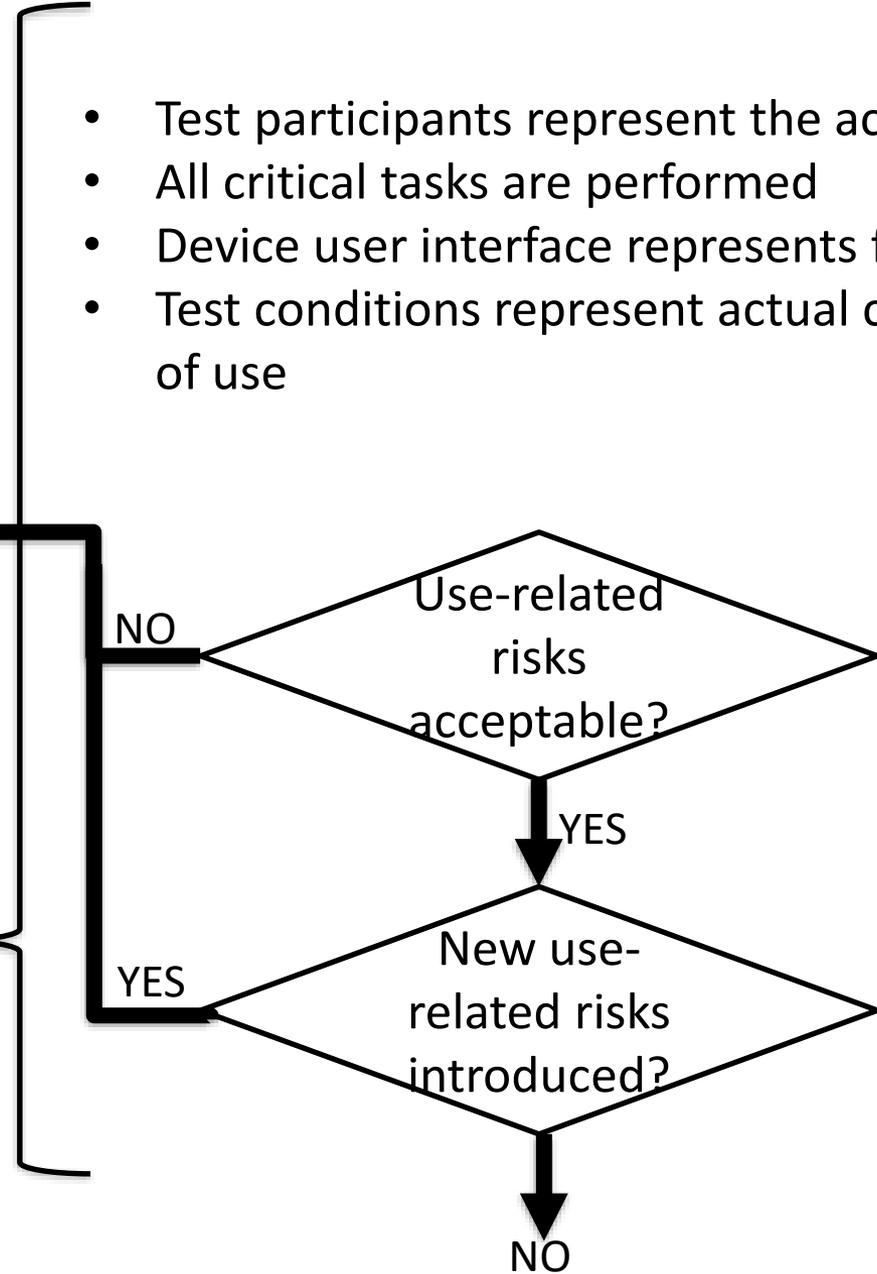
Define intended users, use environments & UI

Identify use-related hazards; identify and categorize critical tasks

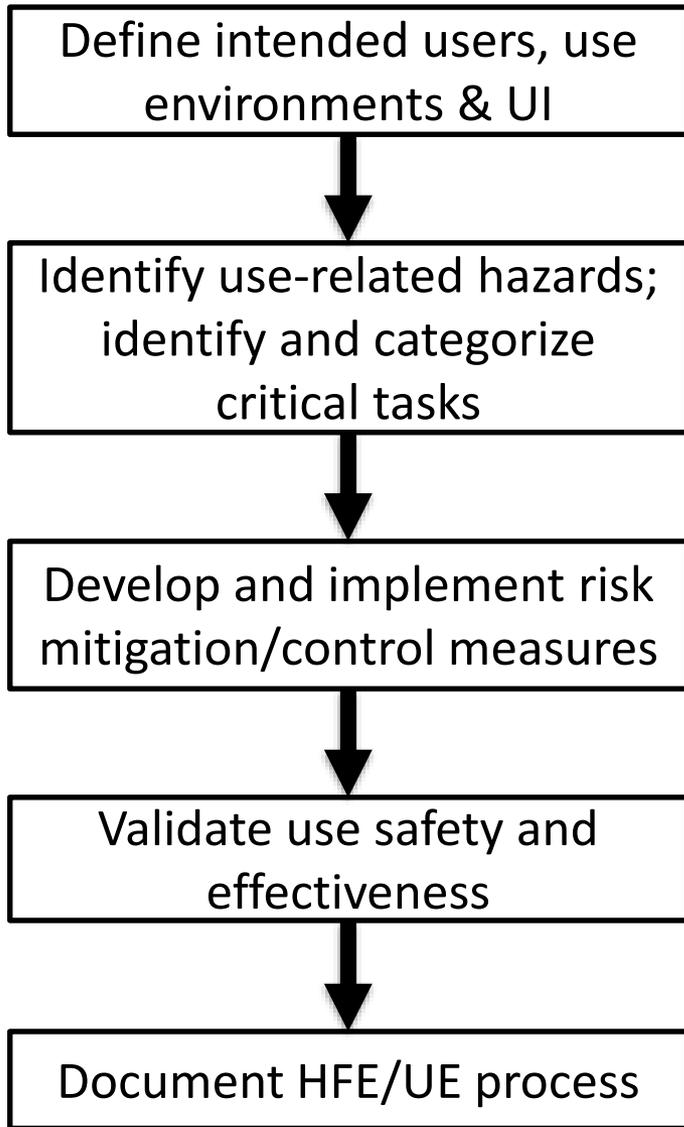
Develop and implement risk mitigation/control measures

Validate use safety and effectiveness

- Test participants represent the actual users
- All critical tasks are performed
- Device user interface represents final design
- Test conditions represent actual conditions of use



# Human Factors Process Flowchart



## Human Factors Recommended Report Outline

1. Conclusion
2. Description of Intended device users, uses, environments and training
3. Description of device user interface
4. Summary of known use problems
5. Analysis of risks associated with use of the device
6. Summary of preliminary analyses and evaluations
7. Description and categorization of critical tasks
8. Details of human factors validation testing

# Combination Product Development and Human Factors Considerations

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Associate Director for Human Factors

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention & Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

REdI Plenary, May 2018

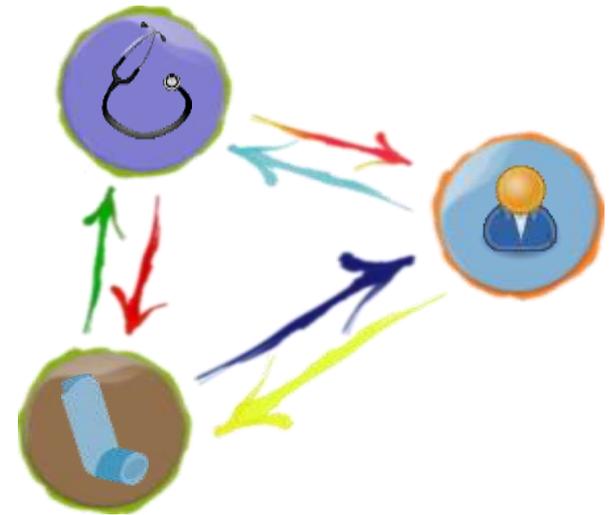
# “I’m Not an Idiot”



# What is 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**.

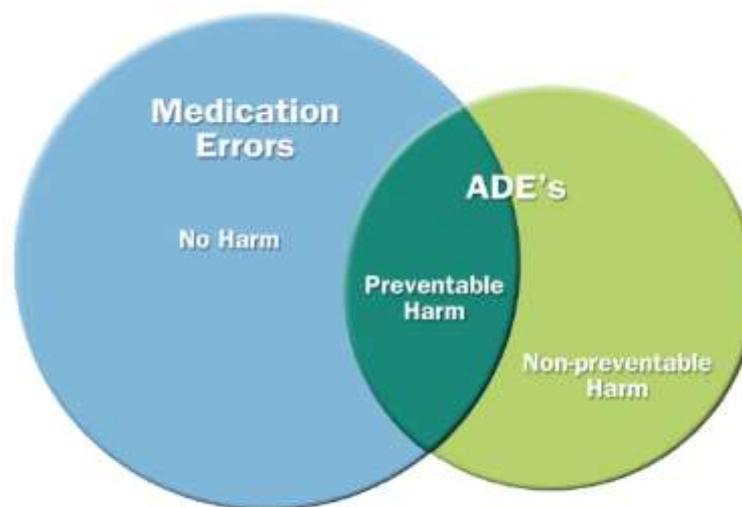


International Ergonomics Association (IEA)

# 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

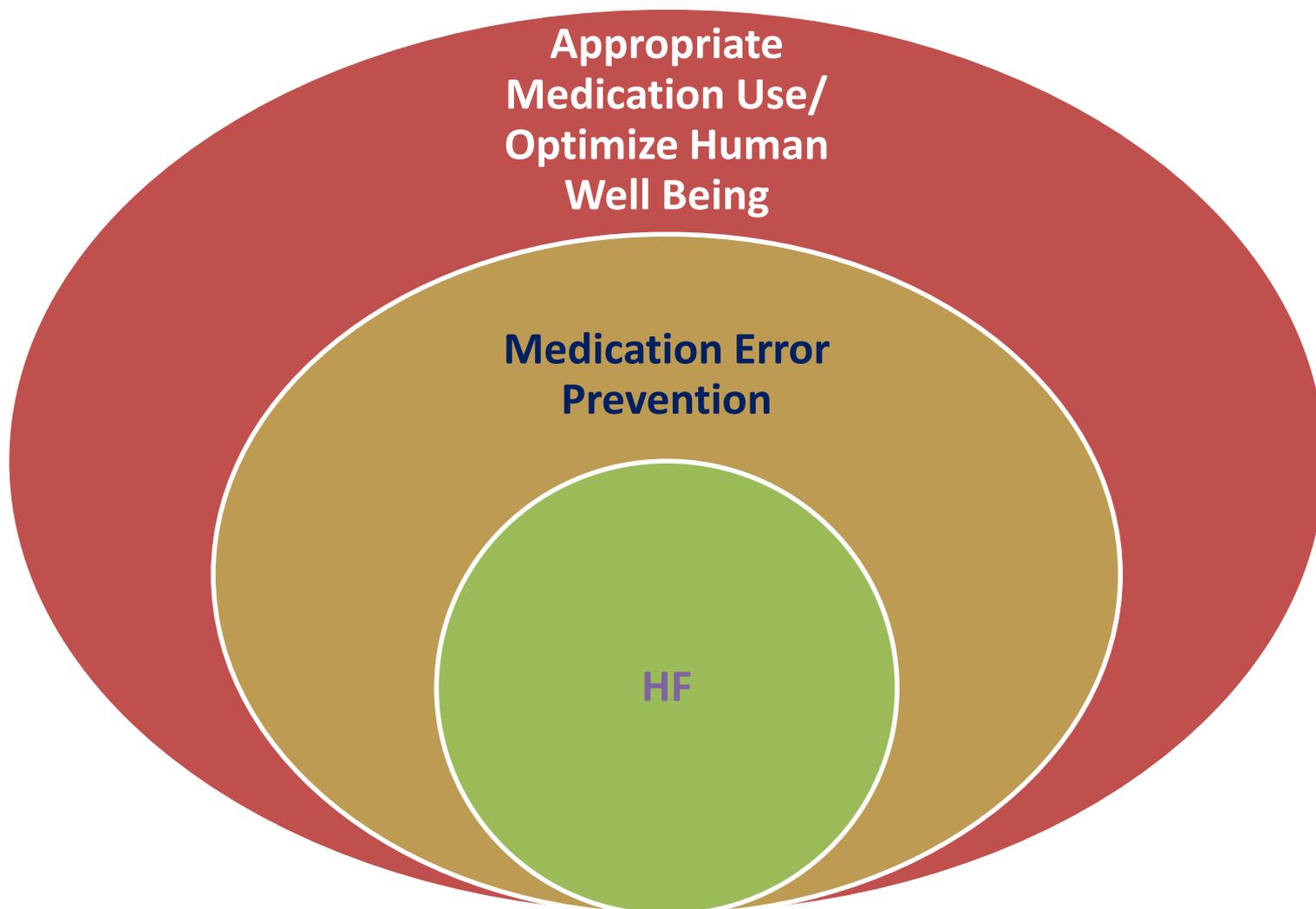
Figure 1: Relationship between medication errors and ADEs



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

National Coordinating Council for Medication Error Reporting and Prevention. Available at: [www.nccmerp.org](http://www.nccmerp.org). Accessed 12/30/2014

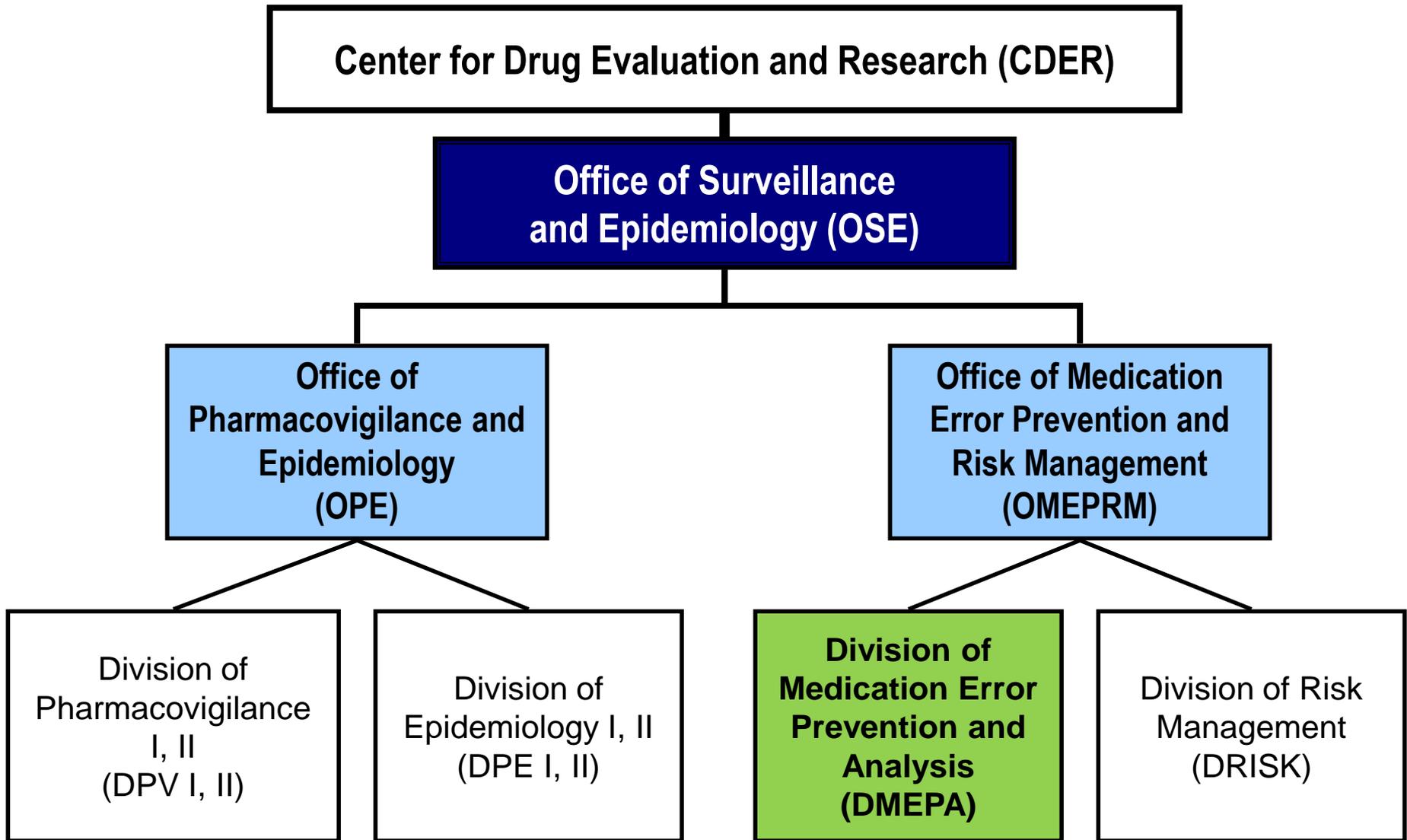
# Medication Error Prevention and HF



# 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





# 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





# HF Evaluation of Drug, Biologic, and Combination Products in CDER

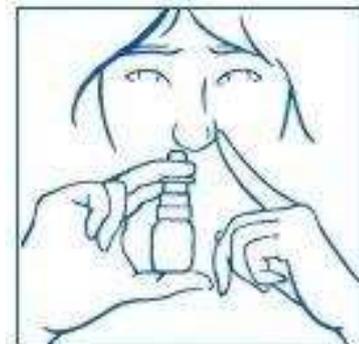
DMEPA leads review of human factors submissions (e.g., protocols, study reports, etc.) within CDER

- Evaluate HF submissions for drugs, biologics, and combination products regulated by CDER
- OSE/DMEPA will identify the need for and issue inter-center consults to the CDRH Human Factors Team as needed
- OSE/DMEPA consults Patient Labeling Team in the CDER's Office of Medical Policy for review of Instructions for Use (IFU) for laypersons in the IND phase

# What Am I?

Combination Product

Not a Combination Product



# 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))

# Where Do I Go?

**Primary mode of action** is the statutory criterion FDA must use to determine **the agency component with primary jurisdiction** for the review and regulation of a combination product: 21 CFR 3.2(k) and (m).



21 U.S.C. § 503(g)



# Primary Mode of Action (PMOA)

Primary mode of action is the **single mode** of action of a combination product that provides the most important therapeutic action of the combination product. The most important therapeutic action is the **mode of action expected to make the greatest contribution** to the overall intended therapeutic effects of the combination product.

21 CFR 3.2(m)

# 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

**interface** to ensure safe and effective use

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.**

# Your User Interface (UI)\* is Not Just the Device

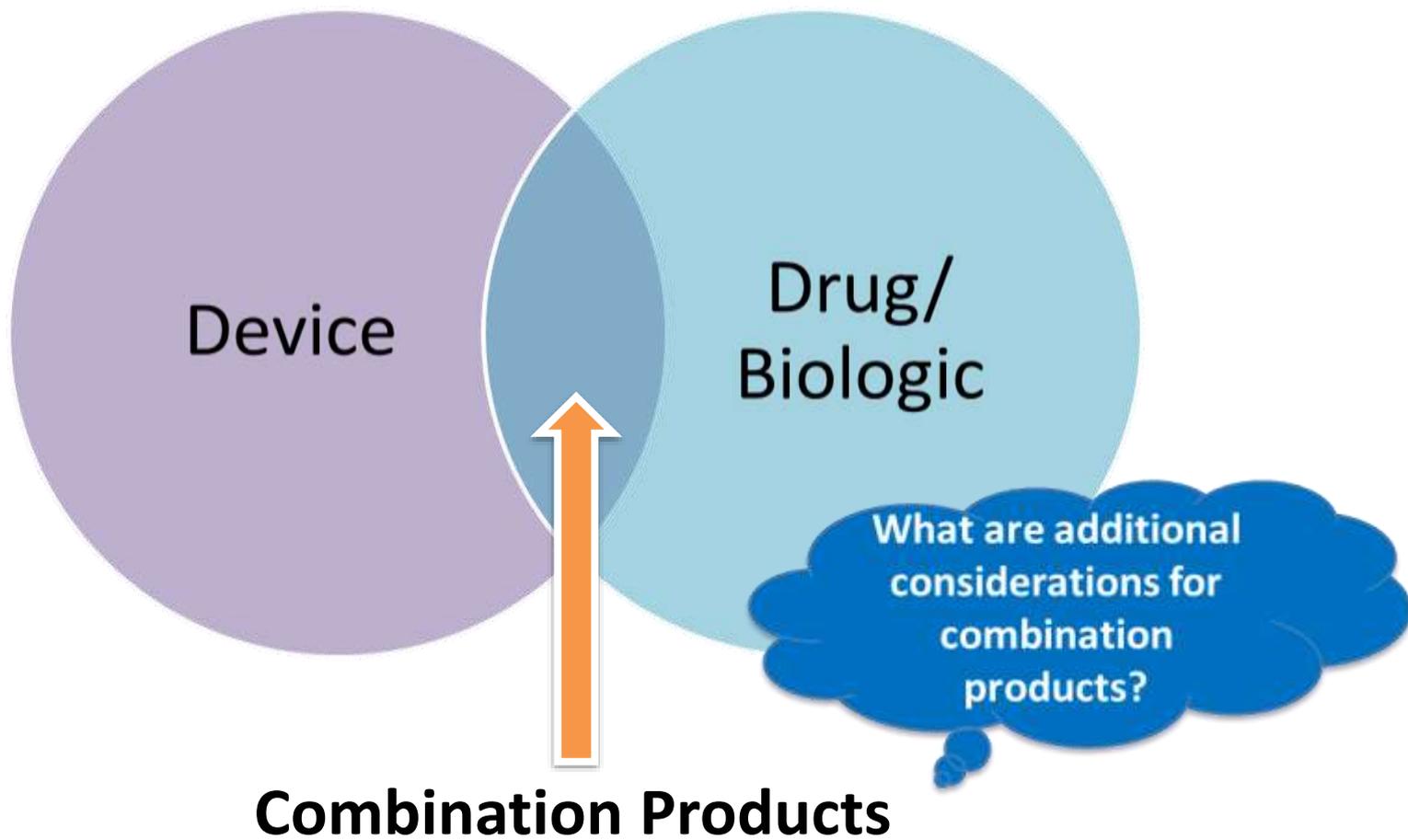
User interface: includes all points of interaction between the product and the user(s) including elements such as displays, controls, packaging, product labels, instructions for use, etc.

E.g.,

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



# We Look at the Entire Product



# Case Study #1

- Drug ABC is already approved on the market in a single-dose vial for use by healthcare providers
- Sponsor X wants to introduce a prefilled syringe presentation for drug ABC intended for use by **laypersons for at-home use**
- What should Sponsor X be thinking about???

Is the product's presentation and its user interface safe and effective for the **intended users, uses, and use environments?**

# Case Study # 1

## Some Considerations for Sponsor X

- Dosing:
  - What is the dose for Drug ABC?
  - Is the product single-dose where users administer the entire contents?
  - Would users need more than one syringe to administer intended dose?
- Intended user group(s):
  - Is the indicated population naïve to prefilled syringes?
- Design of prefilled syringe user interface:
  - Is there anything about the user interface that makes this product unique?

# Case Study # 1: What if...



The dosing for Drug ABC  
was weight-based?



# Case Study # 1: What if...

Drug ABC was for emergency use and users needed to assemble the syringe (i.e., attach the needle to the body of the syringe) prior to administration?



# Case Study # 1:

## Some Considerations for Sponsor X

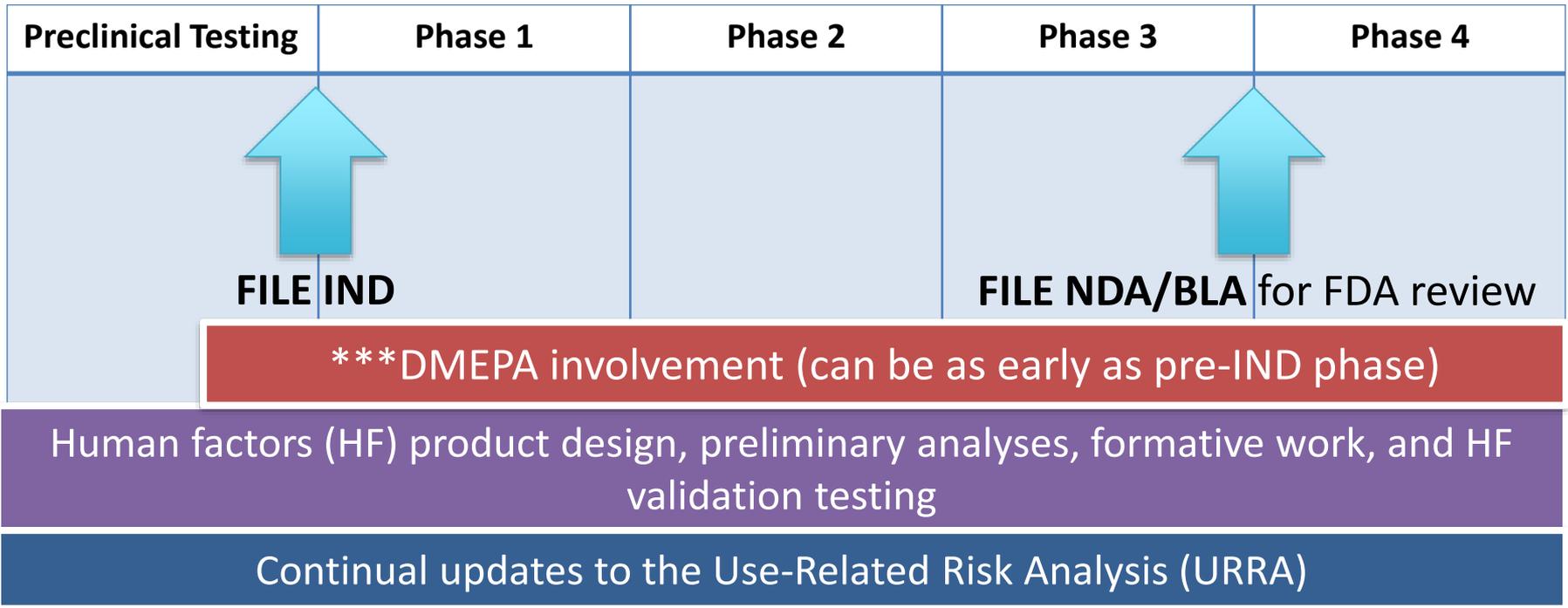
### Drug ABC was weight-based?

- Specific instructions to calculate doses?
- Are there graduation marks on prefilled syringe? Are increments appropriate to achieve required doses?
- Does dosing require users to expel drug out of syringe to achieve required dose?
- Is indicated population naïve to prefilled syringes?

### Drug ABC was for emergency use and required pre-assembly?

- Design of the product user interface: is product assembly feasible during an emergency situation?
- Is indicated population naïve to prefilled syringes?

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



# CDER Regulatory Approval Pathways & Human Factors Considerations



	New Drug	Generic	Biosimilar	Interchangeable
<b>Regulatory Pathway(s)</b>	505(b)(1), 505 (b)(2), 351(a)	505(j)	351(k)	351(k)(4)
<b>Application Type(s)</b>	NDA's, and BLA's	ANDA's	BLA's	BLA's
<b>Related Human Factors Guidance for Industry</b>	<a href="#">Draft Guidance for Industry and FDA Staff: Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development</a>  Released February 2016	<a href="#">Draft Guidance for Industry: Comparative Analyses and Related Comparative Use HF studies for a Drug-Device Combination Product Submitted in an ANDA</a>  Released January 2017	<a href="#">Draft Guidance for Industry and FDA Staff: Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development</a>  Released February 2016	<a href="#">Draft Guidance for Industry: Considerations in Demonstrating Interchangeability with a Reference Product</a>  Released January 2017

# Update to 356h Form

22. Submission Sub-Type <input type="checkbox"/> Presubmission <input type="checkbox"/> Amendment <input type="checkbox"/> Initial Submission <input type="checkbox"/> Resubmission	23. If a supplement, identify the appropriate category. <input type="checkbox"/> CBE <input type="checkbox"/> Prior Approval (PA) <input type="checkbox"/> CBE-30
24. Does this submission contain: <i>Only Pediatric data?</i> <input type="checkbox"/> Yes <input type="checkbox"/> No         Human Factors information? <input type="checkbox"/> Yes <input type="checkbox"/> No	
25. Reasons for Submission	



If the submission contains Human Factors (HF) information, select ‘Yes.’ HF information may include a study protocol, results report, use-related risk analysis, or justification for no HF validation study.

# Update to 1571 Form

Check “other” if you have a use-related risk analysis, HF results report, etc.

11. This submission contains the following *(Select all that apply)*

<input type="checkbox"/> Initial Investigational New Drug Application (IND)	<input type="checkbox"/> Response to Clinical Hold	<input type="checkbox"/> Response To FDA Request For Information
<input type="checkbox"/> Request For Reactivation Or Reinstatement	<input type="checkbox"/> Annual Report	<input type="checkbox"/> General Correspondence
<input type="checkbox"/> Development Safety Update Report (DSUR)	<input type="checkbox"/> Other <i>(Specify)</i> : _____	

<b>Protocol Amendment(s)</b>		<b>Information Amendment(s)</b>		<b>Request for</b>	<b>IND Safety Report(s)</b>
<input type="checkbox"/> New Protocol	<input type="checkbox"/> Human Factors Protocol	<input type="checkbox"/> Chemistry/Microbiology	<input type="checkbox"/> Clinical/Safety	<input type="checkbox"/> Meeting	<input type="checkbox"/> Initial Written Report
<input type="checkbox"/> Change in Protocol		<input type="checkbox"/> Pharmacology/Toxicology	<input type="checkbox"/> Statistics	<input type="checkbox"/> Proprietary Name Review	<input type="checkbox"/> Follow-up to a Written Report
<input type="checkbox"/> New Investigator		<input type="checkbox"/> Clinical Pharmacology		<input type="checkbox"/> Special Protocol Assessment	
<input type="checkbox"/> PMR/PMC Protocol				<input type="checkbox"/> Formal Dispute Resolution	

Check here if you have a protocol for a HF validation study

A large green ribbon graphic with a central rectangular box containing the text "FDA Resources". The ribbon has a 3D effect with shadows on the bottom and sides.

# FDA Resources

# FDA Guidance Timeline

Year	Title	Description
2000	Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management	<ul style="list-style-type: none"> <li>• First HF guidance from FDA</li> <li>• Focused on applying Human Factors Engineering as an <b>essential component of risk management</b></li> <li>• Introduced use error as a source of risk largely separate from device reliability</li> </ul>
2011	Draft Guidance: Applying Human Factors and Usability Engineering to Optimize Medical Device Design	<ul style="list-style-type: none"> <li>• Provides a structure for the manufacturer's HF reporting</li> <li>• Evaluation focused on risk priority of user tasks</li> <li>• Continues to treat use error as separate risk from device failure risks</li> </ul>

# FDA Guidance Timeline

Year	Title	Description
2012	Draft Guidance for Industry: Safety Considerations for Product Design To Minimize Medication Errors	<ul style="list-style-type: none"> <li>• 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</li> <li>• Underscores importance of evaluating the product design using proactive risk assessments before finalizing the design</li> <li>• Recommendations based on postmarket safety information</li> <li>• Discusses concepts of simulated use testing</li> </ul>

# FDA Guidance Timeline

Year	Title	Description
2013	Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors	<ul style="list-style-type: none"><li>• Focused on safety aspects of the container label and carton labeling design</li><li>• Provides a set of principles to promote safe dispensing, administration, and use of products</li><li>• Reinforces importance of evaluating design using proactive risk assessments before finalizing the design</li><li>• Recommendations based on postmarket safety information</li></ul>

# FDA Guidance Timeline

Year	Title	Description
2016	Draft Guidance for Industry and FDA Staff: Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development	<ul style="list-style-type: none"> <li>• First HF guidance from FDA focused on combination product development</li> <li>• Provides recommendations regarding HF data needs in investigational and marketing applications</li> <li>• Describes how HF studies relate to other clinical studies</li> </ul>
2016	Applying Human Factors and Usability Engineering to Medical Devices	<ul style="list-style-type: none"> <li>• Finalized the June 2011 draft guidance</li> <li>• Supersedes “Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management” issued in 2000</li> </ul>
2016	Safety Considerations for Product Design To Minimize Medication Errors	<ul style="list-style-type: none"> <li>• Finalized the December 2012 draft guidance</li> </ul>

# FDA Guidance Timeline

Year	Title	Description
2017	Draft Guidance for Industry: Considerations in Demonstrating Interchangeability with a Reference Product	<ul style="list-style-type: none"> <li>• First guidance developed by FDA to include the concept of comparative analyses (threshold analyses) and comparative use HF studies</li> <li>• Considerations for the design and analysis of a switching study or studies to support a demonstration of interchangeability; considerations for development of presentations</li> </ul>
2017	Draft Guidance for Industry: Comparative Analyses and Related Comparative Use HF studies for a Drug-Device Combination Product Submitted in an ANDA	<ul style="list-style-type: none"> <li>• Leveraged the framework developed for the Draft Guidance for Industry: Considerations in Demonstrating Interchangeability with a Reference Product</li> <li>• Focused on analysis of the proposed user interface, but not intended to address all information necessary to support approval of a generic combination product</li> <li>• Provide clarity on FDA's expectations for the user interface of a generic drug-device combination product when compared to its RLD</li> </ul>

# Additional Information

- Guidance for Industry and FDA Staff – Applying Human Factors and Usability Engineering to Optimize Medical Device Design:  
[www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm259748.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm259748.htm)
- Draft Guidance for Industry – Safety Considerations for Product Design to Minimize Medication Errors:  
[www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM331810.pdf](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM331810.pdf)
- Draft Guidance for Industry – Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors:  
[www.fda.gov/downloads/drugs/guidancecomplianceinformation/guidances/ucm349009.pdf](http://www.fda.gov/downloads/drugs/guidancecomplianceinformation/guidances/ucm349009.pdf)
- Guidance for Industry – Label Comprehension Studies for Nonprescription Drug Products:  
[www.fda.gov/downloads/drugs/guidancecomplianceinformation/guidances/ucm143834.pdf](http://www.fda.gov/downloads/drugs/guidancecomplianceinformation/guidances/ucm143834.pdf)



# Additional Information

- Draft Guidance for Industry – Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development:  
[www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM484345.pdf](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM484345.pdf)
- Guidance for Industry – Formal Meetings Between FDA and Sponsors or Applicants:  
[www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm153222.pdf](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm153222.pdf)
- Guidance for Industry and FDA Staff – Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff:  
[www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf](http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf)

# Questions



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# Your Call To Action

- HF research can be used to inform review of medical product applications.
- HF is not just a check box at the end of development, incorporate HF principles throughout product development.
- Use available resources to meet with FDA and to engage with FDA as early as possible.

