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

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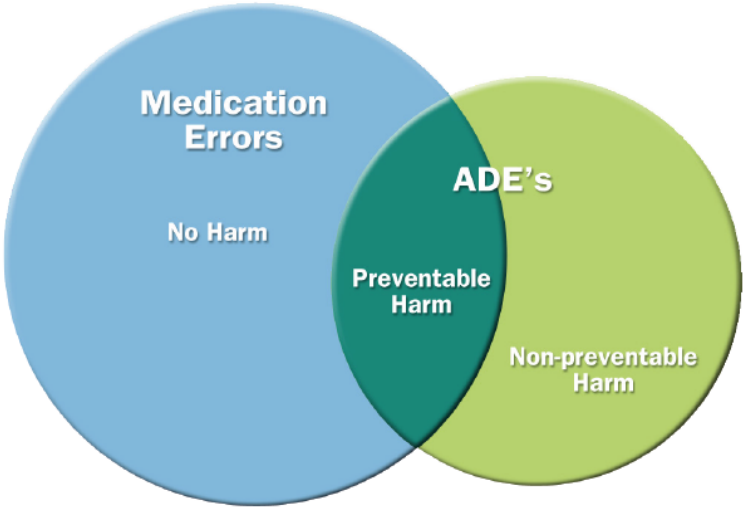
What is a Medication Error?

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



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

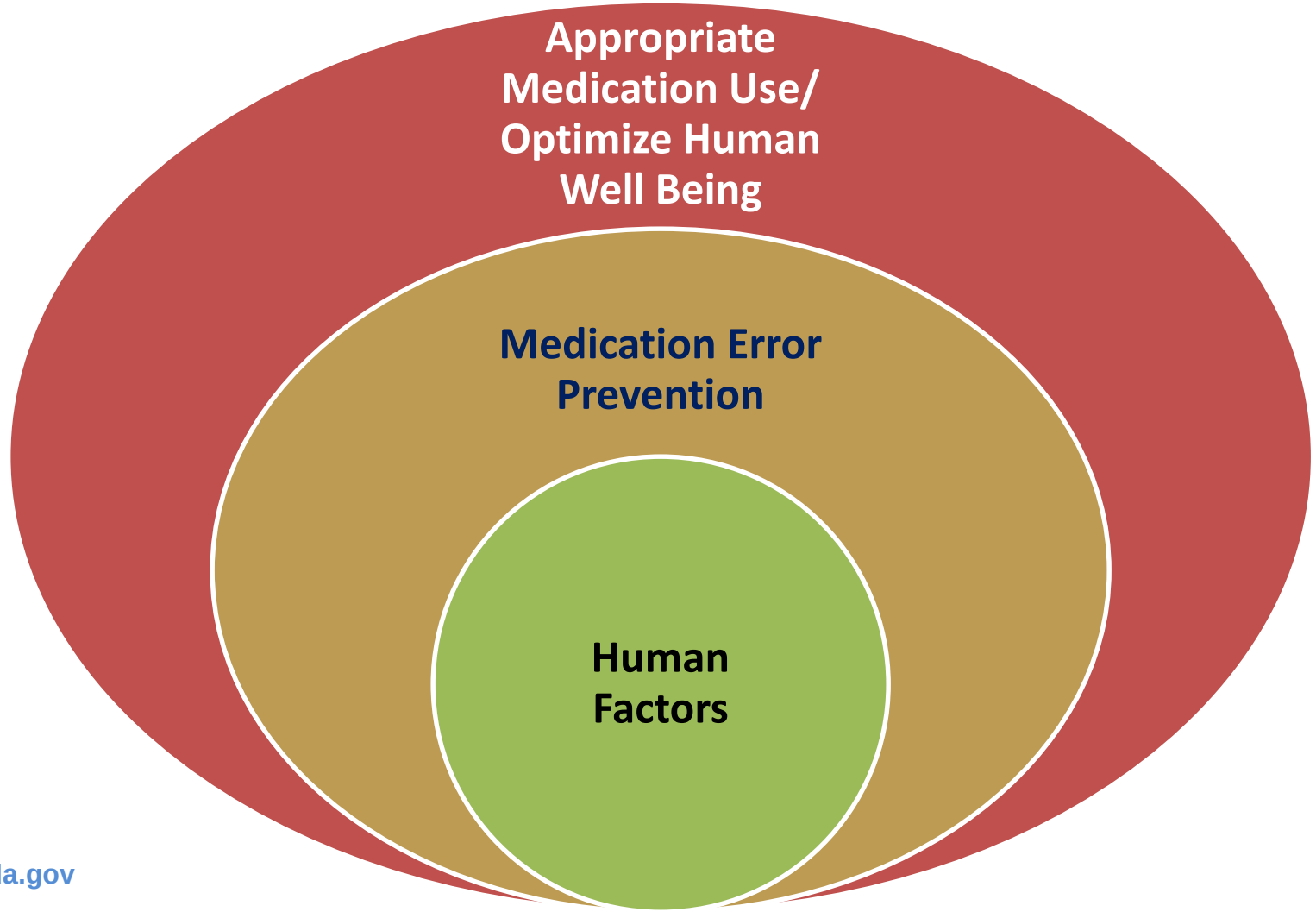
National Coordinating Council for Medication Error Reporting and Prevention. Available at: www.nccmerp.org. Accessed 12/30/2014

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)

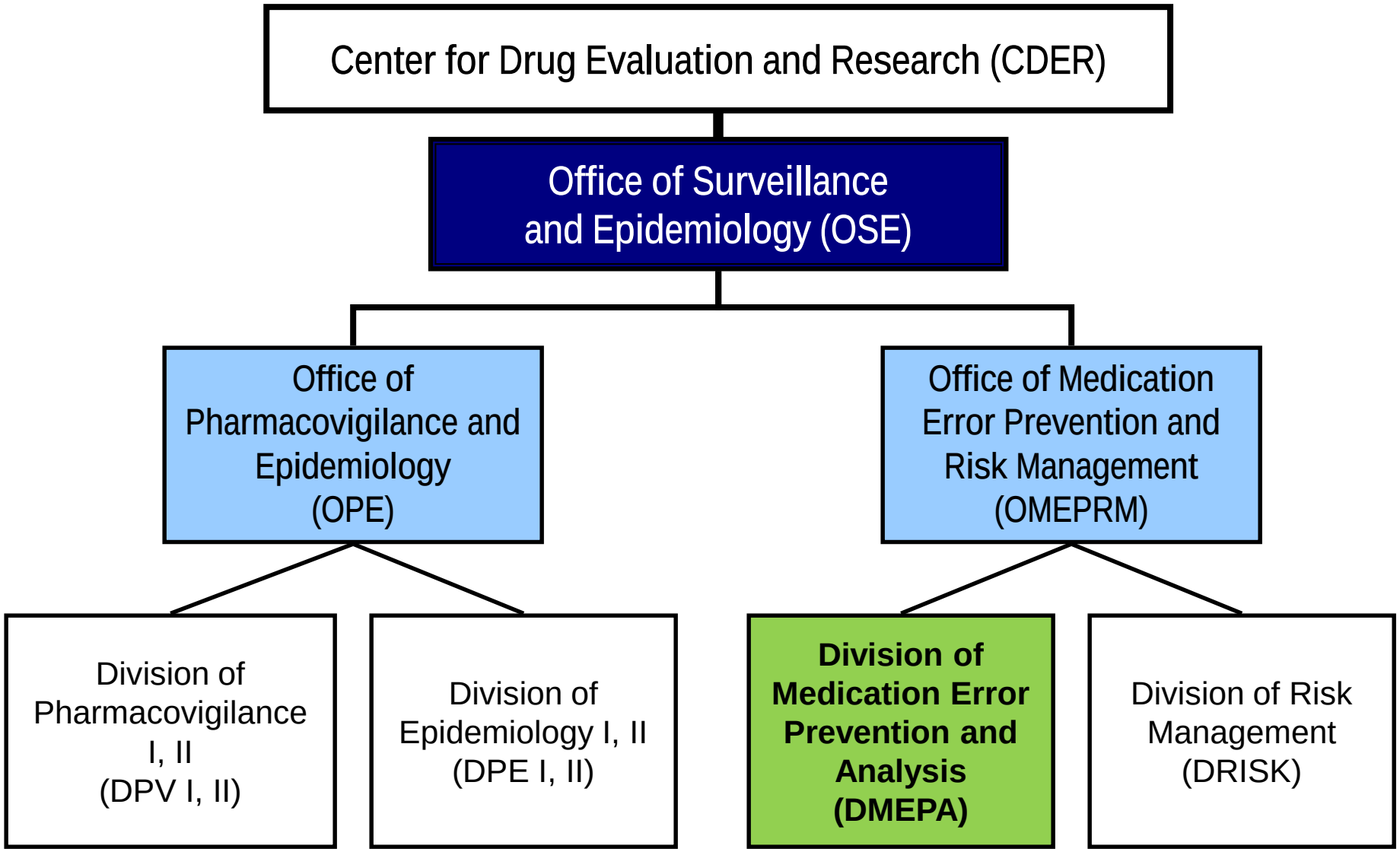
Medication Error Prevention and HF



Who Looks at Medication Errors?

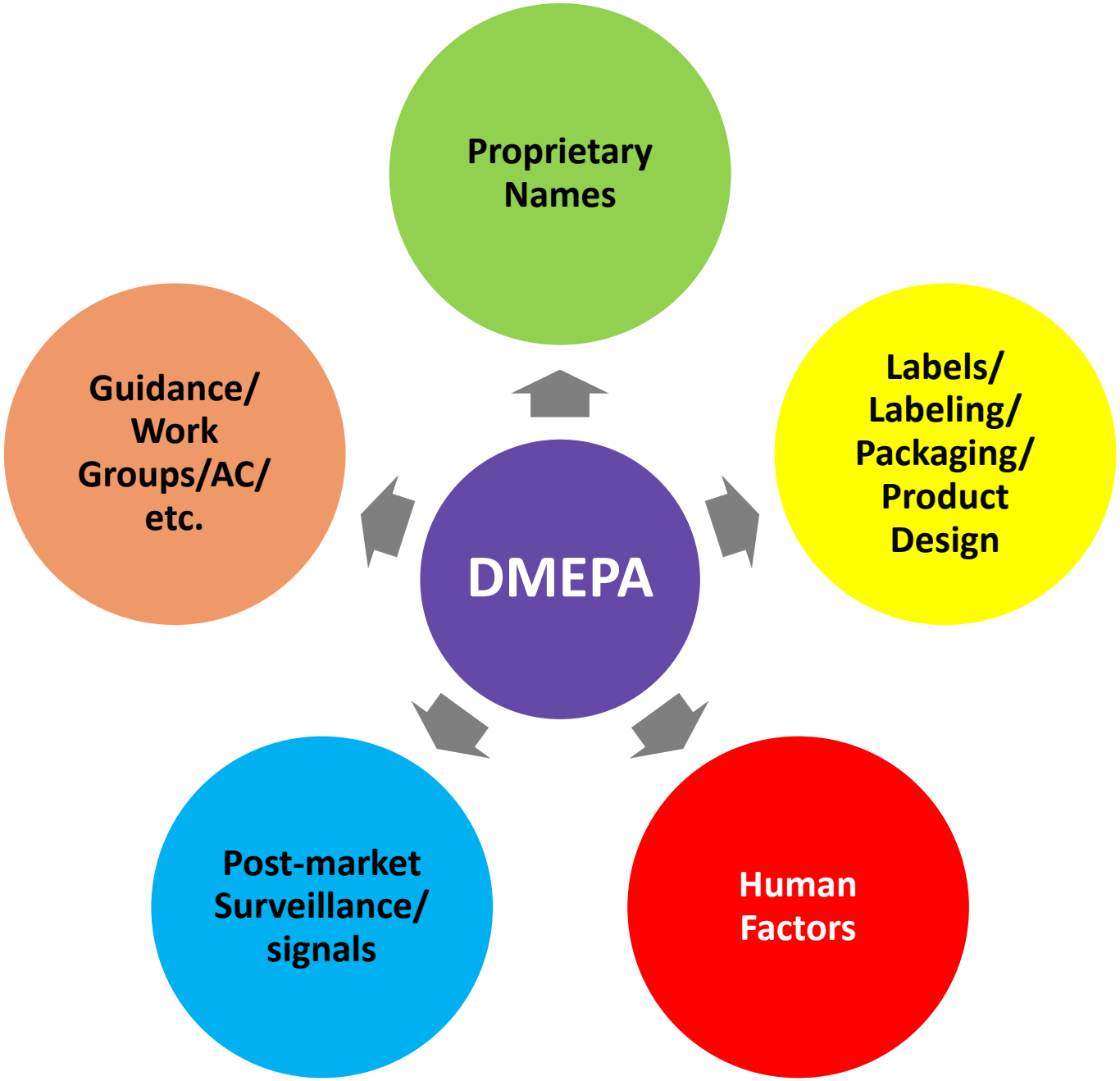
Division of Medication Error Prevention and Analysis (DMEPA)

- 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

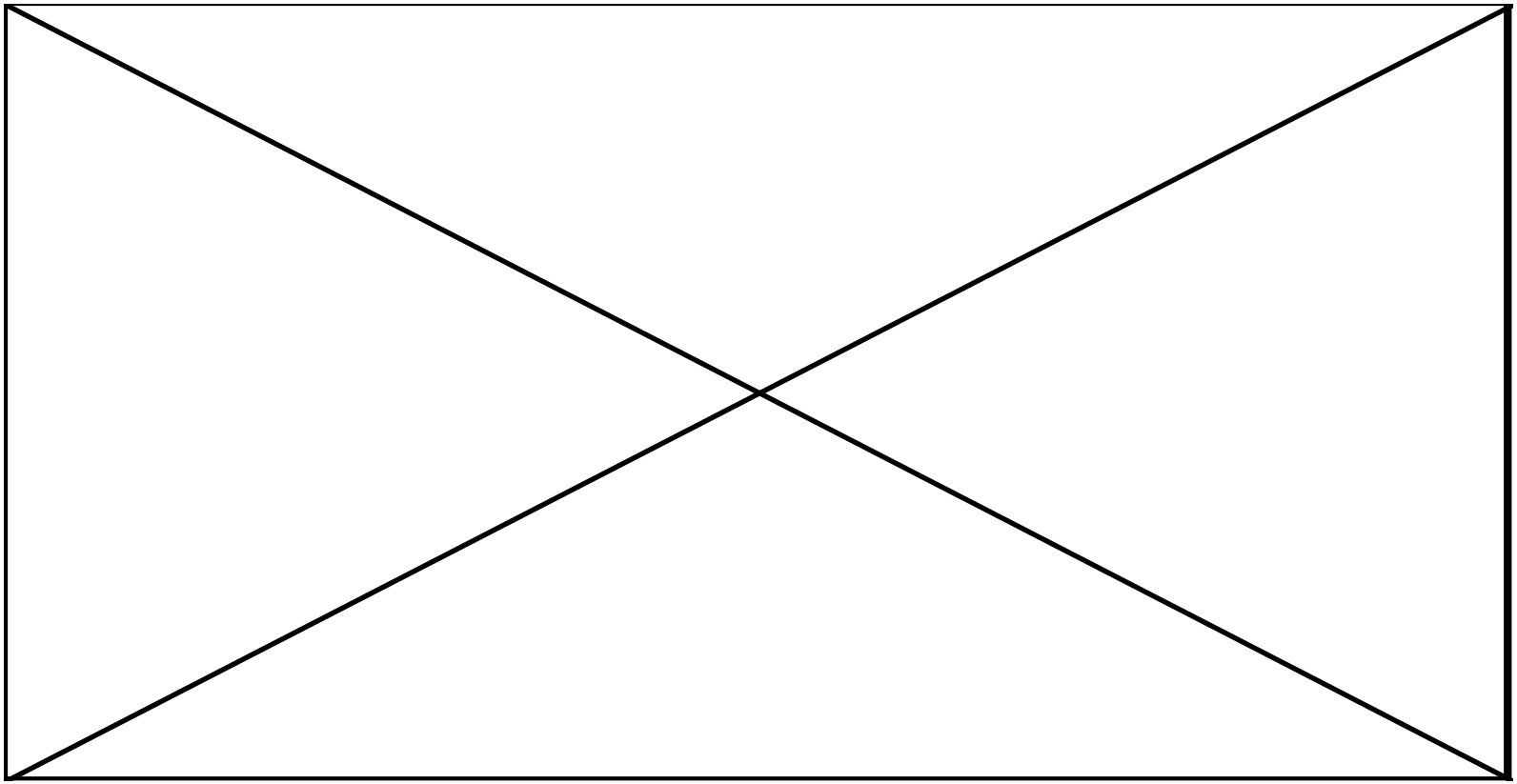

Center for Drug Evaluation and Research (CDER)
Office of Surveillance and Epidemiology (OSE)
Office of Pharmacovigilance and Epidemiology (OPE)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Division of Pharmacovigilance I, II (DPV I, II)
Division of Epidemiology I, II (DPE I, II)
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


Proprietary Names
Labels/ Labeling/ Packaging/ Product Design
Human Factors
Post-market Surveillance/ signals
Guidance/ Work Groups/AC/ etc.
DMEPA

“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

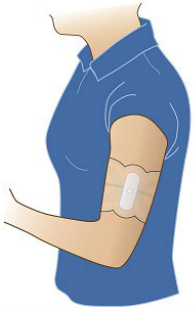
- Formal Definition in 21 CFR 3.2:
  - Therapeutic and diagnostic products
  - Combine >1: drugs, devices, biological products
- They can be:
  - Physically or chemically combined (21 CFR 3.2(e)(1))
  - Co-packaged in a kit (21 CFR 3.2(e)(2))
  - Separate, cross-labeled products (21 CFR 3.2(e)(3) or (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

effective use

Drug:

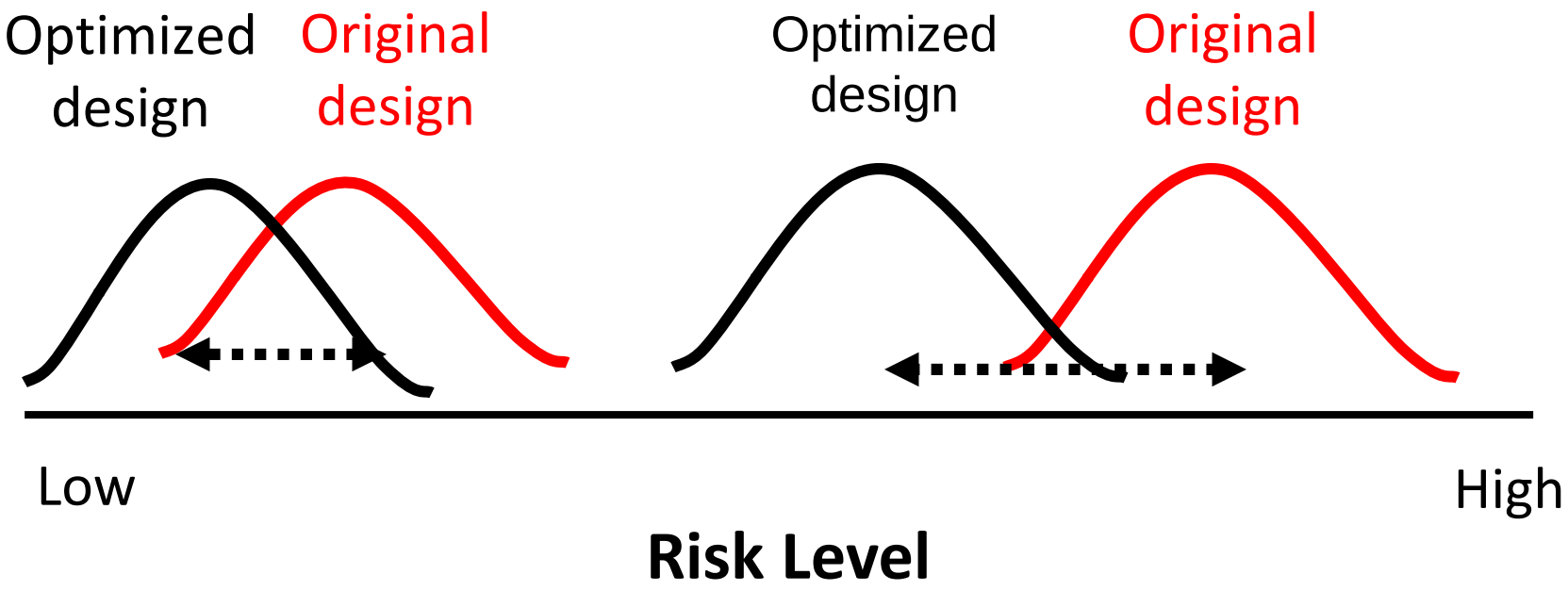
- Kefauver-Harris Amendment to the 1938 Food, Drug and Cosmetic Act

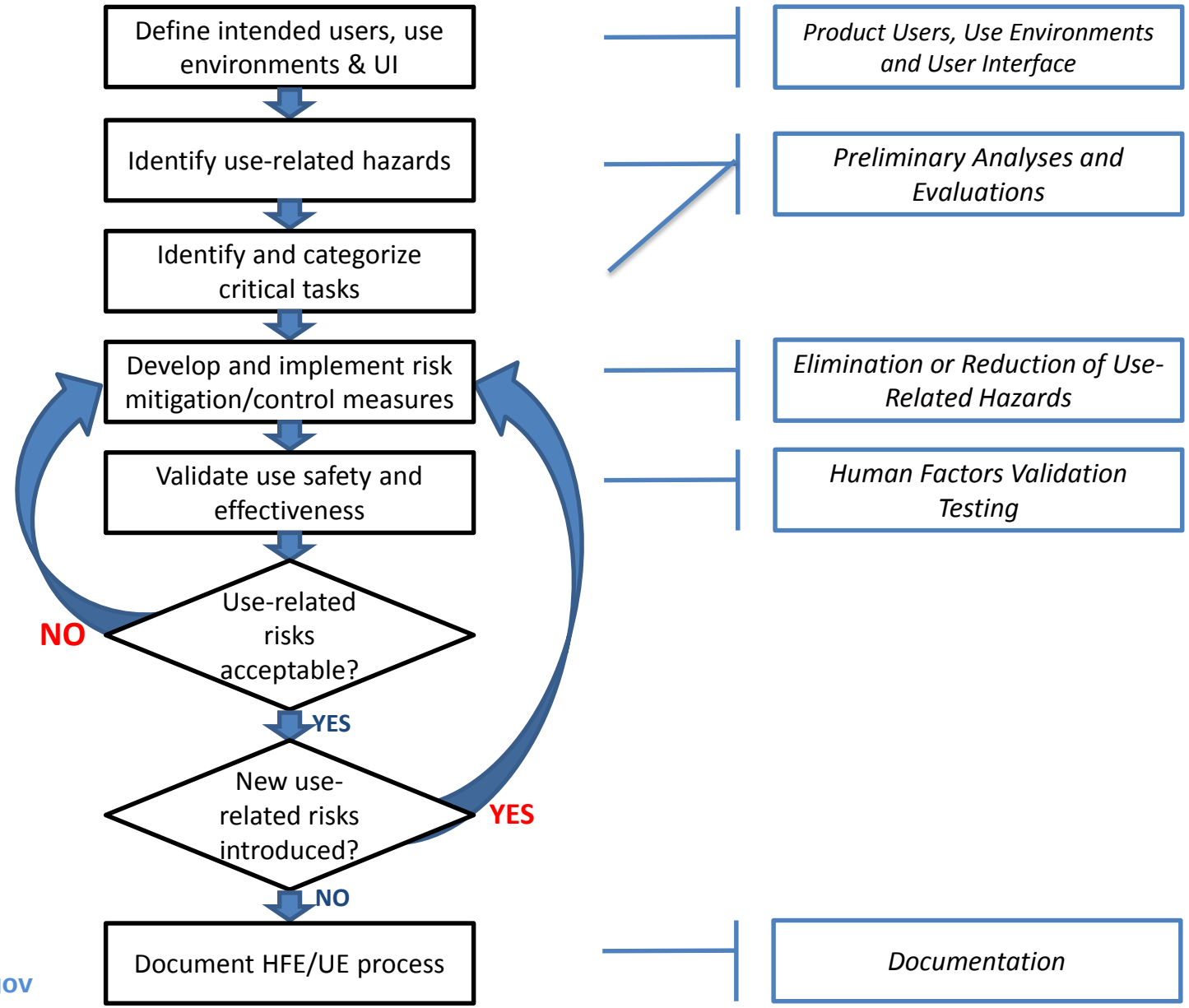
HF studies may be needed to demonstrate elimination/minimization of use-related hazards and medication errors

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

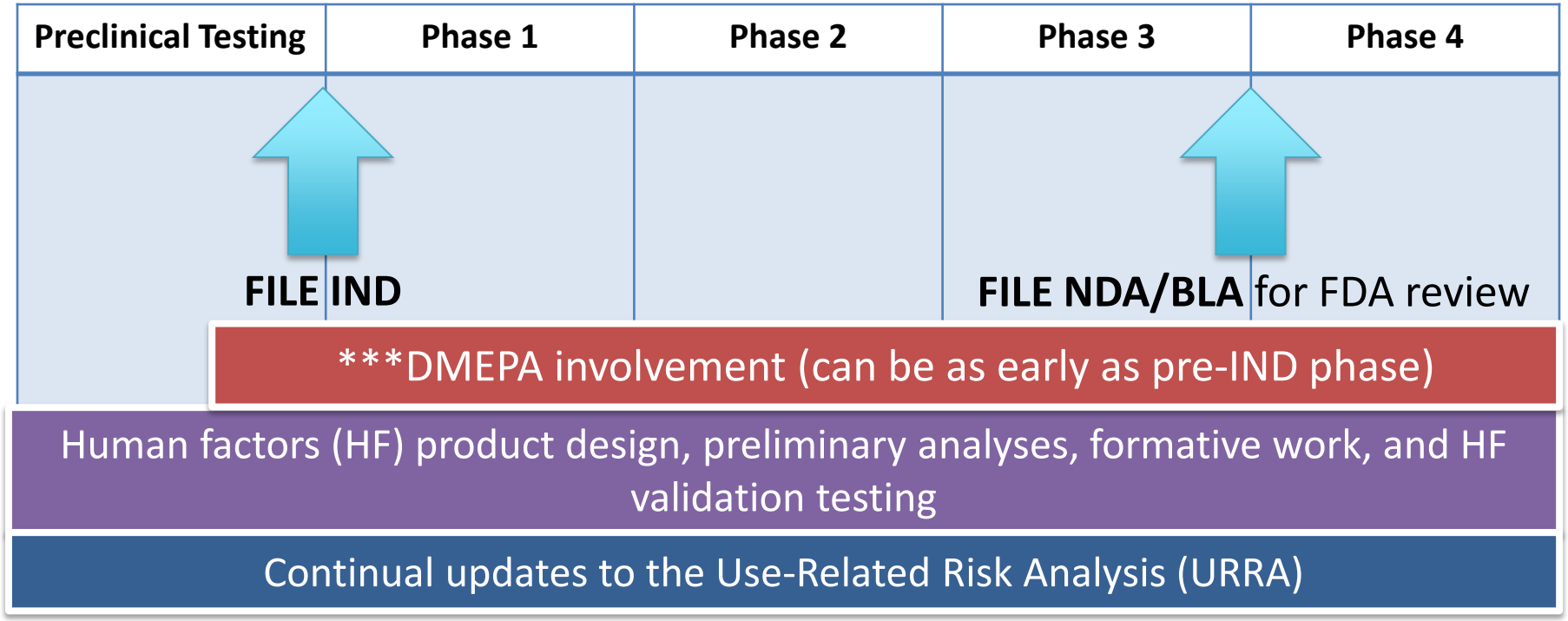



Define intended users, use environments & UI
Identify use-related hazards
Identify and categorize critical tasks
Develop and implement risk mitigation/control measures
Validate use safety and effectiveness
Use-related risks acceptable?
NO
YES
New use-related risks introduced?
YES
NO
Document HFE/UE process
Product Users, Use Environments and User Interface
Preliminary Analyses and Evaluations
Elimination or Reduction of Use-Related Hazards
Human Factors Validation Testing
Documentation

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



CDER Regulatory Approval Pathways & Human Factors Considerations

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

FDA Resources

FDA Guidance Timeline

Year	Title	Description
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

Year	Title	Description
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

FDA Guidance Timeline

Year	Title	Description
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

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	• 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

FDA Guidance Timeline

Year	Title	Description
2017	Draft Guidance for Industry: Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA	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
2017	Draft Guidance for Industry: Considerations in Demonstrating Interchangeability With a Reference Product	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))

Partnership

FDA

Industry

Better Outcomes for Patients

Questions

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