Human Factors Considerations for Combination Products

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Overview

- Introduction to combination products
- Combination product use errors
- Introduction to human factors and new FDA draft HF guidance document
- FDA review process for combination products

Combination Products

- **Formal Definition in 21 CFR 3.2(e):**
  - *Therapeutic and diagnostic products*
  - *Combine >1: drugs, devices, biological products*
- **Involve multiple FDA Centers, e.g.:**
  - Center for Biologics Evaluation and Research (CBER)
  - Center for Drug Evaluation and Research (CDER)
  - Center for Devices and Radiological Health (CDRH)
- **Raise many regulatory, policy, and review management challenges**

Combination Product Examples

- Prefilled Syringes
- Pen Injectors, Autoinjectors
- Pharmaceutical Aerosol Delivery Devices/Inhalation Products
- Transdermal Delivery Systems/Patches

Human Factors and Comb. Products

- **Unlike other medication dosage forms, combination products *require user interaction***
- **Combination products are unique in that their safety profile and product efficacy *depends on user interaction***

Comb. Product Use Errors (1 of 6)

Drug route of administration confusion caused by product container

- Oral or topical drug products packaged in injectable vial containers
- Products that require dilution prior to administration packaged in containers that afford direct administration
- Oral inhalation drug products packaged in capsules
- Topical products in packages that look similar to ones used for oral, nasal, eye, or ear products

Comb. Product Use Errors (2 of 6)

Dosing devices

- **Inappropriate device for the drug product**
  - Related to drug viscosity, dosing, or patient population
- **Use errors due to unit of measure confusion**
  - Units were inconsistent with the dosing directions
  - Units were abbreviated or values had trailing zeros
  - Device markings were uncommon for the device type
  - Device markings were illegible, or were obscured when the drug product was added to the device
  - The device was not able to measure all possible doses

Comb. Product Use Errors (3 of 6)

Pen injectors and autoinjectors

- **Inadequate product differentiation**
  - Within a product line or across similar products
- **Unusual or unexpected device operation**
  - E.g., needle stick injuries due to user holding device upside-down
- **Confusing or complex device controls**
- **Electronic display legibility or message clarity**
  - E.g., font size and visual contrast
  - E.g., confusion from lack of preceding zeroes (.5 mg instead of 0.5 mg) or presence of trailing zeroes (5.0 mg instead of 5 mg)
- **User injury due to lack of protection against incorrect use**

Comb. Product Use Errors (4 of 6)

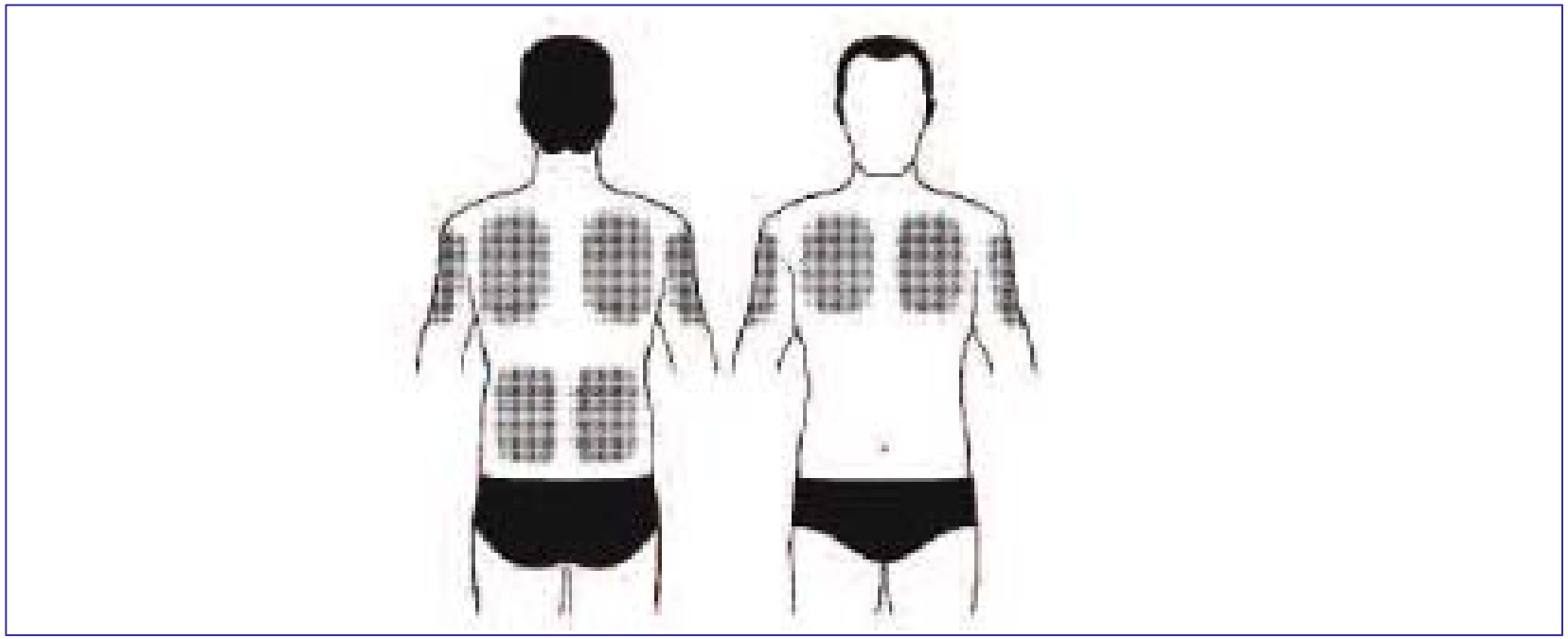
Transdermal Patch Products

- Where to apply?
- How many patches to apply?
- How to apply?
- How long to wear?
- What to do during activities of daily living: showering, swimming, exercise?
- What to do if patch falls off?
- How to remove?
- How and where to dispose?

Comb. Product Use Errors (5 of 6)

Transdermal Patch Products

- **Original user instructions: where to apply patch**

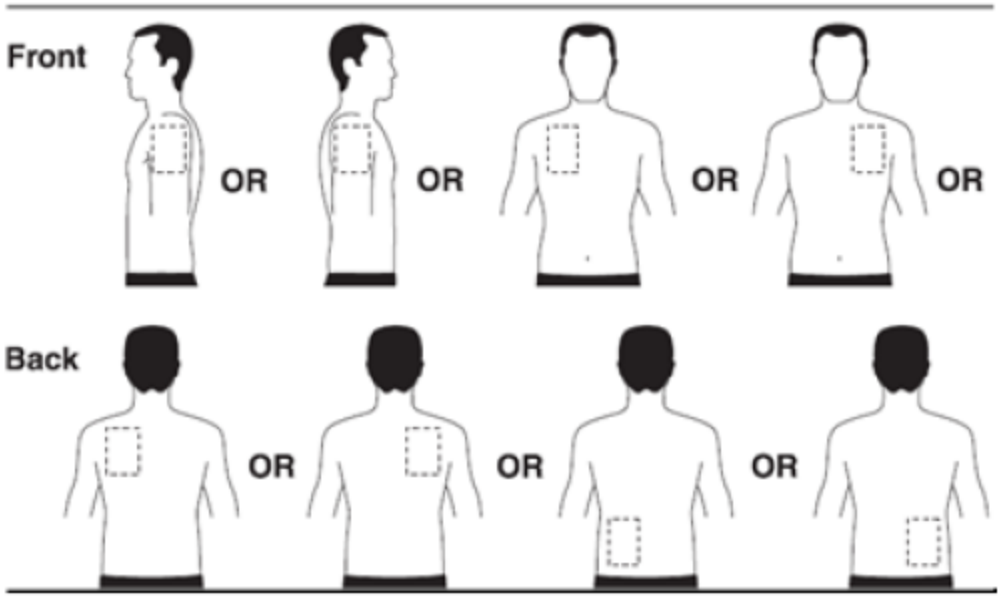


Comb. Product Use Errors (6 of 6)

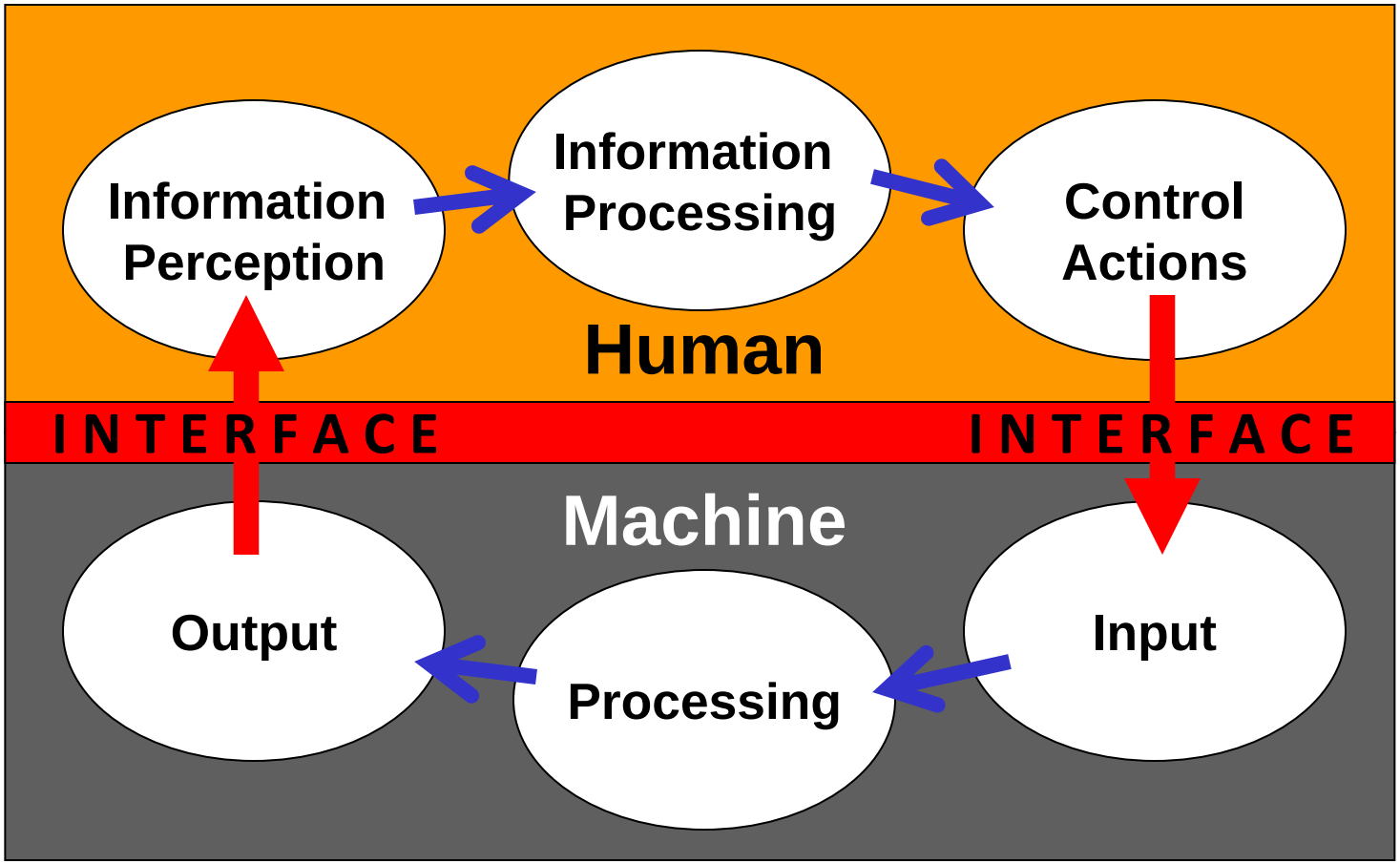
Transdermal Patch Products

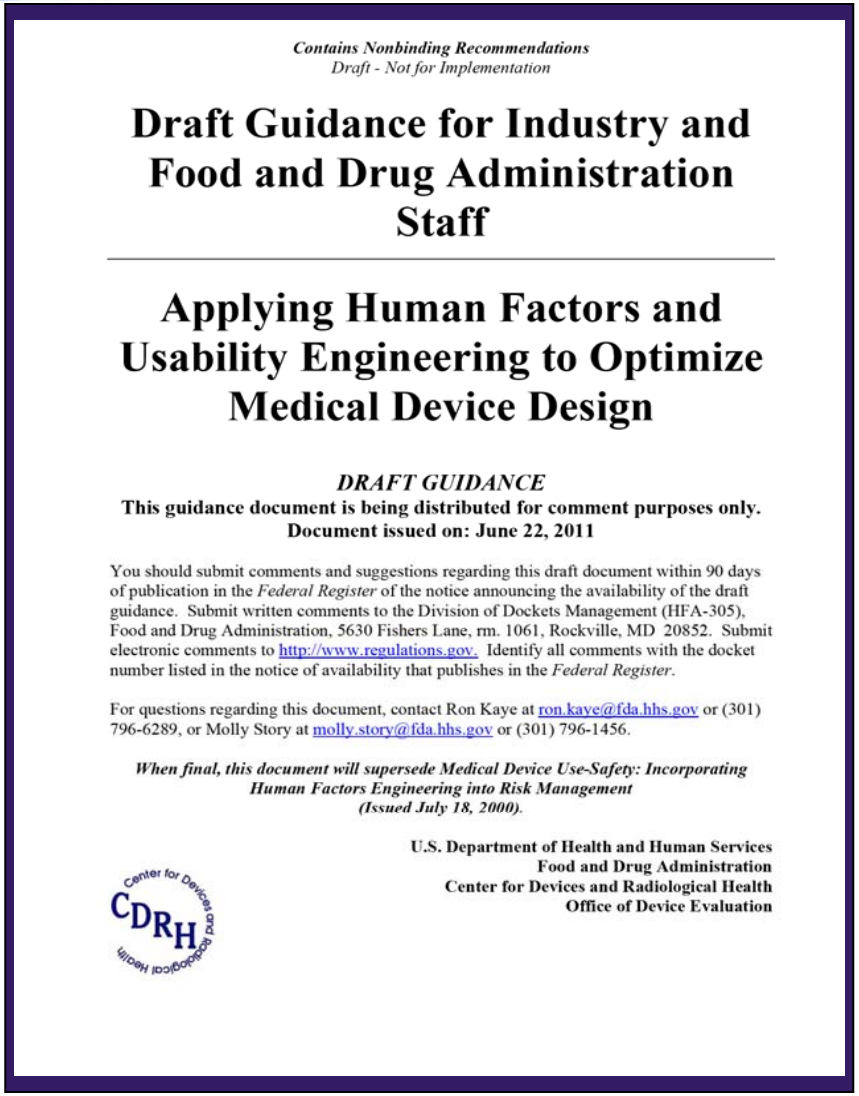
- **Revised user instructions: where to apply patch**

Figure A:
Apply one patch to ONLY ONE of the following possible sites each day.



Device-User Interface





Contains Nonbinding Recommendations
Draft - Not for Implementation

Draft Guidance for Industry and Food and Drug Administration Staff

Applying Human Factors and Usability Engineering to Optimize Medical Device Design

DRAFT GUIDANCE
This guidance document is being distributed for comment purposes only.
Document issued on: June 22, 2011

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact Ron Kaye at ron.kaye@fda.hhs.gov or (301) 796-6289, or Molly Story at molly.story@fda.hhs.gov or (301) 796-1456.

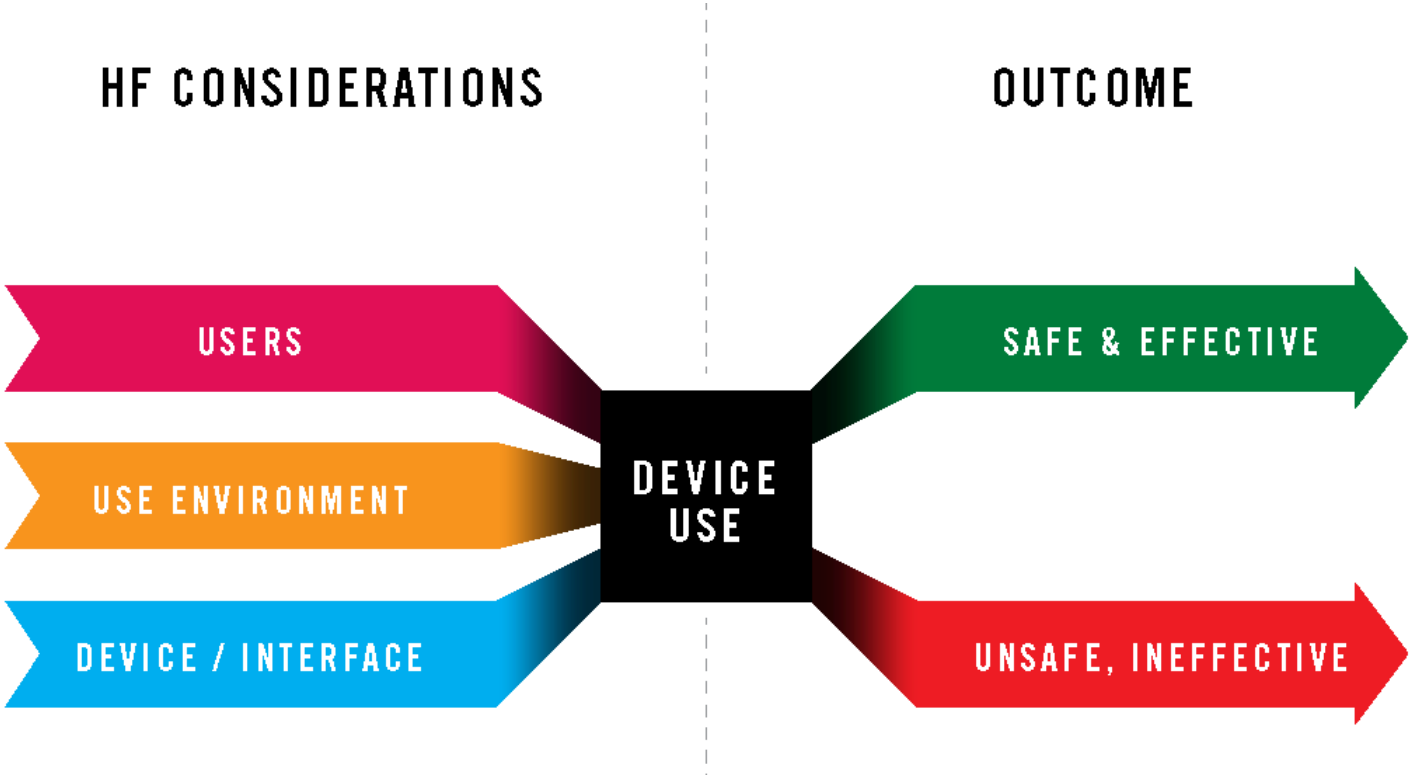
When final, this document will supersede Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management (Issued July 18, 2000).

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

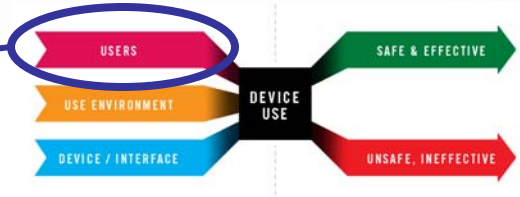
Draft Guidance: Major Sections

- Device Users, Use Environments and User Interfaces
- Preliminary Analysis Methods
- Formative Evaluations and Hazard Mitigation and Control
- Human Factors/Usability Validation

Human Factors of Device Use

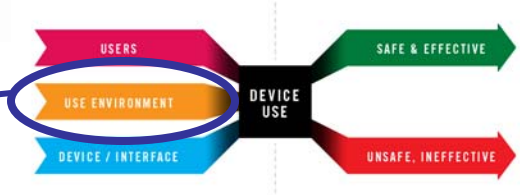


Users



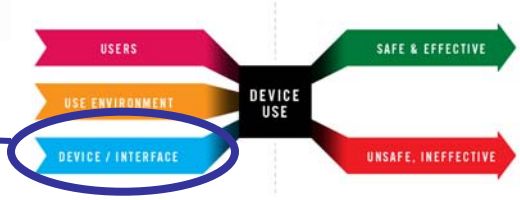
- **Professional or non-professional**
  - Job title and responsibilities
- **Knowledge and experience levels**
- **Age and functional capabilities**
  - Physical, sensory/perceptual, cognitive/intellectual
- **Mental and emotional condition**

Use Environment



- **Clinical environment**
  - Hospital, clinic, etc.
- **Transitional care environment**
  - Rehabilitation, assisted living, long-term care, etc.
- **Home environment**
  - House, mobile home, townhouse, apartment, etc.
- **Community setting**
  - Office, school, retail, outdoors, etc.
- **Mobile environment**
  - Car, plane, train, bus, ambulance, medevac, etc.

User Interface



- **Tasks**
  - Unpacking, assembly/set up
  - Use
  - Supply replenishment, maintenance, repair
- **Interactions**
  - **Input**
    - Knobs/dials, switches, buttons; connections
  - **Output**
    - Visual: displays, lights
    - Auditory: beeps, alerts/alarms, voice
    - Tactile: resistance, vibration, temperature

Preliminary Analyses

Two ways to discover use-related hazards:

1. **Apply analytical techniques**
   - Apply variety of techniques to identify use-related hazards and risks
     - *Can be difficult to anticipate all hazards*
2. **Conduct user-based evaluations**
   - Conduct hands-on testing to identify unanticipated hazards
     - *Sometimes called "Usability Testing" or "Use Testing" or "User Testing" or "Formative" Evaluations*

Formative Evaluations

- **While the device is still under development**
  - Include representative end users
  - Test simple product mock-ups or early prototypes
- **Done early in the design process**
  - At this stage use-related problems can be addressed more easily and less expensively
- **Best when performed iteratively**
  - Repeat until the device is optimized and ready for human factors/usability validation testing

Risk Mitigation

- **Develop a risk mitigation strategy**
  - Modify interface design, user instructions, and/or training to address the problems found
- **Re-test to demonstrate effectiveness of mitigation**
  - Not sufficient to simply state that the device will be modified or that mitigations will be implemented later
- **Residual risk is acceptable if discussed, reasonably limited, not capable of elimination or further reduction, and benefits outweigh it**

Human Factors/Usability Validation

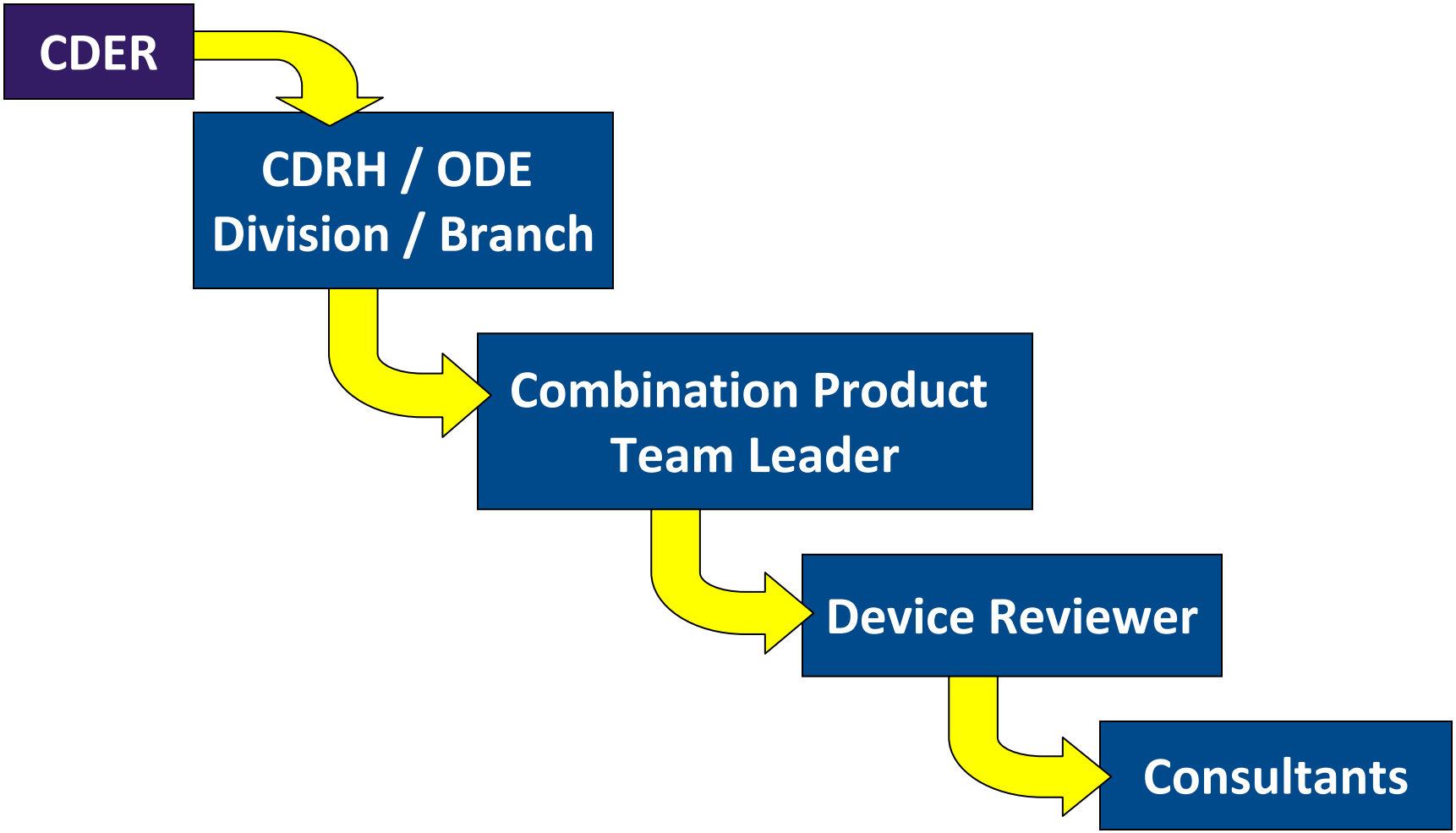
- **Demonstrates and provides evidence that a medical device, as designed, can be used safely and effectively:**
  - By representative intended users
  - Under realistic use conditions
  - For critical (high-risk) and essential tasks
- **Objective and subjective data:**
  - Use errors and failures are observed and recorded
  - User opinion and feedback is collected from users afterward, particularly related to any use problems

CDER Submission Review Team

- **Clinical, Clinical/Pharmacology, Pharmacology/Toxicology**
- **Statistics**
- **Office of New Drug Quality Assessment (ONDQA): Chemistry and Biopharmacology**
- **Division of Medication Errors Prevention and Analysis (DMEPA)**
  - Product naming, labeling, risk management

➢ ***Consult with CDRH on combination products***

CDRH/HF Process with CDER Lead



FDA Expectations for HF Data

- **Conduct a comprehensive risk assessment**
- **Identify and mitigate risks, including use-related**
- **Conduct human factors/usability validation testing on any strategies implemented to mitigate *significant* use-related risks**
  - Use representative users & realistic testing conditions
  - Fully describe testing protocols and results
  - Analyze and justify residual risks
- **Document everything in the Design History File**

Realistic Product Testing Conditions

- **Use finalized device design and labeling**
  - For drug delivery devices, use of placebo is acceptable
  - For injection systems, use of injection pad is acceptable
- **Identify other potential adverse use conditions**
- **Allow realistic interactions, as far as possible**
  - Provide participants with device as they would receive it (e.g., in its original packaging, with all documentation)
  - Allow participants to use the device as they normally would (e.g., without interference from test facilitator)
  - Observe user-device interactions; debrief participant

Selection of Tasks Tested

- **Task selection should be derived from results of an assessment of use-related hazards and risks**
- **Tasks tested do not necessarily include all tasks in the instructions**
  - Include *essential tasks* – i.e., tasks associated with basic product use (e.g., preparatory tasks before an injection)
  - Include *safety-critical tasks* – i.e., tasks that could lead to use errors or failures and have negative clinical impact
- **Include a rationale for your task selection in the study protocol and report**

Realistic Instructions and Training

- **Participant interaction with instructions and training:**
  - Decide: instructions or no instructions
  - Decide: users trained or untrained
- **Conduct separate studies on labeling and training prior to product validation:**
  - Assess the clarity and effectiveness of labeling (e.g., instructions for use, other documentation, packaging)
  - Determine level and nature of training necessary (if any)

Advice: Consult FDA Early

- **Discuss product development plans with FDA before your design is considered "final" (and changes would be difficult)**
  - Experts in CDRH, ONDQA, OND, and DMEPA may have advice to offer based on experience
- **FDA will review human factors/usability testing protocols on request**
  - *Before implementation is recommended!*

FDA Guidance on Human Factors

- Guidance (2000): ***Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management***: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm094460.htm.
- Draft guidance (2011): ***Applying Human Factors and Usability Engineering to Optimize Medical Device Design***: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm259748.htm.
  - *NOTE: This guidance is not yet in effect but it reflects FDA-CDRH's current thinking and approach to human factors.*

Acknowledgment and Questions

My thanks to:

- QuynhNhu Nguyen, FDA / CDRH / ODE / DAGID
- Carlos M. Mena-Grillasca, FDA / CDER / OMEPRM

Contact:

- Molly Follette Story: molly.story@fda.hhs.gov
- FDA/HF web site: www/fda.gov/humanfactors

Considerations for Disabled Users

- **Intended users = design = testing = labeling**
  - **Design for your users and their limitations**
    - Some devices are designed for people with specific medical conditions that are associated with disabilities or impairments – e.g., diabetes, arthritis, allergies
  - **Test a representative sample of these users**
    - Low vision is not the same as blindness
  - **Include information in your labeling about the populations for which the device is appropriate**
  - **Provide a rationale in your FDA submission**