

Agilis

Human Factors: Risks, Rewards and Reason

Renée Bailey, 3 March 2020

Agilis Consulting Group

Agilis Consulting Group is a full-service regulatory human factors engineering, labeling and training firm focused exclusively on medical devices and pharmaceutical drug delivery products.

For almost 20 years, Agilis has successfully helped clients with human factors services, design and development of user labeling and training and human factors regulatory consulting in the US and abroad.

Overview

- How does human factors fit into the overall product development and regulatory submission schedule
- Key differences between clinical studies and human factors studies
- Common myths associated with human factors
- Excerpt of a study to demonstrate differences of human factors and other types of studies
- Case study
 - Regulatory strategy and purpose of the human factors study
 - Results of the study
 - Impact of study results to the regulatory submission and why the impact occurred

Why consider human factors?

- A premarket requirement
- Human factors engineering, usability engineering and risk management are required by Regulatory/Health Authorities around the globe:
 - US 21CFR 820.30
 - Preamble to Final Rule 21 CFR Parts 808, 812, 820 (61 FR 52502)
 - US FDA Human Factors Guidance documents^{1, 2, 3}
 - European Commission Medical Devices Regulation (MDR)
 - IEC 62366⁴
 - ISO 14971⁵

Why consider human factors?

How the human factors strategy is planned for and incorporated within the regulatory/ product development strategy can have a serious impact on:

- Product development timeline and budget
- Planned submission date
- Submission success

Why consider human factors?

FDA has indicated that only 4-11% of human factors submissions are accepted upon first submission.

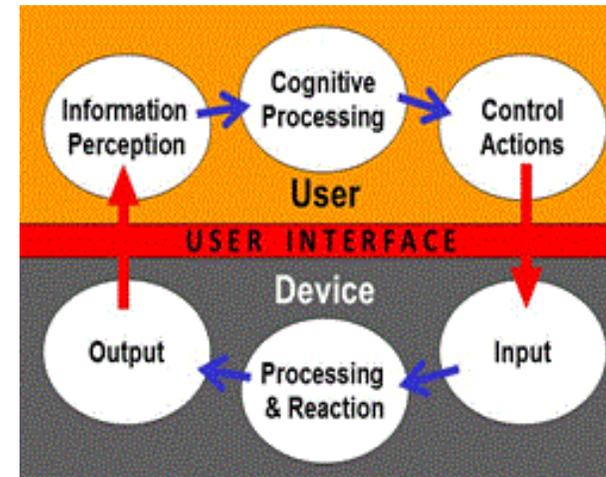
2019 Human Factors and Ergonomics in Healthcare Symposium, Pre-Symposium WK1: CDRH Workshop, Human Factors and Usability Engineering in Medical Product Design and Development, March 24, 2019, Presented by Hanniebey Wiyor, Ph.D., Human Factors Engineer/Reviewer FDA

What is human factors?

US

Human factors/usability engineering focuses on the interactions between people and devices.

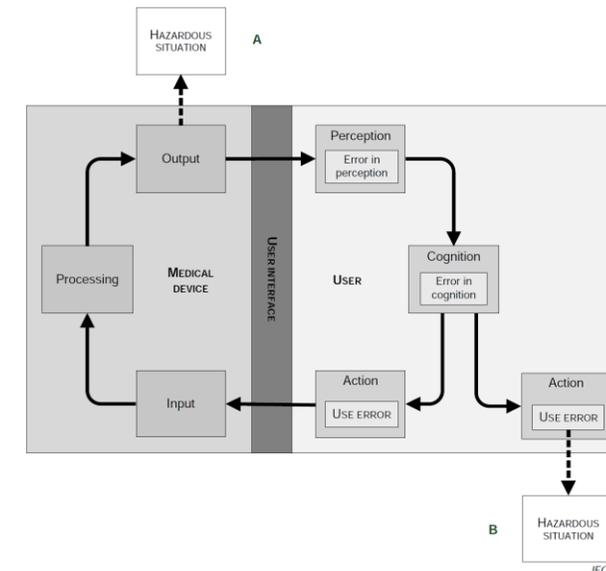
For medical devices, the most important goal of the human factors/usability engineering process is to minimize use-related hazards and risks and then confirm that these efforts were successful and users can use the device safely and effectively.¹



International (EU)

The design of the USER INTERFACE to achieve adequate USABILITY requires a different PROCESS and skill set than that of the technical implementation of the USER INTERFACE.

The USABILITY ENGINEERING PROCESS is intended to identify and minimise USE ERRORS and thereby reduce use-associated RISKS.²



What is the user interface?

All device components the user interacts with to prepare the device for use, use the device, or perform maintenance on the device.



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What is the “human factor”?



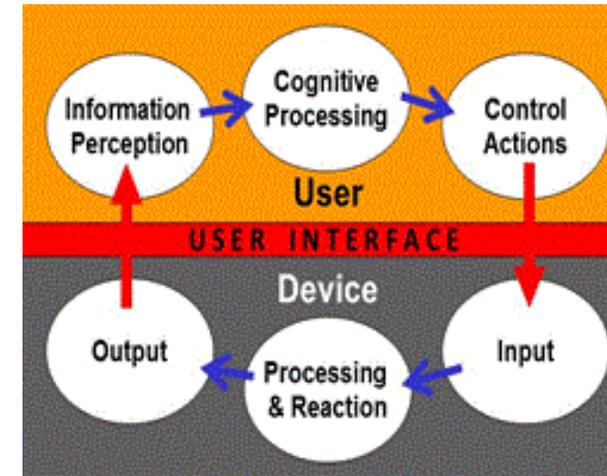
CREDIT: *Steven Day/AP*

How do we assess a medical device for human factors?

US

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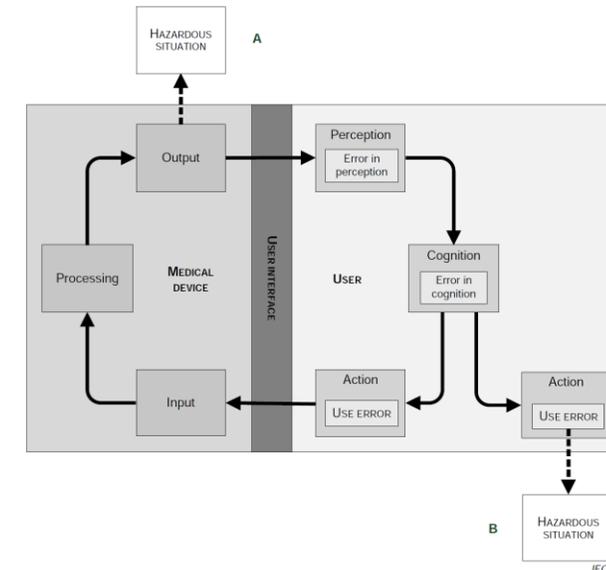
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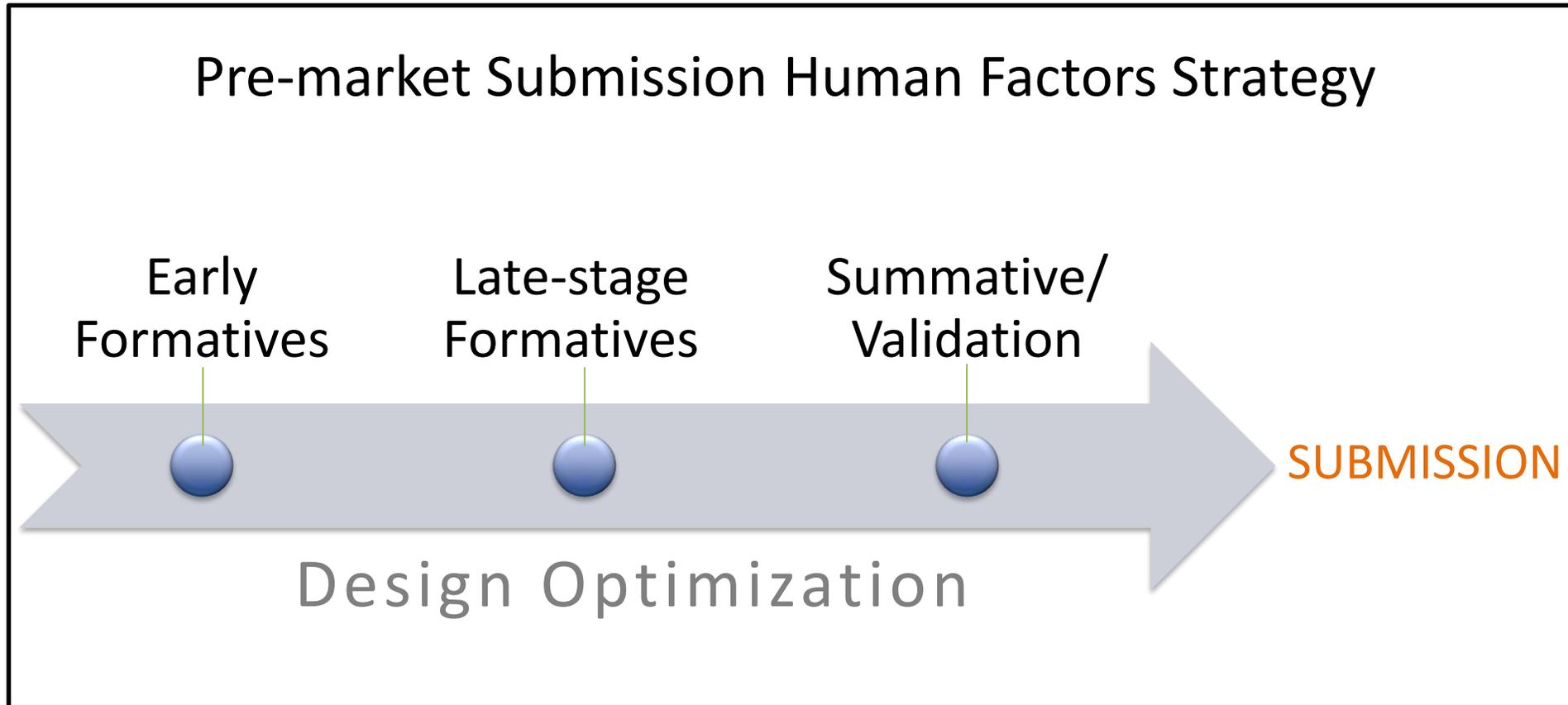
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How do we assess a medical device for human factors?

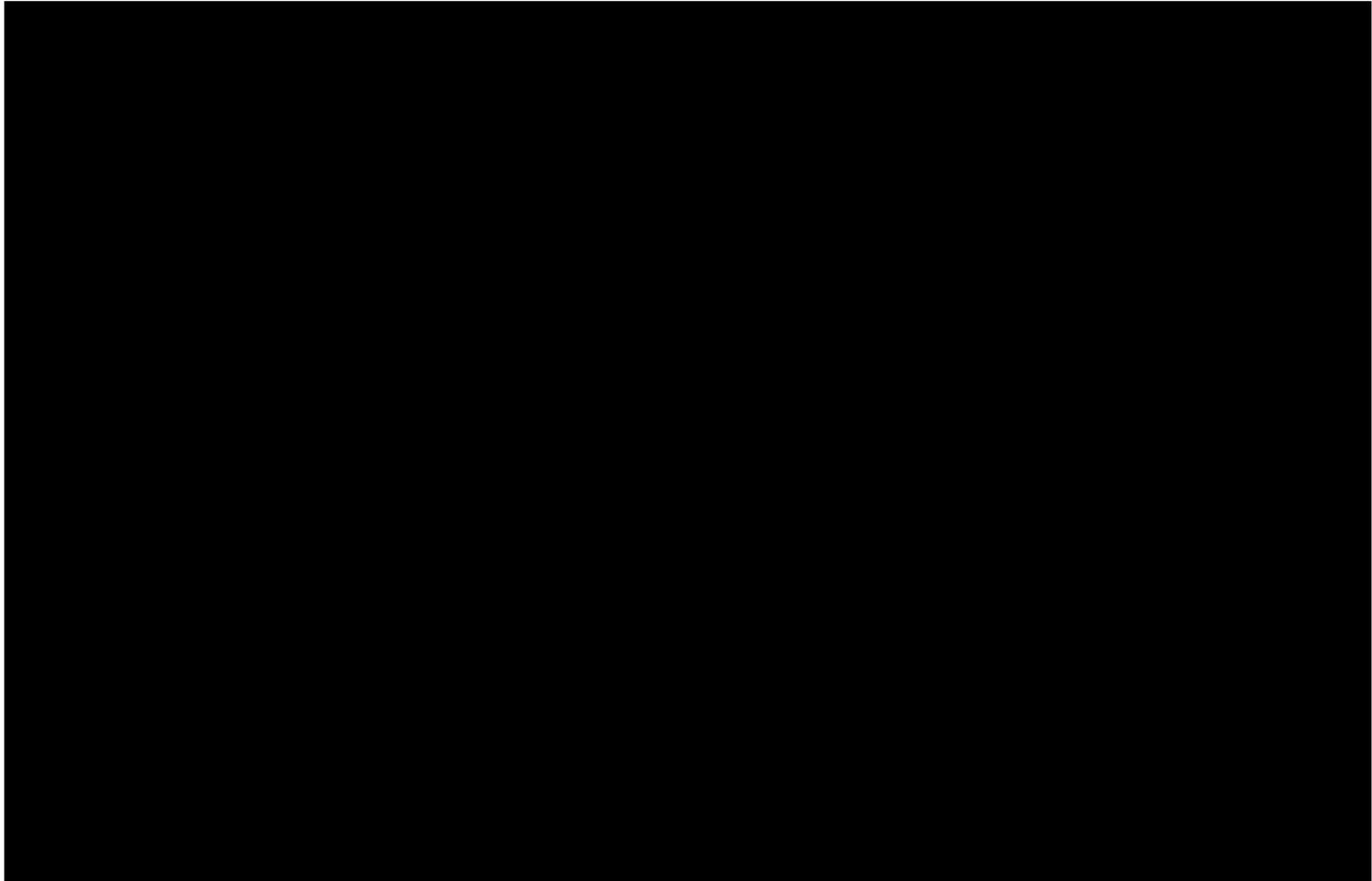


Misconception

Human factors studies require a small sample size and are quick and easy to complete.

Other misconceptions:

- HF is statistical analysis (how many use errors are an acceptable number or %)
- HF is user preference studies
- HF can be substituted with bench testing, engineering data or clinical data
- HF is an endpoint or check-box activity at the end of product development/just before regulatory submission



Planning for the human factors strategy

Human factors studies are **qualitative** in nature and evaluate the **safety and effectiveness** of a device or combination product when in the hands of the user or patient.

- Represent intended users and real-world environment and conditions
- Late stage studies require commercial ready product or device
- Focused on user performance and risks associated with performance difficulties and use errors

Planning for the human factors strategy

Sample size is determined by accepted regulatory standards **per unique user group**

- Appendix B of CDRH Final Guidance 2016¹
- Annex K of IEC 62366: 2015 Part 2⁴
- Minimum 5-8 per user group for formative evaluations
- Minimum 15 per user group for validation/summative studies

Defining user groups

User groups are defined **typically** by differences in functional performance

- Age-related differences and limitations (visual, dexterity/hand strength, cognitive, etc.)
- Condition-related limitations (rheumatoid arthritis, heart failure, cancer, insulin-dependent diabetes, etc.)
- Comorbidities
- Background and education level (especially related to different types of healthcare providers (HCPs) and between HCPs and lay users)
 - Laparoscopic surgeon vs. scrub nurse
 - HCP specialties (nurse vs. phlebotomist)
 - HCP vs. lay patient or caregiver

Types of human factors studies

Early formative studies

- Use a smaller sample size (5-8 users/user group)
- May evaluate focused aspects of the user interface rather than entire user interface
- May evaluate design alternatives and early concepts
- May evaluate user characteristics and preferences, environmental characteristics, etc. to inform design assumptions, device design or selection

Types of human factors studies

Late-stage formative studies

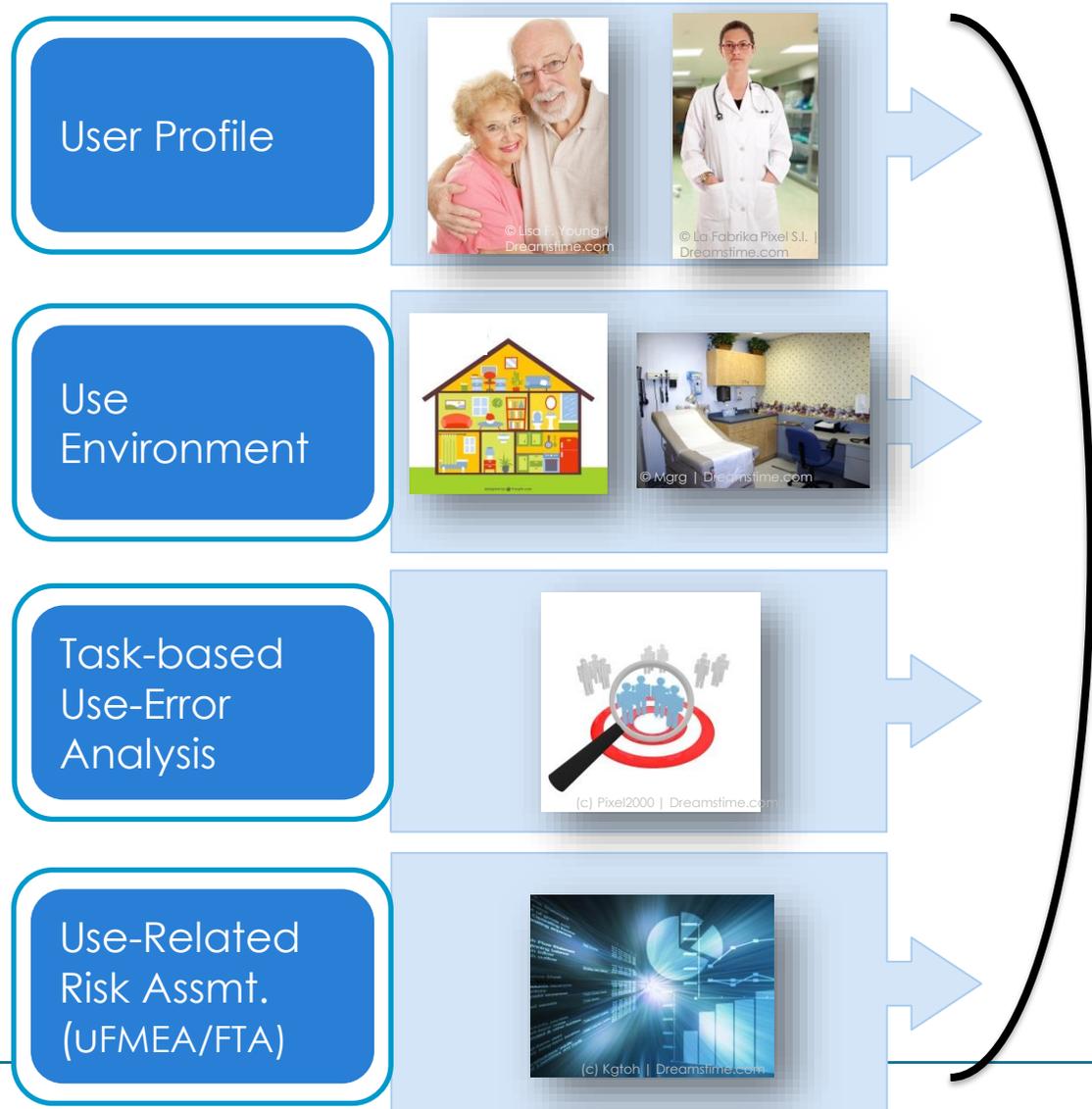
- Use a smaller sample size (5-8 users/user group)
- Bring more aspects of user interface together to evaluate at one time – eventually testing entire user interface and approaching commercial design and validation study methodology
- Inform design of device, packaging, instructions, and/or training
- Build readiness to a successful validation

Types of human factors studies

Summative (Validation) studies

- Use a larger sample size (minimum 15 users/user group)
- Assess the entire user interface with all defined user groups
- Uses the final commercial-ready design of the device or product user interface
- Demonstrates use related safety and effectiveness of the device or product user interface in the hands of the end users

From a regulator...



“ FDA suggests that human factors validation testing is conducted to demonstrate that the device can be used by the intended users without serious user errors or problems, for the intended uses and under the expected use conditions. The testing should be comprehensive in scope, adequately sensitive to capture user errors caused by the design of the user interface and should be performed such that the results can be generalized to actual use. ”

The foundation of all human factors strategies

User Profile



Use Environment



Task-based Use-Error Analysis



Use-Related Risk Assmt. (UFMEA/FTA)



Pose biggest risks to the HF submission (whether pre-market or post-market)

If a regulatory authority disagrees with any of these, it can have significant impacts on submission success, budget and timeline for submission and commercialization.

How long do human factors studies take?

An optimized human factors study plan

Key Milestone	Duration (in Weeks)											
	1	2	3	4	5	6	7	8	9	10	11	12
Average human factors formative study												
Preparing for study (protocol, study site)	■	■	■									
Protocol final/approved				■	■							
Recruitment start				■	■	■						
Study conduct							■					
Data analysis and write report								■	■	■		
Report final/approved											■	■

Variables that impact (lengthen) a study timeline:

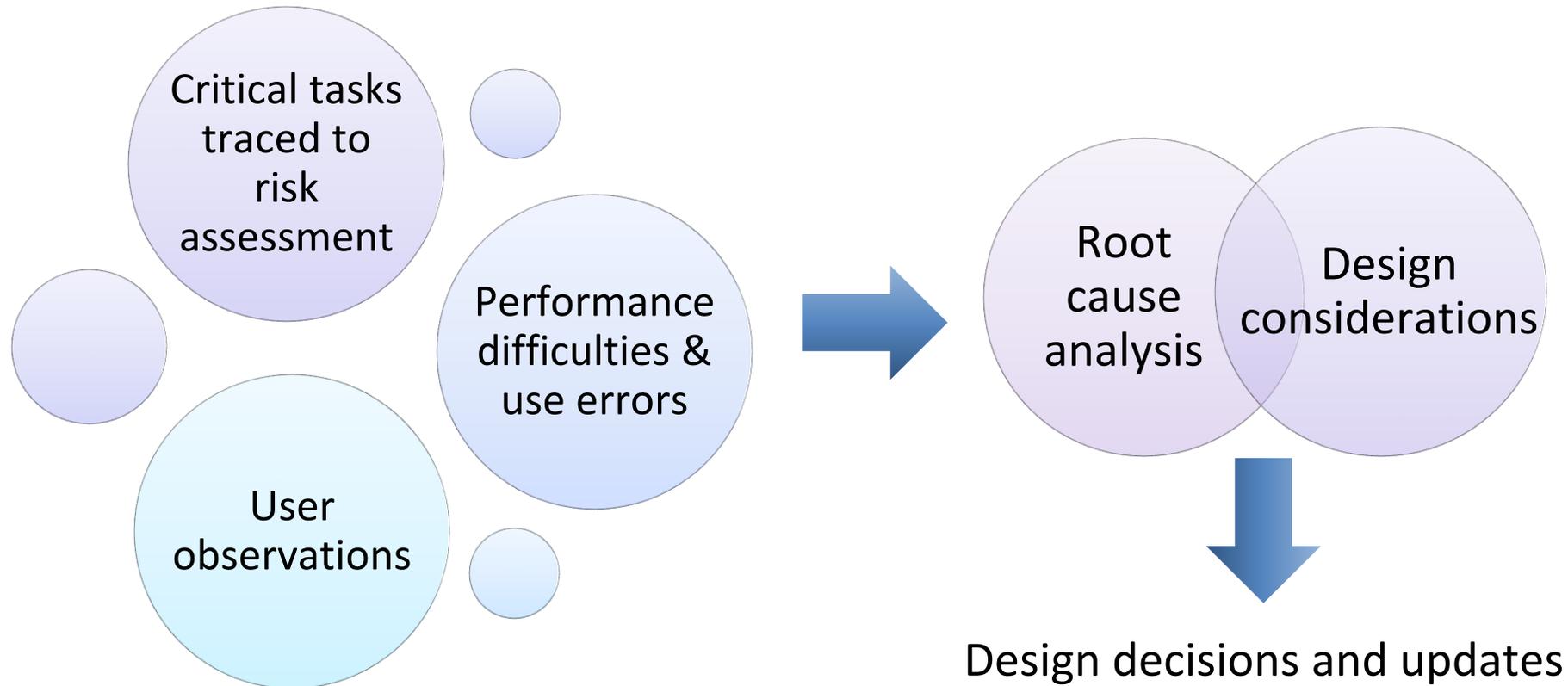
- Number of user groups
- IRB approval
- Training
- Complexity of device interface (study duration)

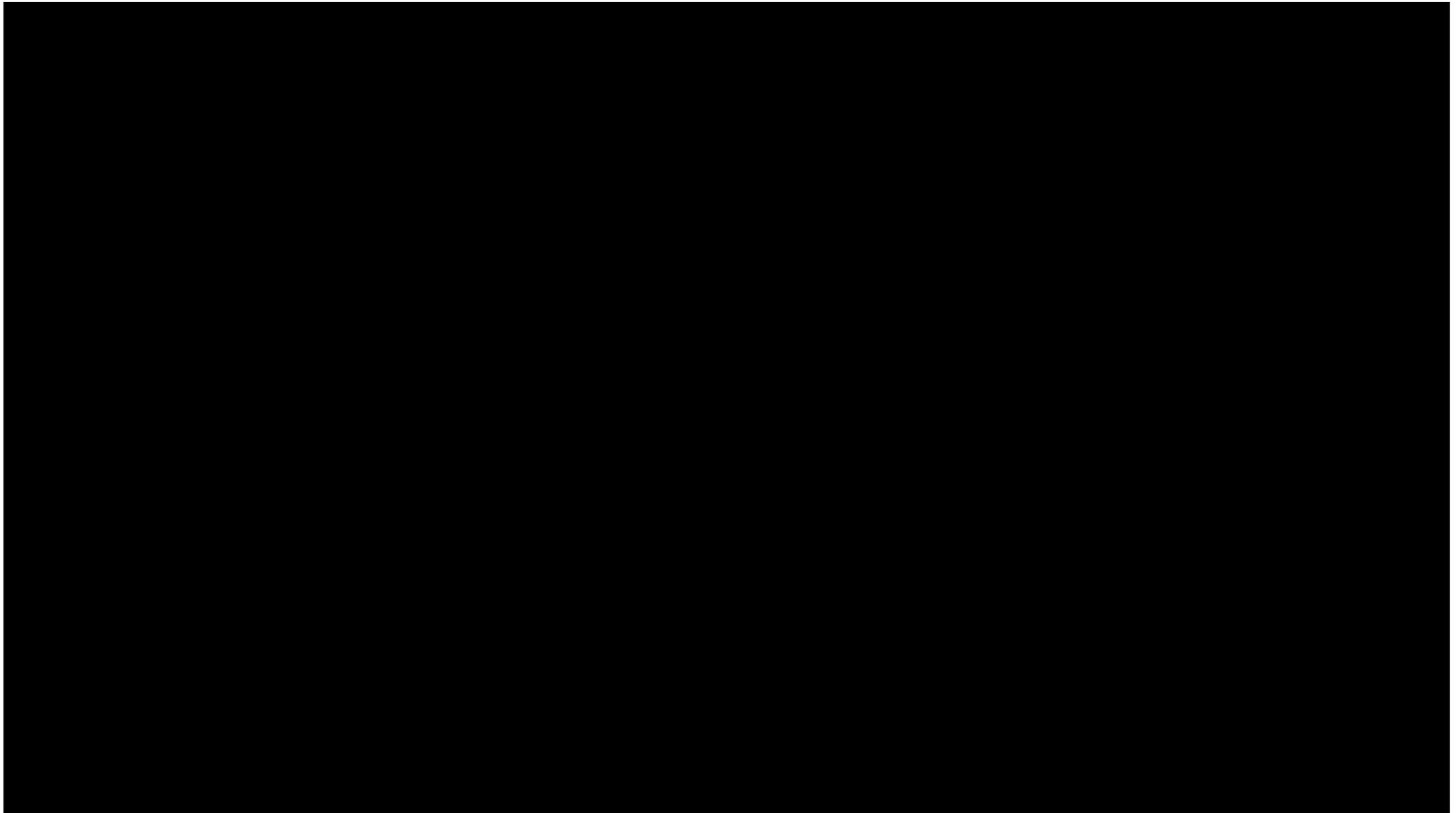
Understanding results of a human factors strategy

- Data gathered during the study are analyzed
- Analysis of data reveals updates to design are necessary
 - Device, packaging, on-device labels, instructions, training – any part of the user interface
- Design updates can impact the submission timeline
 - Depends on the nature of the change
 - Depends on product design and development timeline

Understanding results of a human factors study

Human factors study
data collection





Determining readiness for validation (summative)

- At the point in the process when summative/validation study is conducted, the user interface should be fully optimized
- True residual risk is beyond practicable means of elimination or reduction through modifications to the user interface, labeling, or training (CDRH guidance, 8.1.7)

Assessing residual risk

Serious use errors that are observed during validation testing are not acceptable in premarket submissions unless:

- Results are analyzed well
- Submission shows that further reduction of the likelihood of the use errors is not possible or practical
- Benefits of device use outweigh the residual risks

Residual risk considerations

- Do benefits to the user or patient outweigh the risks?
- Were designs evaluated during formative testing found to be less safe/effective?
- Are implemented design mitigations known best practices?
- Would further design mitigations interfere with the device's essential performance?
- Would further design mitigations make the device unaffordable or significantly delay its availability?

Signs of a successful human factors validation/summative study

- Use errors observed are expected and limited
 - Zero use errors is a red flag to regulatory authorities
 - Successful mitigations to risks and optimizing the user interface are key
 - No surprises
- Use errors have been mitigated to the fullest extent possible
 - Residual risk argument should provide rationale that design has been fully optimized to reduce or eliminate risks (human factors data)
 - Other data can also support residual risks
 - Risk/benefit
 - Clinical data
 - Risk assessment and likelihood of occurrence

Signs of UNsuccessful validation/summative study

- Consistent critical use errors occurring with the first 2-3 participants during the study
- No formative human factors data to support that the user interface has been optimized to reduce observed use errors as much as possible
- Several critical use errors occurred in validation that could be reduced or eliminated by improving the user interface

Pay now or pay later



Successful human factors strategy

STRATEGY

New combination product for diabetic patients

Human factors strategy implemented early in product development

Sought regulatory interaction early, including:

- Pre-submission meetings with FDA CDER
- Pre-submission to FDA CDER/DMEPA for human factors validation protocol review
- Pre-submission commercial labeling review

RESULTS

- Conducted 5 formative evaluations from early product development to pre-summative
 - Optimized device
 - Optimized IFU and packaging
 - Evaluated performance of trained and untrained patients and healthcare professionals
- During FDA reviews, used human factors data to support rationale behind design decisions

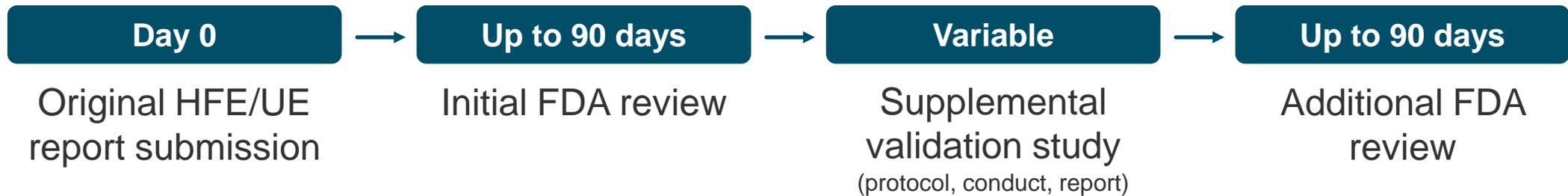
Summative completed 2016

On-time approval by FDA in 2017

Post-Submission Delays are Costly

May require

- Protocol revisions and study conducted again
- Supplemental validation study



6-month+ delay

Case Study - Pay Later

STRATEGY

Engaged with device partner without human factors assessment of device with intended users in the intended environment

Sought regulatory interaction early but changed methodology late in the submission timeline. Late stage interactions included:

- Pre-submission meetings with FDA CDER/DMEPA
- Pre-submission review of human factors validation protocol
- Pre-submission review of commercial labeling and packaging

Case Study - Pay Later

RESULTS

- Initial validation study included all trained participants.
- During FDA review of HFE/UE report, CDER asked for human factors data for untrained participants because, “You indicated that the training will be ‘offered’ to the patient but there is no assurance that all patients are trained.”
- Feedback of subsequent FDA reviews received from the Agency after formative studies were conducted
- Worked with Agilis to re-design IFU, iterate preliminary analyses and conduct validation study.

RESULTS



\$608,000 – Additional HF Strategy Costs

15-month delay to conduct formatives and repeat validation

21-month delay to market due to submission delays

*Excludes costs associated with late stage UI changes and delays to market

Case Study - Pay Later

STRATEGY

Limited regulatory engagement related to submission pathway

Sought limited regulatory feedback that included:

- Pre-submission meetings with FDA CDER
- Pre-submission review of commercial labeling
- Documentation provided for pre-submission reviews was limited

Case Study - Pay Later

RESULTS

- Conducted 6 formative evaluations iterating device and instructional materials throughout the process
- Conducted a validation study with 2 user groups
- During FDA review of HFE/UE report, CDER cited disagreement with:
 - Risk assessment (severity of harms identified and mitigations)
 - Success of human factors validation study due to harms associated with use errors that occurred in the study
 - Training methodology used in the validation study
 - Not using commercial ready product in validation
 - Package labeling, instructions for use and electronic instructions

RESULTS



Additional HF Strategy Costs to redesign device and instructional materials

Undetermined delay to conduct formatives and repeat validation

Undetermined delay to market due to submission delays

*Excludes costs associated with late stage UI changes and delays to market



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Integrating human factors with regulatory early (Pay Now)

- Engage regulatory authority early:
 - Confirm regulatory pathway and related human factors guidance
 - Determine pre-clinical strategy (if combination product)
 - Use pre-submission meetings for questions related to human factors
 - Feedback on risk assessment
 - Feedback on human factors validation protocol for agreement on user groups, risk assessment of individual tasks, testing methods
- Account for the human factors strategy execution in the product development timeline and the regulatory timeline
- Revisit strategy and schedule after each human factors study to accommodate design changes

Integrating human factors with regulatory later (Pay Later)

- Limited or no engagement with regulatory authority
 - No feedback on risk assessment
 - No feedback on human factors strategy
- No human factors testing included in the product development timeline and the regulatory timeline
 - Or, only a validation/summative study is planned
- No early human factors formative evaluations to optimize design of the user interface prior to validation/summative study
 - Hard submission date with no flexibility to optimize design
- No human factors data to support responses to regulatory authority during the submission review process

What is your current strategy costing you?

- Repeated studies
- Validation studies turned formative (unsuccessful validation)
- Costs of redesign during late stages of product development
- Costs of changes in manufacturing lines, package printing, IFU printing and binding, training program design and deployment
- Delays in submission timeline
- Delays in commercialization and revenue generation

Summary Points

- Successful approach is ensuring integration of human factors and regulatory strategies
- Human factors is a regulatory requirement and takes time to implement effectively
- Human factors requires qualitative analysis of user performance with the user interface (it is not marketing research, preference studies or clinical)
- Results of human factors studies could impact the regulatory strategy and submission timeline – it is best to integrate strategies early and ongoingly
- Changes in regulatory strategy can impact the human factors strategy

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for the global medical market

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