Human Factors Compliance and Applications

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Kaleidoscope® Innovation ClearMark

Alison Sathe

CEO Regulatory Mark & ClearMark

- Regulatory Mark™ provides consulting solutions for Medical Device and Combination Products
  - Regulatory strategy and implementation for domestic and international regulatory submissions for medical technology (meetings with FDA and international regulators, submissions, filings, strategies)

- ClearMark™ is an electronic Quality Management System tailored to medical technology
  - Cloud based platform for regulatory and quality management system compliance
  - Specific workflows for 21 CFR 820 and ISO 13485 compliance

Valerie Fenster

Director, Insights and Human Factors

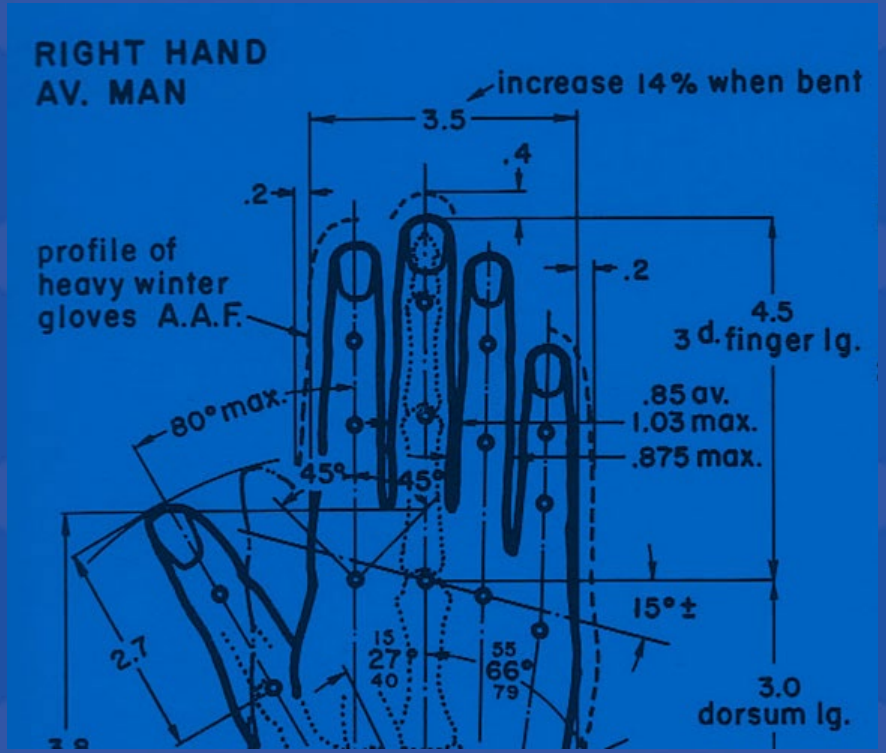
Kaleidoscope Innovation

- Kaleidoscope Innovation™ is a full-service insights, design and development firm innovating across medical, consumer and industrial markets. For over 30 years our clients have partnered with us to improve the human experience.
  - **Insights:** uncovers critical needs that drive product development decisions and enhance the user experience.
  - **Human Factors**: navigates regulatory challenges and conducts studies to produce safe and effective fully supported solutions.

Agenda

- Standards & Guidance
- Human Factors in the Total Product Life Cycle (TPLC)
- Regulatory Submissions - Domestic and International
- Q & A

Standards & Guidance



Benefit of Human Factors Engineering

- FDA and Human Factors Engineering
  - FDA guidance includes an HFE process as part of QMS and Design Control
  - More focused on HFE to demonstrate safe and effective use
  - Recognized benefit of incorporating HFE early in the development process
  - Enforcement Discretion (mobile apps as a medical device)

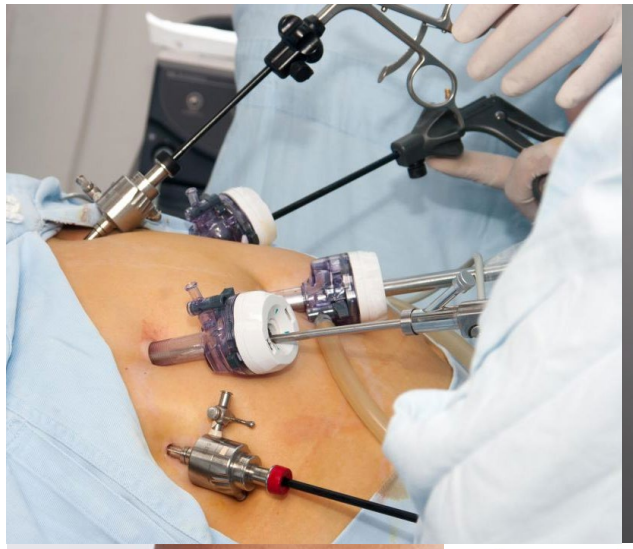
- Human Factors Engineering from the Quality Perspective
  - Focus of today's presentation is HFE from the Quality Perspective
  - Reach out for more information on HFE and Regulatory Submissions

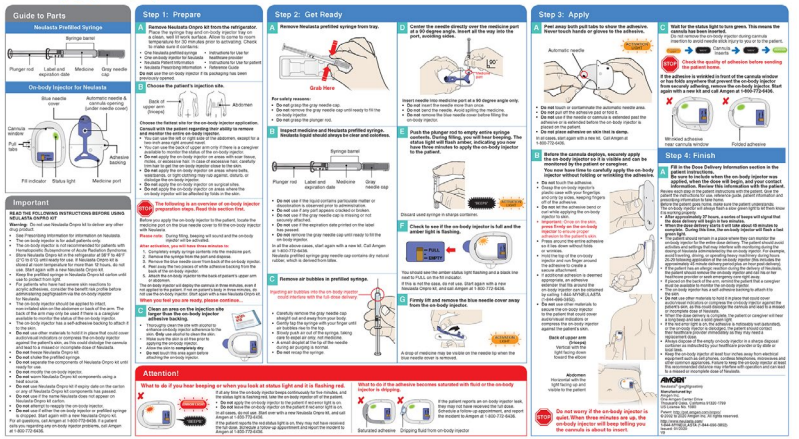
Standards and Guidance

- IEC 62366-1 - Medical devices, Part 1: Application of usability engineering to medical devices
- IEC/TR 62366-2 - Medical devices, Part 2: Guidance on the application of usability engineering to medical devices
- EN 60601-1-6 - Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability
- AAMI/ANSI HE75 - Human Factors Engineering - Design Of Medical Devices
- ISO 14971 - Medical devices — Application of risk management to medical devices
- FDA - Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and Food and Drug Administration Staff
- FDA – List of Highest Priority Devices for Human Factors Review
- FDA - Contents of a Complete Submission for Threshold Analyses and Human Factors Submissions to Drug and Biologic Applications
- FDA - Safety Considerations for Product Design to Minimize Medication Errors Guidance for Industry
- FDA - Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development
- FDA - Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
- NMPA - Technical Review Guidelines of Human Factor Design
- MHRA – Guidance on Applying Human Factors and Usability engineering to Medical Devices including Drug-Device Combination Products in Great Britain

Human Factors Across Regulated Products

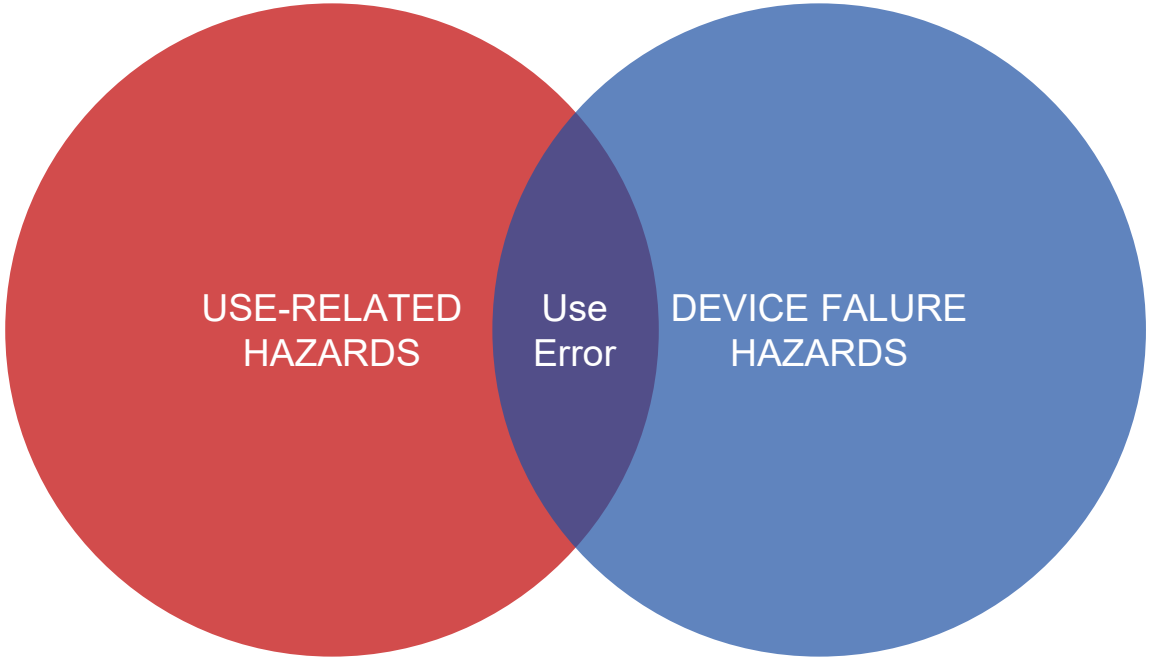
- Medical Devices
  - Professional use devices
  - Home use devices
  - SaMD – mobile apps, web apps
- Drug Products
  - Pediatric use
  - Complex dosing regimens
- Combination Products
  - Drug delivery systems
  - IVD Companion diagnostic device
- Packaging and Labeling
  - Instructions for Use
  - Trays, pouches, cartons, device labels





Human Factors Across Regulated Products

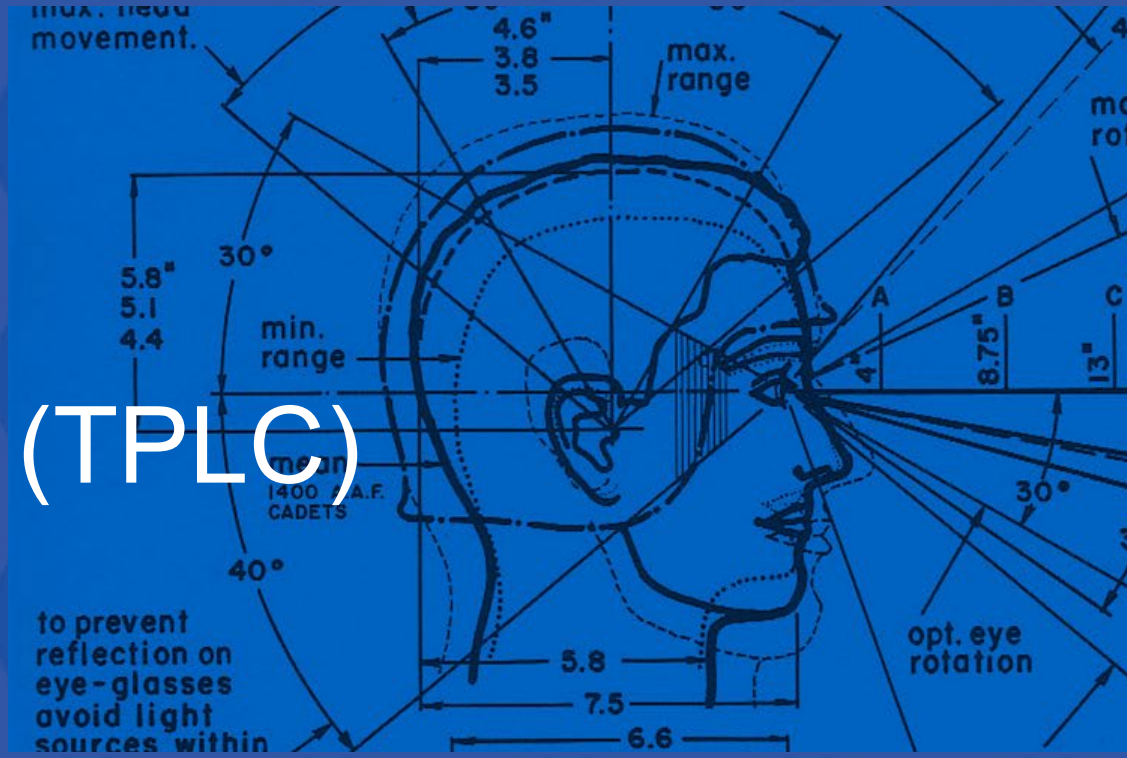
- All types of medical products have usability considerations
- Considerations differ based on
  - Skill level of user(s)
  - Intended user(s) characteristics
  - Product design (user interfaces)
  - Use environment
  - Risk potential and harm
  - Potential abnormal uses
  - Product lifecycle
- How do we address these in the course of development?



21 CFR 820.30, Design Controls

- Human Factors is implied as part of robust design control
  - Design Input
  - Design Verification
  - Design Validation
- Needed in product submissions for high-risk usability features
  - “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))”
  - List of Highest Priority Devices for Human Factors Review, Draft Guidance for Industry and Food and Drug Administration Staff.

Human Factors in the Total Product Life Cycle (TPLC)



QMS and Design Controls Considerations

- Strategy
- Feasibility
- Planning
- Development
- Design Inputs & Outputs
- Verification
- Validation
- Post-market Surveillance
- Regulatory Submissions

Strategy Considerations

Regulatory, Quality and Human Factors

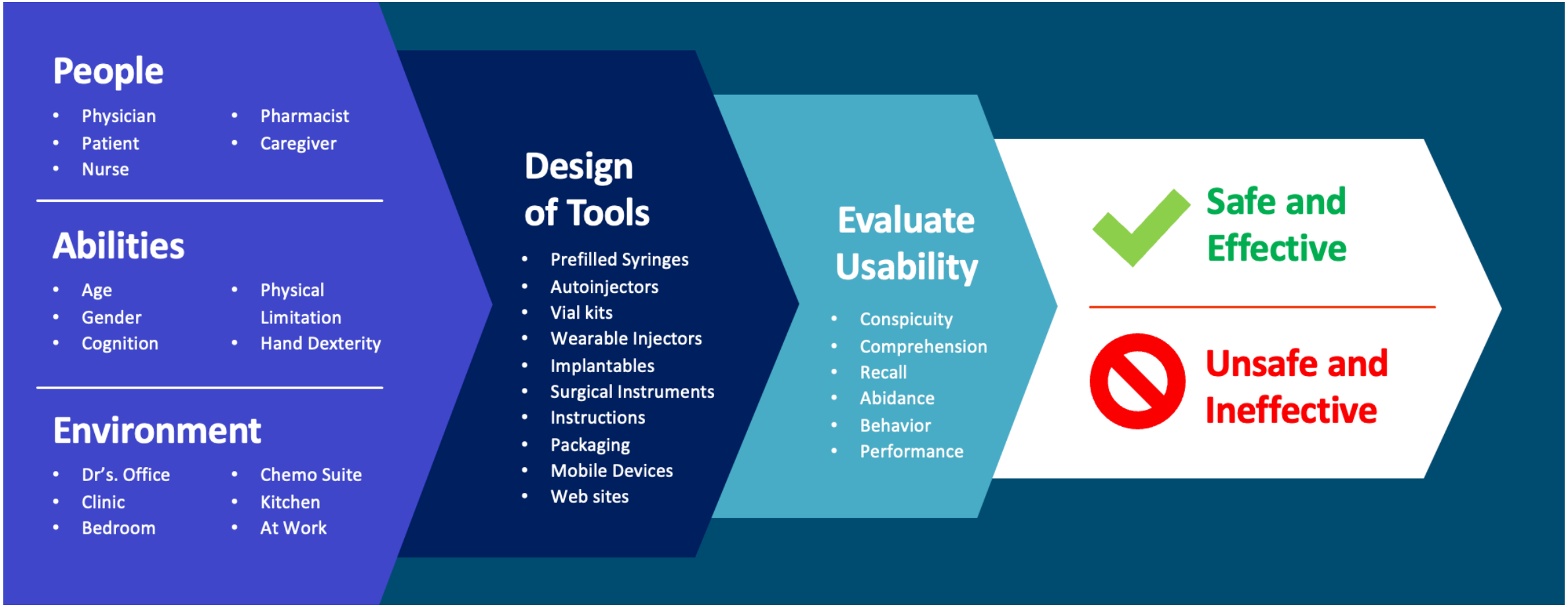
- What is the regulatory path forward?
  - Are we developing new technology or using the same drug delivery device?
  - Do we have available data on known industry problems and will this device help?
  - How many studies need to occur (what usability issues exist and potential impact to risk)?
  - Can we repurpose work and negotiate a reduction in studies with the FDA?
  - Where should studies occur (US only, OUS, as well)?
  - When will Human Factors studies occur (in parallel, before or after clinical trials)?
  - When is Human Factors validation data need to support the filing?

Feasibility Phase

Designing for the User

- Voice of the customer research:
- Identify the user population and determine distinct user groups
  - Explore with users to understand behavior, their mental model(s), physical and cognitive challenges
  - Identify potential use-related hazards, risks and harm
  - Gather and address customer needs, create design alternatives and trade-off using sketches and 3D models
  - Document the customers' needs
- Develop User Needs Requirements (UNR) under design controls

Designing for the User



Planning

Human Factors Engineering Planning

- Product Development Plan
- Regulatory Plan
- Quality Plan
- Usability Plan*
- Risk Management Plan*
- Verification & Validation Plan*

* Integral to Human Factors Engineering activities

Usability Plan (follows Appendix A)

- FDA: “Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and Food and Drug Administration Staff”

  - Descriptions of intended device users, uses, use environments, and training
  - Description of device user interface
  - Summary of known use problems
  - Analysis of hazards and risks associated with use of the device
  - Summary of preliminary and planned analyses and evaluations
  - Description and categorization of critical tasks
  - Details of the planned human factors testing
  - Trace to FDA Guidance and internal client requirements

Risk Management Plan and ISO 14971: 2019

- Minimizes Use Errors Leading to Harm and Maximizes Use and Design Success
  - Risk management
  - Risk analysis
  - Risk evaluation
  - Evaluation of overall residual risk acceptability
- Human Factors documents
  - Hazard analysis & severity of harm
  - Critical steps of operation (Essential Tasks)
  - Task analysis
  - uFMEA (Failure Modes and Effects Analysis)

Did I Make the **Right Product** / Did I Make the **Product Right**:

- 820.30(f) & (g) Design Verification & Validation
  - Verification: Formative studies and Validation: Summative studies
- Identify needed requirements for study development
  - Critical steps of operation (Essential Tasks)
  - Safety-critical steps that could have a significant negative clinical impact
  - Customer Needs Requirements (based on feasibility research)
  - Task Analysis to identify potential use errors
  - Use-related Risk Assessment - (uFMEA)
  - Trace to Labeling Specification Requirements (Product Labeling)

Potential Hazard	Cause	Harm
Unable to access subretinal space	Failure to measure, set caliper, or measure properly or Incision to close to limbus	Adverse Event (retinal perforation, tear, or detachment)
Choroidal bulging /retinal incarceration at incision site	Scleral incision too long	Adverse Event (retinal perforation, tear, or detachment), Excessive scleral bleeding (impairs surgical vision, time delays to stop bleeding)
Tissue Damage (choroid, or retina)	Scleral incision too deep	Adverse event (choroidal bleeding, suprachoroidal hemorrhage, retinal perforation, retinal tear, retinal detachment, loss of vision)
Tissue Damage (choroid)	IOP too high	Adverse event (choroidal bleeding, suprachoroidal hemorrhage)
Tissue Damage (sclera or choroid)	OMR scratches sclera or choroid during placement	Adverse event (ocular irritation, ocular inflammation, scleral bleeding)
Tissue Damage (choroid)	Puncture choroid with OMR tips or OMR expanded too far	Adverse event (choroidal bleeding, suprachoroidal hemorrhage)
Tissue Damage (sclera)	Forceps slip off retractor while bending more open	Adverse event (choroidal bleeding, suprachoroidal hemorrhage)
Tissue Damage (lens, retina, optic nerve)	Scope inserted too deep or at the wrong angle	Adverse Event (retinal perforation, tear, or detachment, lens, optic nerve, loss of vision, IOL displacement)
Unwanted eye rotation from ideal stable position	Aiming endoscope toward sclerotomy inherently creates unintentional rotational forces	Adverse Event (retinal perforation, tear, or detachment) and delays surgery
Tissue Damage (lens, retina, optic nerve)	Difficult to maintain constant position relative to eye (hand fatigue, improper wrist support)	Adverse Event (retinal perforation, tear, or detachment, lens, optic nerve, loss of vision)

Development

Human Factors Study Objectives

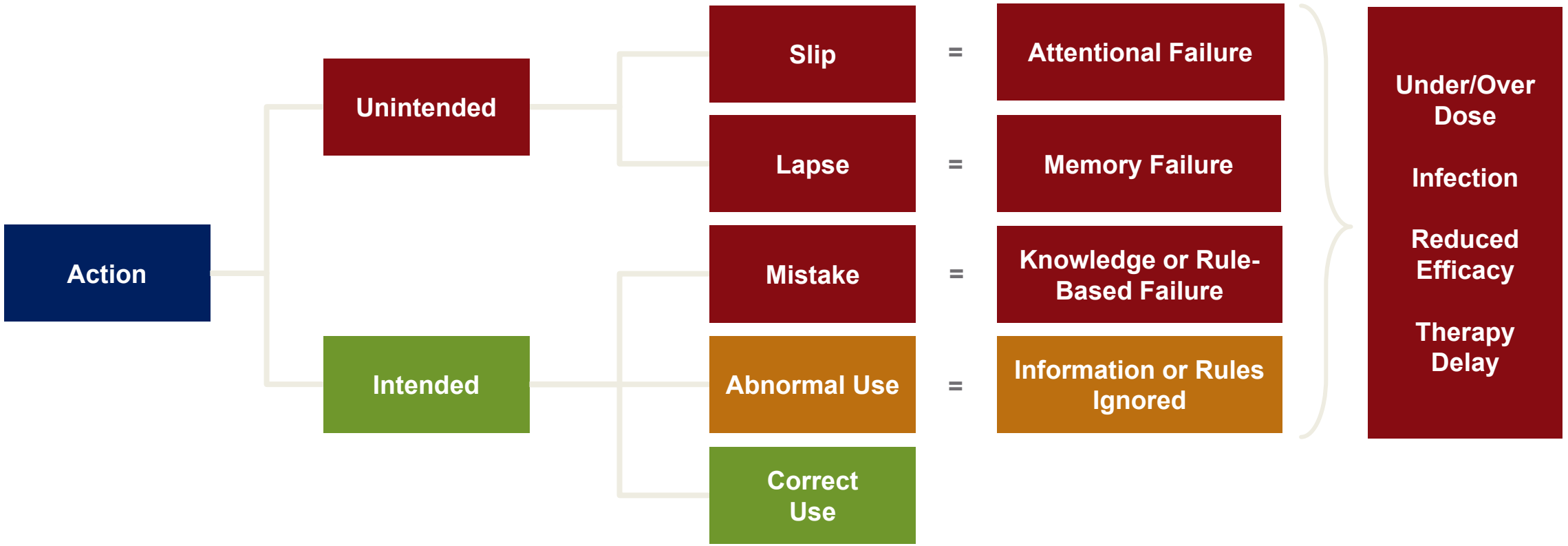
Formative Study

- Aids design/development process
- Tests performance and knowledge
- Evaluates device, packaging and product labeling (entire UI)
- Gathers objective, subjective evidence of success / failure
- Uncovers use errors, and root cause
- Improves and mitigates readability, comprehension, usability issues

Summative Study

- Traces to design controls requirements (UNR, uFMEA, Validation Plan, Usability Plan)
- Tests production-equivalent device, product labeling, packaging.
- Tests critical steps of operation (Essential Tasks), and at minimum, safety-critical steps (from uFMEA)
- Proves requirements are traced to task observations and knowledge-based assessments

What Is A Use Error and its Root Cause?

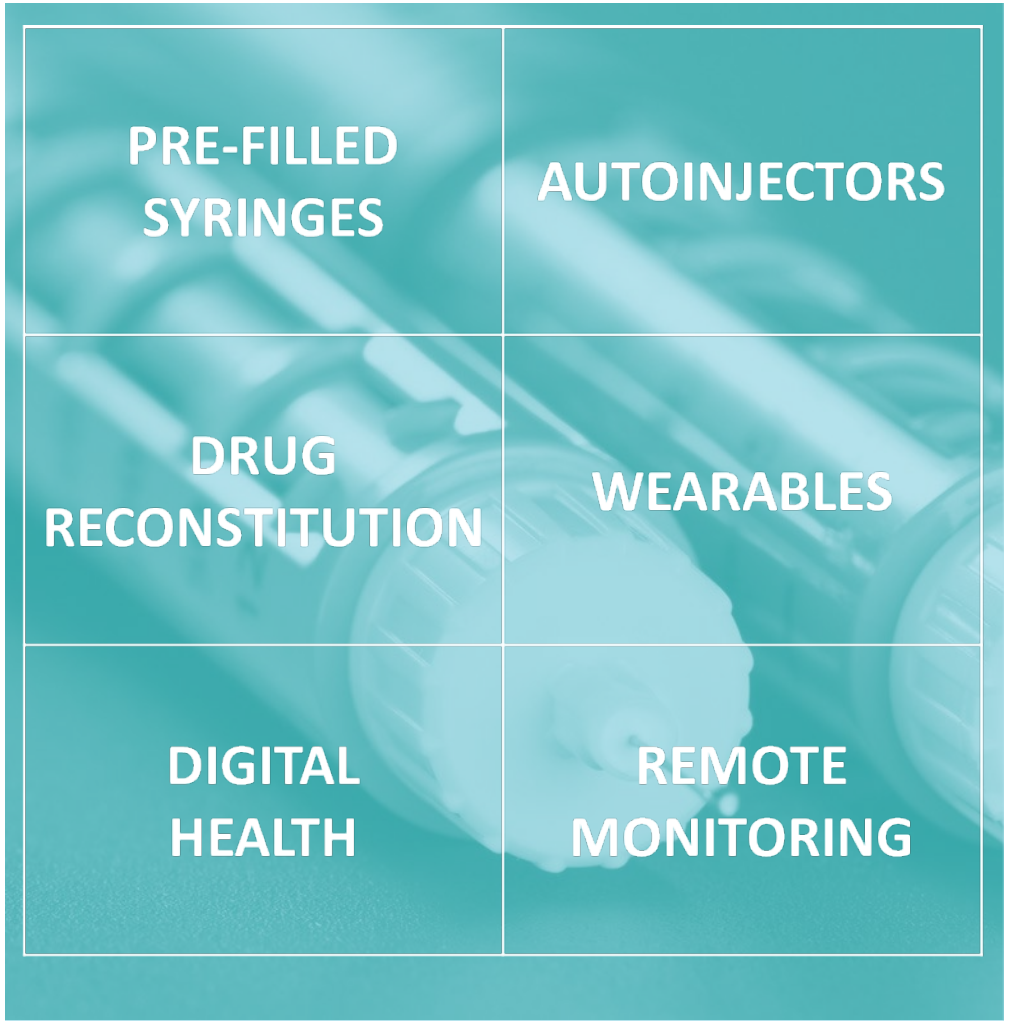


Planning and Conducting the Formative Study

- Determine study type, participant sample, stimuli, topics/tasks
- Include device, packaging and labeling variations and prototypes.
- Develop and test IFUs, user guides.
- Record use errors, operational difficulties.
- Watch and ask “Why” (root cause)
- Update uFMEA after each study.
- “Design out” errors

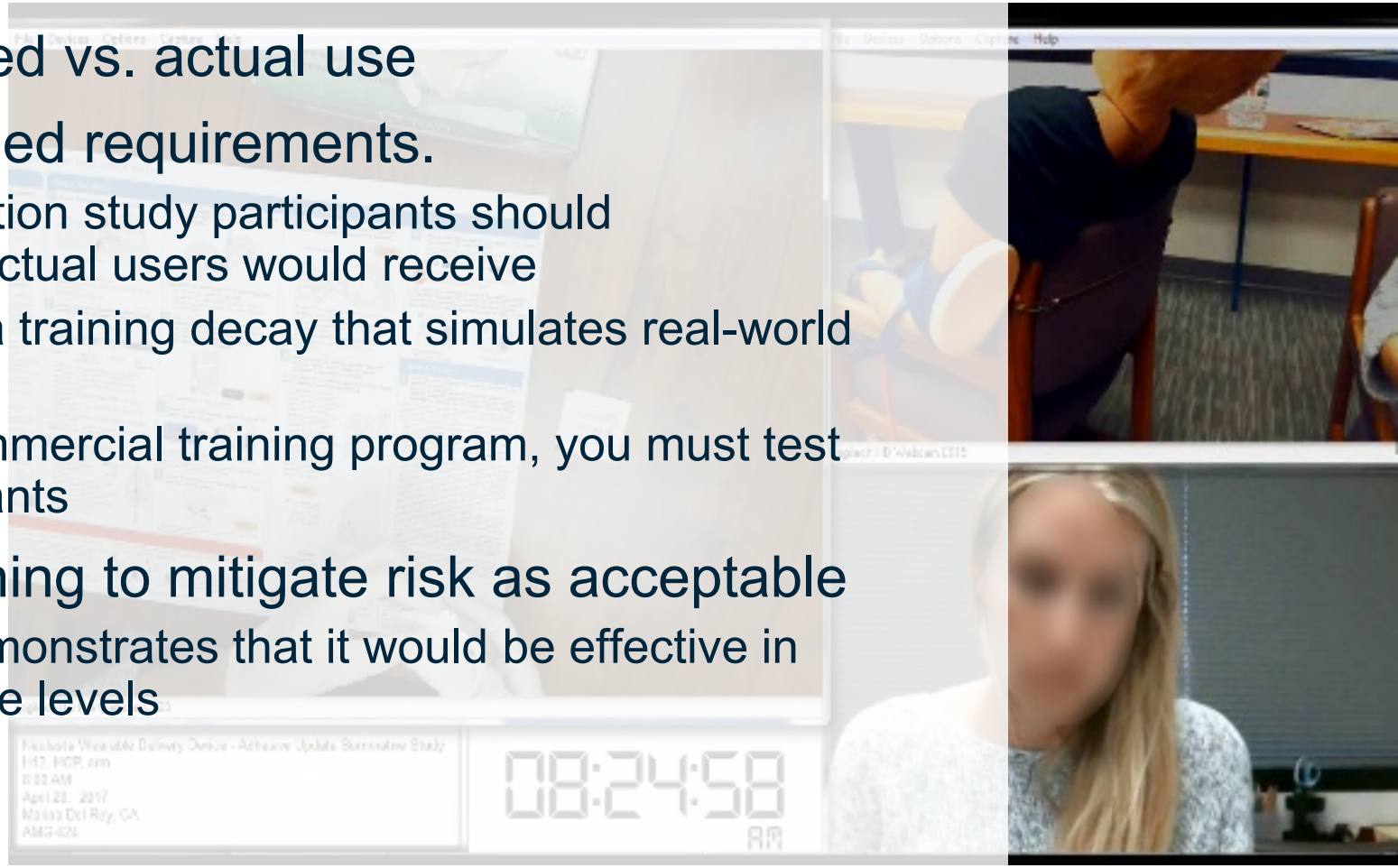
Planning and Conducting the Validation Study

- Include all distinct user groups, emulate context of use (home, surgery suite, office)
- References design controls requirements (UNR, uFMEA, Validation Plan, Usability Plan), internal SOPs) in protocol
- Test production-equivalent device, product labeling, packaging.
- Trace tasks to approved requirements
- Record passes, and use errors resulting in close calls, failures, operational difficulties and foreseeable misuse
- Obtain root cause



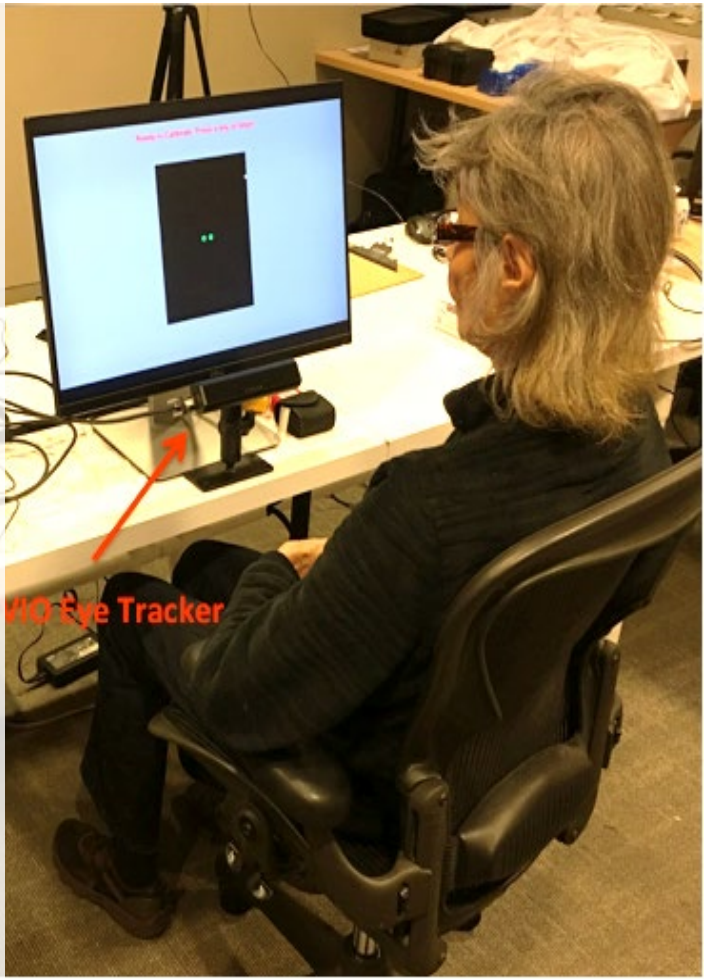
Key Principles in Designing and Executing Human Factors Studies

- Determine if study is simulated vs. actual use
- Determine trained vs. untrained requirements.
  - Training provided to the validation study participants should approximate the training that actual users would receive
  - If training is included, include a training decay that simulates real-world (minimum of one-hour decay)
  - If there is not a mandatory commercial training program, you must test at minimum untrained participants
- Do not expect additional training to mitigate risk as acceptable
  - Unless additional data that demonstrates that it would be effective in reducing the risks to acceptable levels



Human Factors Objective

- Validate the intended user population can demonstrate they can operate the device per its intended use, in the context of use in the intended use environment
- Users **must demonstrate** Critical tasks and Safety-critical tasks while avoiding use errors that could lead to harm.
- Determine that the device user interface has been optimized to its fullest extent without developing a new device
- Update the uFMEA after validation, as this becomes residual risk
- Quality and medical affairs must determine the risk/benefit analysis.
- Any residual risk is outweighed by the therapeutic value of the device (combination product)



After-validation Activities

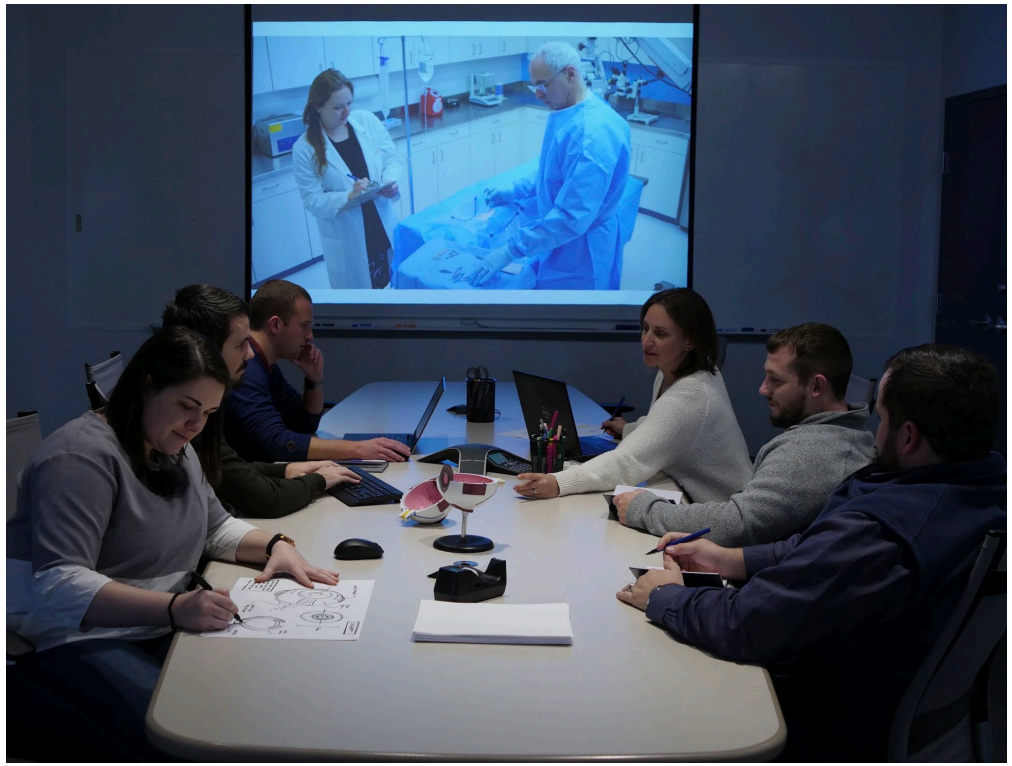
- Open a change record to assess the impact on usability and risk if tested materials were not production-equivalent
  - Document differences, and determine to re-test (supplemental summative)
- Create Usability Engineering File Summary Report:
  - determines HFE activities indicates device is safe and effective for use.
- Health authority makes the final determination regarding study success or acceptance.
  - There is no quantitative threshold of acceptance.
- Disposition of identified risks

Risk Analysis				
Severity (Significance of the effect on the product)	Occurrence Rank (What is the likelihood that the failure mode may occur given the risk reductions as they are today?)	Priority Number (Severity x Occurrence)	Detection Rate (Optional) (Opportunity to detect the effect/failure mode given the risk reductions as they are today)	Risk Priority Number (Severity x Occurrence x Detection)
5	2	10	2	20
5	4	20	3	80
5	2	10	2	20

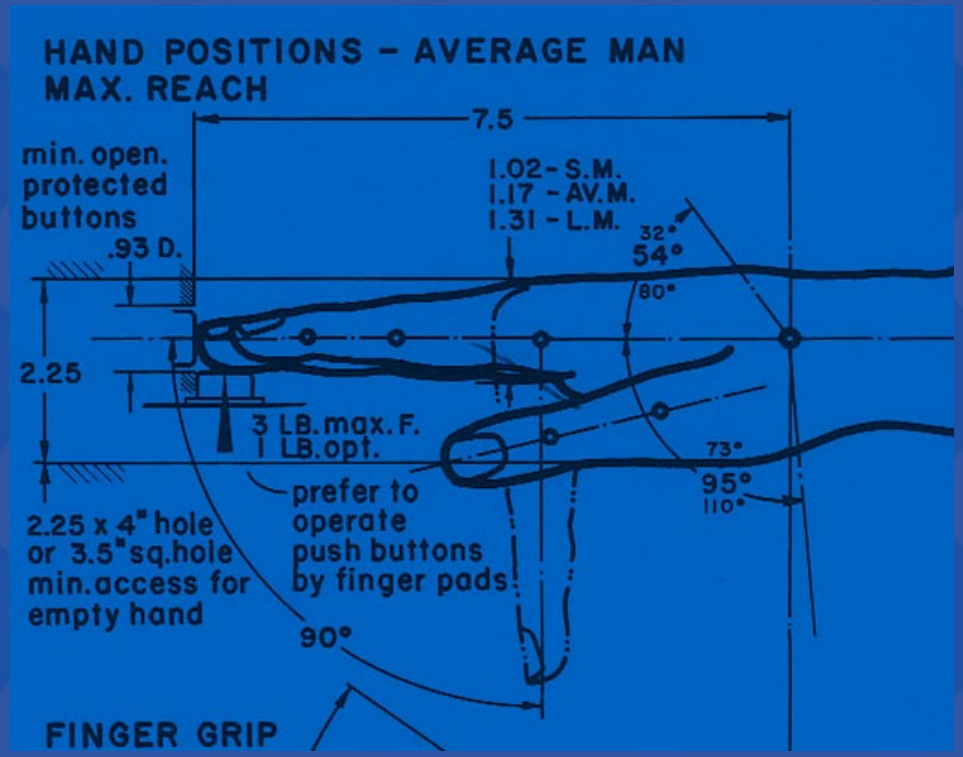
Post-market Surveillance

Field Work, Complaint Mining

- Log and investigate customer complaints as part of your complaint process
- Determine if it is truly the device or the IFU
- Isolate geographic / demographic areas where issues are occurring
- Conduct additional usability studies with targeted users in those geographic / demographic areas
- Continue to design out the errors with additional risk mitigation activities



Regulatory Submissions - Domestic and International



Regulatory Submissions - HFE In International Markets

- US FDA
  - FDA Guidance
  - Focus on class II and III, high priority list

- EU (and MHRA)
  - EU MDR
  - Harmonized Standard 62366

- China NMPA
  - Focus on medium and high-risk products, excludes IVD reagents, Class I medical devices.

FDA

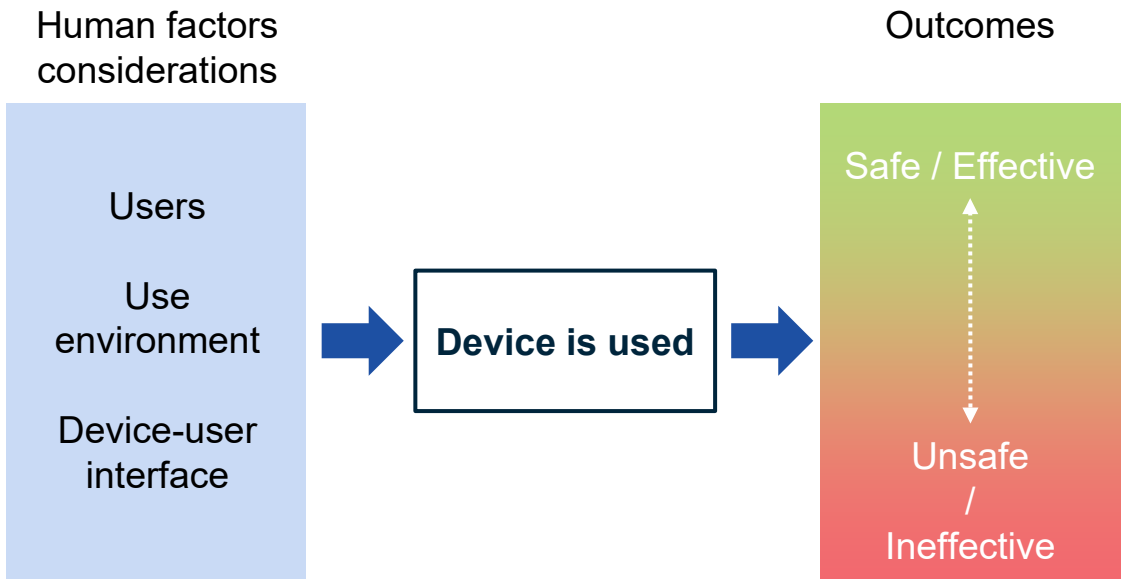
- Recommends seeking IRB approval
- Sample Size
  - No recommendation on sample size for formative studies, however 5-8 is generally acceptable with rationale
  - HF Validation – at least 15 per distinct user group
- Study must be conducted in the USA
- Simulated vs. Actual Use
- Training requirements
  - not detailed in guidance
  - important part of HFE
  - include in validation if required
  - decay period

EU

- While FDA focuses on higher risk deice, in the EU all medical device classifications and IVDs require conformance
  - Scope increases for higher risk MDs
- User profiles
- Training leaves room for interpretation – must document in user interface specification, must include training in validation if needed and include a decay period
- Does not comment on necessity for IRB/EC
  - 62366-2 recommends IRB/EC if risk to participants
- No formal guidance on sample size
  - typically smaller (8/user group) are accepted

MHRA

- Guidance on applying human factors and usability engineering to medical devices including drug-device combination products in Great Britain (Jan 2021)
- All device, combination product classifications
- Minimum sample size – 15 for summative
- Focuses heavily on HFE during development, postmarket changes



NMPA

NATIONAL MEDICAL PRODUCTS ADMINISTRATION
国家药品监督管理局

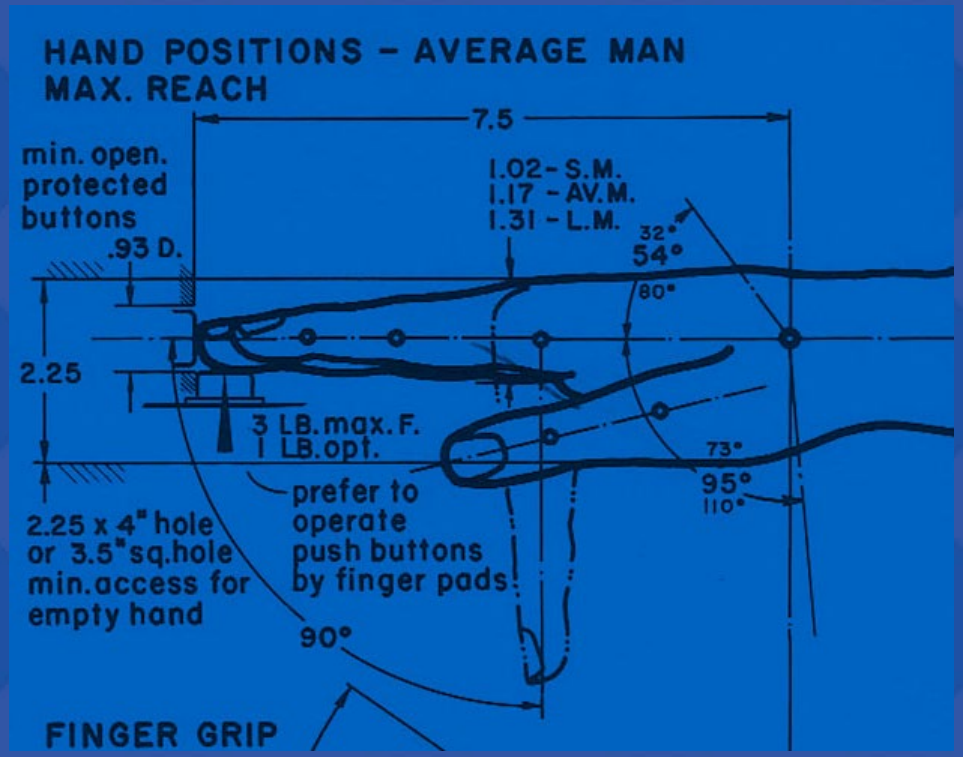
- NMPA guidelines offer slightly different considerations than FDA, both risk based
- Special focus on training – unique requirements for developing training program document for high-risk devices
- Does not currently require IRB
- Sample size justification
  - Formative studies - 5-8 participants per user group
  - Summative studies - more than 20 participants per user groups
  - All participants must be Chinese residents
- State-owned lab is preferred for conduct of testing (i.e. a must!)

Regulatory Submissions - HFE In International Markets

	USA	EU	China
Focus	Focus on class II, III, high priority list	All classifications, scope increases with increased risk	Focus on class II, III
Sample Sizes	Formative – no less than 5/user group Summative – no less than 15/user group	Not specified, typically smaller sample sizes (8-10)	Formative – no less than 5/user group Summative – minimum 15, more than 20/user group recommended
In-country testing requirements	Yes	Not specified (provide rationale)	Yes
Test Facility	NA	NA	State-owned lab
Standards/Guidance	FDA Guidance	62366	NMPA Guidance

- Report content and definitions vary between regions – ensure your documentation addresses these differences!

HFE and Compliance Issues



Meridian Medical Technologies - 483 - June 6, 2019

OBSERVATION 4
Procedures for design validation have not been adequately established.

Specifically, Human factors validation testing has yet to be complete since the Agency's warning letter to MMT (dated September 5, 2017), which detailed the need for validation of the user needs associated with use of the EpiPen products. You have detailed specific user requirements of the EpiPen products in document #: DHF-EPIP-DID-00001, Title: User Requirements Specifications for EpiPen NGA Auto-injector. You also provided a design traceability table for said use requirements in document #: DHF- EP1P-TMA-00017 V3.0, Title Design Traceability Matrix for EpiPen NGA Auto-injector. In the design traceability table, you link the user requirements to the evidence of design validation in a human factors protocol document # DHF-EPIP-DHVO-00048 Title: Human Factors Validation Test Protocol for EpiPen NGA Auto-injector; however according to the MMT Director of Combination Products, this study is not complete and will not be submitted to the Agency until September 2019. Without design validation it is unclear if EpiPen products meet the user requirements. This is a repeat observation.

Pharmacia & Upjohn - 483 - Dec 12, 2018

The device design was not adequately validated. Per Design and Human Factors Validation Plan (INX100324529, Version 1.0;approved 12-Apr-2018), your firm's Gelfoam Sponge validation strategy was limited to reviewing "current post-marketed usability/complaints data for the Gelfoam Sponge." This strategy does not provide objective evidence that the device meets all define user needs and intended uses. Additionally, acceptance criteria for your review of complaint data were not preestablished in the validation plan. C. Per SOP 25806: Unplanned Incidents (Versions 33.0 and 34.0), investigations documented as Quality Assurance Reports (QARs) or Event Reports (ERs) shall include sections for "Corrective Actions." Although not specified by procedure, on 05-Dec-2018, your firm's Sr. Quality Operations Specialist said that the "Corrective Action" section may include "corrections" rather than corrective actions. This distinction was not documented in 9 of 10 closed/approved QAR/ER records sampled. Thus, it is unclear whether requirements such as verification or validation of effectiveness must be completed for such QARs/ERs.

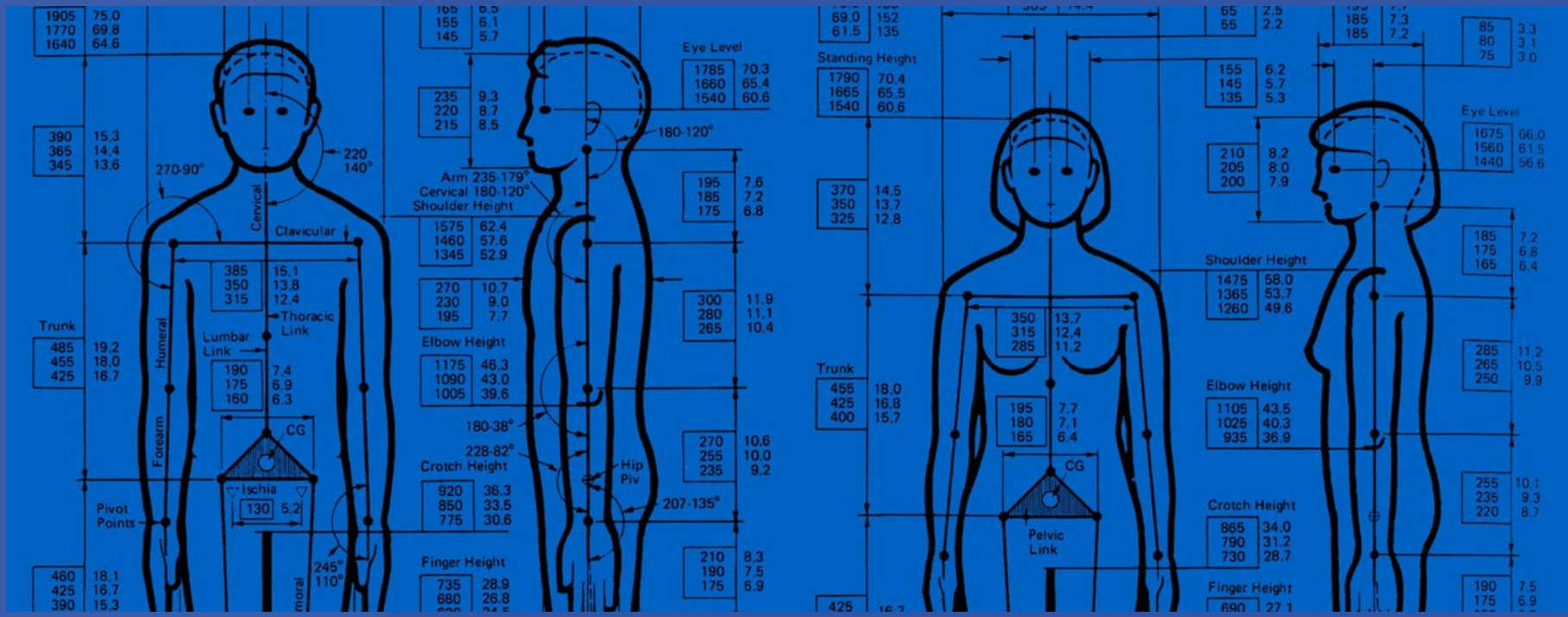
Bio Data Corp - 483, 2012-01-09

OBSERVATION 1

Risk analysis is inadequate.

Specifically, Standard Operating Procedure (b)(4)~~~~~~
~
(b)(4)~~~~~~
~~~~~~ However, your firm failed to identify and prioritize use-related hazards, how significant use-related hazards were mitigated or controlled during design and development, and why strategies used to address use-related hazards were appropriate, on an FMEA Worksheet (b)(4)~~~~~~~~~~ for the PAP-E8 (b)(4)~~~~~~~~~~~~~~~~as per SOP (b)(4)
~~~~~~

Q & A


Trunk
Humeral
Forearm
Cervical
Clavicular
Thoracic Link
Lumbar Link
CG
Ischia
Pivot Points
270-90°
220
140°
245°
110°
Eye Level
Arm 235-179°
Cervical 180-120°
Shoulder Height
Elbow Height
180-38°
228-82°
Crotch Height
Hip Piv
180-120°
207-135°
Finger Height
Standing Height
Pelvic Link
Shoulder Height
Elbow Height
Crotch Height
Finger Height

Thank You!

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