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Industry Perspective: Development of Generic Emergency Use Products

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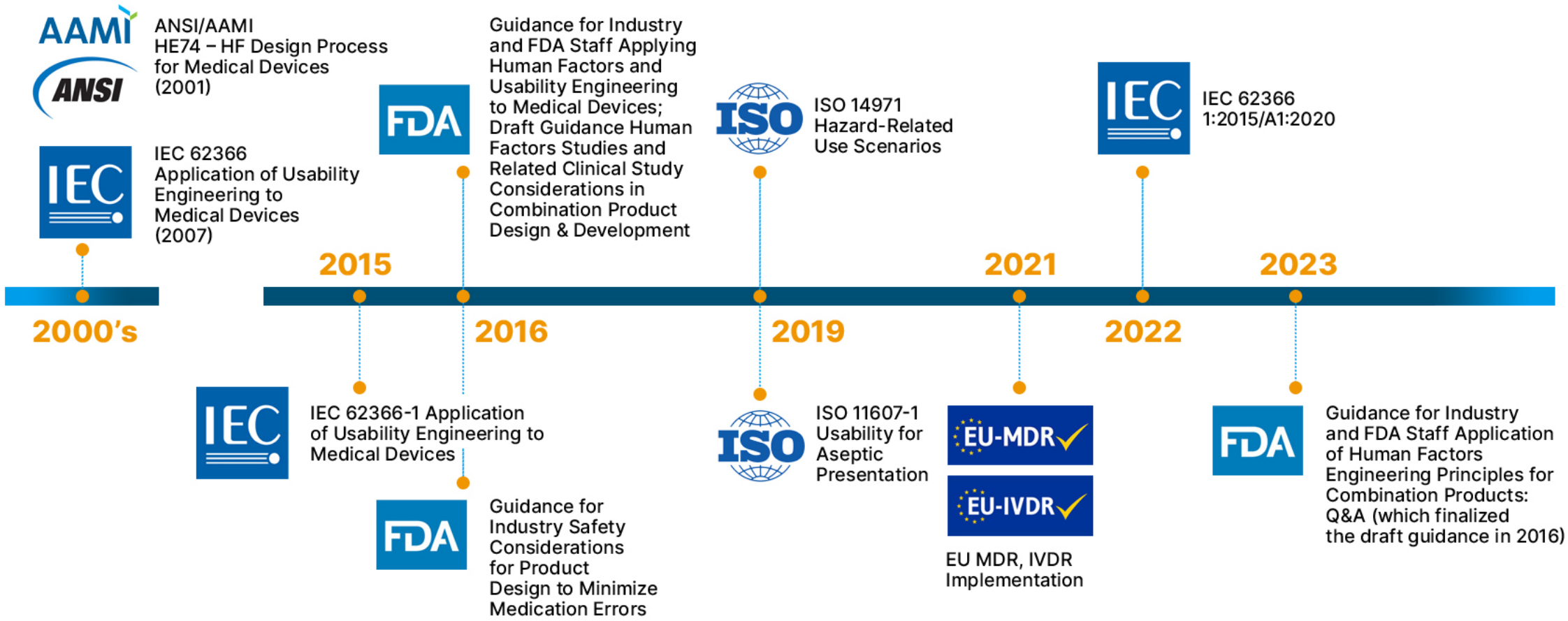
Overcoming Challenges of Siloed Experiences

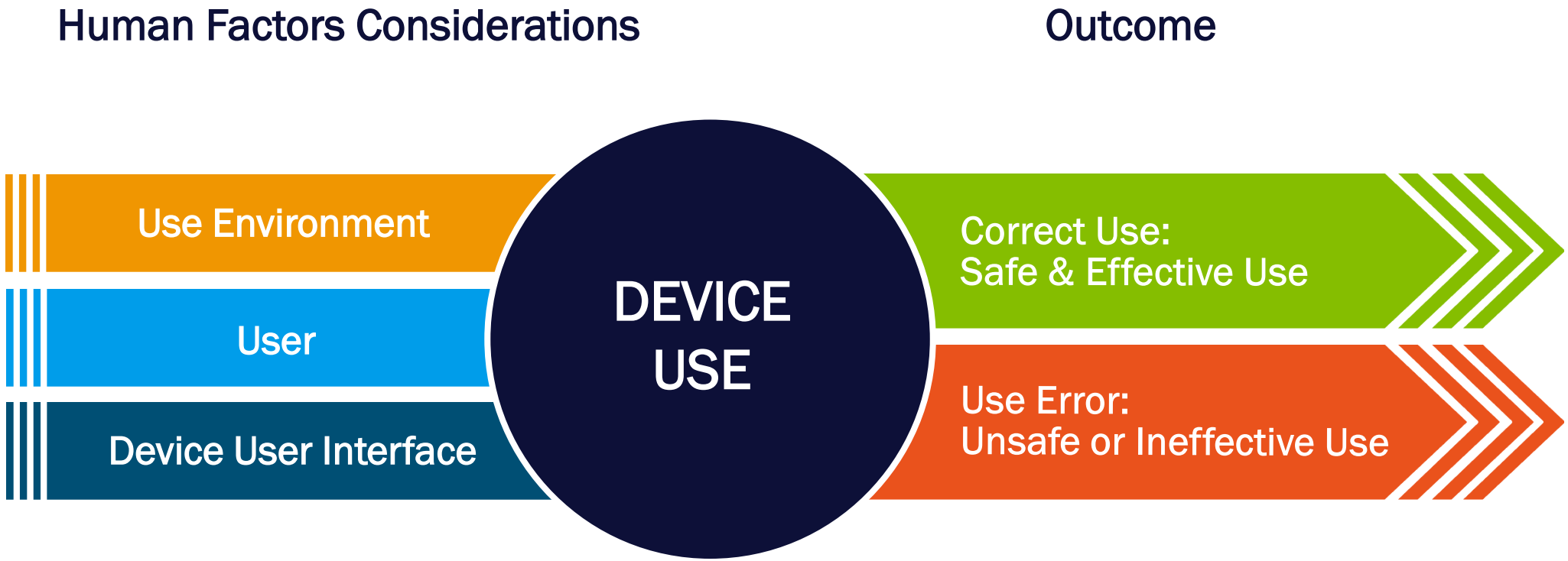
New way of looking at emergency RLD vs. Gx products

Evolution of Regulatory Guidance for Human Factors



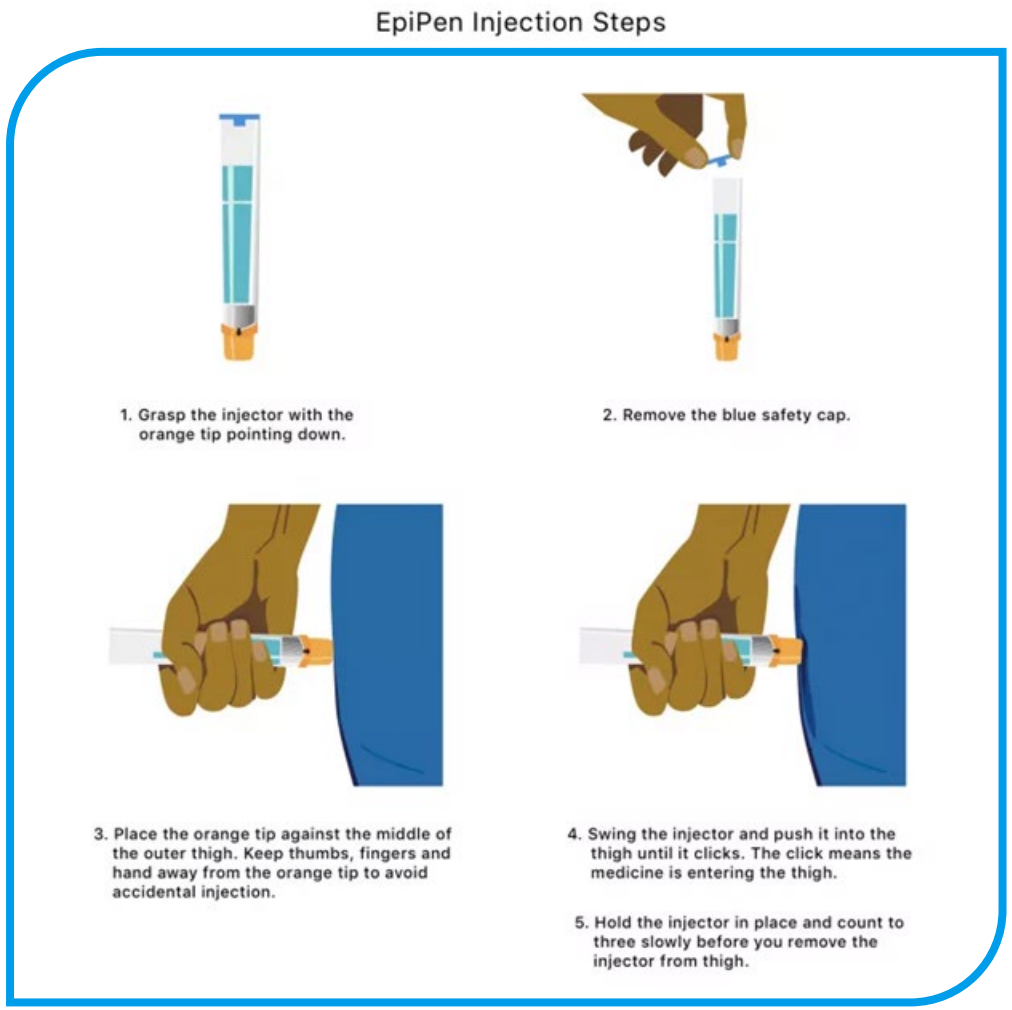
Applying Human Factors Engineering to Drug Development, North Carolina Regulatory Affairs Monthly Seminar, 2023

Human Factors Is a Critical Component of the Risk Management System



FDA, Applying Human Factors and Usability Engineering to Medical Devices , 2016

Emergency Use Autoinjectors

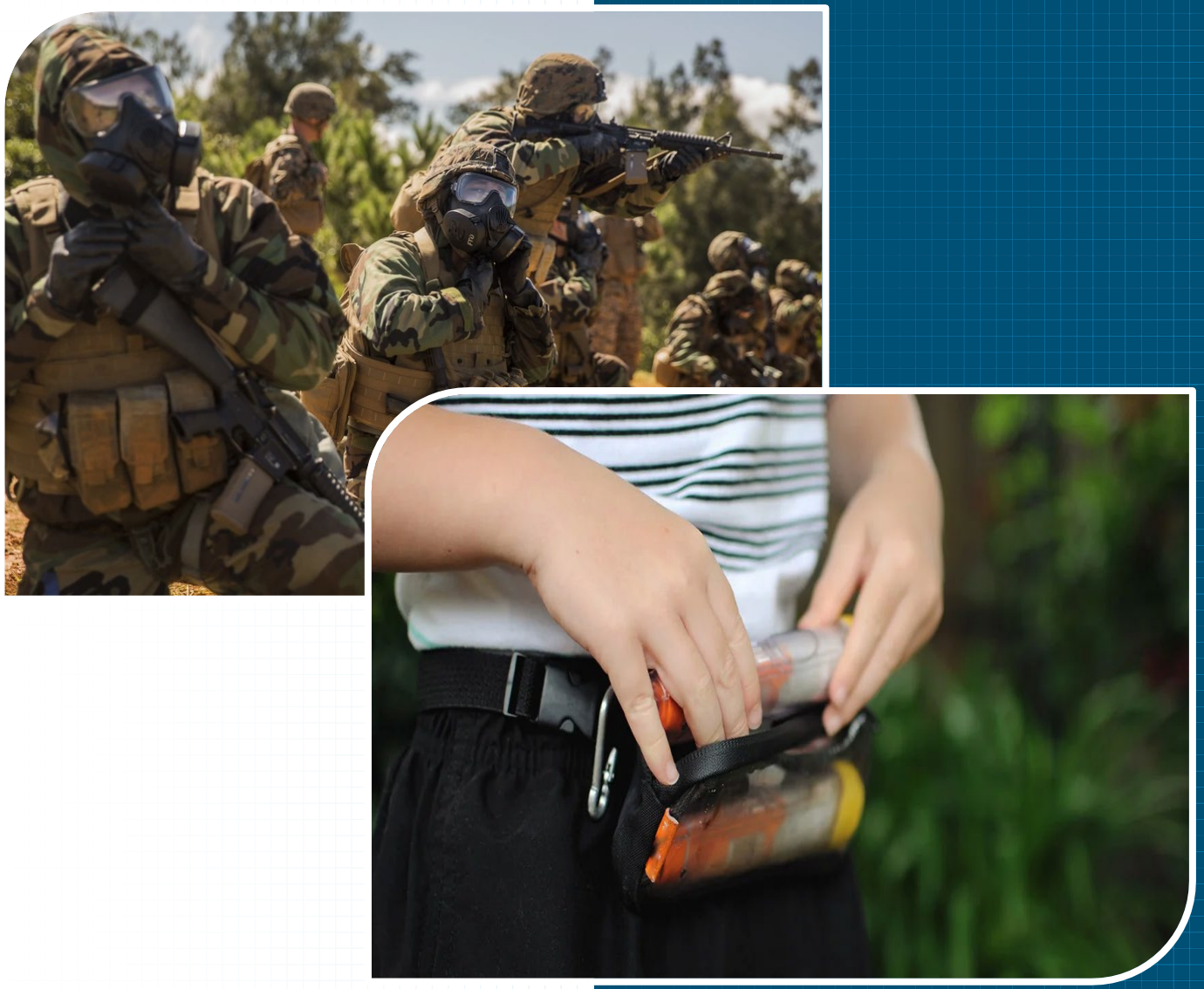


Follow instructions to properly administer EpiPen. "Blue to the sky, orange to the thigh."

- Emergency use autoinjectors, such as those for treating anaphylaxis, are used by patients, caregivers, or first responders outside healthcare environments.
- The FDA recommends that emergency use autoinjectors include design control specifications for successful injection reliability of 99.999% with a 95% level of confidence or a 1:100,000 failure frequency.
- The level of reliability necessary to manufacture a safe and effective combination product directly correlates to the level of risk associated with an unreliable emergency use autoinjector. The reliability specification(s), R(t), represents the probability that the emergency use autoinjector will perform as intended, without failure, for a given time interval under specified conditions.

Context of Use

- Assessment of Identified Differences
- Threshold Analysis
- Reliability
- Emergency Use Gx Products
- Use Related Risk Analysis (URRA)



Context of Use: Assessment of Identified Differences

Minor Design Differences – Guidance describes a design difference as minor if the differences in the user interface of the proposed generic combination product, in comparison to the user interface of the RLD, do not affect an external critical design attribute. External critical design attributes are those features that directly affect how users perform a critical task that is necessary in order to use or administer the drug product.

Other Design Differences – FDA may not view a design difference as minor if any aspect of the threshold analyses suggests that differences in the design of the user interface of a proposed generic combination product as compared to the RLD may impact an external critical design attribute that involves administration of the product.

FDA, Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA: Draft Guidance for Industry, 2017

Context of Use: Threshold Analysis

Q: Is a threshold analysis relevant/necessary for emergency use Gx products?

To Compare Generic and RLD Devices FDA Recommends:

- Labeling side-by-side comparison
- Comparative task analysis
- Physical comparison of delivery devices. If analyses show that user interface differences between generic and RLD products might not be minor:
  - Consider changing the generic design
  - Conduct “comparative human factors study” measuring error rate

Context of Use: Reliability

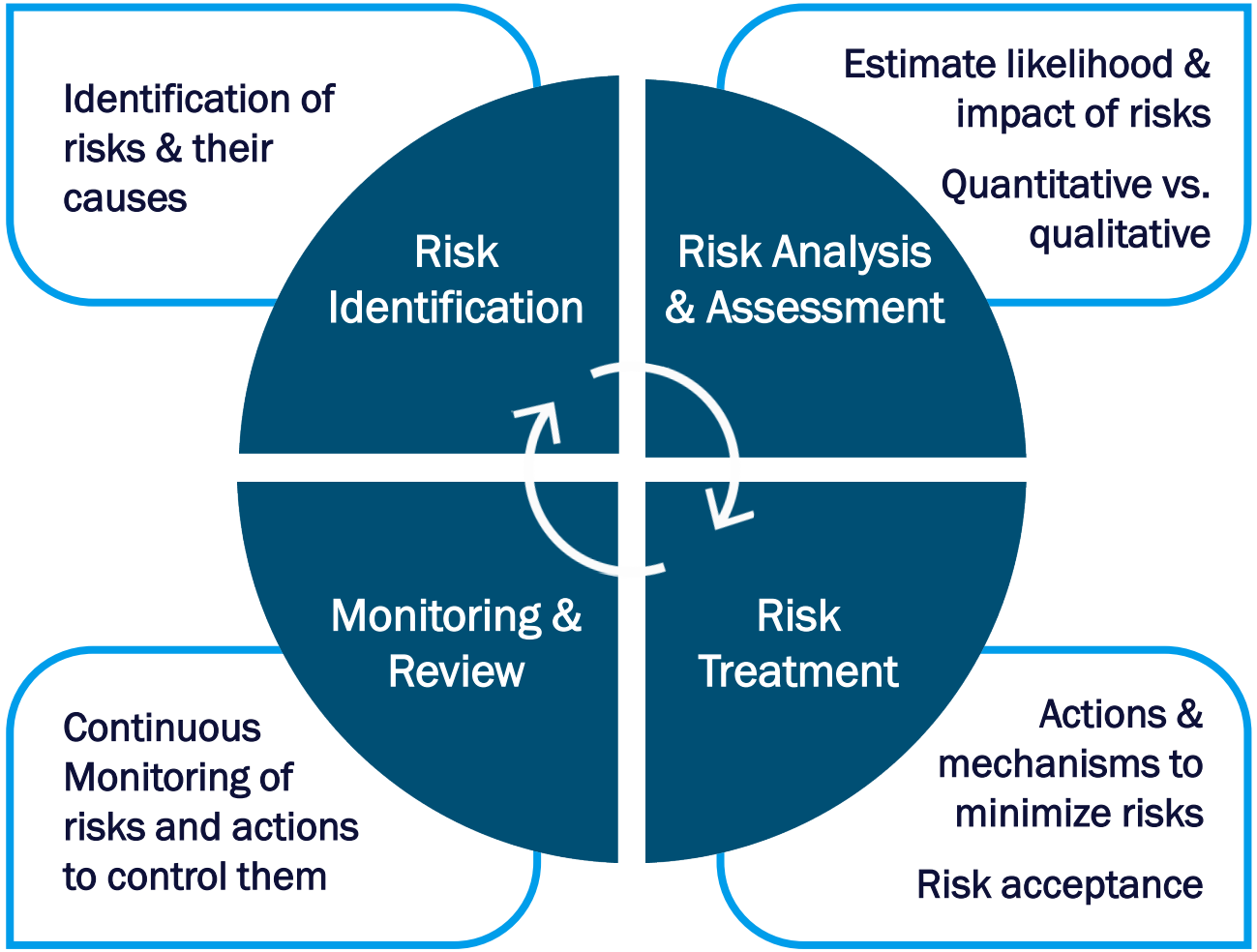
- Meeting reliability is a critical component of emergency Gx products.
- We do this by employing Essential Performance Requirements.
- ISO 11608 ensures that a device reliably performs the minimum activation and operation steps to meet safety requirements and to be reliably operated by different users. And typically considers:
  - Cap removal/Priming force
  - Activation force
  - Injection time
  - Dose accuracy
  - Needle length
  - Needle shield
  - Confirmation of operation (visual, audible, or tactile means)

Context of Use: Emergency Gx Products

- A reliability assessment is specific to the combination product's intended use — risks are likely to be impacted by the condition being treated, environments of use, emergency use autoinjector technology, drug, user characteristics, etc.
- The reliability analysis, in addition to the traditional development activities, should include:
  - Identification of the reliability requirements and specifications
  - Risk analysis
  - Design verification and validation of the reliability requirements and specifications
  - Design transfer of reliability specifications to the correct production specifications
  - The life cycle management benefits of a well-constructed reliability analysis include life cycle management benefits, future improvements in manufacturing controls, and post-market failure investigations. The marketing application should include information to verify and validate that the injector achieves its reliability specifications and related information. The design of an emergency use autoinjector should consider various factors to ensure its reliability, such as intended use, associated risks, risk analysis, use related issues, and use conditions.

Context of Use: Role of URRA

- A Use Related Risk Analysis (URRA) defines all use cases, tasks, and sub-tasks related to the user interface, potential use errors, the potential harm to the patient that results from potential use errors, and the severity of that harm.
- A URRA describes which aspects of the user interface/product design is intended to minimize the identified risks (risk control measures).
- The URRA is a powerful tool because it comprehensively considers the overall HFE product development process.



Overcoming Challenges of Siloed Experiences

- The complexity of combination products arises from the diversity of users, environments, delivery devices, and the combined properties of the drug and the overall user interface, as well as the potential effects of medication errors.
- For emergency use Gx, the URRA comprehensively examines how the drug, device, or combination of the two contribute to risks and identify opportunities to design the product to mitigate those risks.

Overcoming Challenges of Siloed Experiences (cont.)

Utilizing the URRA allows for a comprehensive consideration of overall safety, effectiveness, and reliability of the emergency Gx product.

Because tasks are completed by different user groups and are identified in the URRA to assess risk across potential product users and use environments, it also takes into consideration the EPRs of the emergency Gx product.

Risk control measures identified in the URRA for the RLD against the Gx could provide an alternate means of determination of minor vs. other design differences.

This method provides a nuance and more meaningful assessment for emergency Gx product's way of meeting requirements that may be limited by threshold analyses in the current guidance.

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