Essential Drug Delivery Outputs (EDDOs)

Breakout Session

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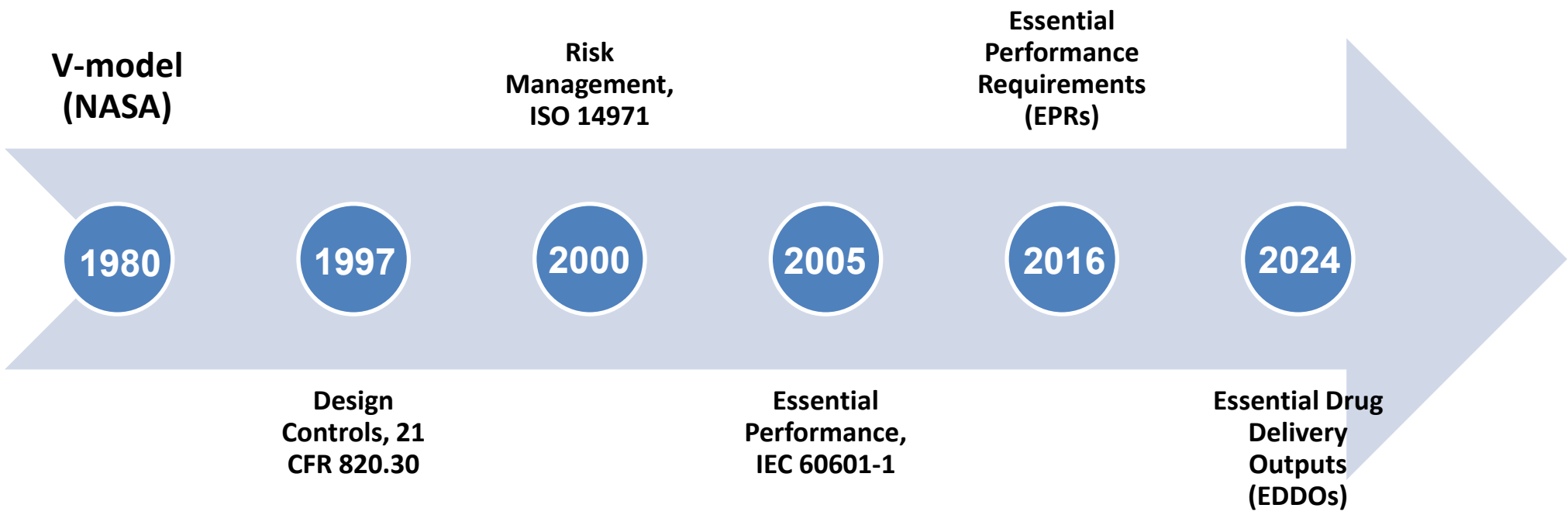
Session Objective

Industry perspective and panel discussion with FDA to understand current agency thinking and expectations on topics such as:

- Understanding when EDDO testing is applicable
- EPRs vs. EDDOs
- Impact of EDDO guidance on shelf-life and stability testing

How We Got to Essential Drug Delivery Outputs



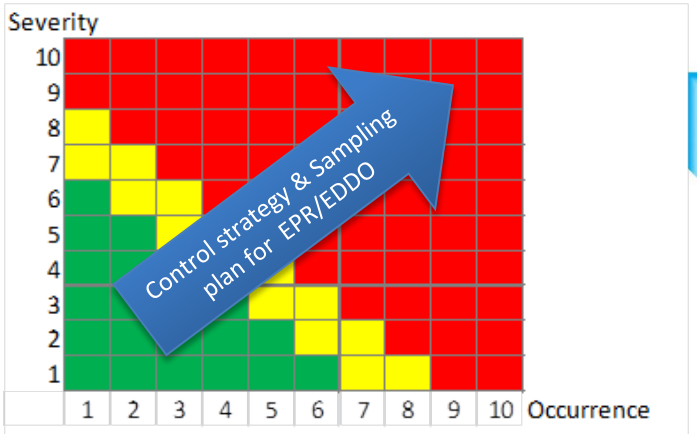
Why EPRs or EDDOs?

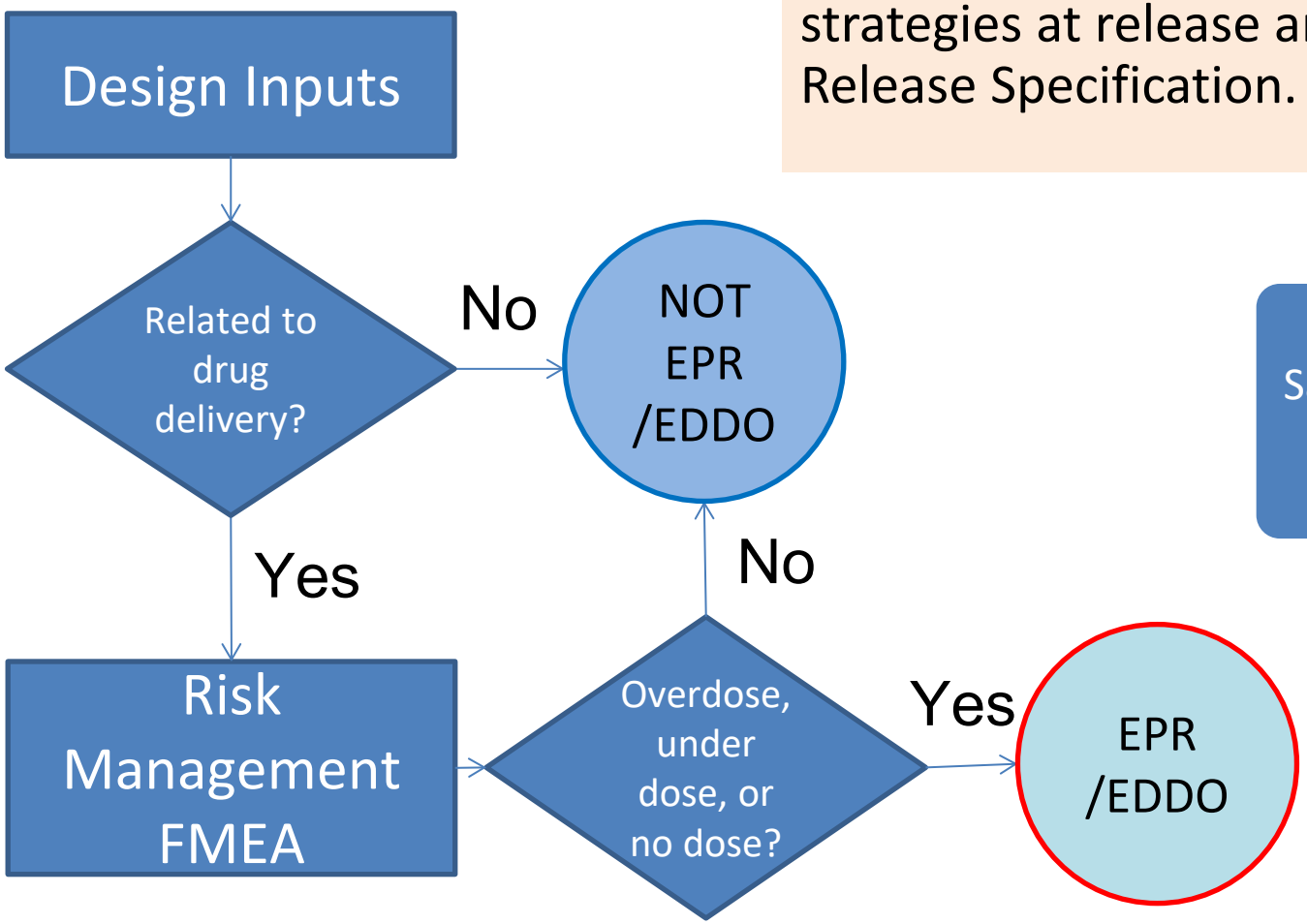
- We don't submit Design History File and Risk Management File to the FDA, so we need an executive summary in our submission!

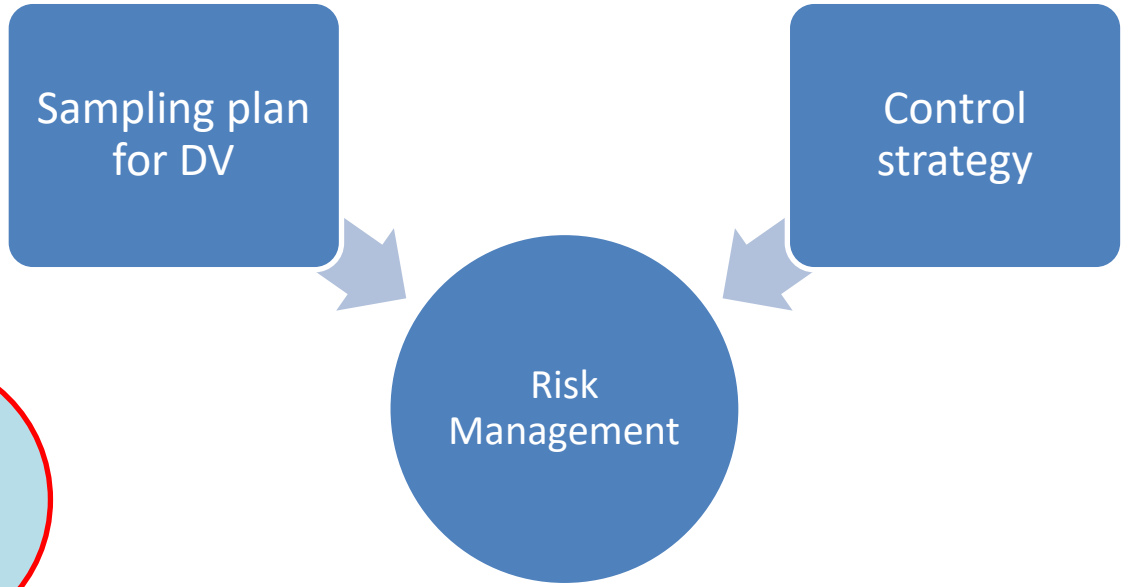
User Needs	Design Inputs	Design Outputs	Control Strategy	Design Verification	Design Validation
A product that is safe, effective, and usable	Delivered volume	Component and assembly specification	Incoming inspection	Dose accuracy testing	Human factors validation testing, comparative use testing, or threshold analysis
	Activation force		In process controls	Activation force testing	
	Injection time			Injection time testing	
	Extended needle length		Release specification	Extended needle length testing	

Identifying EDDOs: Practical Example

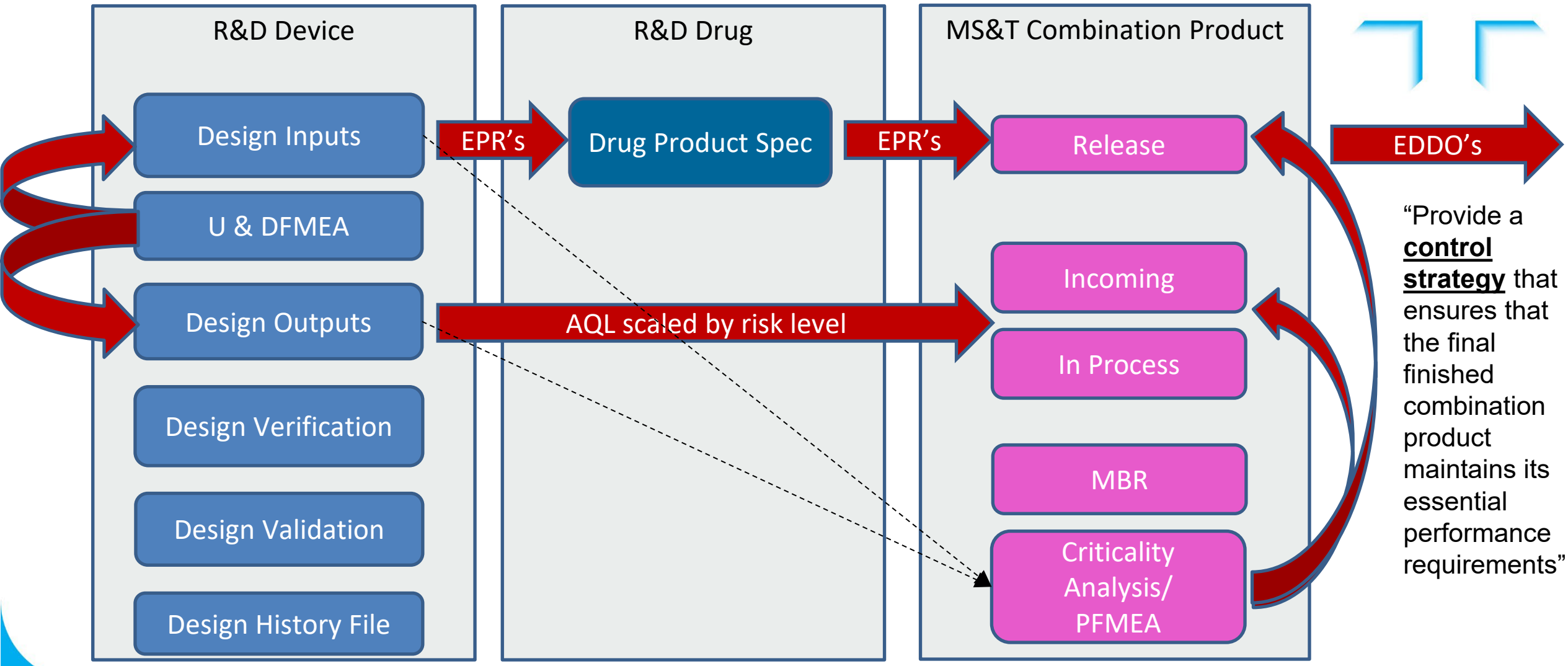
EPRs that are control strategies at release are Release Specification.







EPRs, Control Strategies and EDDOs



"Provide a **control strategy** that ensures that the final finished combination product maintains its essential performance requirements"

EPRs vs. EDDOs

"While the final set of essential performance requirements should be based on your **design control process**, we are providing the following example EPRs for your device type.

Example auto-injectors EPRs:
- Delivered Volume Accuracy
- Activation Force
- Injection Time
- Extended Needle Length

Example prefilled syringe EPRs:
- Delivered Volume Accuracy
- Break loose & Extrusion Force
- Safety needle activation force"

EPRs

Appendix A & B

Example auto-injectors EDDOs:
- Delivered Volume Accuracy
- Activation Force
- Injection Time
- Extended Needle Length

Example prefilled syringe EDDOs:
- Delivered Volume Accuracy
- Break loose & Extrusion Force
- Safety needle activation force

EDDOs

EPRs and EDDOs are the same.

Impact of EDDO on shelf-life and stability testing

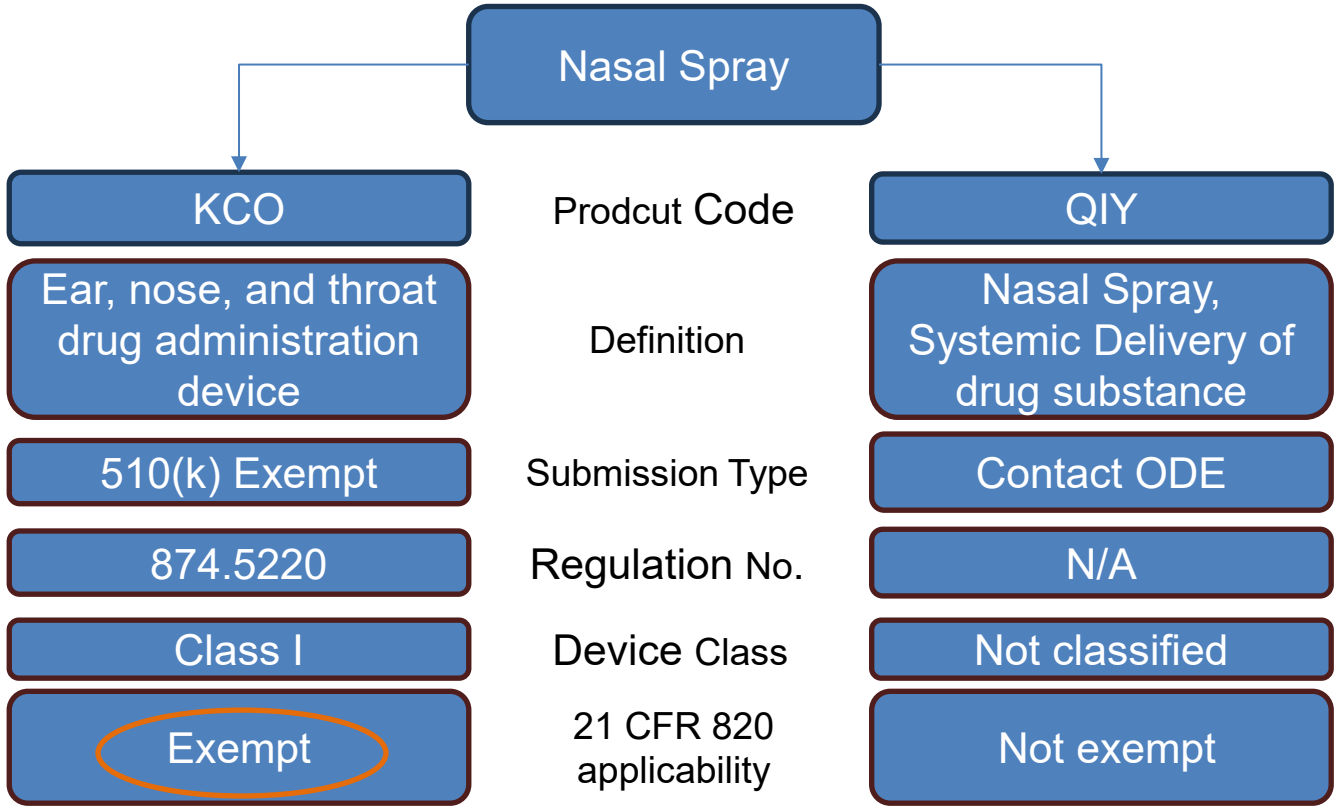
- You will verify all design inputs!
- Some design inputs will rise to the threshold of directly impacting drug delivery (efficacy) or safety and become EDDO's and likely tested at release.
- For the submission, clearly show for EPR's/EDDO's
  - Verification: including shipping and shelf-life
  - Validation: under actual or simulated use conditions
  - Use-related forces justification: side by side comparison or RLD independent testing
  - Control strategies

"Please provide validation testing, either through simulated shipping or actual shipping, that your combination product maintains its essential performance requirements."

"For your future marketing application, the stability program should include device endpoints to verify that the device essential performance, including dose accuracy and injection force, are maintained to the labeled date of expiry."

When EDDO testing is applicable – Nasal spray example

Nasal sprays are classified depending on if they are locally-acting or systemically absorbed, see below example product codes KCO and QIY.



- Exemption applies to medical device manufacturer.
- For combination products, 21 CFR Part 4 applies!
- Scope of the EDDO guidance includes nasal spray devices, thereby bringing nasal spray devices under EDDO testing considerations.

When EDDO testing is applicable – Nasal spray example

Irrespective of the exemption provided to the medical device manufacturer, EDDO testing applies to nasal spray combination products.

- Combination product manufacturer must ensure that EDDO parameters for nasal sprays (pump delivery / spray weight, spray content uniformity, spray pattern, droplet size distribution, particle size distribution and activation force*) are identified, tested, and documented.

- EDDO documentation can reside either in the DHF or QbD documentation, and EDDO testing summary shall be part of the dossier submission.

* Activation force is a new addition coming from the FDA EDDO guidance; rest of the parameters are already part of the FDA guidance on *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation*.

Summary

- EPRs and EDDOs are two names for the same thing (testing EPRs on release made them design outputs).
- Develop under design controls and risk management and you will have EPRs/EDDOs.
- EPRs/EDDOs are a submission paradigm to create an executive summary of your development that most impact safety and efficacy.
- Have control strategies for attributes proportional to the risk to safety and efficacy (more risk/more stringent).
- EDDOs are defined as system parameters from product preparation to dose delivery completion (EPRs were from delivery start to delivery completion) – additional device quality attributes now clearly in scope (e.g., cap removal force).