Kirsten Ritter, PhD
GRx+Biosims 2025

Ophthalmic and nasal combination products

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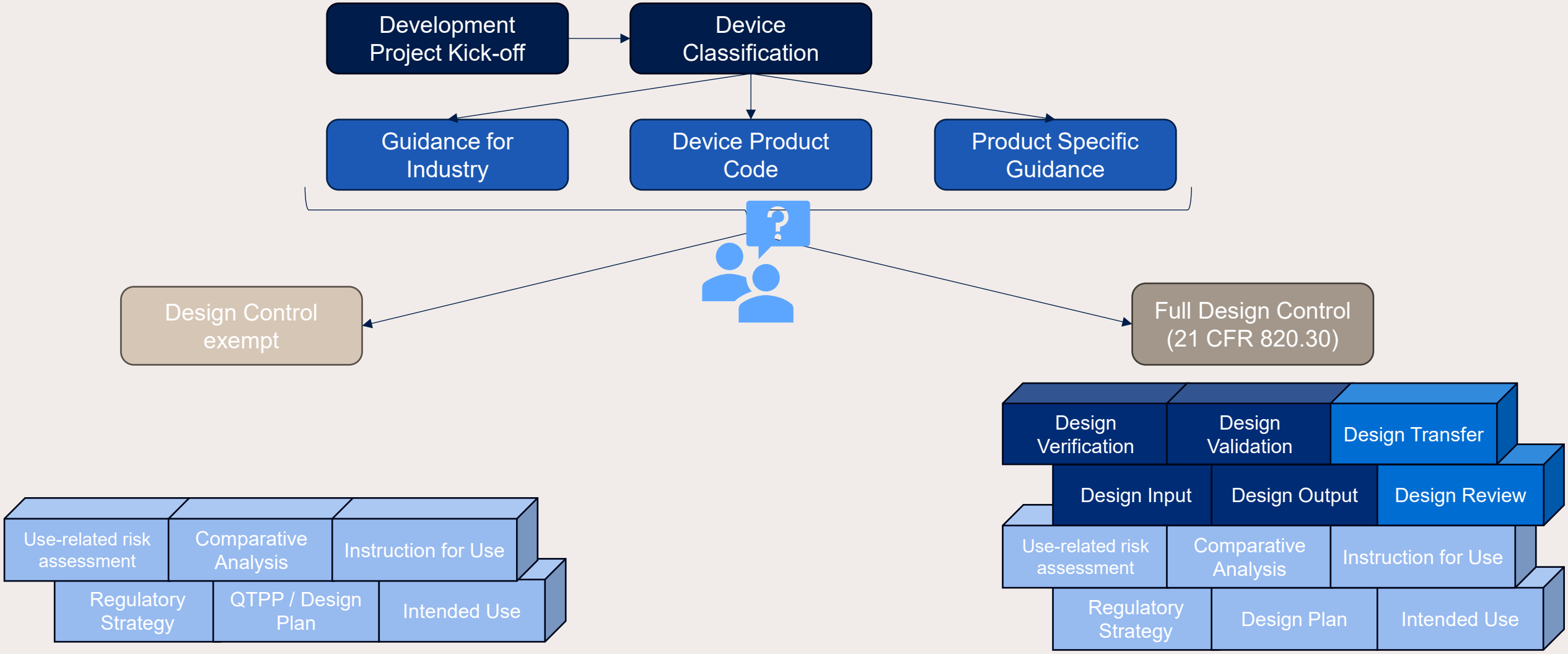
Impact of device classification on documentation



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Nasal Spray classification

Many new Nasal spray products are designed for systemic delivery, targeting various disease indications

FDA NEWS RELEASE

FDA Approves First Nasal Spray for Treatment of Anaphylaxis

For Immediate Release: August 09, 2024

Reuters World Business Markets Sustainability Legal More

US FDA approves nasal spray alternative to EpiPen for allergic reactions

By **Sriparna Roy** and **Christy Santhosh**

August 9, 2024 10:35 PM GMT+2 · Updated August 9, 2024

FDA NEWS RELEASE

FDA Approves First Over-the-Counter Naloxone Nasal Spray

Agency Continues to Take Critical Steps to Reduce Drug Overdose Deaths Being Driven Primarily by Illicit Opioids

FDA NEWS RELEASE

FDA Approves Nasal Spray Influenza Vaccine for Self- or Caregiver-Administration

First Influenza Vaccine That Does Not Need to be Administered by a Health Care Provider

Therapeutic areas for Nasal spray expanded from colds and allergies to migraine, autism spectrum disorders, Alzheimer's disease and depression.

FDA Approves First Nasal Spray for Treatment of Anaphylaxis | FDA
FDA Approves First Over-the-Counter Naloxone Nasal Spray | FDA
FDA Approves Nasal Spray Influenza Vaccine for Self- or Caregiver-Administration | FDA
US FDA approves nasal spray alternative to EpiPen for allergic reactions | Reuters

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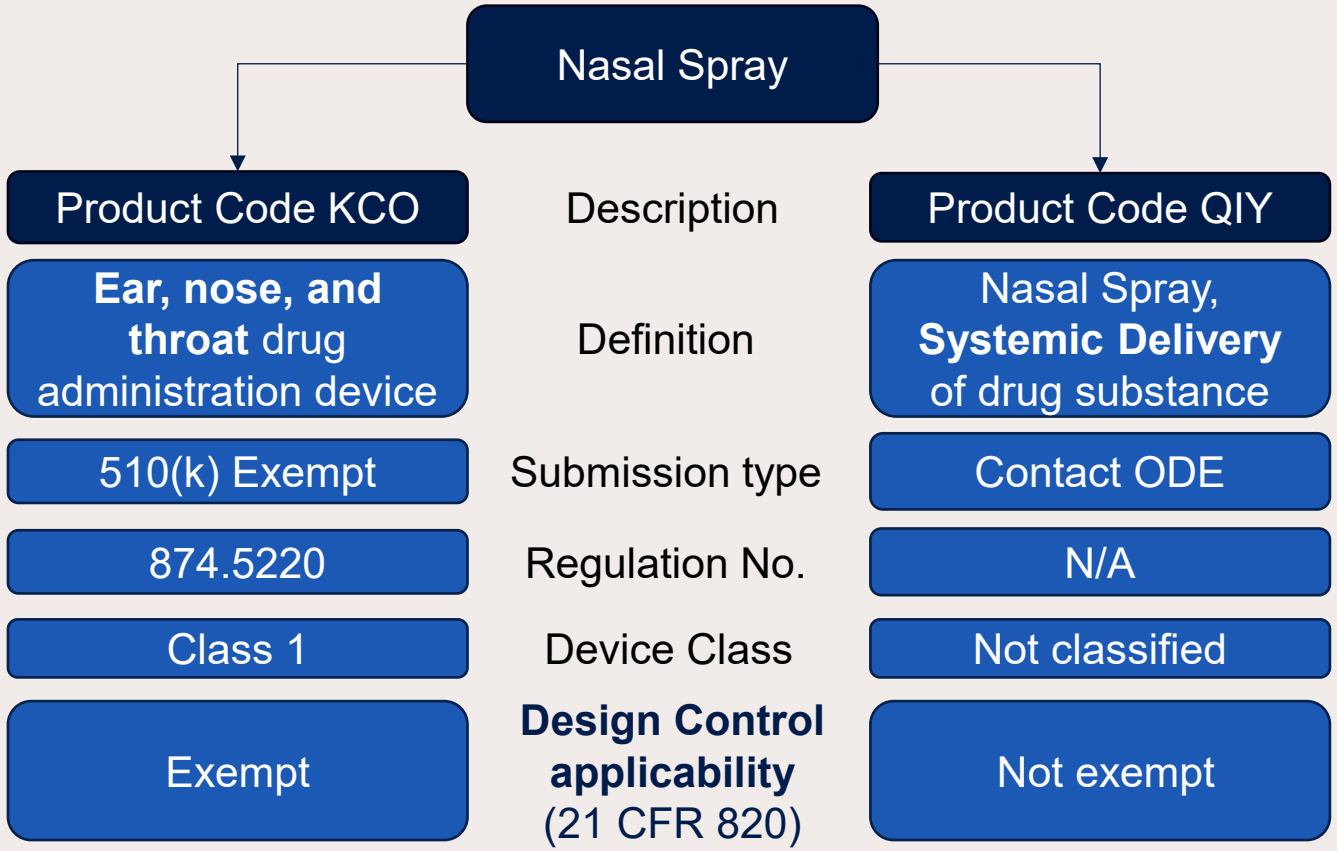
The Local vs systemic mechanism of nasal sprays is a major determinant for the device component requirements



Classification of device component is dependent on their **local or systemic mechanism** of action.

This mechanism is dependent on device characteristics, e.g.,:

- Particle size distribution
- Spray pattern & Plume geometry

but predominantly also on drug properties:

- Solubility
- **Pharmacokinetics**

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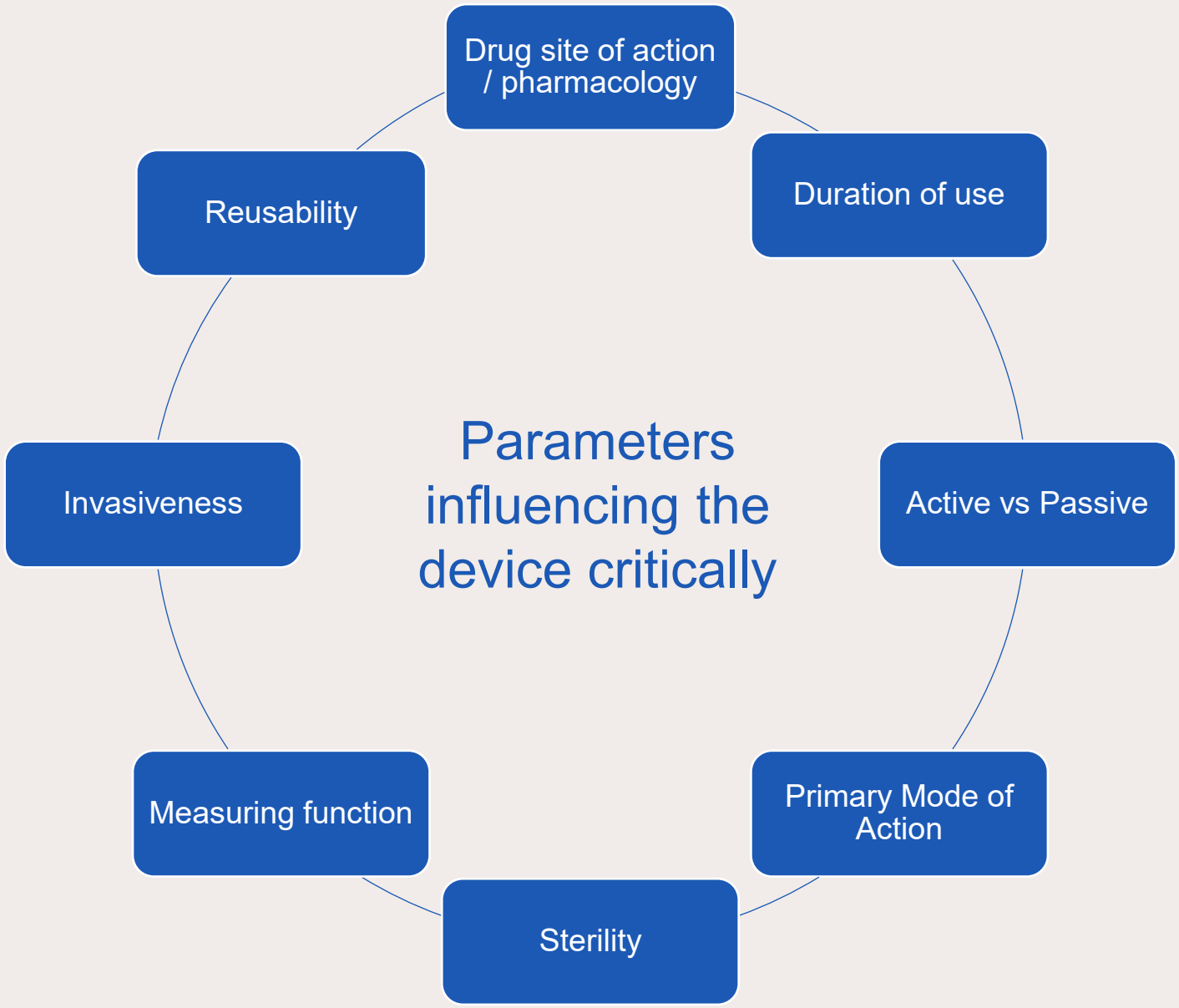

Linking Device classification to critical functional device parameters would ensure product development requirements are matched to patient safety needs

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Ophthalmic Dispenser products classification

For ophthalmic dispensers, „Genus decision“ led to a change in classification from drugs to combination products

21 CFR 200.50(c)

- **Ophthalmic dispensers** packaged together with the ophthalmic drug with which they were intended to be used were **regulated as drugs**
- Products were not regulated as combination products as defined in § 3.2(e) and were **not subject to requirements in part 4**

April 2021: Genus decision

- US Court of Appeals for District of Columbia Circuit decision in **Genus** Medical Technologies LLC v U.S. Food and Drug Administration
- “[e]xcepting combination products, . . . devices must be regulated as devices and drugs — if they do not also satisfy the device definition — must be regulated as drugs.

21 CFR Part 4

- Products are classified as “**drug-led combination products** composed of a drug constituent part that provided the primary mode of action and a device constituent part (an ophthalmic dispenser)”

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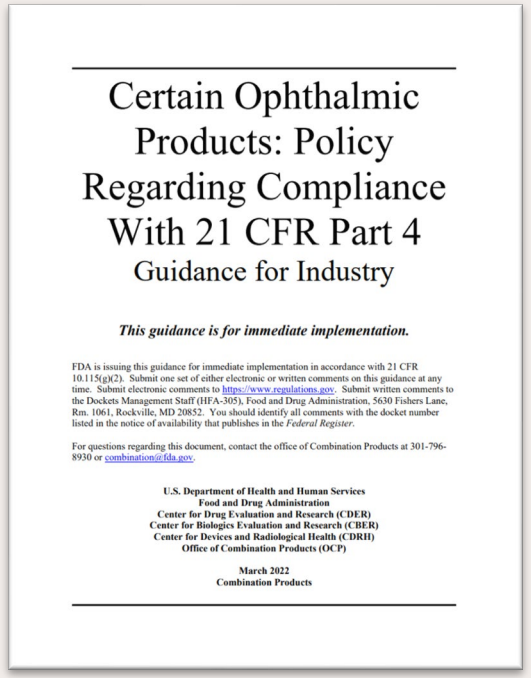
The impact of the reclassification on products with lower-risk device constituent parts is still outstanding

"Additionally, some ophthalmic products […] incorporate **lower-risk device constituent parts**, for example, eye dropper bottles/ampules that administer the drug directly to the eye.

The Agency is **evaluating the application of part 820 (*design control*)** quality system (QS) requirements to combination products that include such constituent parts.

Until FDA has further considered the application of these requirements to these combination products, the **Agency generally does not intend to take action with respect to noncompliance** with any applicable part 820 requirements for these ophthalmic products."



Certain Ophthalmic Products: Policy Regarding Compliance With 21 CFR Part 4

Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(2). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should 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 the office of Combination Products at 301-796-8930 or combination@fda.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Combination Products (OCP)

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Combination Products

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Key questions

- **Future Guidance for lower-risk Ophthalmic dispenser products:** What is the status of the evaluation of design control requirements (21 CFR 820) for lower-risk ophthalmic dispenser products?
- **Ophthalmic dispenser product code:** Does the FDA plan to create **device product codes** for (lower-risk) ophthalmic dispenser products?
- **Module 3 submission content for ophthalmic dispensers**: Beyond Design Control, could FDA provide guidance on their expectations for the scope and content of device constituent part testing data in Module 3 for lower-risk class ophthalmic dispenser products?
- **Module 3 submission content for nasal sprays**: Beyond Design Control, could FDA provide guidance on their expectations for the scope and content of device constituent part testing data in Module 3 for locally-acting vs systemically-acting nasal sprays?

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