

# What's New Regulatory Edition

## FDA Updates

### Guidance Documents

#### **1. Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations**

This draft guidance [issued July 3, 2025] is intended to clarify the key factors in calculating the aluminum content to ensure that the total aluminum exposure in parenteral nutrition (PN) does not exceed an acceptable threshold. It also provides FDA's recommendations regarding the aluminum concentration limits for small volume parenterals (SVPs) packaged as single doses or SVPs packaged in pharmacy bulk packages (PBPs). Additionally, this draft guidance is intended to assist sponsors and applicants in determining the appropriate placement of information on aluminum toxicity in SVP and large volume parenteral (LVP) Prescribing Information and container and carton labeling. This draft guidance revises and replaces the draft guidance for industry of the same name published on December 7, 2022.

#### **2. E21 Inclusion of Pregnant and Breastfeeding Women in Clinical Trials**

This draft guideline [issued July 18, 2025] provides recommendations for the appropriate inclusion and/or retention of pregnant and/or breastfeeding women in clinical trials and facilitate the generation of robust clinical data that allow for evidence-based decision making on the safe and effective use of medicinal products by these women and their healthcare providers (HCPs). The scope of this guideline includes pre- and postmarketing clinical trials of investigational products (see ICH E6(R3)) for indications in the general population and indications specific to pregnant or breastfeeding women.

#### **3. Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products Guidance for Industry**

This final guidance [issued July 18, 2025] provides recommendations to industry on formal meetings between FDA and sponsors or applicants relating to the development and review of biosimilar or interchangeable biological products regulated by the Center for Drug Evaluation

and Research (CDER) or the Center for Biologics Evaluation and Research (CBER). The guidance discusses the principles of good meeting management practices and describes standardized procedures for requesting, preparing, scheduling, conducting, and documenting formal meetings. This final guidance for industry revises and replaces the draft guidance of the same name issued in August 2023.

# What's New Regulatory Edition

## Health Canada Updates

### General Notices

#### **1. Notice: Revisions to the Drug Product Database's terminology page**

[published: July 4, 2025]

Health Canada is pleased to announce revisions to the [Drug Product Database's \(DPD\) Terminology Page](#). This page provides end users of the [Drug Product Database \(DPD\)](#) with information on the terms used throughout the DPD.

This page has been revised to better define the "Schedule" field and update the schedules to reflect the applicable Acts, Regulations, and other categories, including descriptions for each schedule. Other minor revisions to provide clarity are also included throughout this page.

While the drug product records are being revised to align with these updates, some may still list the former schedules.

Questions or concerns related to the Drug Product Database's Terminology Page should be directed to the Office of Submissions and Intellectual Property at: [din@hc-sc.gc.ca](mailto:din@hc-sc.gc.ca).

#### **2. Notice of amendment: Nicotine tablets exempted from the Prescription Drug List**

[published: July 21, 2025]

The purpose of this notice of amendment is to announce that Health Canada has added a new part to the qualifier of the "Nicotine or its salts" listing on the human use part of the Prescription Drug List (PDL). The new part provides for the non-prescription status of some orally disintegrating or sublingual nicotine tablets (see part "f" which will become part "g" in the future once further amendments are made to the other qualifiers specific to nicotine pouches).

### **3. Notice: Classification of topical products containing human-derived exosomes, human extracellular vesicles, and/or human cell-conditioned media**

[published: August 14, 2025]

The purpose of this Notice is to communicate Health Canada's position on the classification and regulation of topical products at the cosmetic-drug interface that contain human-derived exosomes, human extracellular vesicles, and/or human cell-conditioned media to industry, practitioners, and the public. This intended approach is based on available evidence to date.

This Notice outlines the considerations applied in determining whether a topical product containing human-derived exosomes, human extracellular vesicles, and/or human cell-conditioned media is classified and regulated as a drug product or cosmetic product. It is intended to provide information to regulated parties on compliance with the Food and Drugs Act and its regulations, and is intended to be used in conjunction with other existing guidance documents and policies

### **4. Notice: Multiple additions to the Prescription Drug List (PDL)**

[published: August 28, 2025]

The purpose of this Notice of Amendment is to announce the addition of artesunate, crovalimab, osilodrostat, and quizartinib to the [Prescription Drug List](#) (PDL) for human and veterinary use (see [Table 1](#)), and the amendment to the qualifier of the "Benzoyl peroxide" PDL entry for human use (see [Table 2](#)).

# Health Canada Updates

## Guidance Documents

### **1. Nitrosamine impurities in medications: Guidance**

[updated: August 1, 2025]

An updated version of Health Canada's [Guidance on nitrosamine impurities in medications](#), including an updated list of established Acceptable Intake (AI) limits ([Appendix 1](#)), has been posted online. Several updates have been incorporated into the Nitrosamines guidance document, including:

Health Canada's current expectations for the Step 3 timeline of our Call for Review, notably:

- For those nitrosamine impurities with an established AI limit published in Appendix 1 of this guidance document prior to August 1, 2025, MAHs are permitted to have a Corrective

and Preventative Action (CAPA) implementation timeline of up to 3 years from August 1, 2025 (i.e., up to August 1, 2028).

- For those nitrosamine impurities with an established AI limit published in Appendix 1 on August 1, 2025 or later, MAHs are permitted to have a CAPA implementation timeline of up to 3 years from the publication date of the AI limit.
- Considering the risk profiles of nitrosamines and the possibility of an additive biological effect, the AI limits published in Appendix 1 are considered appropriate by Health Canada for lifetime and less-than-life (LTL) administration of a drug product, including during the 3 year CAPA implementation timeline (i.e., LTL-based AI limits are not to be applied during or after 3 year CAPA implementation timeline).

#### General and Quality:

- Confirmatory testing expectations for nitrosamine impurities which can be controlled according to the ICH Q3A and ICH Q3B guidelines (number 12)
- Additional guidance concerning Supplements, Notifiable Changes and Post-DIN Change submissions where the quality changes do not increase the risk of presence of nitrosamine impurities relative to the approved drug product (number 20 and Appendix 2)
- Validating the limit of quantitation for analytical procedures (number 33)
- The potential for alternative control strategies where the root cause of nitrosamine presence is well understood (number 34)

#### Appendix 1:

- seventeen (17) additional nitrosamine impurities and their corresponding Carcinogenic Potency Categorization Approach (CPCA)-derived AI limits
- revised AI limit for N-nitroso-N-desmethyl-doxylamine (from 18 ng/day to 100 ng/day)
- The list of established AI limits can be filtered by date to identify the most recent additions

#### Appendix 5:

- A new appendix concerning bioequivalence studies for reformulated drug products with nitrosamine suppressing agents such as antioxidants and pH modifiers