What's New Regulatory Edition

FDA Updates

General Notices

1. **FDA qualifies drug development tool to facilitate clinical trial research on alcohol use disorder**

FDA's Center for Drug Evaluation and Research (CDER) has a qualifying tool to support the development of treatments for alcohol use disorder (AUD). This tool provides a new endpoint option for researchers and drug developers alongside abstinence and no heavy drinking days. With this qualification, investigators can now determine if their proposed treatment works as they expect based on whether it reduced risk drinking levels by two levels in clinical trials.

2. **Determining Recommended Acceptable Intake Limits for N-nitrosamine Impurities in Pharmaceuticals: Development and Application of the Carcinogenic Potency Categorization Approach**

FDA and international regulators developed a methodology, the Carcinogenic Potency Categorization Approach (CPCA), that uses the chemical structure of a nitrosamine impurity to recommend AI limits by assignment to 1 of 5 predicted potency categories reflecting carcinogenic risk.

The application of the CPCA to determine recommended AI limits for nitrosamine impurities has expedited the regulatory review of drug safety assessments submitted by drug companies as an AI limit can be identified more efficiently and with greater transparency and predictability.-Further development of the CPCA is expected as new experimental studies help identify additional features and properties that may be appropriate to include.

CDER continues to work with international regulators in the development and use of this modeling approach to identify recommended AI limits for nitrosamines and to more effectively address the potential impact of these impurities on the drug supply.

3. **FDA issues class-wide labeling changes for testosterone products**

FDA informed sponsors of testosterone products about new labeling changes following the agency's review of the findings from the Testosterone Replacement Therapy for Assessment of Long-term Vascular Events and Efficacy Response in Hypogonadal Men (TRAVERSE) clinical trial and the results from required post-market ambulatory blood pressure (ABPM) studies.

FDA Updates

Guidance Documents

1. **Considerations for Complying with 21 CFR 211.110**

This guidance, when finalized, will describe considerations for complying with the requirements in 21 CFR 211.110 to ensure batch uniformity and drug product integrity. In addition, this guidance discusses related quality considerations for drug products that are manufactured using advanced manufacturing. It also discusses how manufacturers can incorporate process models into commercial manufacturing control strategies. This guidance applies to the manufacture of human drug products, including biological products, and animal drug products; these will be collectively referred to as drug products in this guidance. This guidance does not apply to the manufacture of active ingredients.

2. **Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products Questions and Answers**

This guidance describes FDA's enforcement policy regarding certain firm-initiated communications of scientific information on unapproved use(s) of the firm's approved/cleared medical products to health care providers (HCPs) engaged in prescribing or administering medical products to individual patients. This guidance finalizes the revised draft guidance of the same title issued in October 2023. The October 2023 revised draft guidance revised and replaced the draft guidance entitled "Distributing Scientific and Medical Publications on Unapproved New Uses--Recommended Practices," issued in March 2014, which itself revised the final guidance entitled "Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices," issued in January 2009. This guidance is not for current implementation, pending the Office of Management and Budget's (OMB's) decision on the collection of information.

3. **Interim Policy on Compounding Using Bulk Dug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act**

This guidance describes FDA's interim policy concerning compounding by human drug product compounders that are not outsourcing facilities using bulk drug substances while FDA develops the list of bulk drug substances that can be used in compounding under the applicable section of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This guidance finalizes the draft guidance of the same title issued in December 2023 and replaces the final guidance of the same title issued in January 2017.

4. **Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act**

This guidance describes FDA's interim regulatory policy concerning compounding by outsourcing facilities using bulk drug substances while FDA develops the list of bulk drug substances that outsourcing facilities can use in compounding under the applicable section of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This guidance finalizes the draft guidance of the same title issued in December 2023 and replaces the final guidance of the same title issued in January 2017.

5. **Study of Sex Differences in the Clinical Evaluation of Medical Products**

This guidance provides recommendations for increasing enrollment of females in clinical trials, analyzing and interpreting sex-specific data, and including sex-specific information in regulatory submissions of medical products. Clinical trials and non-interventional studies of medical products should be designed to enroll sufficient numbers of females and males to reflect the prevalence of the disease or condition for which the medical product is being investigated to help ensure the generalizability of results and facilitate exploration of potential differences in effects by sex. When finalized, this guidance will replace the guidance entitled "Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs" issued in July 1993.

6. **Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products**

This guidance provides recommendations to sponsors and other interested parties on the use of artificial intelligence (AI) to produce information or data intended to support regulatory decision-making regarding safety, effectiveness, or quality for drugs. Specifically, this guidance provides a risk-based credibility assessment framework that may be used for establishing and evaluating the credibility of an AI model for a particular context of use (COU).

7. Developing Drugs for Optical Imaging

The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Developing Drugs for Optical Imaging.” The purpose of this guidance is to provide recommendations to sponsors regarding clinical trial design features that support development and approval of optical imaging drugs that are used in conjunction with imaging devices and intended as intraoperative aids for the detection of pathology such as tumors or to enhance the conspicuity of normal anatomical structures.

8. Obesity and Overweight: Developing Drugs and Biological Product for Weight Reduction

The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Obesity and Overweight: Developing Drugs and Biological Products for Weight Reduction.” This guidance provides recommendations to industry regarding the development of drugs and biological products regulated within the Center for Drug Evaluation and Research intended for reduction and long-term maintenance of body weight in patients with obesity or overweight. This guidance revises and replaces the draft guidance for industry “Developing Products for Weight Management” issued in February 2007. This guidance is being distributed for comment purposes only.

What's New Regulatory Edition

Health Canada Updates

General Notices

1. **Updated: Validation rules for regulatory transaction in non-eCTD format**

Health Canada has updated the validation rules for regulatory transactions submitted in the non-eCTD format.

Version of the non-eCTD validation rules: 5.3

Effective date: May 31, 2025

2. **Updated: Validation rules for regulatory transactions in electronic Common Technical Document (eCTD) format**

Health Canada has updated the validation rules for regulatory transactions submitted in the electronic Common Technical Document (eCTD) format, to reflect recent and upcoming changes in our processes.

Version of the eCTD validation rules: 5.3

Effective date: May 31, 2025

3. **Notice – Implementation of International Council for Harmonisation (ICH) S1B(R1): Testing for Carcinogenicity of Pharmaceuticals**

By way of this Notice, Health Canada is advising of its implementation of ICH S1B(R1): Testing for Carcinogenicity of Pharmaceuticals. The ICH Assembly endorsed the final draft and recommended its implementation on August 4, 2022. Health Canada implemented ICH S1B(R1) on June 20, 2023. ICH S1B(R1) should be read in conjunction with this accompanying notice and with the relevant sections of other applicable Health Canada guidances.

4. **Notice to Stakeholders – Consultation on the Impacts of Implementation of ICH M13A: Bioequivalence for Immediate Release Solid Oral Dosage Forms**

By way of this Notice, Health Canada is advising Canadians that it anticipates implementation of ICH M13A: Bioequivalence for Immediate Release Solid Oral Dosage Forms in fall 2025 and is seeking feedback on a proposal to extend the application of the bioequivalence standards outlined in ICH M13A to modified-release dosage forms.

5. **Updates to Mutual Recognition Agreement between Canada and Switzerland**

Drug Establishing Licensing Bulletin #187, January 31, 2025:

As of January 31, 2025, Canada and Switzerland agreed to expand the scope of the existing Mutual Recognition Agreement (MRA).

Health Canada Updates

Guidance Documents

1. **Updated: Guidance Document: Patented Medicines (Notice of Compliance) Regulations**

The Guidance Document has been amended to align with existing Health Products and Food Branch policies and the Office of Patented Medicines and Liaison's current practices as they relate to the administration of the Patented Medicines (Notice of Compliance) Regulations.

2. **What we heard: Draft guidance on expanded access clinical trials**

The Draft guidance on expanded access clinical trials was published on August 2, 2024, and opened to the public for consultation until October 31, 2024.

This "what we heard" report:

- provides background and context for the draft guidance
- summarizes the consultation approach and
- gives an overview of the comments we received

3. **Updated: Guidance Document: Regulatory Requirements for Drug Identification Numbers (DINs)**

This guidance document applies to all drugs that have been assigned a DIN (i.e., human and veterinary drugs, biologics, disinfectants, and radiopharmaceuticals). The guidance was updated on February 18, 2025, to provide additional clarification on the designation “DIN” on the label of a biocide.

4. Submitting risk management plans guidance document

This guidance document on submitting risk management plans, published on February 24, 2025, will come into effect on July 1, 2025.

In the meantime the Guidance Document - Submission of Risk Management Plan and Follow-up Commitments published in June 2015 will remain in effect, along with the supporting notices:

- Notice of clarification to drug manufacturers and sponsors - Risk Management Plans - Update (August 13, 2020)
- Notice of clarification to drug manufacturers and sponsors: Canadian-specific considerations in risk management plans (November 12,2020)

For more information on risk management plans guidance, and transitioning to the new regulations, consult:

- New agile regulatory provisions and updated guidance document for submitting risk management plans: Notice