US FDA Update

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IMDRF International Medical Device Regulators Forum

Overview

- Final Rule: Quality Management System Regulation (QMSR)
- Proposed Rule: Laboratory Developed Tests (LDTs)
- Digital Health
- Cybersecurity
- The Accreditation Scheme for Conformity Assessment (ASCA)

Quality Management System Regulation (QMSR)

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Quality Management System Regulation (QMSR)

FDA published the final amendment to 21 CFR Part 820: **Quality Management System Regulation (QMSR)** on **February 2, 2024**; harmonizing the current Quality System regulation for medical devices by converging its requirements with international quality management system requirements

Revisions to Part 820 replace most of the existing regulation with an incorporation by reference (IBR) to the 2016 edition of International Organization for Standardization (ISO) 13485 - *Medical Devices - Quality Management Systems - Requirements for Regulatory Purposes*

The transition period from the Quality System Regulation (prior 820) to the Quality Management System Regulation ("new" 820) is two (2) years from **February 2, 2026**.

Overview of the QMSR

- Withdraws most of the requirements in the previous part 820
  - Retains the scope and some definitions from the Quality System Regulation
- Incorporates by reference ISO 13485:2016
  - Minimal called out provisions/country specific requirements
    - Includes definitions and requirements to ensure consistency with other applicable FDA requirements
- Incorporates by reference Clause 3 of ISO 9000:2015, Quality management systems--Fundamentals and vocabulary
  - Terms and definitions necessary for the application of ISO 13485
- Includes conforming edits to Part 4 (cGMPs for combination products)
  - Does not impact the CGMP requirements for combination products

Laboratory Developed Tests (LDTs)

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Laboratory Developed Tests (LDTs) Rulemaking

Oct 3, 2023

- Notice of Proposed Rulemaking published
- Opened docket for public comment

Dec 4, 2023

- Docket closed
- >6,500 comments received

Spring 2024

- Projected publication of final rule per Unified Agenda

Notice of Proposed Rulemaking

Would amend FDA's regulations to make explicit that IVDs are devices under the FD&C Act including if the manufacturer is a laboratory

Would phase out FDA's general enforcement discretion approach for most LDTs so IVDs manufactured by laboratories generally fall under the same enforcement policies as other IVDs

1 year from final rule
- Medical Device Reporting
- Correction and Removal Reporting

2 years from final rule
- Establishment Registration & Device Listing
- Labeling Requirements
- Investigational Requirements

3 years from final rule
- Quality System Requirements

3.5 years from final rule
- Premarket Review for High Risk IVDs

4 years from final rule
- Premarket Review for Low* and Moderate Risk IVDs

*Most Low Risk IVDs are exempt from premarket review

Digital Health Updates

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Digital Health Advisory Committee (DHAC)

Purpose: Solicit views from technical and scientific subject matter experts to improve the FDA's understanding of the Digital Health Technologies (DHT's) that supports safe and effective regulation while encouraging innovation.

Charter

- **Topics**
  - AI, digital diagnostics, digital therapeutics, AR/VR, real-world data, real-world evidence, patient-generated health data, interoperability, personalized medicine/genetics, decentralized clinical trials, cybersecurity, others.

- **Duties**
  - Advise the FDA on issues related to Digital Health Technologies (DHTs). Provide expertise and perspective to improve Agency understanding of the benefits & risks,
  - New approaches to develop and evaluate DHTs.
  - Promote innovation, identifying barriers.
  - Consider unintended consequences from policy or regulation.

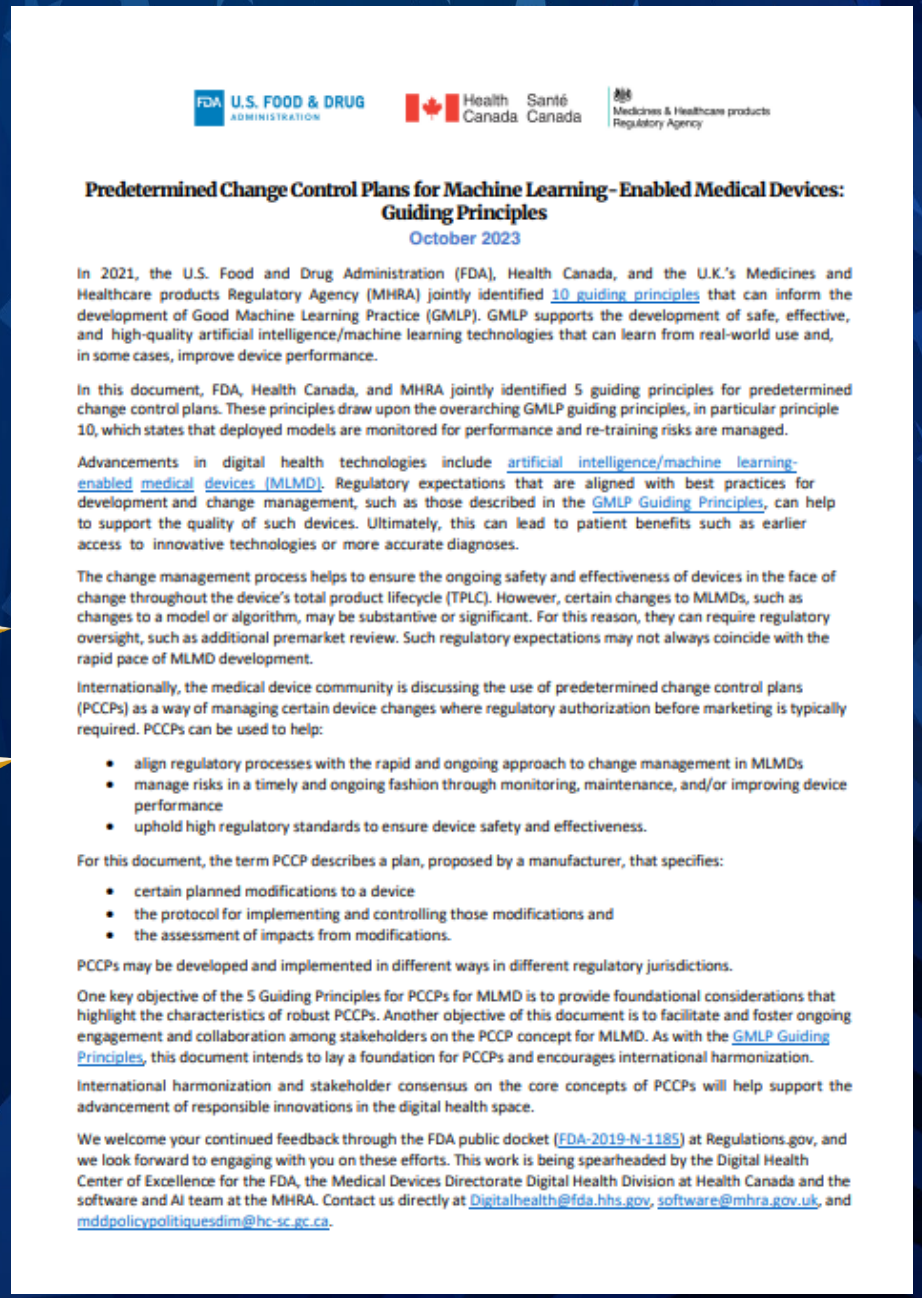
Committee

- **Standing members**
  - *(8) Academic/practitioners*
  - *(1) Consumer representative (nominated by consumer orgs.)*

- **Industry representative**
  - *Non-voting; (1) nominated by industry per meeting/topic*

- **Temporary members**
  - Qualified pool of scientific and technical experts.
  - The number of temporary members selected for a particular meeting will depend on the meeting topic.

- **Meetings**
  - The committee should be fully operational in 2024.



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Predetermined Change Control Plans for Machine Learning-Enabled Medical Devices: Guiding Principles

October 2023

In 2021, the U.S. Food and Drug Administration (FDA), Health Canada, and the U.K.'s Medicines and Healthcare products Regulatory Agency (MHRA) jointly identified 10 guiding principles that can inform the development of Good Machine Learning Practice (GMLP). GMLP supports the development of safe, effective, and high-quality artificial intelligence/machine learning technologies that can learn from real-world use and, in some cases, improve device performance.

In this document, FDA, Health Canada, and MHRA jointly identified 5 guiding principles for predetermined change control plans. These principles draw upon the overarching GMLP guiding principles, in particular principle 10, which states that deployed models are monitored for performance and re-training risks are managed.

Advancements in digital health technologies include artificial intelligence/machine learning-enabled medical devices (MLMD). Regulatory expectations that are aligned with best practices for development and change management, such as those described in the GMLP Guiding Principles, can help to support the quality of such devices. Ultimately, this can lead to patient benefits such as earlier access to innovative technologies or more accurate diagnoses.

The change management process helps to ensure the ongoing safety and effectiveness of devices in the face of change throughout the device's total product lifecycle (TPLC). However, certain changes to MLMDs, such as changes to a model or algorithm, may be substantive or significant. For this reason, they can require regulatory oversight, such as additional premarket review. Such regulatory expectations may not always coincide with the rapid pace of MLMD development.

Internationally, the medical device community is discussing the use of predetermined change control plans (PCCPs) as a way of managing certain device changes where regulatory authorization before marketing is typically required. PCCPs can be used to help:

- align regulatory processes with the rapid and ongoing approach to change management in MLMDs
- manage risks in a timely and ongoing fashion through monitoring, maintenance, and/or improving device performance
- uphold high regulatory standards to ensure device safety and effectiveness.

For this document, the term PCCP describes a plan, proposed by a manufacturer, that specifies:

- certain planned modifications to a device
- the protocol for implementing and controlling those modifications and
- the assessment of impacts from modifications.

PCCPs may be developed and implemented in different ways in different regulatory jurisdictions.

One key objective of the 5 Guiding Principles for PCCPs for MLMD is to provide foundational considerations that highlight the characteristics of robust PCCPs. Another objective of this document is to facilitate and foster ongoing engagement and collaboration among stakeholders on the PCCP concept for MLMD. As with the GMLP Guiding Principles, this document intends to lay a foundation for PCCPs and encourages international harmonization.

International harmonization and stakeholder consensus on the core concepts of PCCPs will help support the advancement of responsible innovations in the digital health space.

We welcome your continued feedback through the FDA public docket (FDA-2019-N-1185) at Regulations.gov, and we look forward to engaging with you on these efforts. This work is being spearheaded by the Digital Health Center of Excellence for the FDA, the Medical Devices Directorate Digital Health Division at Health Canada and the software and AI team at the MHRA. Contact us directly at Digitalhealth@fda.hhs.gov, software@mhra.gov.uk, and mddpolicypolitiquesdim@hc-sc.gc.ca.

Predetermined Change Control Plans

- Joint document issued between US FDA, Health Canada, and MHRA in October 2023
- Identifies 5 guiding principles for predetermined change control plans:
  1. Focused and Bounded
  2. Risk-Based
  3. Evidence-Based
  4. Transparent
  5. Total Product Lifecycle (TPLC) Perspective

Cybersecurity

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Medical Device Cybersecurity Program

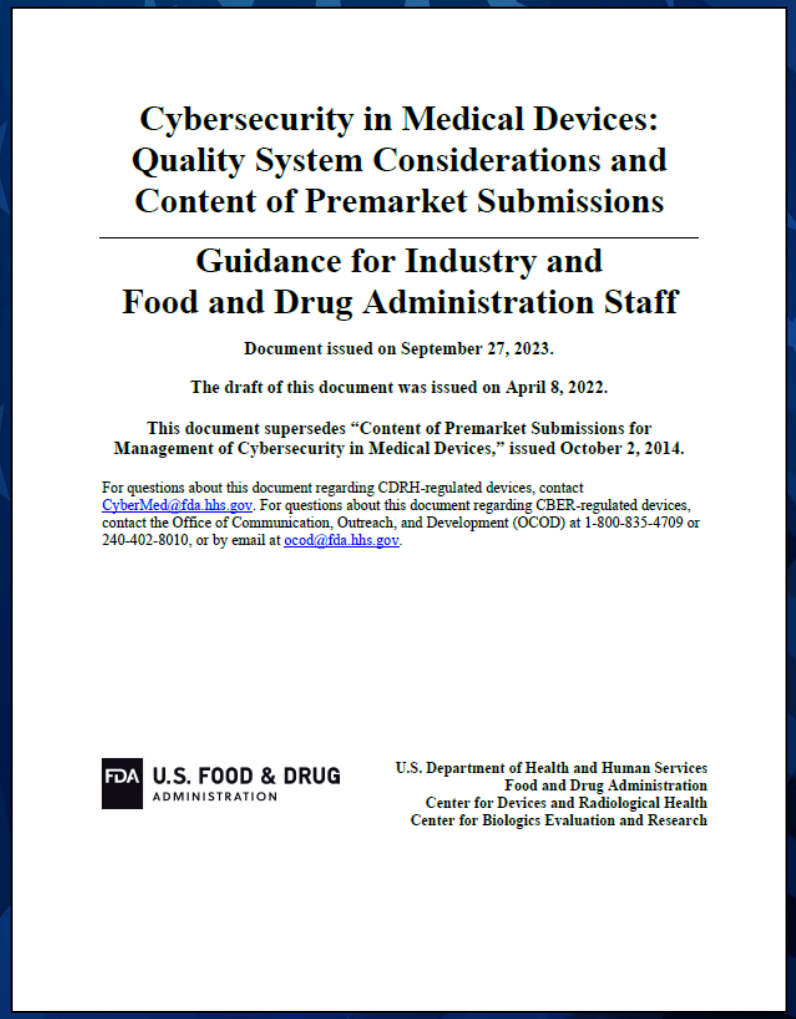
Celebrated 10-year anniversary in 2023

More than doubled the number of dedicated cybersecurity personnel

Division of Medical Device Cybersecurity formed in 2024 within FDA/CDRH

Continue to develop resources, collaborate with other federal partners, and private/public sector working groups.

Collaborated with sector partners to develop 31 cybersecurity resources available to use.



Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 27, 2023.

The draft of this document was issued on April 8, 2022.

This document supersedes "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices," issued October 2, 2014.

For questions about this document regarding CDRH-regulated devices, contact CyberMed@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Cybersecurity in Medical Devices Guidance Document

FDA's Cybersecurity in Medical Device: Quality System Considerations and Content of Premarket Submissions

- Issued September 27, 2023
- Recommendations are intended to help manufacturer comply with requirements under Section 524B of the FD&C Act:
  - Have policies and procedures for addressing vulnerabilities and exploits;
  - Design, develop, and maintain processes and procedures to provide reasonable assurance that device and related systems are cybersecure;
  - Ensure device can be updated and patched;
  - Provide SBOM.
- Addresses how cybersecurity fits into the Quality System Requirements (21 CRF Part 820) and premarket submission documentation requirements

Accreditation Scheme for Conformity Assessment (ASCA)

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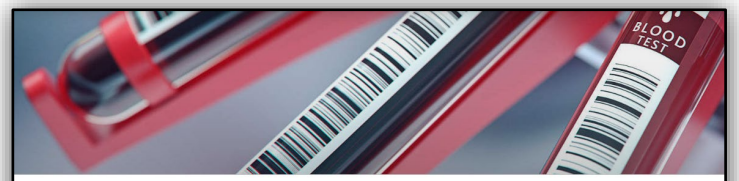
The Accreditation Scheme for Conformity Assessment (ASCA)

- Voluntary program leveraging a well-established international conformity assessment infrastructure
  - ASCA-recognized accreditation bodies accredit testing laboratories.
  - ASCA-accredited testing laboratories provide test results to device manufacturers.
  - Device manufacturers include Declarations of Conformity and supplemental documentation in their premarket submissions to FDA.
- Capitalizes on voluntary consensus standards in device development and review
- **Transitioned from a pilot to a permanent program on September 19, 2023**

ISO/IEC 17011:2017
Conformity assessment — Requirements for accreditation bodies accrediting conformity assessment bodies



← Popular standards
ISO/IEC 17025
Testing and calibration laboratories

ASCA Goals

- Streamlines conformity assessment in device submissions
- Enhances the FDA's confidence in test methods and results
- Decreases the need for additional information related to conformance with a standard
- Promotes consistency, predictability, and efficiency in the medical device review process
- Serves as a least burdensome approach to conformity assessment

ASCA By the Numbers

80*

Standards included in ASCA

105

ASCA-accredited testing laboratories

56

ASCA Submissions

6%

ASCA submissions for which FDA requested complete test reports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