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QMSR Final Rule: Meeting FDA's New Requirements

20 March 2024

PRESENTED BY:
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Profile

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Eric is a Senior Quality Systems and Compliance Advisor in the FDA & Life Sciences Practice of the law firm King & Spalding. He is a 35-year industry veteran and since 2018 has provided advisory and consulting services focused on regulatory compliance, enforcement, and policy matters for industries regulated by the FDA. Eric's guidance focuses on FDA requirements to professionals in medical device manufacturing, including but not limited to quality systems requirements, inspection preparedness and post-market obligations. He also advises corporate management and boards on their responsibilities and expectations of the FDA.

In addition to his work at K&S, Eric is also a strategic committee member of the AI Global Healthcare Initiative, where he co-chairs the Good Machine Learning Practices (GMLP) working team and collaborates with organizations such as the FDA, National Academy of Medicine, Duke University, and the Office of National Coordinator for Health IT within HHS on a number of AI-related projects. He has published numerous white papers and articles and speaks frequently on regulatory compliance, software design controls, cybersecurity, and AI. Eric's presentation work includes volunteering for Pathway for Patient Health, where he provides fundamental quality and regulatory education to undergraduate college students in life science-related majors.

Prior to King & Spalding, Eric led global technical and quality organizations at Philips, Medtronic, GE Healthcare, Boston Scientific, and Hologic.

Prior to entering the medical device industry, Eric held software and business operations leadership roles in the financial securities, health insurance, and retail industries.

The Quality System Regulation (QSR) (i.e. 21 CFR Part 820) and Its Scope

The Quality System Regulation

- Effective 1 June 1997
- Replaced 1978 GMP for medical devices
- Harmonized to ISO 13485:1996

Scope

- Domestic and foreign manufacturers of finished medical devices (FMDs) (not component manufacturers although supplier controls may influence expectations at this level)
- Methods and facilities involved in design, manufacturing, packaging, labeling, storage, installation, and servicing of FMDs (may extend beyond FMD manufacturers)
- Finished medical devices intended for use in the U.S. (including territories, DC, PR)

The One Fundamental Requirement (21 CFR §820.5)

- “Each manufacturer shall establish and maintain a quality system that is appropriate for the specific medical device(s) designed or manufactured, and that meets the requirements of this part.”
- A product not manufactured in compliance with the QSR is deemed “adulterated” and subject to regulatory action (even if it meets specifications and is safe and effective).

High-Level Walkthrough of 21 CFR Part 820 (1 of 2)

- ***Management Controls (*)***
  - Quality Policy
  - Organization
    - Manager with Executive Responsibility
    - Management Representative
  - Management Review
  - Quality Planning
  - Quality System
  - Quality Audit
  - Personnel (Training, Education, Experience)

- ***Design Controls (*)***
  - Design and Development Planning
  - Design Inputs
  - Design Outputs
  - Design Review
  - Design Verification
  - Design Validation
  - Design Transfer
  - Design Change
  - DHF
- ***Document Controls***
  - Approval
  - Changes
- ***Purchasing Controls***
  - Evaluation
  - Maintenance

(*) QSIT Element

High-Level Walkthrough of 21 CFR Part 820 (2 of 2)

- ***Production and Process Controls (*)***
  - Process changes
  - Environmental Controls, Personnel, Contamination Controls, Buildings, Equipment, Material Management
  - Software Validation
  - Inspection / Test Equipment, Calibration
  - Process Validation (or verification)
  - Nonconforming Product
  - Acceptance
- ***Corrective Action / Preventive Action (*)***
  - Investigation
  - Data Analysis (including statistical analysis)
  - Containment
  - Correction
  - Corrective Actions
  - Preventive Actions
  - Verification of Effectiveness
- ***Product Identification***
  - Identification
  - Traceability
- ***Packaging / Labeling***
- ***Handling, Storage, Distribution, Installation***
- ***Records***
  - DMR
  - DHR
  - Quality System Records
  - Complaints
- ***Service***
- ***Statistical Techniques***

(*) QSIT Element

What is Happening to the QSR?

- 1996 – Present: No significant changes to QSR
- 2018: FDA announced plans to reexamine the QSR to blend with requirements of ISO 13485 and align with other regulatory authorities
- 2018 – 2022: FDA missed at least five internal deadlines to modify the QSR
- 23 February 2022: FDA published a proposed rule to amend 21 CFR Part 820 and Part 4 (Combination Products) to incorporate by reference ISO 13485:2016 (QSR renamed QMSR)
- 2 March 2022: FDA convened the Device Good Manufacturing Practice (DGMP) Advisory Committee in a public meeting to review and make recommendations regarding the proposed rule (Section 520(f)(1)(B) of the FD&C Act)
- 24 May 2022: Comment period on the proposed rule closed
- 2 February 2024: FDA issued the final rule amending 21 CFR Part 820 (QMSR) and Part 4– more on this later
- 2 February 2026: The final rule will become effective. Firms must comply with QSR until that date.

Why ISO 13485?

ISO 13485

- Initial version in 1996 as an adaptation of ISO 9001 (general quality management system requirements)
- Governs Quality Management System (QMS) requirements for medical device manufacturing
- Recognized in a variety of geographies (e.g., the European Union (harmonized under EU MDR), Canada, Australia, Japan)

Scope of ISO 13485

- Organizations that provide medical devices and related services including design and development, production, storage and distribution, installation, or servicing of a medical device and design and development or provision of associated activities (e.g., technical support).
- External parties that provide product, including quality management system-related services to such organizations.

Relationship Between FDA and ISO 13485

- FDA was a key participant in the 1996 initial release of ISO 13485
- FDA continues to be heavily involved in ISO/TC 210 through the American National Standards Institute (ANSI)
- FDA participates in the Medical Device Single Audit Program (MDSAP), which is based on ISO 13485:2016, and accepts MDSAP audit reports in lieu of routine FDA inspections
- ISO 13485:2016 remains "substantially similar" to the QSR

Current part 820 [1]	ISO 13485 requirements [1]	Proposed rule
Subpart A—General Provisions	Clause 1. Scope, Clause 4. Quality Management System.	Requirements substantively similar.
Subpart B—QS Requirements	Clause 4. Quality Management System, Clause 5. Management Responsibility, Clause 6. Resource Management, Clause 8. Measurement, Analysis, and Improvement.	Requirements substantively similar.
Subpart C—Design Controls	Clause 7. Product Realization	Requirements substantively similar.
Subpart D—Document Controls [2]	Clause 4. Quality Management System	Differences addressed in 820.35.
Subpart E—Purchasing Controls	Clause 7. Product Realization	Requirements substantively similar.
Subpart F—Identification and Traceability	Clause 7. Product Realization	Requirements substantively similar.
Subpart G—Production and Process Controls	Clause 4. Quality Management System, Clause 6. Resource Management, Clause 7. Product Realization.	Requirements substantively similar.
Subpart H—Acceptance Activities	Clause 7. Product Realization, Clause 8. Measurement, Analysis, and Improvement.	Requirements substantively similar.
Subpart I—Nonconforming Product	Clause 8. Measurement, Analysis, and Improvement.	Requirements substantively similar.
Subpart J—Corrective and Preventive Action	Clause 8. Measurement, Analysis, and Improvement.	Requirements substantively similar.
Subpart K—Labeling and Packaging Control	Clause 7. Product Realization	Differences addressed in 820.45.
Subpart L—Handling, Storage, Distribution, and Installation.	Clause 7. Product Realization	Requirements substantively similar.
Subpart M—Records	Clause 4. Quality Management System	Differences addressed in 820.35.
Subpart N—Servicing	Clause 7. Product Realization	Differences addressed in 820.35.
Subpart O—Statistical Techniques	Clause 7. Product Realization, Clause 8. Measurement, Analysis, and Improvement.	Requirements substantively similar.

FDA's Authority to Make this Change

"We are issuing this rule under the same authority that FDA initially invoked to issue the QS regulation and combination product regulations…"
Preamble to the Final Rule

"The Secretary may, in accordance with subparagraph (B), prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation … , packing, storage, and installation of a device conform to current good manufacturing practice, as prescribed in such regulations, to assure that the device will be safe and effective and otherwise in compliance with this Act …" — FD&C Act § 520(f)(1)(A)

Structure of the Final Rule (101 pages)

Preamble (includes)

- Executive Summary
  - ➢Purpose
  - ➢Major Provisions
  - ➢Legal Authority
- Background
  - ➢Introduction (History)
  - ➢Need for the regulation
  - ➢FDA's current regulatory framework
  - ➢General overview (summarizes changes from the proposed rule)
  - ➢Incorporation by reference
- Legal authority
- Comments on the proposed rule and FDA response (fewer than 100 comments addressed in 83 comment categories)

21 CFR Part 4 (Regulation of Combination Products)

21 CFR Part 820 (Quality Management System Regulation)

21 CFR Part 4

Changes references from QSR to QMSR and ISO 13485:2016

Section 820.1 (Scope)

Largely identical to QSR:

- In scope: Finished devices and human cells, tissues, and cellular and tissue-based products (HCT/Ps)
- Out of scope: Components and parts of finished devices
  - FDA has statutory authority to bring these into scope "should that become appropriate"
  - FDA encourages component manufacturers to voluntarily comply with QMSR

Describes how to address conflicts between Federal Food, Drug, and Cosmetic Act (FD&C Act) and implementing regulations.

Describes how to address conflicts between FD&C Act and ISO 13485:2016 (2 examples):

- "Device" and "labelling" in FD&C Act supersedes ISO 13485:2016 definitions of "medical device" and "labelling"
- "Safety and performance" in ISO 13485:2016 equivalent to "safety and effectiveness" in FD&C Act

Section 820.3 (Definitions)

Incorporates by reference Clause 3 of ISO 9000:2015 (change from proposed rule drove removal of several definitions): • "Customer" • "Design validation" • "Non-conformity" • "Process validation" • "Product" • "Top management" (was "management with executive responsibility in QSR) • "Verification"	"Establish" is gone (FDA resisted pushback from industry on removing this term).	DHF, DMR, DHR are gone. • Design History File (DHF) is now the design and development file from ISO 13485:2016 • Device Master Record (DMR) is now the Medical Device File from ISO 13485:2016 • Device History Record (DHR) is now the medical device or batch record from ISO 13485:2016	"Risk" definition pulled from ISO 14971:2019 (Medical devices – Application of risk management to medical devices), but FDA does not incorporate ISO 14971:2019 by reference.	Where FDA definitions supersede ISO 13485:2016: • "Device" from FD&C Act • "Labeling" from FD&C Act • "Manufacturer" from QMSR

Section 820.7 (Incorporation by Reference)

"Congress authorized incorporation by reference in the Freedom of Information Act (5 U.S.C. 552) to reduce the volume of material published in the Federal Register and CFR (see 5 U.S.C. 552(a) and 1 CFR part 51). The legal effect of incorporation by reference is that the material is treated as if it were published in the Federal Register and CFR. This material, like any other properly issued rule, has the force and effect of law."	The final rule removes most of the contents of the existing 21 CFR Part 820 and replaces them with three elements: • Reference to ISO 13485:2016: Instead of rewriting the QSR section by section, FDA makes the proposed 21 CFR Part 820 a pointer to ISO 13485:2016 content. • Reference to Clause 3 of ISO 9000:2015 (change from the proposed rule – sort of): ISO 13485:2016 references definitions in ISO 9000:2015, where ISO 13485:2016 does not define a term. FDA agreed with comments to make this an explicit reference in the QMSR. • Additional and clarified definitions and requirements: The QMSR identifies those limited areas in which FDA proposes to depart from ISO 13485.	ISO 13485:2016 and ISO 9000:2015 are copyrighted material. • View as read-only (no copying or printing) format from the American National Standards Institute (ANSI) Incorporated by Reference (IBR) Portal. • Purchase from ISO.	Future updates to ISO 13485:2016 (as early as 2026) will not result in automatic updates to the QMSR. FDA will review and consider updates using the rulemaking process, as appropriate.

Section 820.10 (Requirements for a Quality Management System)

Incorporates ISO 13485:2016, while ensuring other FDA regulations are maintained: •21 CFR Part 803 (Medical Device Reporting) •21 CFR Part 806 (Corrections and Removals) •21 CFR Part 821 (Medical Device Tracking) •21 CFR Part 830 (Unique Device Identification)	Clarifies devices subject to design and development requirements (ISO 13485:2016 (Clause 7.3)) are the same as QSR design controls (21 CFR §820.30): •Class II •Class III •Some Class I	Extends ISO 13485:2016 traceability requirements for implantable devices to devices that support or sustain life.	Failure to comply with QMSR renders a device adulterated.

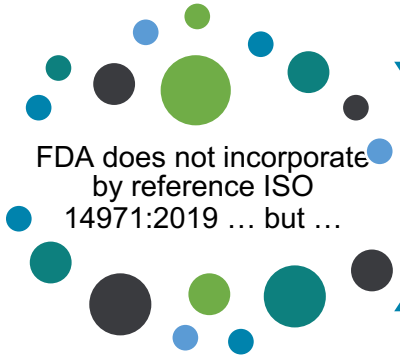
Section 820.35 (Control of Records)

Removes proposed rule requirement to "obtain the signature for each individual who approved or re-approved the record, and the date of such approval, on that record and include the below information in certain records" in favor of ISO 13485 approval requirements.	Defines content requirements for complaint records and service records.	Adds complaint requirements not in proposed rule: • When a complaint investigation must be initiated: Complaints that involve "the possible failure of a device, labeling, or packaging to meet any of its specifications." • FDA clarified how organizations should manage multiple complaint-handling units by admonishing firms to "define its corporate complaint handling procedure to ensure consistency throughout the different complaint handling units." • Identify a single group or unit "ultimately responsible for coordinating all complaint handling functions."	Adopts ISO 13485:2016 concepts of corrective actions and preventive actions • Different from FDA corrective and preventive actions in QSR's 21 CFR §820.100. • Adds "corrections" to CA/PA vocabulary especially regarding complaints.

Section 820.45 (Device Labeling and Packaging Controls)

FDA considers ISO 13485:2016 treatment of control and inspection of labeling and packaging as inadequate. ("ISO 13485 fails to provide additional requirements for labeling and packaging and does not specifically address the inspection of labeling by the manufacturer.")	QMSR requires manufacturers to inspect the accuracy of device labels with respect to certain elements prior to release, consistent with the requirements in current 21 C.F.R. § 820.120(b)e. (e.g., Recalls resulting from automated readers not catching label errors requires physical examination of representative sample prior to release)

Risk Management



FDA does not incorporate by reference ISO 14971:2019 … but …

ISO 13485:2016 treatment of risk management was a key driver behind the QMSR.

FDA recognizes ISO 14971:2019 as a consensus standard.

I strongly recommend compliance with ISO 14971:2019 as part of QMSR compliance.

ISO 13485:2016 references ISO 14971:2019 without mandating compliance.

- Compliance with ISO 14971:2019 is not required, but…
- FDA views compliance as a way to meet its regulatory requirements for risk management.

Effectiveness and Transition

Effective 2 February 2026

- This doubles the transition period in the proposed rule.
- “FDA recognizes that it is important for manufacturers to prepare to align their practices with the QMSR as soon as practical, and some manufacturers may choose to begin complying with the QMSR before the effective date. However, FDA does not intend to require compliance with the QMSR until its effective date. Until then, manufacturers are required to comply with the QS regulation.”

Points of ambiguity

- Will FDA inspections prior to 2 February 2026 comment on QMSR compliance?
- How will PMA submissions submitted prior to 2 February 2026 but subject to final decision after 2 February 2026 be treated?

Expect a short-term regulatory burden of compliance with both QMSR and QSR.

Inspection Considerations

QMSR does not impact FDA's inspectional authority

Quality System Inspection Technique (QSIT) will be replaced – no details provided

FDA inspections will not result in the issuance of ISO 13405:2016 certificates

ISO 13485:2016 certificates do not exempts firms from FDA inspection

Medical Device Single Audit Program (MDSAP) will continue to exempt firms from routine FDA inspections – impact to MDSAP not fully assessed yet

Management review, internal audits, and supplier audits no longer exempt from inspection review

Final Thoughts on Industry and FDA Impacts

Industry

If 13485:2016 certified, relatively small changes to accommodate QMSR – likely a net reduction in regulatory burden

If not 13484:2016 certified, possibly significant changes to accommodate QMSR (including adoption of ISO 14971:2019)

FDA

QSIT updates

Office of Medical Device & Radiological Health Operations (OMDRHO) training required

Unknown impact from CDRH reorg (e.g., ORA-to-OII)

Potential conflicts with current statutory authority

- Implementation of ISO 13485:2016 may cause unforeseen conflicts with current statutory authority under the FD&C Act

Questions?