FDA's Quality Management System Regulation (QMSR) and What it Means for Industry

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Summary of this Presentation

- FDA's Rationale for the QMSR
- Walkthrough of the QMSR – clause-by-clause
- Industry Feedback

Evolution of Medical Device QMS Requirements

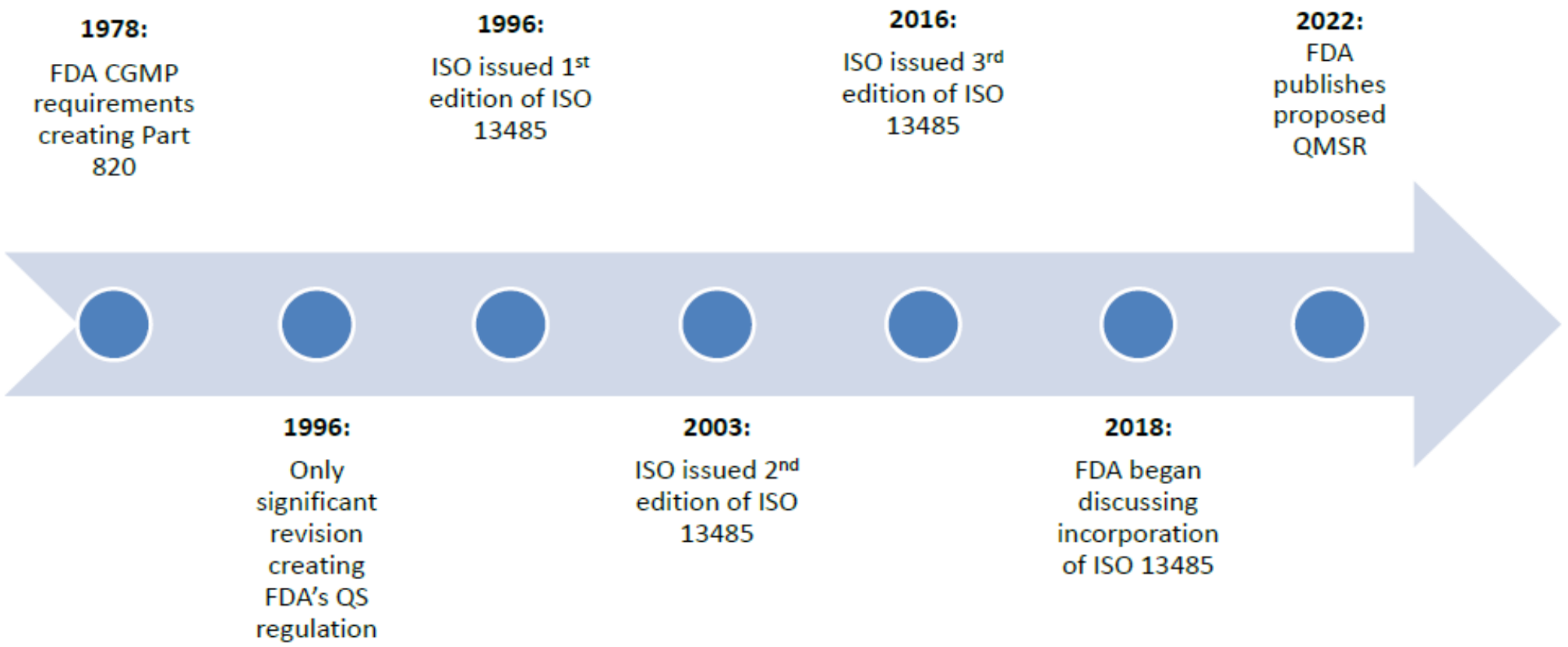

Figure from "Overview: 21 CFR 820 Amendment Proposed Rule Quality Management System Regulation", Melissa Torres, FDA, March 2, 2022

FDA's Rationale for the QMSR

- Regulatory expectations for a QMS have evolved since 21 CFR 820 was implemented 25 years ago
- ISO 13485:2016 is used by regulatory authorities worldwide as basis for medical device QMS requirements
  - "Regulatory metric system"
- ISO 13485 was revised in 2016 to more closely align with 21 CFR 820
- Programs such as MDSAP demonstrated feasibility of global QMS harmonization
- Reduce burden on manufacturers by aligning FDA's expectations with globally harmonized QMS requirements

Areas of Difference Between QSR and ISO

21 CFR 820	ISO 13485:2016	Section of Proposed QMSR where differences are addressed
Subpart D: Document Controls	Clause 4: Quality Management System	21 CFR 820.35
Subpart K: Labeling and Packaging control	Clause 7: Product Realization	21 CFR 820.45
Subpart M: Records	Clause 4: Quality Management System	21 CFR 820.35
Subpart M: Servicing	Clause 7: Product Realization	21 CFR 820.35

FDA considers other aspects of the 21 CFR 820 regulation to be substantially similar to ISO 13485:2016

Adapted from "21 CFR 820 Amendment Proposed Rule Quality Management System Regulation", Keisha R. Thomas, FDA, March 2, 2022

Structure of the Proposed QMSR

820.1	Scope
820.3	Definitions
820.7	Incorporation by Reference
820.10	Requirements for a Quality Management System
820.15	Clarification of Concepts
820.35	Control of Records
820.45	Device labeling and packaging controls

21 CFR 820.1 Scope – Proposed Changes

- Clarify that conflicting regulations that are more specific are controlling only to the extent of the conflict
- Rearrange content for better clarity and improved flow
- Remove the paragraph listing authority, because the CFR already lists the legal authority for the regulation as a separate entry
- Relocate the enforcement provision to 21 CFR 820.10

21 CFR 820.3 Definitions – Proposed Changes

- Terms that do not appear in ISO 13485 but are necessary for the purposes of part 820 – retain the definition with minor revisions:
  - Maintain: “Act”, “Rework”, “Component”, “Finished Device”, “Human cell, tissue, or cellular or tissue-based product (HCT/P) regulated as a device”, “design validation”, “remanufacturer”, “nonconformity” and “verification”
  - Replace “Management with Executive Responsibility” with “Top Management”
  - Remove “Device Master Record (DMR)”
  - Clarify “Process Validation”
  - Add “Customer”
    - “Customer means persons or organizations, including users, that could or do receive a product or a service that is intended for or required by this person or organization. A customer can be internal or external to the organization.”
- Terms defined in ISO 13485 that will not be incorporated into the QMSR because they are inconsistent with the FD&C act: device, labeling
- Retain “manufacturer”, “product”

Proposed 21 CFR 820.7 (new)

Certain material is incorporated by reference into this part … it is available from the following source(s):

(a) *The International Organization for Standardization (ISO),* BIBC II, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland; +41-22-749-01-11; *customerservice@iso.org*, *https://www.iso.org/store.html*.

(1) ISO 13485, "Medical devices—Quality management systems—Requirements for regulatory purposes," third edition, dated March 2016; IBR approved for §§ 820.1; 820.3; 820.10; 820.15; 820.35; 820.45.

Proposed 21 CFR 820.10 – Requirements for a QMS

- Document a QMS that complies with ISO 13485 and this part
- Applicable regulatory requirements

ISO 13485 clause	Applicable CFR reference
7.5.8 – Identification	Part 830, Unique Device Identification (UDI)
7.5.9.1 – Traceability, general	Part 821, Medical Device Tracking Requirements
8.2.3 – Reporting to Regulatory Authorities	Part 803, Medical Device Reporting
7.2.3 – Customer-related processes, communication 8.2.3 – Reporting to Regulatory Authorities 8.3.3 – Actions in response to nonconforming product detected after delivery	Part 806, Medical Devices, Reports of Corrections and Removals

- Design and Development – incorporates the existing 21 CFR 820.30(a) – applicability of design controls
- Devices that support or sustain life – reference to ISO 13485 clause 7.5.9.2
- Enforcement

21 CFR 820.15 – Clarification of Concepts

Manufacturers…shall construe the following terms in ISO 13485… as follows:

(a) *Organization* = “manufacturers” as defined in this part.

(b) *Safety and performance* = “safety and effectiveness” for the purposes of this part. The phrase “safety and performance” does not relieve a manufacturer from any obligation to implement controls or other measures that provide reasonable assurance of safety and effectiveness.

(c) *Validation of processes* = “process validation” as defined in this part.

21 CFR 820.35 – Control of Records

- In addition to the requirements of Clause 4.2.5 in ISO 13485 (incorporated by reference, see § 820.7), Control of Records, the manufacturer must 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 as follows:
  - Records of complaint
  - Records of servicing activities
  - UDI
  - Confidentiality

21 CFR 820.45 – Device Labeling and Packaging Controls

Note: 21 CFR 820.45 essentially replaces 820.120 and 820.130. Per FDA there is no ISO equivalent to these regulations.

- In addition to the requirements of Clause 7.5.1 of ISO 13485 (incorporated by reference, see § 820.7), Control of production and service provision, each manufacturer must establish and maintain procedures that provide a detailed description of the activities to ensure the integrity, inspection, storage, and operations for labeling and packaging, during the customary conditions of processing, storage, handling, distribution, and where appropriate, use of the device.

  (a) The manufacturer must ensure labeling and packaging has been examined for accuracy prior to release or storage, where applicable, to include the following:

  (1) The correct unique device identifier (UDI) or universal product code (UPC), or any other device identification(s);

  (2) Expiration date;

  (3) Storage instructions;

  (4) Handling instructions; and

  (5) Any additional processing instructions.

  (b) The release of the labeling for use must be documented in accordance with Clause 4.2.5 of ISO 13485.

  (c) The manufacturer must ensure labeling and packaging operations have been established and maintained to prevent errors, including, but not limited to, inspection of the labeling and packaging immediately before use to assure that all devices have correct labeling and packaging, as specified in the medical device file. Results of such labeling inspection must be documented in accordance with Clause 4.2.5 of ISO 13485.

Industry Feedback – Sources

- Public Meeting Industry Presentations
  - Jamie Wolszon, AdvaMed
  - Diane Wurzburger, MITA
  - Peter Linders, Chair of ISO/TC 210
  - Mark Swanson, QRx Partners (public comments portion of meeting)
- Panel industry representatives
  - Robert Phillips, Siemens
  - Scott Sardeson (3M)
- Stakeholder comments to the docket (March 2-May 24, 2022)

Industry Feedback - Summary

- Transition Period
  - FDA proposing a 1-yr transition period after final rule – industry stakeholders prefer 2-3 years
  - Transition challenging for small companies, US-only companies, need to find and hire experts – these same resources are needed to help companies update their QMS for MDR/IVDR
  - Transitioning to a more comprehensive use of risk management
- Inspections
  - Training of inspectors, educational resources for industry, harmonization with NB inspections
  - Different mix of incentives vs. inspectional target. ISO 13485 more specific, FDA incentivized to find problems while NB incentivized to support industry
  - FDA stated that an ISO cert is not necessary or sufficient for compliance
  - MDSAP impact
  - ISO process approach vs. FDA compliance approach
  - How risk management will be inspected
- Avoid ISO 13485 plus
  - FDA's initial QMSR proposal does appear to be ISO 13485 plus

Industry Feedback – Summary (cont.)

- Can a US law refer to an international standard?
  - What happens if the standard is changed?
  - Can FDA require you to purchase a standard?
  - Will FDA use the NOTEs in the standard as requirements?
  - What about nonapplicable parts of the standard (e.g. 0.5 – Compatibility with Other Management Systems)
- Loss of the current 21 CFR 820.180(c) – Exceptions prohibiting FDA from looking at management review, internal audit or supplier audits during an inspection
- Postmarket surveillance is a requirement of ISO 13485; is this now required by FDA (currently PMS only required by FDA upon request, 21 CFR 822)
- Concern about the new definition of "customer"
- Impact of a greater focus on risk management – more explicit use of risk-based decision-making
- Timing – concurrent with MDR/IVDR QMS implementation

What Happens Now

- FDA will go through all of the comments from the docket
- FDA will revise the QMSR accordingly, and provide responses to each comment regardless of whether or not the suggestion is incorporated into the QMSR
- FDA will publish a Final Rule
- The transition period (TBD) will be established to start on the date the Final Rule is published.
- There will be lots of training and education (hopefully!)

Take Home Messages

- Most stakeholders agree that in principle, the QMSR is a sensible approach to international standardization of QS requirements
- The devil is in the details, as always

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