DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 4 and 820

[Docket No. FDA–2021–N–0507]

RIN 0910–AH99

Medical Devices; Quality System Regulation Amendments

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is issuing a final rule to amend the device current good manufacturing practice (CGMP) requirements of the Quality System (QS) regulation to harmonize and modernize the regulation. We are harmonizing to align more closely with the international consensus standard for devices by converging with the quality management system (QMS) requirements used by other regulatory authorities from other jurisdictions (*i.e.,* other countries). We are doing so by incorporating by reference an international standard specific for device quality management systems. Through this rulemaking we also establish additional requirements and make conforming edits to clarify the device CGMP requirements for such products. This action will continue our efforts to align our regulatory framework with that used by regulatory authorities in other jurisdictions to promote consistency in the regulation of devices and provide timelier introduction of safe, effective, high-quality devices for patients.

DATES: This rule is effective February 2, 2026. The incorporation by reference of certain material listed in this rule is approved by the Director of the Federal Register February 2, 2026.

ADDRESSES: For access to the docket to read background documents or comments received, go to *https://www.regulations.gov* and insert the docket number found in brackets in the heading of this final rule into the "Search'' box and follow the prompts, and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

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SUPPLEMENTARY INFORMATION:

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I. Executive Summary

A. Purpose of the Final Rule

FDA has historically recognized the benefits of harmonization with other regulatory authorities and, over time, has taken a number of actions to promote consistency with its regulatory counterparts. As part of such activities, FDA is revising its medical device CGMP requirements as set forth in the QS regulation, codified in part 820 (21 CFR part 820). FDA is accomplishing this primarily by incorporating by reference the 2016 edition of ISO 13485 (ISO 13485). Through this rulemaking, FDA is harmonizing quality management system requirements for medical devices with requirements used by other regulatory authorities.

B. Summary of the Major Provisions of the Final Rule

We are amending part 820, primarily through incorporating by reference the quality management system requirements of ISO 13485.[1] We have determined that the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the QS regulation, providing a similar level of assurance in a firm's quality management system and ability to consistently manufacture devices that are safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act). As such, we are retaining the scope of the QS regulation, and amending many of the provisions. We are also amending the title of the regulation and establishing additional requirements and provisions that clarify certain expectations and certain concepts used in ISO 13485. These additions ensure that the incorporation by reference of ISO 13485 does not create inconsistencies with other applicable FDA requirements. This revised part 820 is referred to as the Quality Management System Regulation (QMSR). FDA has made conforming edits to part 4 (21 CFR part 4) to clarify the device Quality Management System (QMS) requirements for combination products. These edits do not impact the CGMP requirements for combination products.

C. Legal Authority

We are issuing this rule under the same authority that FDA initially invoked to issue the QS regulation and combination product regulations, as well as the general administrative provisions of the FD&C Act: 21 U.S.C. 351, 352, 353, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, 383; 42 U.S.C. 216, 262, 263a, 264.

D. Costs and Benefits

We estimate that the QMSR will result in an annualized net cost savings (benefits) of approximately $532 million at a 7 percent discount rate (cost savings: $540M, costs: $8.2M) and approximately $554 million in annualized net cost savings at a 3 percent discount rate (cost savings: $561M, costs: $7.29M). In addition to the cost savings to the medical device industry, the qualitative benefits of the

[1] In this rulemaking, FDA uses the terms below in the following manner: when referring to this rulemaking, FDA uses the term "QMSR." When referring to the rule that was formerly effective, FDA uses the term "QS regulation." Because both the QMSR and the former QS regulation are located in part 820, wherever possible, FDA has used the terms "QS regulation" and "QMSR."

rule include quicker access to newly developed medical devices for patients leading to improved quality of life of the consumers. The rule will also align part 820 with other related programs potentially contributing to additional cost savings.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation/acronym	What it means
ANPRM	Advance Notice of Proposed Rulemaking.
CFR	Code of Federal Regulations.
CGMP	Current Good Manufacturing Practice.
CPG	Compliance Policy Guide.
EO	Executive Order.
EIR	Establishment Inspection Report.
FD&C Act	Federal Food, Drug, and Cosmetic Act.
FDA	U.S. Food and Drug Administration.
GHTF	Global Harmonization Task Force.
GMP	Good Manufacturing Practice.
IMDFR	International Medical Device Regulators Forum.
ISO	International Organization for Standardization.
ISO 13485	Medical devices—Quality management systems—Requirements for regulatory purposes—ISO 13485:2016.
ISO 9000	Quality Management Systems—Fundamentals and Vocabulary—ISO 9000:2015.
ISO 14971	Medical Devices—Application of Risk Management to Medical Devices.
MDR	Medical Device Reporting.
MDSAP	Medical Device Single Audit Program.
OMB	Office of Management and Budget.
QMS	Quality Management System.
QMSR	Quality Management System Regulation.
QS	Quality System.
QSIT	Quality System Inspection Technique.
UDI	Unique Device Identifier/Unique Device Identification.

III. Background

A. Introduction

QMSs specify requirements to help manufacturers ensure that their products consistently meet applicable customer and regulatory requirements and specifications (Ref. 1). In the United States, authority to prescribe regulations requiring conformance to CGMP is found under section 520(f) of the FD&C Act (21 U.S.C. 360j(f)). In the **Federal Register** of July 21, 1978 (43 FR 31508), FDA issued a final rule for CGMP requirements, which also created part 820 (Ref. 2).

As described later in this section, FDA significantly revised part 820 in a final rule published in the **Federal Register** of October 7, 1996 (61 FR 52602) (1996 Final Rule), which established the QS regulation. The QS regulation included requirements related to the methods used in, and the facilities and controls used for, designing, manufacturing, packaging, labeling, storing, installing, and servicing of devices intended for human use. These requirements have been effective in providing assurance that devices are safe and effective and otherwise in compliance with the FD&C Act. FDA has not undertaken a significant revision of part 820 since the 1996 Final Rule.

Also in 1996, ISO issued the first version of ISO 13485, "Quality Systems—Medical Devices—Particular Requirements for the Application of ISO 9001," as a voluntary consensus standard to specify, in conjunction with the application of ISO 9001, the QMS requirements for the design and development and, when relevant, installation and servicing of medical devices (Refs. 3 and 4). Over time, ISO 13485 has evolved into a stand-alone standard outlining QMS requirements for devices (Ref. 1).

With each revision, the requirements in ISO 13485 have become more closely aligned with, and similar to, the requirements set forth in FDA's QS regulation. This alignment and similarity are particularly true for the 2016 version of ISO 13485. Recognizing this progression, FDA sees an opportunity for regulatory harmonization by amending part 820 to incorporate by reference the QMS requirements of ISO 13485 and, thereby, replace the QS regulation with the new QMSR. ISO 13485 is used internationally by many regulatory authorities either as a foundation for or as that regulatory authority's QMS requirements for device manufacturers and is utilized in regulatory harmonization programs such as the Medical Device Single Audit Program (MDSAP), in which FDA and regulatory authorities from four other countries participate (Ref. 5).

The QS regulation applied to many different devices and, thus, did not prescribe in detail how a manufacturer was to design and manufacture a specific device. Rather, the regulation was developed to be a mandatory and flexible framework, requiring manufacturers to develop and follow procedures and processes, as appropriate to a given device, according to the current state-of-the-art for manufacturing and designing such a device. Successful compliance with this regulation provided the manufacturer with a framework for achieving quality throughout the organization (Ref. 1).

While the QS regulation effectively addressed the requirements for a QMS, FDA has long recognized the value of, and has been exploring ways to effect, global harmonization for the regulation of devices. For example, FDA has actively participated in the development of internationally harmonized documents and standards on risk management since their inception, including the development of the Global Harmonization Task Force (GHTF) guidance document entitled "Implementation of Risk Management Principles and Activities Within a Quality Management System," dated May 20, 2005, which outlines the integration of a risk management system into a QMS (Ref. 6). FDA also participated in the development of the various versions of ISO 14971 "Medical Devices—Application of Risk Management to Medical Devices" (Ref. 7).

In 2012, FDA developed a voluntary audit report submission pilot program, which is no longer operational, in which FDA accepted a manufacturer's

ISO 13485:2003 audit report (Ref. 8). Through this program, FDA established the feasibility of using ISO 13485 audit reports in lieu of FDA's routine inspections covering the QS regulation requirements. Additionally, FDA participates in the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world focused on regulatory harmonization and convergence (Ref. 9). IMDRF developed MDSAP in 2012.

Under MDSAP, audits performed by third parties are conducted based on core ISO 13485 requirements with additional country-specific requirements. In determining whether to participate in MDSAP and which FDA-specific provisions were needed for the United States, FDA conducted a thorough review and comparison of ISO 13485 and the QS regulation and concluded that very few FDA-specific requirements needed to be added to this audit model, demonstrating not only the similarities between the QS regulation and ISO 13485, but also the comprehensive QMS approach provided by ISO 13485. This has allowed FDA to participate in MDSAP and accept certain MDSAP audits as a substitute for its own routine surveillance of device quality systems (Ref. 5).

Through participation in MDSAP, FDA has gained experience with ISO 13485 and determined that it provides a comprehensive and effective approach to establishing a QMS for medical devices. As such, in this rulemaking, FDA is amending the device CGMP requirements of part 820 by incorporating by reference the 2016 edition of ISO 13485. We are also publishing additional requirements that help connect and align ISO 13485 with other FDA requirements. The 2016 version of ISO 13485 provides requirements for a QMS that allow a manufacturer to demonstrate its ability to provide devices and related services that consistently meet customer requirements and regulatory requirements applicable to such devices and services (Ref. 1). These requirements can be used by "an organization involved in one or more stages of the life cycle of a medical device, including design and development, production, storage and distribution, installation, servicing and final decommissioning and disposal of medical devices" (Ref. 1).

FDA believes the global harmonization of medical device regulation can help provide safe, effective, and high-quality devices and contributes to public health through timelier patient access to such devices. Harmonizing differing regulations removes unnecessary duplicative regulatory requirements and impediments to market access and removes barriers to patient access and lowers costs.

B. Need for the Regulation

Device manufacturers registered with FDA must comply with part 820. In addition, registered manufacturers in many other jurisdictions and domestic manufacturers that export devices must comply with ISO 13485, which is substantially similar to the QS regulation. As a result, there is redundant effort for some manufacturers in complying with both the QS regulation and ISO 13485. The redundancy of effort to comply with two substantially similar requirements creates inefficiency. For example, FDA expects that the aligned requirements will reduce the burden on industry to prepare documents and/or records for inspections and audits. In addition, the final rule will result in establishments conducting internal audits and management reviews based on aligned requirements as opposed to auditing and assessing separately to comply with the requirements of the previous QS regulation and ISO 13485 individually. The harmonization of requirements will reduce training costs of industry in that internal training can now cover an aligned set of requirements. To address this inefficiency, we are incorporating by reference ISO 13485 to align substantially similar requirements. Although the requirements under the QS regulation are effective and substantially similar to those in ISO 13485, incorporating ISO 13485 by reference will further the Agency's goals for regulatory simplicity and global harmonization and should reduce burdens on regulated industry overall, thereby providing patients more efficient access to necessary devices (Ref. 9).

C. FDA's Current Regulatory Framework

The FD&C Act, as amended, and its implementing regulations establish a comprehensive system for the regulation of devices intended for human use. The device CGMP requirements in the QS regulation were authorized by section 520(f) of the FD&C Act, which was among the authorities added to the FD&C Act by the Medical Device Amendments of 1976 (Pub. L. 94–295). Under section 520(f) of the FD&C Act, FDA issued the QS regulation, which was last revised in 1996.

In addition, section 520(f)(1)(B) of the FD&C Act directs the Agency to afford the Device Good Manufacturing Practice Advisory Committee (DGMP Advisory Committee) an opportunity to submit recommendations for proposed CGMP regulations, to afford an opportunity for an oral hearing, and to ensure that such regulations conform, to the extent practicable, with internationally recognized standards defining QMSs, or parts of the standards, for devices (see 21 U.S.C. 360j(f)(1)(B)). The DGMP Advisory Committee reviews regulations proposed for promulgation regarding good manufacturing practices and makes recommendations to the Agency regarding the feasibility and reasonableness of the proposed regulations.

On March 2, 2022, the Agency convened a DGMP Advisory Committee meeting and afforded an opportunity for an oral hearing to discuss this proposal and to make recommendations that FDA considered when finalizing this rule (Ref. 10). The meeting included presentations by both FDA and stakeholders and also discussions regarding various topics, including the requirements within the proposed rule; the use of a consensus standard for regulatory purposes and accompanying considerations; impact to stakeholders; implementation questions related to education, training, inspections, and timing; as well as considerations for transition planning and options for guidance for stakeholders. The DGMP generally agreed with FDA's proposal for harmonization as set forth in the proposed rule and noted that using global standards can help increase overall compliance with regulatory requirements.

Further, the provisions of section 501(a)(2)(B) and (h) of the FD&C Act (21 U.S.C. 351(a)(2)(B) and (h)) require the manufacture of drugs and devices to comply with CGMP requirements, and section 520(f) of the FD&C Act specifically authorizes the issuance of CGMP regulations for devices, including device constituent parts of products that constitute a combination of a drug, device, and/or biological product, as defined in 21 CFR 3.2(e) ("combination products"). Combination products that include device constituent parts have a distinct regulatory framework for CGMP requirements because the product, by definition, also includes non-device constituent parts (*e.g.,* a drug or a biological product). In the **Federal Register** of January 22, 2013 (78 FR 4307), FDA issued a final rule codifying the CGMP requirements applicable to combination products at part 4. We issued the part 4 regulations, in part, under sections 501(a)(2)(B) and (h) and 520(f) of the FD&C Act, and we are

amending part 4 under the same authorities in this rulemaking.

The regulatory requirements for combination products arise from the statutory and regulatory requirements applicable to drugs, devices, and biological products, which retain their discrete regulatory identities when they are constituent parts of a combination product. At the same time, combination products comprise a distinct category of medical products that can be subject to specialized regulatory requirements, where appropriate. Specialized regulatory requirements for combination products generally are designed to address the overlaps and distinctions between the statutory and regulatory requirements applicable to the drug, device, and biological product constituent parts that comprise them. Part 4 clarifies the applicability of the various CGMP requirements to provide a streamlined option for practical implementation for co-packaged and single-entity combination products (see 78 FR 4307 at 4320, 81 FR 92603 and part 4). Because of the similarity of the drug and device CGMP requirements, FDA considers demonstrating compliance with one of these two sets of regulations (*e.g.,* device CGMP requirements) along with demonstrating compliance with the specified provisions from the other set (*e.g.,* drug CGMP requirements) identified in part 4 as demonstrating compliance with all CGMP requirements from both sets (see 78 FR 4307 at 4320 and § 4.4 (21 CFR 4.4)).

D. History of This Rulemaking

This rulemaking is the first major revision of part 820 since 1996. As previously described, FDA has had a longstanding interest and history of participation in efforts to harmonize its regulatory requirements with the requirements used by other regulatory authorities from other jurisdictions (*i.e.,* other countries). This rulemaking is a continuation of these efforts and harmonizes FDA's QMS regulation with requirements of the international standard ISO 13485, which is used by other regulatory authorities. Harmonizing FDA regulations with the ISO standard will have benefits for manufacturers because many firms producing devices for sale within the United States and abroad have to comply with both standards. This rule will require compliance with more closely aligned requirements.

On July 21, 1978, FDA issued a final rule in the **Federal Register** (43 FR 31508), establishing CGMP requirements for medical devices under section 520(f) of the FD&C Act. This rule became effective on December 18, 1978, and is codified under part 820.

The Safe Medical Devices Act of 1990 (SMDA) (Pub. L. 101–629) amended section 520(f) of the FD&C Act to provide FDA with the authority to add preproduction design controls to the CGMP regulation. This change in law was based on findings that a significant proportion of device recalls were attributable to faulty product design. The SMDA also added section 803 to the FD&C Act (21 U.S.C. 383), which, among other things, authorizes the Agency to enter into agreements with foreign countries to facilitate commerce in devices, and in such agreements, FDA must encourage the mutual recognition of GMP regulations under section 520(f) of the FD&C Act (see 21 U.S.C. 383(b)(1)).

To implement the SMDA changes to section 520(f) of the FD&C Act, FDA issued the 1996 Final Rule, which revised the CGMP requirements for medical devices and promulgated the QS regulation under part 820 in its previous form. As part of that revision, FDA added the design controls authorized by the SMDA in addition to other changes to achieve consistency with QMS requirements worldwide. At the time, the Agency sought to harmonize the CGMP regulations, to the extent possible, with the requirements for QMSs contained in then-applicable international standards. In particular, FDA worked closely with the GHTF and ISO Technical Committee 210 (TC 210) to develop a regulation consistent with both ISO 9001:1994, Quality Systems—Model for Quality Assurance in Design, Development, Production, Installation, and Servicing; and the ISO committee draft (CD) revision of ISO/CD 13485 Quality systems—Medical Devices—Supplementary Requirements to ISO 9001 (see 61 FR 52602 at 52604).

In the **Federal Register** of February 23, 2022 (87 FR 10119), FDA published a proposed rule to amend the device CGMP requirements of the QS regulation. In this rulemaking, FDA is finalizing the proposed rule, taking into account the comments submitted to the docket and the recommendations from the DGMP Advisory Committee.

E. Summary of Comments to the Proposed Rule

In the **Federal Register** of February 23, 2022, FDA published a proposed rule to amend the device CGMP requirements of the QS regulation. The comment period for the proposed rule closed on May 24, 2022. FDA received many comments on the proposed rule from entities including medical device associations, industry, medical and healthcare professional associations, law firms, and other stakeholders, including individuals. While several comments object to particular sections or subsections of the proposed rule, almost all comments voice support for the objective of the proposed rule, to update and modernize the CGMP requirements of the QS regulations by incorporating ISO 13485.

Some comments raise concerns or request clarification regarding:

- the effective date of the rulemaking,
- the scope of the rulemaking,
- FDA's proposed definitions, as well as specific defined terms in the proposed rule,
- recordkeeping requirements,
- implementation, including the process for inspections conducted after the effective date,
- the implications of certification to ISO 13485, and
- traceability requirements.

F. General Overview of the Final Rule

We are amending part 820, primarily to incorporate by reference ISO 13485, Medical Devices—Quality Management System Requirements for Regulatory Purposes. While the QS regulation provided sufficient and effective requirements for the establishment and maintenance of a QMS, regulatory expectations for a QMS have evolved since the QS regulation was implemented over 20 years ago. By incorporating ISO 13485 by reference, we are explicitly requiring current internationally recognized regulatory expectations for QMS for devices subject to FDA's jurisdiction. This resulting regulation is referred to as the QMSR.

The previous QS requirements were, when taken in totality, substantially similar to the requirements of ISO 13485. Where ISO 13485 diverges from the QS regulation, these differences were generally consistent with the overall intent and purposes behind FDA's regulation of QMSs. Almost all requirements in the QS regulation corresponded to requirements within ISO 13485. Therefore, we are amending part 820 by incorporating by reference ISO 13485. Despite these changes, this rulemaking does not fundamentally alter the requirements for a QS that existed previously, and as noted throughout this document, FDA maintains its expectations regarding an effective QMS.

We recognize, however, that reliance on ISO 13485 without clarification or modification could create inconsistencies with FDA's statutory and regulatory framework. Therefore, as detailed in this rulemaking, we are

adding additional definitions and provisions.

One goal for this rulemaking is to simplify and streamline the regulation. Where possible, we either are accepting the incorporated requirement without modification or are creating a requirement that will supersede the correlating requirement in ISO 13485. There are a few exceptions where we are clarifying concepts or augmenting specific clauses in ISO 13485 but overall, we are not modifying the clauses in ISO 13485. This approach helps further regulatory convergence.

As discussed in section VI. of this document (regarding implementation), this rule is only amending the requirements of part 820 and does not impact our inspectional authority under section 704 of the FD&C Act (21 U.S.C. 374). We are also making conforming edits to part 4 to clarify the device QMS requirements for combination products. These edits do not impact the CGMP requirements for combination products.

FDA considered all comments received on the proposed rule and made changes, primarily for clarity and accuracy and to improve understanding of the requirements of the QMSR. On its own initiative, FDA is also making minor technical changes to further align the QMSR with requirements of the FD&C Act and its implementing regulations. The changes from the proposed rule include the following more significant revisions, additions, and removals to the codified section:

- Revise § 4.2 terms to replace "QMSR for devices'' with "QMSR."
- Revise § 4.4(b)(1) to replace the term "QMSR requirements" with "QMSR."
- Revise § 4.4(b)(1)(i) to revise the term "management responsibility" by adding the phrase "general requirements'' and adding § 820.10 to the section.
- Revise § 4.4(b)(1)(ii) to add the requirement that "[t]he organization shall document one or more processes for risk management in product realization. Records of risk management activities shall be maintained."
- Revise § 4.4(b)(1)(iv) to revise the term "improvement" by adding the phrase "analysis of data" and "complaint handling" and adding Clause 8.2.2 and § 820.35(a) to the section.
- Revise § 820.1(c) to align with statutory language in sections 501 and 801 (21 U.S.C. 381) of the FD&C Act.
- Revise § 820.3(a) to clarify use of definitions from ISO 13485 and ISO 9000 in this rulemaking.
- Remove from § 820.3(a) definitions for the terms "customer,'' "design validation,'' ''nonconformity,'' ''process agent," ''process validation," ''rework,'' "top management,'' and "verification.''
- Revise § 820.3(b) to clarify use of definitions from ISO 13485 and ISO 9000 in this rulemaking.
- Remove from § 820.3(b) the definition for the term ''product'' and add to § 820.3(b) the definition for the term "rework."
- Incorporate certain portions of proposed § 820.15, Clarification of Concepts, into § 820.3(b), not including § 820.15(c), "validation of processes." Delete proposed § 820.15.
- Revise clarification of term "safety and performance'' in § 820.3(b) to apply only to Clause 0.1 of ISO 13485.
- Add to § 820.3(b) clarification of term "implantable medical device."
- Remove from § 820.35 the requirement that a manufacturer must "obtain the signature for each individual who approved or re-approved the record, and the date of such approval, on that record."
- Revise § 820.35(a) to clarify expectations for record keeping related to complaint handling.
- Revise § 820.35(a)(6) to add "correction."
- Revise § 820.45 to replace the term "establish'' with the term "document," and replace the term "where appropriate'' with the term "as appropriate."
- Revise § 820.45(c) to remove the term "immediately'' with respect to inspection of labeling and packaging.

G. Incorporation by Reference

FDA is incorporating by reference the International Standard, ISO 13485:2016(E), *Medical devices—Quality management systems—Requirements for regulatory purposes,* Third Edition, 2016–03–01. ISO is an independent, nongovernmental international organization with a membership of national standards bodies. ISO 13485 specifies requirements for a QSM that can be used by a manufacturer involved in one or more stages of the life cycle of a medical device, including design and development, production, storage and distribution, installation, servicing and final decommissioning and disposal of medical devices, or provision of associated activities. Incorporating ISO 13485 by reference in the QMSR will reduce the volume of material published in the Code of Federal Regulations (CFR) and it will have the same force and effect as language explicitly stated in the codified.

FDA is also incorporating by reference Clause 3 of ISO 9000:2015(E), *Quality management systems—Fundamentals and vocabulary,* (ISO 9000) (Ref. 11). ISO 9000 contains terms and definitions that are indispensable for the application of ISO 13485.

You may view ISO 13485 and ISO 9000 at the Food and Drug Administration, Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The materials can also be read in a read-only format at the American National Standards Institute (ANSI) Incorporated by Reference (IBR) Portal, *https://ibr.ansi.org/Standards/iso1.aspx,* or you may purchase a copy of the materials from the International Organization for Standardization, 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.* In addition, the terms and definitions given in ISO 9000 are available for viewing, without cost, at *https://www.iso.org/obp/ui#iso:std:iso:9000:ed-4:v1:en.*

FDA is incorporating by reference the current 2016 version of ISO 13485 and the current 2015 version of Clause 3 of ISO 9000. Any future revisions to these standards would need to be evaluated to determine the impact of the changes and whether this rule should be amended. If deemed necessary and appropriate, FDA will amend the final regulation in accordance with Federal law, including the Administrative Procedure Act (5 U.S.C. 553), and obtain approval of any changes to the incorporation by reference in accordance with 1 CFR part 51.

IV. Legal Authority

We are issuing this rule under the same authority that FDA initially invoked to issue the previous Quality System Regulation (part 820) and Regulation of Combination Products (part 4), as well as the general administrative provisions of the FD&C Act: 21 U.S.C. 321, 351, 352, 353, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360*l,* 371, 374, 381, 383; 42 U.S.C. 216, 262, 263a, 264.

V. Comments on the Proposed Rule and FDA Response

We received fewer than 100 timely filed comments on the proposed rule, each containing one or more comments on one or more issues. We received comments from medical device associations, industry, medical and healthcare professional associations, law firms, and other stakeholders, including individuals.

We describe and respond to the comments in this section. We have numbered each comment to help distinguish between different

comments. We have grouped similar comments together under the same number, and, in some cases, we have separated different issues discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment's value or importance or the order in which comments were received.

A. General Comments on Proposed Rule

(Comment 1) FDA received many comments that express support for the proposed QMSR. Many comments made general remarks supporting the proposed rule without focusing on a particular provision. Many comments agreed with FDA's goal to harmonize the QMSR with an internationally recognized standard. Multiple commenters agreed with FDA that this rulemaking will streamline regulations regarding quality management systems. Some comments express support for the reduced administrative burden of complying with multiple regulatory schemes. Other comments express support for the provisions of the rulemaking addressing risk management. Some comments express hope that FDA's rulemaking sets an example for other regulators, and expressed their desire that the rulemaking will inspire other regulators to follow a similar approach. Some commenters opined that international harmonization would enhance competition and help remove barriers to market access; another noted that harmonization will improve imported devices' compliance with regulatory requirements; and some commenters noted that the rule will help to ensure safe and effective devices.

(Response) FDA appreciates the public support for the proposed rulemaking. FDA notes that harmonizing the regulation of devices will help provide safe, effective, and high-quality devices, contributing to public health through timelier access for patients. FDA agrees that harmonizing regulations from different regulatory jurisdictions will remove unnecessary duplicative regulatory requirements and may limit impediments to market access, resulting in increased competition. Reducing barriers to patient access and increasing competition have the potential to bring down costs as well. FDA believes that the more explicit integration of risk management throughout ISO 13485 and incorporated into the QMSR will help best meet the needs of patients and users and facilitate access to quality devices along with the progress of science and technology.

B. Scope

(Comment 2) FDA received several comments regarding the scope of the QMSR. One commenter acknowledged that this rulemaking has not changed the scope of this regulation from the QS regulation, but suggested that FDA does not have legal authority to extend the QMSR to components or parts of finished devices, should the need arise.

(Response) FDA agrees with the portion of the comment that notes that the scope of the rule is appropriate and unchanged from the QS regulation.

FDA disagrees with the portion of the comment suggesting that FDA does not have the legal authority to extend the scope of the rule to components or parts of finished devices, should that become appropriate. FDA's legal authority to promulgate the QMSR derives from its statutory authority to develop regulations to assure that a device conforms to CGMP, to assure that the device will be safe and effective and otherwise in compliance with the FD&C Act. See section 520(f) of the FD&C Act. Section 201(h)(1) of the FD&C Act (21 U.S.C. 321(h)(1)) defines a device to include any component, part, or accessory of that device. Thus, while FDA's authority to promulgate quality systems regulations for devices extends to the components and parts of those devices, FDA has chosen, in this regulation, not to require components and parts to comply with the requirements of this rulemaking. FDA's determination not to extend this regulation to manufacturers of components and parts does not preclude any contract between manufacturers that requires compliance with this rulemaking and is consistent with Clause 0.1 of ISO 13485. This scope also is consistent with the previous scope in the QS Regulation. See also section IV. Limiting the application of that authority to the finished products that are within the scope of this rulemaking, however, does not alter the broader authority granted by the FD&C Act.

(Comment 3) FDA received several comments regarding specific entities within and outside the scope of the QMSR. One comment recommended that FDA should incorporate third-party servicers and refurbishers into the scope of this rulemaking. Another comment recommended that FDA extend the scope of the regulation to any entity required to register.

(Response) FDA disagrees with the comments that recommend FDA change the scope of the regulation to include third-party servicers and refurbishers. FDA has considered the comment's observation that ISO 13485 requires manufacturers who require servicing to document those processes and verify that such requirements are met. However, ISO 13485 does not impose the entirety of its requirements on third-party servicers or refurbishers, and because the purpose of this rulemaking is both to harmonize with international standards where possible and to retain the scope of the QS regulation, at this time FDA declines to incorporate third-party servicers and refurbishers into this rulemaking.

FDA has also considered the comment asking the Agency to apply the QMSR rulemaking to all entities required to register under section 510 of the FD&C Act (21 U.S.C. 360(h)). The Agency disagrees; the scope of the QMSR and the scope of the registration requirements serve different objectives. Section 510 of the FD&C Act requires all entities that manufacture, prepare, propagate, compound, or process devices to register their establishments, unless that entity and/or its activities are exempted by section 510(g) of the FD&C Act. FDA has determined that registering manufacturing entities is important, because knowing where devices are made helps FDA to conduct both pre- and postmarket inspections, which help to ensure that devices are manufactured in a safe and effective manner.

Section 520(f) of the FD&C Act addresses more activities than those enumerated in section 510, and makes the entities participating in those broader categories subject to the QMSR. Entities who, among other things, design, package, validate, manufacture, and store devices must establish and follow quality systems to help ensure that their products consistently meet applicable requirements and specifications. Therefore, FDA disagrees that it would be appropriate to use registration requirements to determine which entities are subject to the QMSR.

(Comment 4) A comment asked FDA to discuss how the least burdensome concept was considered in the rulemaking.

(Response) As FDA has explained in the guidance document entitled "The Least Burdensome Provisions: Concept and Principles," the least burdensome principles should be consistently and widely applied to the regulation of medical devices to help remove or reduce unnecessary burdens so that patients can have earlier and continued access to high-quality, safe, and effective devices (Ref. 12). This rulemaking to develop and use standards published by international

development organizations intends to converge and harmonize international medical device standards, and it is consistent with the least burdensome principles stated in the Agency's guidance document. As stated in the economic analysis, we believe this harmonization can help reduce overall documentation burdens on manufacturers without compromising safety and effectiveness.

(Comment 5) One commenter noted that while manufacturers of components or parts of finished devices are not subject to this rule, FDA should direct such manufacturers to any and all specific regulatory provisions that manufacturers of such devices should consider. Another comment requested that FDA define the term "appropriate," as that term is used in the QMSR to note that manufacturers of components or parts of finished devices are encouraged to consider provisions of this regulation "as appropriate.''

(Response) FDA agrees that manufacturers of components or parts of finished devices are not subject to the QMSR. We also note that, although the scope of the QMSR remains unchanged, FDA has the legal authority to inspect component manufacturers under the FD&C Act should the need arise. However, FDA encourages manufacturers to consider provisions of this regulation as appropriate. FDA declines to specify in this rulemaking the specific provisions "appropriate for" manufacturers of components or parts of finished device. FDA encourages manufacturers of components and parts of finished devices subject to the QMSR to also review this rule and consider its provisions as guidance, and to develop and follow processes and procedures aligned with the current best practices for manufacturing and designing that are applicable to such component or part. Voluntary compliance with the QMSR will provide manufacturers of components or parts of finished devices a framework for achieving quality throughout the organization. FDA notes that because ISO 13485 clarifies the term "as appropriate" in section 0.2, "Clarification of concepts," in the manner requested by the commenter, we do not need to add such a definition to this rule.

(Comment 6) A commenter asked for examples of a clause in ISO 13485 conflicting with a provision of the FD&C Act and/or its implementing regulations, where FDA would consider the FD&C Act and/or its implementing regulations to control.

(Response) In response to the comment seeking clarification about how FDA will address any conflict between a clause of ISO 13485 and any provision of the FD&C Act, FDA notes that, to the extent that any clauses of ISO 13485 conflict with any provisions of the FD&C Act and/or its implementing regulations, the FD&C Act and/or its implementing regulations will control. Elsewhere in this rulemaking, FDA gives two such examples: (1) the definitions of "device" and "labeling," in sections 201(h) and (m) of the FD&C Act, respectively, supersede the correlating definitions for "medical device" and "labelling'' in ISO 13485; and (2) although ISO 13485 often refers to "safety and performance'' as a standard to measure medical devices, we have clarified in response to Comment 51 that FDA construes "safety and performance'' in Clause 0.1 of ISO 13485 to mean the same as "safety and effectiveness'' in section 520(f) of the FD&C Act.

When there is a conflict between regulations in part 820 and a specifically applicable regulation located elsewhere in Chapter I of Title 21 of the CFR, the regulations that specifically apply to the device in question supersede other generally applicable requirements that conflict. A reader should not interpret this provision to mean that the specifically applicable regulation renders the rest of the part 820 regulation completely inapplicable; the generally applicable part 820 regulations apply to the extent they do not otherwise conflict with the specifically applicable regulation.

C. Incorporation by Reference

(Comment 7) FDA received several comments opining that, for various reasons, it is inappropriate for FDA to incorporate ISO 13485 by reference. Some of those comments claim that the standard is not meant to establish regulatory requirements. Others suggest that ISO 13485 is inconsistent with the MDSAP, and thus utilizing ISO 13485 to set regulatory requirements creates a conflict with that program.

(Response) FDA disagrees with the comments. Incorporation by reference is used primarily to enable Federal Agencies to give legal effect to privately developed technical standards or materials that are published elsewhere. 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.

FDA is utilizing the standard appropriately to form the basis of regulatory requirements. FDA notes that manner. In addition, ISO 13485 instructs that "this International Standard can also be used . . . to assess the organization's ability to meet customer and regulatory requirements . . ." (Ref. 1), at Clause 0.1. ISO 13485 acknowledges that there may be different applicable regulatory requirements for any individual jurisdiction. For example, Clause 0.1 of the standard states with respect to definitions, "the definitions in applicable regulatory requirements differ from nation to nation and region to region. The [manufacturer] needs to understand how the definitions in this International Standard will be interpreted in light of regulatory definitions in the jurisdictions in which the medical devices are made available."

FDA also disagrees that incorporating ISO 13485 creates a conflict with MDSAP.

MDSAP sets ISO 13485 as its core requirements, but MDSAP also allows for additional country-specific requirements for each jurisdiction that uses the standard. FDA is acting consistently with that flexibility by incorporating ISO 13485 with the additional requirements appropriate for compliance with the FD&C Act and its implementing regulations. FDA notes that it intends to assess its policies, procedures, and guidance documents, including any documents that address the MDSAP program, which may be impacted by this rulemaking and where appropriate may amend such documents in accordance with applicable procedures.

(Comment 8) Several commenters noted the manner in which the current rulemaking impacts their compliance obligations in the following ways:

(1) some commenters asked FDA to confirm that compliance with the QMSR satisfies ISO 13485 requirements;

(2) other commenters asked FDA to confirm that compliance with ISO 13485 demonstrates compliance with the QMSR; and

(3) additional commenters asked FDA to clarify whether compliance with the QMSR demonstrates compliance with other countries' regulatory requirements.

(Response) FDA responds to the commenters according to the numbered questions outlined above:

(1) FDA partially agrees with the comment. FDA agrees that harmonizing part 820 with ISO 13485 by

incorporating ISO 13485 by reference will create an aligned set of requirements, instead of two different ones. The redundancy of effort to comply with two substantially similar requirements creates inefficiency. To address this inefficiency, we are incorporating by reference ISO 13485 requirements in the QMSR. FDA expects that compliance with the QMSR will largely satisfy the standard set forth at ISO 13485. See also Comment 79.

(2) FDA disagrees with the comment and confirms that compliance only with ISO 13485 does not fully satisfy the QMSR. With the incorporation of ISO 13485 in the QMSR, the requirements of ISO 13485 become the foundational requirements for device CGMPs. FDA has added limited additional requirements to the QMSR where appropriate, and thus device manufacturers must meet those additional QMSR requirements in addition to those set forth in ISO 13485 (see *e.g.,* § 820.10(b)(i) through (iv)). Any additional requirements are intended to help manufacturers satisfy requirements within the FD&C Act or other FDA regulations. FDA also refers the commenter to FDA's response to specific comments more fully set forth later in this rulemaking. FDA notes, as is stated elsewhere in this rulemaking, that manufacturers are responsible for complying with all the applicable requirements of the FD&C Act and its implementing regulations.

(3) It is inappropriate for FDA to take a position in this rulemaking on whether compliance with ISO 13485 will meet any other jurisdiction's regulatory or statutory or legal requirements. As stated above, FDA cannot provide any assurances that meeting the QMSR or ISO 13485 demonstrates compliance with any other regulatory authority's requirements.

(Comment 9) Commenters inquired whether incorporating ISO 13485 by reference also means that FDA is incorporating any of the additional standards referenced in ISO 13485.

(Response) In response to comments received, in this rulemaking, FDA is incorporating Clause 3 of ISO 9000, in addition to ISO 13485, by reference. Therefore, consistent with Clause 3 of ISO 13485, unless otherwise specified in this rulemaking, the terms and definitions given in Clause 3 of ISO 9000 apply. Aside from Clause 3 of ISO 9000, FDA does not, in this rulemaking, incorporate ISO 14971 or any other standards referenced by, or listed as a source in, ISO 13485, but acknowledges that these other standards may be helpful in understanding application of ISO 13485.

(Comment 10) Comments suggested that FDA should not utilize any notes included in ISO 13485 as statutory requirements.

(Response) FDA agrees with the comment that the notes do not set forth statutory or other legal requirements. However, the notes provide an explanation for the provisions of ISO 13485, and those explanations can be helpful for understanding those provisions.

(Comment 11) One comment recommended that FDA incorporate only certain sections of the ISO 13485 introduction, which the commenter described as "key parts" of the introduction. In particular, the comment requested that FDA clarify whether FDA intends to incorporate Clauses 0.1 (General), 0.2 (Clarification of Concepts), and 0.4 (Relationship with ISO 9001) of the Introduction to ISO 13485.

(Response) FDA disagrees with the comment recommending that FDA incorporate only certain sections of the ISO 13485 introduction. This final rule incorporates the entire introduction from ISO 13485, which sets forth important concepts. FDA confirms that the QMSR incorporates ISO 13485:2016 by reference, including Clauses 0.1 (General), 0.2 (Clarification of Concepts), and 0.4 (Relationship with ISO 9001) of the Introduction of the standard.

(Comment 12) One commenter recommended that FDA retain in the QMSR § 820.100(a)(6) and (7) from the QS regulation, and noted that these provisions are not specifically listed in ISO 13485. The commenter stated that retaining these provisions was both important and beneficial to a quality management system to ensure that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems.

(Response) FDA agrees that § 820.100(a)(6) and (7) of the QS regulation, which require that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of the product or the prevention of such problems and that relevant information on quality problems, as well as corrective and preventative actions, is submitted for management review, are not specifically listed in ISO 13485 but disagrees that the substance of those provisions is not accounted for in ISO 13485 and, thus, in the QMSR. Clauses 8.2.2, 8.5.2, and 8.3.1 of ISO 13485 address investigations of complaints, sharing relevant information between the organization and any external party involved in the complaints, determining the need to investigate nonconformities and any need to notify an external party responsible for a nonconformity, and evaluating any need for actions to ensure that nonconformities do not recur. Also, FDA notes that use error may be a type of nonconformity and may require investigation, as appropriate.

Nonconforming product discovered before or after distribution should be investigated to the degree commensurate with the significance and risk of the nonconformity, consistent with Clause 8.3 of ISO 13485 and its subclauses. At times an in-depth investigation will be necessary, while at other times a simple investigation, followed by trend analysis or other appropriate tools will be acceptable. Consistent with Clauses 8.2.5 and 8.2.6 of ISO 13485, among other things, the requirement for measurement and monitoring applies to process and quality system nonconformities, as well as product nonconformities. For example, if a molding process with its known capabilities has a normal 5 percent rejection rate and that rate rises to 10 percent, an investigation into the nonconformance of the process must be performed. We also note that, consistent with Clause 8.3.2 of ISO 13485, acceptance by concession of nonconforming product is allowed only if "justification is provided, approval is obtained and applicable regulatory requirements are met." FDA believes that the justification should be based on scientific evidence, which a manufacturer should be prepared to provide upon request. Concessions should be closely monitored and not become accepted practice.

(Comment 13) Commenters suggested that the QMSR does not emphasize the importance of ensuring that personnel who perform verification and validation be qualified and trained, as set forth at § 820.20(b)(2) of the QS regulation. One commenter noted that ISO 13485 does not include the term "special process" and recommended that the QMSR use that phrase, as the commenter believed that phrase is set forth at § 820.75(b)(1) of the QS regulation.

(Response) FDA agrees with the commenter that it is important to have competent personnel to conduct validation activities and adds that one of the principles on which the quality systems regulation is based is that all processes require some degree of

qualification, verification, or validation, and manufacturers should not rely solely on inspection and testing to ensure processes are adequate for their intended use. FDA considers Clause 6.2 of ISO 13485 to capture the intent of the previous § 820.75(b)(1) adequately, by requiring that any individuals doing work that impacts quality should be competent on the basis of appropriate education, training, skills, and expertise. Examples of such individuals may include internal and external personnel performing work impacting product quality, full-time and part-time personnel, contractors, and/or consultants. All education, training, skills, and experience of employees need to be carefully recorded.

FDA disagrees that it is necessary to keep the language of § 820.20(b)(2) from the QS regulation in the QMSR to maintain the requirements of the section, which are addressed by Clause 6.2 of ISO 13485. FDA also agrees that the term "special process" does not appear in ISO 13485 but would like to clarify that the phrase "special process" does not appear in § 820.75(b)(1) of the QS regulation, and thus, no additional changes to the rule are necessary to address this comment.

(Comment 14) One commenter recommended that FDA retain in the QMSR the provisions of the previous § 820.150, as the commenter suggested that ISO 13485 lacks requirements to prevent a manufacturer from using an obsolete product.

(Response) FDA agrees that the specific language from the previous § 820.150 does not appear in ISO 13485 but disagrees that the same concept is not covered within ISO 13485. Specifically, Clause 7.5.11 of ISO 13485 allows a device manufacturer to have the flexibility to use a risk-based approach to develop a process to preserve conformity of devices to requirements during processing, storage, handling, and distribution. FDA emphasizes that this process should take into consideration that a nonconformity may not always rise to the level of a product defect or failure, and we note that a product defect or failure will typically constitute a nonconformity. This process should ensure that devices distributed conform to established distribution criteria and are not otherwise obsolete.

More broadly, we note that one objective of the QMSR is to correct and prevent poor practices, not simply bad product. Consistent with Clauses 8.1, 8.2.4, 8.2.5 and 8.2.6, FDA expects that correction and prevention of unacceptable QS practices should result in fewer nonconformities related to product. These and other provisions of the QMSR address problems within the QS itself. As additional examples, FDA expects that a QMSR-adherent QMS will identify and correct improper personnel training, the failure to follow procedures, and inadequate procedures, among other things.

(Comment 15) One commenter suggested that FDA maintain the titles and subparts of the QS regulation, which the commenter further suggested would avoid the need to substantially modify existing cross references and citations within industry and Agency systems.

(Response) FDA disagrees with the comment and suggestion. The titles and subparts have been modified as set forth in the codified language to be consistent and to harmonize with the terminology in ISO 13485. Thus, this rulemaking titles part 820 "PART 820 QUALITY MANAGEMENT SYSTEM REGULATION'' and includes Subpart A—General Provisions, and Subpart B—Supplemental Provisions. Subparts C through O of the QS regulation have been removed and reserved.

(Comment 16) Several commenters inquired as to how FDA intended to manage updates to ISO 13485, and some commenters suggested that FDA utilize this rulemaking to communicate in advance its plan for managing any future revisions to the standard.

(Response) FDA agrees that ISO 13485 will likely be updated, but disagrees that this rulemaking is the appropriate instrument for addressing how FDA will address any such future revisions. Any future revisions to this standard would need to be evaluated to determine the impact of the changes and whether the QMSR should be amended. If deemed appropriate, FDA will update this regulation in accordance with Federal law, including the Administrative Procedure Act (5 U.S.C. 553), and obtain approval of any changes to the incorporation by reference in accordance with 1 CFR part 51. Also, FDA actively participates in the ISO technical committee responsible for ISO 13485 (ISO TC 210). As a participant in ISO TC 210, we are actively monitoring and engaged in the process of making changes to the standard.

(Comment 17) FDA received a comment disagreeing that a revision to part 820 was needed given the similarity of the requirements between ISO 13485 and the QS regulation.

(Response) FDA recognizes that the effort necessary to comply with two substantially similar requirements can lead to some potential redundancy and inefficiency. To reduce this potential for inefficiency while retaining the same high standards for safety and effectiveness for medical devices, we have incorporated by reference ISO 13485 requirements into part 820 so that compliance with ISO 13485 and the new QMSR would more closely align. Although the requirements under the QS regulation were effective and substantially similar to those in ISO 13485, incorporating ISO 13485 by reference furthers the Agency's goals for regulatory simplicity and global harmonization and should reduce burdens on regulated industry, thereby providing patients more timely access to safe and effective medical devices.

(Comment 18) Commenters suggested that, in this rulemaking, FDA map the requirements of the QS regulation to ISO 13485 and/or the QMSR. Comments noted that ISO 13485 differs in wording, phraseology, and organization from the QMSR.

(Response) FDA agrees with the comments that note there are some differences between the QS regulation, the QMSR, and ISO 13485, but disagrees with the comments that suggest FDA should map the requirements of the QS regulation to ISO 13485 and/or the QMSR. The QMSR replaces the QS regulation, and FDA disagrees that providing a 1-to-1 comparison of the former regulation would be useful to understand and comply with the new QMSR. The concepts and requirements contained in the QS regulation, when viewed holistically, are contained in ISO 13485. However, ISO 13485 is organized differently from the QS regulation such that providing a direct comparison of the former QS regulation to the QMSR would be cumbersome and not a useful tool to help firms comply with this rulemaking.

The QMSR requirements are, when taken in totality, substantially similar to the requirements of ISO 13485. Where FDA's statutory framework requires additions to ISO 13485, these requirements are generally consistent with the overall intent and purposes behind FDA's regulation of QMSs. This rulemaking does not fundamentally alter the requirements for a QS that exist in either the former QS regulation or the new QMSR. This rulemaking harmonizes the QS regulation with the QMS requirements of ISO 13485, while continuing to provide the same level of assurance of safety and effectiveness under the FD&C Act and its implementing regulations.

(Comment 19) FDA received several comments regarding the role of risk and risk management in the QMSR. Some comments agreed that the embedded risk management concepts present in ISO 13485 emphasize risk management

throughout the total product life cycle, while another disagreed that ISO 13485 requires a complete risk management system. One comment suggested that FDA's guidance documents addressing risk management may conflict or overlap after this rulemaking. Another comment suggested that FDA is shifting its focus to speed of access, rather than quality of devices.

(Response) FDA disagrees that it has changed its primary objective; FDA's expectations associated with risk management remain consistent: providing reasonable assurance of safety and effectiveness through the appropriate regulatory processes. FDA agrees that the embedded risk management concepts present in ISO 13485 emphasize risk management throughout the total product life cycle. Although the integration of risk management principles throughout ISO 13485 does not represent a shift in philosophy, the explicit integration of risk management throughout the clauses of ISO 13485 more explicitly establishes a requirement for risk management to occur throughout a QMS and should help industry develop more effective total product life-cycle risk management systems. Effective risk management systems provide the framework for sound decision making within a QMS and provide assurance that the devices will be safe and effective (see section 520(f) of the FD&C Act). The QS regulation explicitly addressed risk management activities in the former § 820.30(g) (21 CFR 820.30(g)). In adopting ISO 13485, the QMSR incorporates risk management throughout its requirements and explicitly emphasizes risk management activities and risk-based decision making as important elements of an effective quality system (see *e.g.,* Clauses 4.1, 7.1, 7.3, 7.4, 7.5, 7.6, and 8.2 and certain subclauses therein of ISO 13485).

FDA also disagrees that ISO 13485 does not require a complete risk management system. Because the standard is intended to guide development of a quality system to meet regulatory requirements for medical devices, the ISO prioritizes that an effective quality system systematically identify, analyze, evaluate, control, and monitor risk throughout the product life cycle to ensure that the devices they manufacture are safe and effective. This includes the review and update of risk documentation when a manufacturer becomes aware of previously unforeseen risks or new information that suggests that known risks need to be updated to ensure appropriate control measures are implemented.

In response to the comment suggesting that FDA's guidance documents may need to be reevaluated after this rulemaking, FDA notes that it intends to assess all of its policies, procedures, regulations, and guidance documents that are impacted by the QMSR, and make conforming revisions, as appropriate.

(Comment 20) One commenter noted that ISO 13485 separates the terms "corrective action" and "preventive action," suggested that FDA should not combine the two concepts in the QMSR's corrective action process, and further suggested that use of the term "Preventive Action" in ISO 13485 is not consistent with FDA's previous use of that term.

(Response) FDA agrees with the portion of the comment that notes that ISO 13485 has one Clause outlining expectations regarding corrective action (Clause 8.5.2) and has another Clause outlining the expectations regarding preventive action (Clause 8.5.3). FDA has incorporated the corrective action and preventive action requirements of ISO 13485 by reference into the QMSR and disagrees that it has combined the two subjects in the manner the commenter describes. In the QS regulation, FDA's prior interpretation of the term "preventive action" did not apply solely to preventing recurrence of quality problems, and we disagree that adoption of the definition in ISO 13485 represents a change in expectation. FDA continues to believe that it is essential that the manufacturer establish procedures for implementing corrective action and preventive action, and that these procedures must provide for control and action to be taken on quality systems, processes, and products with actual or potential nonconformities.

The degree of corrective or preventive action taken to eliminate or minimize actual or potential nonconformities shall be appropriate to the magnitude of the problem and commensurate with the risks encountered, and includes processes such as developing procedures for assessing the risk, the actions that need to be taken for different levels of risk, and the methods that correct or prevent the problem from recurring.

FDA notes that, as more fully set forth in section V.D., FDA utilizes many of the definitions in ISO 13485 and ISO 9000 to harmonize the QMSR to the greatest extent possible with ISO 13485 and to reduce the potential for misinterpretation of the QMSR requirements.

(Comment 21) Commenters noted that ISO 13485 is a copyrighted document that may be associated with a fee and thus may not be accessible to all entities, and suggested that FDA make the standard available and cost-free.

(Response) FDA agrees with the portion of the comment that notes that ISO 13485 is a copyrighted document but advises that a mechanism exists to enable any entity to access ISO 13485 and ISO 9000 through the ANSI Standards Incorporated By Reference portal. The website for the portal is located at *https://ibr.ansi.org/Standards/iso.aspx*. Utilizing the web address will give the user access to a read-only version of ISO 13485 and Clause 3 of ISO 9000, at no cost to the user. As noted, the definitions set forth in ISO 9000 are also available to users at no cost at *https://www.iso.org/obp/ui#iso:std:iso:9000:ed-4:v1:en.*

D. Definitions

(Comment 22) One comment opined that because ISO 13485 sets forth its own definitions, the Agency does not have the authority to promulgate definitions that differ from ISO 13485.

(Response) FDA disagrees with the comment. FDA's legal authority to promulgate the QMSR derives from its statutory authority, more fully set forth above, at section IV. That legal authority includes the ability to retain and modify regulatory definitions in the QMSR, as appropriate. In addition, ISO 13485 itself anticipates that each jurisdiction may have its own definitions (see ISO 13485, at Clause 0.1). FDA also notes that there are, however, certain definitions in ISO 13485 that FDA cannot adopt because they conflict with or differ from definitions established in the FD&C Act or by regulations in other parts in Title 21 of the CFR.

(Comment 23) One comment asked FDA to clarify its expectations regarding how manufacturers should update their existing quality management systems to ensure that all terms, definitions, and documentation are consistent with the new QMSR. The commenter asked that FDA provide guidance for how organizations are to update their QMS.

(Response) Because each organization's QMS is unique to its operations, FDA is not able to provide advice about how each organization should evaluate its existing QMS for consistency with the QMSR. Similarly, FDA is not able provide advice on how to revise specific documents or otherwise update an existing QMS within an organization.

(Comment 24) Some comments recommended that FDA fully align the QMSR's definitions with those in ISO 13485. Other comments suggested FDA clarify how terms in ISO 9000 function in the QMSR. Multiple commenters also

asked FDA to clarify where there are similarities and differences between definitions in the former QS regulation, the QMSR, ISO 13485, and ISO 9000.

(Response) FDA partially agrees with the suggestion that FDA more fully align the definitions in the QMSR with the definitions in ISO 13485 and has modified the proposed § 820.3 in response. There are, however, certain definitions in ISO 13485 that FDA cannot adopt because they either conflict with or differ from definitions established in the FD&C Act or its implementing regulations in other parts in Title 21 of the CFR (see § 820.3(b)).

ISO 13485 uses ISO 9000 as a normative reference and Clause 3 of ISO 13485 states that for the purposes of ISO 13485, "the terms and definitions in ISO 9000 apply." In this rulemaking, except as specified in § 820.3, we take the same approach. This will help harmonize the QMSR to the greatest extent possible with ISO 13485 and to reduce the potential for misinterpretation of the QMSR requirements.

FDA acknowledges that some terms that appeared in the former QS regulation no longer appear in the QMSR. FDA further acknowledges that certain terms that appear in the QMSR do not appear in ISO 13485, and thus are not defined in that document. While we have not provided comparisons between all definitions in the QMSR and the QS regulation or ISO 13485, subsequent responses in this section address specific terms for which we received questions. Finally, although ISO 13485, the QMSR, and the former QS regulation use some different terms, the requirements remain substantially the same.

As discussed previously, FDA considers the terms and definitions in ISO 9000, as used in ISO 13485, to be incorporated by reference into the QMSR except for those terms and definitions FDA has determined are necessary to define in § 820.3 to satisfy requirements within the FD&C Act or its implementing regulations. This includes the corresponding notes for terms defined in ISO 9000, and as stated previously, FDA considers these notes as providing important context for understanding and implementing the standard rather than setting forth regulatory requirements. By incorporating these terms and definitions by reference, FDA intends to minimize the regulatory burden on device manufacturers, which will allow for a harmonized application of the ISO 13485 standard across regulatory jurisdictions to the extent permissible by, and consistent with, the FD&C Act. FDA reiterates that it does not intend to incorporate any definitions for terms that are inconsistent with definitions set forth in the FD&C Act.

We also note that ISO 13485 only references the terms and definitions in Clause 3 of ISO 9000, which are being incorporated by reference here, and does not reference the remainder of the document; FDA considers the remainder of ISO 9000 to fall outside the scope of the QMSR. Organizations may choose to incorporate concepts, processes, or other aspects of ISO 9000 into their organization's QS and, so long as the resultant system is compliant with the QMSR established in this rulemaking, we do not take a position here on those choices. For additional details on specific terms, please see the discussions below in responses to comments 26 through 30.

(Comment 25) One comment suggested that because FDA proposed to include definitions in the QMSR that are different from those in ISO 13485, the QMSR has created a second, alternate standard with which manufacturers would need to comply.

(Response) FDA disagrees that we are creating a second, alternate standard. Rather the QMSR must be consistent with the FD&C Act and its implementing regulations and, as noted throughout this rulemaking, any differences between the QMSR and the ISO 13485 are intended to help manufacturers satisfy requirements within the FD&C Act and its implementing regulations. FDA has added limited additional requirements to the QMSR where appropriate, and device manufacturers must meet those requirements in addition to those set forth in ISO 13485 (see *e.g.,* §§ 820.10 through 820.45). Additionally, in response to other comments FDA has adopted, to the extent possible, the definitions used in ISO 13485 in this rulemaking, the extent of potential differences between the QMSR and ISO 13485 has been reduced compared to the proposed rule.

(Comment 26) Many comments recommended that FDA revise its proposed definitions for specific terms. Some comments recommended that FDA adopt the definitions set forth in ISO 9000 for the terms "customer,'' "nonconformity," and "verification.'' Multiple comments noted that because these terms are defined in ISO 9000, FDA can adopt those definitions for the QMSR, and does not need to create new definitions in this rulemaking.

(Response) FDA agrees with these comments and has adopted for the final QMSR the definitions set forth in ISO 9000, including the terms "customer," "nonconformity," and "verification.'' With respect to the definition for "customer," we note that when considering the requirements related to customer property in Clause 7.5.10, manufacturers must comply with this provision to the extent necessary to assure the safety and effectiveness of the devices being manufactured, consistent with the requirements of section 520(f) of the FD&C Act. For example, a manufacturer is expected to ensure that the integrity of a component provided by a contract manufacturer is not compromised before it is incorporated into the device being manufactured. To the extent any customer property requirements may be interpreted to go beyond the safety and effectiveness of the devices being manufactured, FDA does not intend to enforce this provision for such activities.

(Comment 27) Multiple commenters recommended that, to harmonize with ISO 13485 and to avoid redundancy, FDA should either adopt the definition of "top management'' from ISO 9000, or retain both the term "management with executive responsibility" and the definition of that term from § 820.3(n) of the QS regulation. One commenter suggested that the term "management with executive responsibility'' conveys the intent of the term more clearly than the definition set forth in ISO 13485.

(Response) FDA agrees with the comments recommending FDA avoid redundancy and harmonize with the standard and further agrees that the QMSR should utilize the definition set forth in ISO 9000 for the term "top management." FDA disagrees with those comments that suggested FDA retain either the term "management with executive responsibility" or its definition from the QS regulation. Utilizing the definition in ISO 9000 for the term "top management'' does not change that FDA expects medical device manufacturers, led by individuals with executive responsibilities, to embrace a culture of quality as a key component in ensuring the manufacture of safe and effective medical devices that otherwise comply with the FD&C Act.

A culture of quality meets regulatory requirements through a set of behaviors, attitudes, activities, and processes. Top management ensures that applicable regulatory requirements are met through the integration of QMS processes. For example, quality cannot be inspected or tested into products or services. Rather, the quality of a product or service is established during the design of that product or service, and achieved through proper control of the manufacture of that product or the performance of the service. Because FDA is incorporating the definition of

"top management,'' it is, therefore, unnecessary to retain the definition of "management with executive responsibility" in the QS regulation.

(Comment 28) Multiple comments noted that FDA's proposed definition of the term "product" differed from the definition in ISO 13485 and recommended either adopting the definition from ISO 13485, or using an alternative definition than the one proposed by FDA.

(Response) FDA agrees with the comments recommending that it adopt the definition set forth in ISO 13485 for the term "product." FDA disagrees with those comments that suggested an alternate definition for the term, as FDA considers the definition in ISO 13485 to be appropriate, and an alternate definition would not further the goal of harmonizing device CGMP requirements to the extent possible. Further, establishing other definitions would not serve the purpose of this rulemaking; *i.e.,* harmonization with ISO 13485. We note, in adopting ISO 13485's definition of "product," that we consider this definition to include, but it is not limited to, components, in-process devices, finished devices, services, and returned devices. For example, services may be parts of the manufacturing or quality system that are contracted to others, such as, plating of metals, testing, consulting, and sterilizing, among other services.

(Comment 29) One comment noted that the terms "correction,'' "corrective action,'' and "preventive action,'' although defined in ISO 9000 and important for use in ISO 13485, were not addressed in the proposed rule, and asked FDA to introduce definitions for these terms in the final QMSR.

(Response) FDA agrees that the proposed rule did not address the terms "correction," "corrective action," and "preventive action." This final rule provides that the definitions set forth in ISO 9000 apply for the terms "correction," "corrective action," and "preventive action." FDA considers part 806 (21 CFR part 806) to apply to manufacturers who conduct corrections or take corrective actions that occur after the product is released. Additionally, "correction" may also refer to scrap, repair, rework, or adjustment and relates to eliminating a nonconformity, whereas "corrective action" relates to the elimination of the cause of nonconformity and to prevent recurrence. FDA clarifies that consistent with the former QS regulation, as part of an effective quality system, manufacturers must verify or validate corrective and preventive actions to ensure that such actions are effective and do not adversely affect the finished device.

After consideration, we have included in § 820.3 one definition for "batch'' or "lot" consistent with the definition of these terms in § 820.3(m) of the QS regulation. We note that these terms are utilized in ISO 13485 and are not defined there or in ISO 9000. We consider maintaining the definition of these terms to be important for implementing a QMS consistent with this rule. Additionally, in keeping with FDA's intent to align terminology more fully in the QMSR with ISO 13485, we have decided not to finalize the proposed definitions for the terms "process validation,'' and "design validation." These terms are not defined in either ISO 13485 or ISO 9000, and FDA considers definitions for these terms to be unnecessary because the concepts and intents underlying these terms are encompassed by other terms as used in the standards, including but not limited to "process," "validation,'' and "design and development."

(Comment 30) Many comments asked that FDA retain the term "establish" in the QMSR. Commenters noted that the QS regulation defined the term "establish'' to mean "to define, document, and implement,'' and comments suggested that retaining that definition would provide continuity between the QS regulation and the new QMSR and would help provide clarity regarding an organization's responsibilities under the QMSR. Some comments opined that the term "document" as utilized in ISO 13485 does not have the same meaning as the term "establish'' used in the QS regulation.

(Response) FDA disagrees with these comments and affirms that retaining the previous definition of the term "establish'' is not necessary in this rulemaking. FDA agrees that the terms "document" in ISO 13485 and "establish'' in the QS regulation do not have the same meaning, and it was not FDA's intention to replace the term "establish'' with "document." Clause 0.2 in ISO 13485 clarifies that "document" encompasses the activities of establishing, implementing, and maintaining. FDA considers the term "document" as used in ISO 13485 to be appropriate for implementation of the QMSR and has determined that retaining a separate definition for "establish'' in § 820.3 would be redundant, could lead to confusion, and would unnecessarily increase the potential for misinterpretation and apparent conflicts with QMS requirements in other regulatory jurisdictions.

(Comment 31) Some comments noted that the terms "device master record" (DMR), "design history file" (DHF), and "device history record" (DHR) do not appear in ISO 13485 and were not separately defined in the proposed rule and asked FDA to clarify whether those terms remain part of this rulemaking. Commenters observed that the term DMR is used in the previous QS regulation, but does not appear in the QMSR. Commenters did not agree that the concepts included in the previous term DMR are adequately covered under the requirements for a medical device file (MDF), discussed in Clause 4.2.3 of ISO 13485. One commenter asked that FDA provide a direct comparison of the terms DMR and MDF, multiple commenters suggested that the proposed definitions would further confuse expectations, and multiple commenters suggested that the term DMR has a long history of use and is not interchangeable with the term MDF. For these reasons, commenters opined that it would be unnecessarily burdensome and complicated for organizations to update their existing QMS to comply with the term "medical device file."

(Response) FDA agrees with the comments to the extent that they correctly identify that ISO 13485 does not contain requirements for record types specified in the QS regulation, such as quality system record (QSR), DMR, DHF, and DHR. As stated in the QMSR proposed rule, we are not retaining separate requirements for these record types in the QMSR and have eliminated terms associated with these specific record types because we believe the elements that comprise those records are largely required to be documented by ISO 13485, including Clause 4.2 and its subclauses, and Clause 7 and its subclauses. For example, many of the requirements previously in the DHR are largely required to be in the medical device or batch record, as described in Clause 7.5.1.

Similarly, consistent with the former DHF, Clause 7.3.10 requires the design and development file to contain or reference all the records necessary to establish compliance with design and development requirements, including the design and development plan and design and development procedures.

Clause 4.2.3 requires that the MDF will contain or reference the procedures and specifications that are current on the manufacturing floor. The final design output from the design phase, which is maintained or referenced in the design and development file, forms the basis or starting point for the MDF. Previously, product specifications,

procedures for manufacturing, measuring, monitoring, and servicing, and requirements for installation were included in a manufacturer's DMR and will now be located in the manufacturer's MDF.

The recordkeeping requirements in ISO 13485 are substantively similar to those in the QS regulation and, because there is no reference to these terms in ISO 13485, we have eliminated this terminology as it is no longer necessary. Retaining the definition of the DMR in the QMSR would, therefore, be redundant and could lead to confusion and misinterpretation of the requirements of the QMSR.

FDA disagrees that compliance with the concept of a MDF in the QMSR will be overly burdensome as we expect the burden to be similar to requirements associated with record types in the QS regulation. It is important to ensure that records and documentation are maintained to meet the requirements of the QMSR for each organization, and recognizes that each organization will implement a QMS specific to its requirements regarding device safety and effectiveness, including with respect to records and documentation.

(Comment 32) FDA received one comment recommending that FDA expand the definition of "risk" to encompass both the concept of regulatory obligations and the consequences of failure to meet those obligations, as the commenter suggested that the definition set forth in ISO 13485 was insufficient without that language.

(Response) FDA disagrees partially with this comment and considers the definition of the term "risk" as utilized by ISO 13485 to be appropriate. FDA agrees with the commenter that organizations involved in the life cycle of a medical device must comply with the appropriate regulatory requirements and responsibilities. To the extent that these regulatory requirements intersect with an organization's QMS, we agree that the QMS should address those requirements. In addition, ISO 13485 Clause 0.2 states that "when the term 'risk' is used, the application of the term within the scope of this International Standard pertains to safety or performance requirements of the medical device or meeting applicable regulatory requirements." For these reasons, we do not believe that a definition for "risk" unique to the QMSR is necessary and are retaining the unmodified definition in ISO 13485.

(Comment 33) FDA received multiple comments asking FDA to clarify the term "component.'' Some comments recommended that FDA specify that a component that meets the definition of a device in section 201(h) of the FD&C Act is subject to the applicable provisions of the QMSR. Other comments asked FDA to identify the circumstances under which a component of a medical device would be subject to the requirements of the QMSR. Some comments requested additional clarification on the differences between a component and an accessory or a raw material.

(Response) FDA disagrees with the comments suggesting that FDA modify the definition of the term "component.'' The definition of the term is unchanged from the definition used in the QS regulation, and we note that a raw material is already explicitly included within this definition; that is, a "raw material'' may be a "component'' of a finished medical device for the purposes of the QMSR. FDA considers an accessory, on the other hand, to be itself a finished device in this rulemaking. See Comment 34 for additional discussion of the term "accessory."

To distinguish raw material and components from "finished devices," FDA notes that finished devices are all devices that are capable of functioning, including those devices that could be used even though they are not yet in their final form. For example, devices that have been manufactured or assembled, and need only to be sterilized, polished, inspected and tested, or packaged or labeled by a purchaser/manufacturer are clearly not components but are now in a condition in which they could be used, therefore meeting the definition of a "finished device."

Additionally, the distinction between "components'' and "finished devices" was not intended to permit manufacturers to manufacture devices without complying with CGMP requirements by claiming that other functions, such as sterilization, incoming inspection (where sold for subsequent minor polishing, sterilization, or packaging), or insertion of software, will take place. The public would not be adequately protected in such cases if a manufacturer could claim that a device was not a "finished'' device subject to the CGMP regulation because it was not in its "final" form. We also note that it is not necessary for a device to be in commercial distribution to be considered a "finished device."

The scope of the QMSR is the same as the QS regulation and explicitly applies to manufacturers of medical devices and requires that manufacturers of finished devices apply an ongoing risk-informed assessment of suppliers to ensure the provision of quality products or services, including related to components. As stated in the proposed rule, FDA's intent is to harmonize medical device CGMP requirements while maintaining consistency with our statutory and regulatory framework. Manufacturers must clearly document the type and extent of control they intend to apply to products and services. Thus, a finished device manufacturer may choose to provide greater in-house controls to ensure that products and services meet requirements or may require the supplier to adopt measures necessary to ensure acceptability, as appropriate.

FDA generally believes that an appropriate mix of supplier and manufacturer quality controls are necessary. However, finished device manufacturers who conduct product quality control solely in-house must also assess the capability of suppliers to provide acceptable product. Where audits are not practical, this may be done through, among other means, reviewing historical data, monitoring and trending, and inspection and testing. FDA further notes that certification may not provide adequate assurances of supplier quality without further evaluation. Just as with the QS regulation, the provisions of the QMSR do not apply to manufacturers of components or parts of finished devices, but such manufacturers are encouraged to consider provisions of this regulation as appropriate.

(Comment 34) One comment asked that FDA include a definition for the term "accessory'' in the QMSR.

(Response) FDA disagrees that it is appropriate to define the term "accessory" in the QMSR, because a medical device is subject to the requirements of the QMSR whether or not it is an "accessory.'' The term "device" as defined in section 201(h)(1) of the FD&C Act includes "any component, part, or accessory.'' See Comment 33.

In this rulemaking, FDA considers an accessory to be a finished device. That determination is consistent with the FD&C Act, its implementing regulations, and FDA's guidance discussing classification pathways for accessories under section 513(f)(6) of the FD&C Act (21 U.S.C. 360c(f)(6)) (Ref. 13). For example, FDA considers an accessory to be a finished device for purposes of classifying a device under section 513 of the FD&C Act. Further, in conducting such a classification analysis, FDA has stated that it considers an accessory to be a finished device that is intended to support, supplement, and/or augment the performance of one or more other

devices. While distinguishing whether a device is an accessory is helpful for identifying potential classification mechanisms under section 513 of the FD&C Act, FDA considers it immaterial to whether an accessory is subject to the provisions of the QMSR because accessories are finished devices and are therefore subject to the provisions of the QMSR.

(Comment 35) One comment addressed the use of the term "record" in the proposed rule. The commenter seemed to interpret that "record" could mean either procedures or quality activity results depending on the section of the QS regulation. The comment considered the proposed rule for the QMSR to properly use the term "record." The commenter also noted that within the family of ISO standards, "document" and "record" have distinct meanings.

(Response) FDA partially agrees with the comment to the extent that it supports FDA's use of the term "record'' within the QMSR, as described in the proposed rule. FDA also agrees that there is a clear distinction between the terms "document'' and "record'' in ISO 13485 and the relevant portion of ISO 9000. Clause 4.2.4 of ISO 13485 specifies that documents required by the quality management system shall be controlled. Records are a special type of document and shall be controlled according to the requirements given in 4.2.5. FDA adds that the term "specification'' is also a distinct term. For example, a record and a specification are types of documents as defined in ISO 9000.

Because this comment is supportive of FDA's proposed use of these definitions in the QMSR, we have determined that revisions to the relevant portions of the rule are not necessary.

(Comment 36) One comment noted that in ISO 13485, the definition of the term "distributor" appeared to the commenter to be broader than the definition of the term in part 803 (21 CFR part 803). In particular, the commenter understood the term "distributor" as defined in part 803 not to include retailers, in contrast to the definition in ISO 13485, which does.

(Response) FDA recognizes that the definitions for the term "distributor" used in ISO 13485 and 21 CFR 803.3(e) are not identical, and that the definition of "distributor" in the QMSR may include retailers, as retailers further the availability of a medical device to the end user, per the definition in ISO 13485. We note that FDA intends to evaluate a firm's conformity to the requirements of the QMSR related to distribution through the initial consignee. ISO 13485 requires entities to develop and maintain a quality management system appropriate for the activities of the organization, including the requirements relevant to distribution (see ISO 13485, Clause 3.5). The regulation at part 803, by contrast, establishes the requirements for medical device reporting for device user facilities, manufacturers, importers, and distributors.

Although terminology may differ, the requirements that are applicable to distributors in the QMSR and the requirements that apply to distributors under part 803 are appropriate for their purposes. We do not consider there to be conflict between the two and do not expect confusion regarding interpretation of the requirements under these respective provisions. We are therefore retaining the definition of "distributor" as written in ISO 13485 for the purposes of compliance with the QMSR, which additionally will help accomplish the goal of harmonization. Similarly, in this rulemaking, we are not amending the definition of "distributor" in part 803 for the purposes of compliance with that part.

(Comment 37) One comment suggested that including definitions for the terms "labeling'' and "marketing" would help clarify when promotional materials for a product are considered labeling.

(Response) FDA disagrees that definitions for the terms "labeling'' and "marketing'' should be included in the QMSR. The FD&C Act defines the terms "label'' and "labeling" in section 201(k) and (m) of the FD&C Act, respectively, and we consider it unnecessary and redundant to include those definitions in the QMSR. The term "advertising'' is used throughout the FD&C Act and encompasses promotional materials (*e.g.,* section 201(n), regarding information FDA may use to assess whether a device is misbranded includes an evaluation of whether "the labeling or advertising is misleading......"). For the purposes of compliance with the QMSR, a separate definition for "marketing'' is unnecessary, as marketing is not addressed in ISO 13485.

(Comment 38) Two comments suggested that replacing the term "manufacturing material" in the QS regulation with "process agent" in the QMSR would create a conflict with ISO 13485. These comments seemed to interpret Clause 7.5.2 of ISO 13485 to require that process agents be removed from the product during manufacture, but that the definition for "process agent" in the QMSR suggests that the process agent may be "present in or on the finished device as a residue or impurity not by design or intent of the manufacturer."

(Response) FDA partially disagrees with this comment because it misinterprets Clause 7.5.2 of ISO 13485. In particular, Clause 7.5.2 of ISO 134385 does not require that process agents are to be removed from all products. This Clause discusses "cleanliness of product" within the context of "production and service provision" and states that in certain cases, the organization "shall document requirements for cleanliness of product or contamination control of product." Section (e) of the Clause states that when "process agents are to be removed from product during manufacture'' such documentation requirements apply. FDA expects removal of a process agent if it is reasonably expected to have an effect on product quality. The process agent should be removed or limited to an amount that does not adversely affect the device quality. To further clarify our position, process agents must be assessed, found acceptable for use, and controlled in a manner that is commensurate with their risk. Further, we note that a process agent is a "product" as defined in ISO 13485, consistent with note 1 in the definition for the term "product," which explains that "processed materials" are one of four generic product categories.

Although we do not consider the proposed definition for "process agent" in the QMSR to conflict with the use of the term "manufacturing material" in the QSR, we have determined that it is not necessary to finalize the separate definition for "process agent." In an effort to harmonize with ISO 13485 to the fullest extent possible, we are not finalizing certain FDA-specific definitions for terms in the QMSR where the terms are consistent with our existing regulatory and statutory framework (see response to Comments 24 and 26 through 29).

(Comment 39) Some comments asked that FDA incorporate the definition for "rework'' found in ISO 9000 and asked for clarification on FDA's intended interpretation of the term within the context of the medical device life cycle.

(Response) FDA disagrees with this comment. FDA is not adopting the definition of rework in ISO 9000 and has determined that is important to finalize the proposed definition of "rework" in § 820.3 for consistency with our existing statutory and regulatory framework for postmarket monitoring and reports, including those governing corrections, repairs, removals, and recalls (see sections 518 and 519(g) of the FD&C Act (21 U.S.C. 360h and

360i(g)), and 21 CFR parts 7, 806, and 810. In particular, FDA considers it important that the definition make clear that actions taken by an organization on a nonconforming product after a device has been released for distribution should not be considered a type of rework, as the existing statutory and regulatory requirements, and this final rule, consider rework to be action(s) taken before the device is released for distribution, and not after distribution. This distinction is not addressed by the definition of "rework" in ISO 9000.

(Comment 40) A comment suggested that the QMSR should include a definition for the term "critical supplier" as that term is defined and used in MDSAP.

(Response) FDA disagrees with this comment and does not consider a definition of the term "critical supplier" to be needed in the QMSR. We acknowledge that purchased products and the suppliers of those products can be critical to ensuring safety and effectiveness throughout a medical device's life cycle. The QMSR describes a process of continuous evaluation to address products and suppliers. Clause 7.4 of ISO 13485 specifies that an organization must evaluate suppliers of purchased products in terms of ability and performance of the supplier, commensurate with the "effect of the purchased product on the quality of" the final finished device and in terms of the "proportionate risk associated with" the final finished device. Additionally, monitoring and reevaluation of suppliers and the performance of purchased products is required. Because ISO 13485 already requires quality- and risk-focused continuous evaluation of all purchased products and suppliers, FDA has concluded that an additional definition of "critical supplier" would be redundant and is not necessary for this rulemaking. FDA notes that a consultant may supply advice and/or information to a firm (*i.e.,* a service) and the QMSR requires that a manufacturer determine what it needs to adequately carry out the requirements of the regulation and to assess whether the consultant can adequately meet those needs.

(Comment 41) One comment suggested that § 820.15, Clarification of Concepts, in the proposed rule is unnecessary and should instead be incorporated into § 820.3.

(Response) FDA agrees with this comment and has revised the rule to remove § 820.15 and move the clarification of certain concepts and terms to § 820.3(b). Because the information in this section is intended to help clarify how terms in the QMSR should be interpreted, we consider this section to have a similar intent to that of the definitions provision. We also think that combining these sections should help improve readability and ease interpretation of the overall QMSR. See section V.F for additional discussion of comments received regarding § 820.15 of the proposed rule.

E. Requirement for a Quality Management System

(Comment 42) FDA received multiple comments regarding proposed § 820.10(b), which requires that manufacturers establish and maintain a quality management system and comply, as appropriate with the other "applicable regulatory requirements" including, but not limited to, those requirements listed in the codified. One comment asked that FDA list the other sections of ISO 13485 that apply to medical device manufacturers, for the purposes of complying with § 820.10. Another comment asked FDA to clarify whether parts 803 and 806 remain applicable to device manufacturers after this rulemaking.

(Response) There are many portions of ISO 13485 that refer to "applicable regulatory requirements." We have included FDA requirements that are relevant to the phrase "applicable regulatory requirements'' to assist manufacturers in understanding how ISO 13485 relates to other regulatory requirements for devices. We have identified certain instances of the phrase "applicable regulatory requirements," and therefore, the list is not intended to be comprehensive. Regulated manufacturers are responsible for identifying and meeting all applicable requirements, even if such requirements are not specifically called out in § 820.10.

To the extent the comment is asking what sections of ISO 13485 apply to device manufacturers, FDA notes that all sections of ISO 13485 apply to device manufacturers. In particular, FDA considers compliance with the unique device identification (UDI) provisions of the FD&C Act to be necessary to comply with Clause 7.5.8 of ISO 13485. To comply with Clause 7.5.9.1, a manufacturer is required to document procedures for traceability in accordance with the requirements of part 821 (21 CFR part 821) if that provision is applicable. Also, to comply with Clause 8.2.3 of ISO 13485, manufacturers are required to notify FDA of complaints that meet the reporting criteria of part 803. And, to comply with Clauses 7.2.3, 8.2.3, and 8.3.3 of ISO 13485, this rulemaking requires manufacturers to handle advisory notices in accordance with the requirements of part 806. Because parts 803, 806, 821, and 830 are particularly relevant to meeting the requirements set forth in the ISO 13485 Clauses listed in § 820.10(b), FDA is not making any changes to the listed requirements.

The QMSR also allows for flexibility such that if a manufacturer engages in only some operations subject to the requirements of the QMSR but not in others, the QMSR allows organizations to identify and document the requirements of the QMSR that are not applicable to that organization. FDA recognizes, however, that organizations are seeking guidance and clarification on FDA's expectations regarding an organization's implementation of, and compliance with, the QMSR. To help facilitate understanding, FDA is in the process of evaluating its existing policies, procedures, and guidance for industry to be consistent with the QMSR.

(Comment 43) A comment implied that specific sections of proposed § 820.10(b)(1) through (3) were not needed for several reasons, including that:

- the requirements in proposed § 820.10(b)(1) are already addressed by § 820.3(cc) of the QS regulation and by reference to part 830,
- the requirements in proposed § 820.10(b)(2) are already addressed by § 820.65 (21 CFR 820.65) of the QS regulation and by part 821, and
- the requirements in proposed § 820.10(b)(3) are already addressed by § 820.198(a)(3) (21 CFR 820.198(a)) of the QS regulation and part 803.

(Response) FDA disagrees that § 820.10(b)(1) through (3) are not needed, because FDA is removing the majority of requirements in the QS regulation previously in part 820 and is revising the remainder of the part to harmonize with FDA's statutory and regulatory framework. Sections 820.3(cc), 820.65, and 820.198(a)(3) of the QS regulation have been withdrawn, and the new QMSR no longer includes these provisions.

The requirements enumerated in the new § 820.10(b)(1) through (3) make explicit that compliance with other parts of Title 21 is central to a comprehensive QMS system. Further, they are necessary because ISO 13485 directs the manufacturer to follow "applicable regulatory requirements.'' We have included FDA requirements that are relevant to the phrase "applicable regulatory requirements,'' to assist manufacturers in understanding how ISO 13485 relates to other regulatory requirements for devices. We have only identified certain instances of

the phrase "applicable regulatory requirements," and therefore, the list is not intended to be comprehensive. Regulated manufacturers are responsible for identifying and meeting all applicable requirements, even if such requirements are not specifically listed in § 820.10.

(Comment 44) FDA received comments asking that FDA remove the reference to Clause 7.5.8 of ISO 13485 in the proposed § 820.10(b)(1). One commenter suggested that the reference to Clause 7.5.8 seemed to require that organizations assign a UDI to products throughout the product development cycle, while part 830 only requires UDI for finished devices. This comment also asked that FDA remove the reference to part 821 in the proposed § 820.10(b)(2) because the reference to part 821 is confusing, as the commenter opined that traceability requirements in Clause 7.5.9.1 are not the same as the requirements for device tracking under part 821.

(Response) FDA disagrees with the comment's interpretation of the regulations, and takes this opportunity to clarify its expectations regarding compliance with parts 830 and 821 for the purposes of the QMSR. First, we note that Clause 7.5.8 of ISO 13485 requires that as part of its QMS, an organization must document a process for product identification and, if required by applicable regulatory requirements, must document a system to assign UDI. The QMSR clarifies the applicable regulatory requirements for UDI in § 820.10(b)(1), which states that the system for assigning UDIs must comply with part 830. The QMSR, therefore, requires that an organization document a process to identify a product by "suitable means throughout product realization" and also that an organization document a system to adequately identify devices through distribution and use, consistent with part 830. In light of those provisions, FDA does not consider the QMSR to require an organization to assign a UDI to devices under development because the provisions in part 830 apply to a device in commercial distribution. Similarly, FDA does not take a position in this rulemaking on whether an organization should incorporate UDI as part of its documented process for identification of devices that are not in commercial distribution, so long as the requirements of the QMSR are met.

FDA also disagrees with the portion of the comment addressing compliance with § 820.10(b)(2). FDA does not consider the reference to part 821 to create a general requirement that an organization's traceability procedures adhere to the requirements of part 821. Rather, this reference makes explicit that when a device is subject to the requirements of part 821, an organization shall, among other things, document procedures for those requirements in its QMS in accordance with Clause 7.5.9 of ISO 13485.

(Comment 45) FDA received multiple comments regarding proposed § 820.10(c) Design and Development. In the preamble to the proposed rule, FDA proposed to clarify that Clause 7.3 Design and Development of ISO 13485 applies only to the manufacturers of the class I devices that are listed in § 820.10(c) in addition to all manufacturers of class II and III devices. Multiple commenters asked FDA to clarify this concept and to remove the word "only" to avoid the potential for confusion regarding to which devices this provision applies. One comment stated that under ISO 13485 a manufacturer of any type of class I device needs to follow design controls and that FDA's exclusion of most class I devices differs from ISO 13485. One comment asked FDA to clarify whether class I devices that are constituent parts of combination products will be subject to design and development requirements.

(Response) FDA appreciates the numerous questions regarding the scope of the QMSR with respect to design and development. The QMSR, as proposed, retains the scope of the previous § 820.30(a) of the QS regulation and does not modify which devices are subject to these requirements. Manufacturers of class II and class III, and certain class I devices described in § 820.10(c) must comply with the requirements in Design and Development, Clause 7.3 and its subclauses in ISO 13485. We further note that the device and development requirements, like other QMSR requirements, apply to all finished devices, including devices licensed under section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) (*e.g.,* in vitro diagnostic devices that are intended for blood donor screening and compatibility testing). FDA understands the comments recommending the removal of the term "only" from the preamble of the proposed rule explaining that Clause 7.3 Design and Development of ISO 13485 applies to the manufacturers of the class I devices that are listed in § 820.10(c) in addition to all manufacturers of class II and class III devices.

FDA disagrees with the comment asserting that FDA's decision to limit the applicability of the design and development requirements to a subset of class I devices is inconsistent with ISO 13485. To the extent that ISO 13485 addresses how the standard may be applied in a particular regulatory jurisdiction, the standard explicitly defers to those jurisdictions. Specifically, § 820.10(c) is consistent with clause 1 of ISO 13485, which recognizes that there may be exclusions by the regulatory authority from the Design and Development requirement and directs the manufacturer to document such in its justification for exclusion. For all devices to which design and development requirements apply, FDA does not expect manufacturers to maintain records of all changes proposed during the very early stages of the design process. However, a successful QMS requires a manufacturer to document design changes made after the initial design inputs have been approved, and/or any changes made to correct design deficiencies once the design has been released to production.

To address the comment asking for clarification regarding how the requirements in § 820.10(c) apply to combination products, we note that § 4.3 (21 CFR 4.3) lists all of the CGMP regulations that may apply to a combination product, depending on the constituent parts of the product. We are not revising § 4.3 in this rulemaking, and its language and the general policies around its implementation remain unchanged. We note also that FDA has previously addressed compliance with CGMP requirements for combination products in the final rule for part 4 (78 FR 4307, January 22, 2013) and in a subsequent guidance document entitled "Current Good Manufacturing Practice Requirements for Combination Products", including with regard to device constituent parts that are or would be classified as class I and exempt from design and development requirements (Ref. 14).

(Comment 46) Multiple comments noted that the proposed QMSR did not appear to them to include the requirement found in the QS regulation in § 820.30(e) that each stage of design review shall include an individual(s) who does not have direct responsibility for the design stage being reviewed.

(Response) FDA agrees that the final QMSR differs from the previous QS regulation and does not include the explicit requirement that each stage of design review must include an individual(s) who does not have direct responsibility for the design stage being reviewed. We note that Clause 7.3.5 of ISO 13485 requires that design and development review include representatives of functions concerned with the stage under review as well as

other specialist personnel. FDA considers Clause 7.3.5 of ISO 13485 to provide adequate flexibility for organizations to balance management of personnel and other resources in the organization with the important contribution of independent review to the design and development process; manufacturers may to choose which individual(s) to include in each stage of design review to comply with the requirements.

FDA considers that a successful quality management system under Clause 7.3.3 and 7.3.4. will require a similar approach to design review and validation as those developed under the QS regulation. For instance, the purpose of conducting design reviews during the design phase is to ensure that the design satisfies the design input requirements for the intended use of the device and the needs of the user. Design review includes the review of design verification data to determine whether the design outputs meet functional and operational requirements, the design is compatible with components and other accessories, the safety requirements are achieved, the reliability and maintenance requirements are met, the labeling and other regulatory requirements are met, and the manufacturing, installation, and servicing requirements are compatible with the design specifications. Design reviews should be conducted at major decision points during the design phase.

For a large manufacturer, design review provides an opportunity for all those who may have an impact on the quality of the device to provide input, including manufacturing, quality assurance, purchasing, sales, and servicing divisions. While small manufacturers may not have the broad range of disciplines found in a large company, and the need to coordinate and control technical interfaces may be lessened, the principles of design review still apply. The requirements under § 820.30(e) allow small manufacturers to tailor a design review that is appropriate to their individual needs.

(Comment 47) A comment requested that FDA specify which regulatory requirements would be applicable under Clause 7.3.7 of ISO 13485, which states that as part of design and development validation, an "organization shall perform clinical evaluations or performance evaluations of the medical device in accordance with applicable regulatory requirements."

(Response) Because the regulatory requirements that may apply to clinical evaluations are provided elsewhere, FDA declines to list such information in the codified portion of this rulemaking. Clinical studies of medical devices in the United States are generally governed by the set of regulations and requirements known as good clinical practices. These regulations apply to the manufacturers, sponsors, clinical investigators, institutional review boards, and the medical device. The primary regulations in Title 21 that govern the conduct of clinical studies of medical devices include, but are not limited to, part 812 (21 CFR part 812), Investigational Device Exemptions; 21 CFR part 50, Protection of Human Subjects; 21 CFR part 56, Institutional Review Boards; and 21 CFR part 54, Financial Disclosure by Clinical Investigators. FDA notes that prototypes used in clinical studies involving humans may be shipped in accordance with the investigational device exemption provisions in part 812. We also note that regulations in other parts of the CFR may apply to clinical evaluation, for example those in 45 CFR part 46, Protection of Human Subjects.

(Comment 48) FDA received many comments regarding the proposed § 820.10(d) concerning traceability for implantable devices, discussed here and in the two following sets of comments and responses. This provision requires manufacturers of devices that support or sustain life to comply with the requirements in Clause 7.5.9.2 in ISO 13485. Commenters asked FDA whether the QMSR would retain § 820.65 from the QS regulation and to clarify the relationship between Clauses 7.5.9.1 and Clause 7.5.9.2 of ISO 13485 and § 820.65 and part 821 of this Title.

(Response) In response to the comment suggesting that the QMSR retain § 820.65 of the QS regulation, FDA reiterates that much of the QS regulation is being removed or amended, including § 820.65. Instead, the QMSR incorporates the traceability requirements set forth in Clause 7.5.9 of ISO 13485, including Clause 7.5.9.2, and § 820.10(d) requires that manufacturers of devices that support or sustain life comply with these traceability requirements.

(Comment 49) Comments requested that FDA reconsider the scope of § 820.10(d), suggesting that its requirements be limited to class III devices, devices that require traceability, or to implantable devices with an alternative traceability requirement developed for non-implantable devices. Some comments believed that the risks associated with devices that support or sustain life are not necessarily the same as those associated with implanted devices. Comments asked FDA to define specific terms in § 820.10(d), including the phrase "support or sustain life," and to explain how firms are to determine which devices support or sustain life. One comment suggested that § 820.10(d), as drafted, could be interpreted to apply to all medical devices and recommended that FDA delete the provision to avoid confusion.

(Response) FDA considers the scope of devices subject to this provision under the final QMSR to be substantially similar to the scope in the QS regulation and declines to limit the scope of this provision in the manner suggested by the comments.

In response to the comments suggesting that it would be useful to define specific terms in § 820.10(d), FDA notes that § 820.65 of the QS regulation did not include a definition for the phrase "support or sustain life." Further, it is not necessary to include a definition in the QMSR because the phrase is explained in 21 CFR part 860 and that meaning has historically been applied to CGMP requirements. Section 860.3 (21 CFR 860.3) defines the term "life-supporting or life-sustaining device" as "a device that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life." These meanings are helpful and well understood, and FDA does not consider additional definitions to be necessary to assess compliance with the QMSR.

We additionally note that the term "implant'' is defined in § 860.3 as "a device that is placed into a surgically or naturally formed cavity of the human body. A device is regarded as an implant for the purpose of this part only if it is intended to remain implanted continuously for a period of 30 days or more, unless the Commissioner determines otherwise to protect human health." FDA intends to consider this definition when interpreting the QMSR. To incorporate this definition more clearly into the QMSR, FDA has revised the "clarification of concepts" provision in § 820.3(b) to explain that the term "implantable medical device" as used in ISO 13485 has the same meaning as "implant'' as described above and defined in § 860.3.

(Comment 50) Multiple comments suggested that proposed § 820.10(d) was overly burdensome. One comment stated that the requirements found in previous § 820.65 of the QS regulation were less burdensome than the requirements in ISO 13485 Clause 7.5.9.2, and another comment suggested that the perceived increased burden would itself cause devices to be less

available. A comment was concerned that this provision will increase documentation requirements and is redundant with established processes required by other testing standards and European postmarket reporting requirements. Some comments noted that it may be difficult for manufacturers to maintain records of components and to comply with these requirements for devices incorporating off the shelf technology.

(Response) We disagree that it will be overly burdensome for manufacturers to comply with this provision. The traceability requirements, and the manner in which they are applied in the QMSR, the FD&C Act, and in its implementing regulations, are substantially similar to those found in the QS regulation. For example, the requirements found in § 820.10(d) and Clause 7.5.9.2 of ISO 13485 reflect portions of the QS regulation (including 21 CFR 820.60, 820.65, 820.160, and 820.70(c)), including that a manufacturer is to establish and maintain procedures to identify devices throughout development and identify components where appropriate, to maintain distribution records, and to adequately control environmental conditions when those conditions could impact product quality.

We also have considered the comments regarding the requirement that manufacturers maintain records of components that could cause the medical device not to satisfy its specified safety and effectiveness requirements, and we consider such records to be essential to a comprehensive QMS.

Similarly, we recognize that other jurisdictions may have requirements for medical devices that are similar to those in § 820.10(d) of the QMSR, and those similarities were an important consideration in incorporating ISO 13485. We note, further, that this is consistent with our goal of harmonizing to the extent possible FDA's QMSR requirements with global standards and the requirements of other regulatory jurisdictions.

F. Clarification of Concepts

(Comment 51) FDA received comments asking FDA to clarify use of the phrases "safety and performance'' and "safety and effectiveness" within the QMSR. Commenters seemed to interpret that FDA had used the two phrases interchangeably in the proposed rule and asked that FDA revise the proposed use of the phrase "safety and performance" because its meaning is not the same as "safety and effectiveness.'' One commenter suggested that because the terms are different, they require different outcomes. Another commenter asked FDA to cite the source of the concept of "safety and effectiveness."

(Response) FDA agrees that the phrases "safety and effectiveness" and "safety and performance'' are not interchangeable, and although the proposed rule explained that FDA was not proposing that the terms were interchangeable, we have nevertheless revised this rule to avoid the potential for confusion. In accordance with section 520(f) of the FD&C Act, and as stated in § 820.1, the requirements of the QMSR are intended to assure that finished devices will be safe and effective and otherwise in compliance with the FD&C Act. FDA acknowledges that ISO 13485 and the FD&C Act utilize different phrasing related to device function and use, because ISO 13485 includes criteria related to safety and performance by which to evaluate medical devices. FDA's intention is to reinforce that, despite the difference in terminology, the QMSR as a whole is intended to assure that finished devices will be manufactured to meet the statutory requirement for safety and effectiveness. The quality management system requirements specified in ISO 13485 are complementary to the technical requirements that are necessary to meet applicable regulatory requirements for safety and performance. To help clarify this position, we have revised the "clarification of concepts" section of the rule (proposed § 820.15, which is now included in § 820.3(b)) so that "safety and performance'' has the meaning of "safety and effectiveness'' only within the introduction in Clause 0.1 of ISO 13485. In the context of Clause 0.1 of ISO 13485, "safety and performance'' means "assessment of the performance of the device to assure the device is safe and effective" as required by section 520(f) of the FD&C Act. The term "safety and performance'' does not relieve a manufacturer from obligations related to ensuring that finished devices are safe and effective.

G. Supplementary Provisions

1. Control of Records (§ 820.35)

(Comment 52) Some comments noted that the requirements set forth in the QMSR, at § 820.35, appear to add additional requirements regarding control of records to ISO 13485.

(Response) FDA agrees with the comments. The QMSR includes specific and limited requirements for control of records in addition to those in ISO 13485 to ensure consistency and alignment with other requirements in the FD&C Act and its implementing regulations.

FDA considers the additional requirements specified in § 820.35 (*i.e.,* requirements that are not specified in ISO 13485) regarding control of records to be necessary to implement a QMSR that is consistent with applicable statutory and regulatory requirements. Manufacturers must meet the requirements in ISO 13485 clause 4.2.5 (any other applicable clauses of ISO 13485; for example, complaint handling shall be conducted in accordance with the requirements set forth at 8.2.2), and also meet the requirements of § 820.35. We think that these additional requirements will help ensure that records are established and maintained in a manner that is useful to FDA and manufacturers.

We have included specific requirements to ensure that the information required by part 803, Medical Device Reporting, is captured on certain records of complaints and servicing activities. We are also requiring that firms document the UDI for each medical device or batch of medical devices in accordance with part 830 in its records. Last, we are retaining the clarification from § 820.180 (21 CFR 820.180) of the former QS regulation that governs the confidentiality of records FDA receives. This reminds firms that FDA protects such records in accordance with part 20 (21 CFR part 20). As set forth in this rulemaking, manufacturers must meet the requirements in ISO 13485 Clause 4.2.5 and also meet the requirements of § 820.35.

(Comment 53) Comments noted that § 820.35 of the proposed QMSR requires that manufacturers "obtain the signature for each individual who approved or re-approved the record." Many comments noted that the signature requirements described in the proposed rule appeared to apply to all records and were drafted to appear to be more stringent, and thus more burdensome, than the QS regulation. Multiple comments sought clarification on the manner and method of the signature requirement.

(Response) FDA agrees with the comments that noted that the signature requirements in the proposed rule appear to be more expansive than those in either ISO 13485 or the former QS regulation. In response to the comments and to maintain continuity with the requirements of the QS regulation and ISO 13485, FDA has revised this rule to remove the requirement that the manufacturer obtain the signature for each individual who approved or reapproved the record, and the date of such approval on the record.

FDA notes that where ISO 13485 uses the term "approved," that term means that an approved document, or certain record of a type that requires approval by ISO 13485, has a signature and date. Additionally, we note that FDA will consider signatures that utilize the method the Agency determines fulfills electronic signature requirements to be compliant with this requirement. Manufacturers can choose to develop electronic records and electronic methods for denoting approval. Our focus is on whether the substance of the requirements is met and not the physicality of the record or signature methodology.

(Comment 54) Commenters requested that FDA elaborate on the specific requirements for maintaining complaint records, records of servicing, and for documenting UDI. Some commenters noted that proposed § 820.35(a)(4) requires that complaint records include the name and contact information of the complainant, and requested clarification regarding what information would satisfy that requirement. Other commenters suggested that an electronic address, rather than a physical address, would be appropriate on complaint records. With respect to documenting servicing records, one commenter noted that § 820.35(b)(6) requires manufacturers to record any test and inspection data that is conducted as part of the manufacturer's servicing activities and noted that manufacturers should not be required to perform such testing if it is beyond the scope of the individual servicing activity. One commenter requested that FDA clarify when the QMSR requires manufacturers to document the UDI, and another commenter asked FDA to modify § 820.35(c) to state that the UDI could be "recorded/included'' for each medical device or batch of medical devices.

(Response) The information required by part 803, Medical Device Reporting, must appear on certain records of complaints and of servicing activities in § 820.35(a). To the extent the medical device reporting regulations permit contact information to include an electronic address, rather than a physical address, compliance with part 803 would be compliant with this rule. To provide additional clarity regarding complaint handling, we have revised § 820.35(a) to describe the circumstances under which an investigation of a complaint must be initiated and records related to that complaint must be retained. Clause 8.2.2 and § 820.35(a) require that if any complaint is not investigated, the firm shall document the reason it has not investigated that complaint. For example, if the information required for an investigation cannot be obtained, then the manufacturer must document the efforts it made to ascertain the information.

Consistent with the QS regulation, FDA expects that a firm will make a reasonable and good faith effort to obtain the information required for an investigation. Additionally, we note that if a corporation chooses to operate with different complaint handling units for products and/or establishments, the manufacturer must clearly describe and define its corporate complaint handling procedure to ensure consistency throughout the different complaint handling units. A system that would allow multiple interpretations of handling, evaluating, categorizing, investigating, and following up, would be unacceptable. Each manufacturer should establish in its procedures which one group or unit is ultimately responsible for coordinating all complaint handling functions.

FDA agrees with the comment regarding interpretation of § 820.35(b)(6) and does not consider this section to require test and inspection data for all servicing activities. Rather, when an organization's QMSR does require such test and inspection data to be generated as part of the servicing activities, those data must be included as part of the record per § 820.35(b)(6). Regarding requirements for documentation of UDI, we reaffirm our position—as stated in the proposed rule—that this rule requires that firms document the UDI for each medical device or batch of medical devices in accordance with part 830. Similarly, we disagree that the requirement in § 820.35(c) should be modified; the phrasing of this provision allows a manufacturer to comply with § 820.35(c)'s requirements in the manner appropriate for the device and its manufacturing process.

(Comment 55) FDA received numerous comments regarding the lack of an exception for management review, quality audits, and supplier audit reports, which formerly existed in the QS regulation, at § 820.180(c). Most such comments requested that FDA maintain the exceptions set forth in § 820.180(c), some suggested that FDA adopt specific language to do so, and the remainder requested that FDA clarify whether such records are exempted from inspector access. One commenter in particular noted that the current quality system inspection technique (QSIT) guide also states that management review, internal audit, and supplier audit records are exempted from inspection. Several comments expressed concern that the exception was necessary to ensure manufacturers' audit and management review reports continue to be complete and/or useful.

(Response) FDA disagrees that it should maintain the exceptions set forth at § 820.180(c). One of the primary purposes for this rulemaking effort is to move as closely as possible toward global harmonization and alignment. From a global perspective, the exceptions the comment references are not available to manufacturers being inspected by other regulators or being audited by other entities (*e.g.,* MDSAP auditing organizations), and thus, such manufacturers will not be additionally burdened by making these records available. Similarly, FDA does not consider it to be a large burden to the manufacturers who may have taken advantage of the exceptions to make these records available, as such records are maintained in the regular course of business and should be readily available. Additionally, FDA notes that its investigators have already had access to data used to inform management reviews, such as nonconformances and complaints, and any corrective actions resulting from internal and supplier audits.

FDA emphasizes that robust management review, as well as internal and supplier audit programs, are fundamental to the culture of quality discussed previously in this rulemaking and which FDA expects firms to embrace. Further, FDA intends to modify its inspectional processes consistent with this rulemaking, and does not consider this rulemaking to be the appropriate vehicle to describe any future implementation activities, including inspectional processes.

(Comment 56) One comment suggested that when ISO 13485 refers to providing evidence, FDA should allow manufacturers to determine the most appropriate type of data (qualitative or quantitative).

(Response) FDA disagrees with this comment. In this rulemaking, FDA requires that manufacturers document a quality management system that complies with ISO 13485, as modified by part 820. In general, when ISO 13485 refers to providing evidence, FDA recommends that manufacturers record quantitative data, as appropriate and commensurate with risk. Such information will assist manufacturers in monitoring the performance of their products, processes, and effectiveness of their controls. We recognize that there may be circumstances under which it is not possible or practical for an organization to generate and record appropriate quantitative data, and we consider the QMSR framework to

provide adequate flexibility to accommodate such situations in accordance with Clause 0.2 of ISO 13485.

(Comment 57) One commenter noted that in the QMSR, § 820.35(a)(6) requires manufacturers to keep a record of any corrective action and that FDA should add the term "correction" to the term "corrective action," which FDA interprets to be parallel to the requirement in ISO 13485 at Clause 8.2.2.

(Response) FDA agrees with the commenter that adding the term "correction" to the term "corrective action" would align the QMSR with ISO 13485 and has made such modifications within § 820.35(a)(6). The QS regulation utilized the term "corrective action," whereas ISO 13485 references both "correction" and "corrective action." To harmonize with the standard, we have added the term "correction" to the codified for completeness. See also Comment 29.

(Comment 58) One comment inquired about how FDA interprets the requirement that records be "readily identifiable and retrievable," including how FDA intends foreign manufacturers to comply with these requirements.

(Response) FDA considers this phrase to be substantially similar to the requirement in the QS regulation that records be "reasonably accessible" and "readily available.'' Consistent with the QS regulation, that means that records will be made available during the course of an inspection. If the manufacturer maintains records at remote locations, records will be produced by the next working day or two, at the latest. FDA continues to believe that records can be kept at other than the inspected establishment, provided that they are made "readily available" for review and copying (see 61 FR 52602 at 52637). FDA considers records that a manufacturer makes available as described herein to be "readily identifiable and retrievable." FDA notes that although it has made changes to revise § 820.1(c) to align with the statutory language in sections 501 and 801 of the FD&C Act, it has not changed a foreign manufacturer's obligations under this part.

2. Controls for Device Labeling and Packaging (§ 820.45)

(Comment 59) FDA interprets one comment to note that utilizing the term "establish" in this section creates a potential for confusion, as ISO 13485 defines the process of "documenting'' as including the processes of "establishing," "implementing," and "maintaining."

(Response) FDA agrees with the comment, to the extent it suggests that it would be less confusing to use the term "documenting'' in place of the phrase "established and maintained'' in that portion of the rulemaking. FDA has made changes to the codified rule to accommodate this recommendation and notes that the clarified requirement to document includes the requirements to establish and maintain (see section V.D., Definitions).

(Comment 60) FDA received a comment suggesting that ISO 13485 fails to provide sufficient requirements for labeling and packaging, and does not address how manufacturers inspect their products' labels. The comment recommended that FDA add additional requirements to align with FDA's draft guidance document entitled "Remanufacturing of Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff."

(Response) FDA agrees that ISO 13485 does not specifically address the inspection of labeling by the manufacturer, which is why FDA is retaining in this rule requirements from the QS regulation that strengthen controls for labeling and packaging operations. FDA notes that many device recalls are related to labeling and packaging. Section 820.45(a) requires that manufacturers inspect their labeling and packaging for accuracy to include the requirements set forth at § 820.45(a)(1) through (5) to ensure that release of the labeling is documented in accordance with Clause 4.2.5 of ISO 13485 and so that the manufacturer ensures that labeling and packaging operations have been documented to prevent errors. Section 820.45 specifically requires that manufacturers inspect labeling and packaging before use to assure that all devices have the correct labeling and packaging, in accordance with Clause 4.2.3 and that manufacturers document that inspection.

FDA notes that in its experience, manufacturers have recalled devices where automated readers have not caught label errors. The requirement to inspect labeling and packaging does not preclude automatic readers where that process is followed by human oversight. A designated individual must examine, at a minimum, a representative sampling of all labels that have been checked by automatic readers. Further, automated readers are often programmed with only the base label and do not check specifics, such as control numbers and expiration dates, among other things, that are distinct for each label. The regulation requires that labeling be inspected for these items prior to release. FDA believes that these provisions will better assure the manufacture of safe and effective devices.

FDA disagrees that additional requirements are necessary to ensure that labeling and packaging is sufficiently addressed by this rulemaking. FDA also notes that its guidance documents set forth FDA's current thinking on a subject, but do not set forth regulatory requirements to which this rule could be aligned.

(Comment 61) One comment suggested that manufacturers subject to special controls regarding labeling and/or packaging under sections 510 and/or 513(a) of the FD&C Act may wrongly consider their devices exempt from § 820.45 because this rulemaking states that conflicting regulations that are more specific are controlling only to the extent of the conflict and also states that the generally applicable part 820 regulations apply to the extent they do not otherwise conflict with the specifically applicable regulation.

(Response) Special controls are not in conflict with the requirements of § 820.45, and thus, devices subject to special controls are subject to the requirements of § 820.45. Special controls and the labeling and packaging requirements in § 820.45 serve different purposes and are not in conflict as described in § 820.3(b). Special controls are requirements in addition to those set forth in this rulemaking and are those which FDA has determined are necessary to provide reasonable assurance of the safety and effectiveness of the device. Special controls are device-specific, and may include, among other things, special labeling requirements. Section 820.45 addresses the labeling process itself, not the content of the label (see Scope, supra).

(Comment 62) One comment recommended that FDA delete the phrase "immediately before use" in the requirement in § 820.45 that the manufacturer inspect the labeling and packaging immediately before use, as the commenter suggested that that phrase places an additional and new burden on manufacturers.

(Response) FDA partially agrees with the comment, and agrees that the term "immediately'' is not necessary to accomplish FDA's goal to require manufacturers to inspect labeling and packaging to ensure that an accurate label is applied to the correct device. An effective quality system will include a process for inspecting the label for accuracy and to ensure that it is applied to the correct device before the device is distributed. FDA has made that modification in the codified text.

(Comment 63) One commenter recommended that FDA provide a definition for the term "medical device file" as it is used in § 820.45(c) to require that the manufacturer ensure that labeling and packaging operations have been established and maintained to, among other things, assure that all devices have correct labeling and packaging, as specified in the medical device file.

(Response) FDA disagrees that it would be appropriate and/or helpful to define the term "medical device file" in this rulemaking, as a definition for the term is set forth at ISO 13485 Clause 4.2.3. We note that additional discussion of the term "medical device file" within this rulemaking may be found in response to Comment 31.

(Comment 64) One comment recommended that FDA remove § 820.45(a)(2) through (5), as the commenter suggested that Clause 7.5.1 of ISO 13485 already establishes the need for labeling process controls, making these requirements duplicative and requiring uniformity where the commenter believed it not to be necessary.

(Response) FDA disagrees with the comment. Clause 7.5.1(e) of ISO 13485 states that "defined operations for labelling and packaging shall be implemented.'' However, ISO 13485 fails to provide additional requirements for labeling and packaging and does not specifically address the inspection of labeling by the manufacturer. FDA is therefore retaining requirements from the QS regulation that would strengthen controls for labeling and packaging operations, given that many device recalls are related to labeling and packaging. FDA believes that these provisions will better assure the manufacture of safe and effective devices. Regulated industry must meet the requirements in ISO 13485 7.5.1 and § 820.45. Consistent with the previous QS regulation, FDA continues to expect that manufacturers will retain records of labeling operations to include the primary identification label and/ labeling used for each production unit, lot, or batch record.

As stated above, we have added additional requirements to ISO 13485, which it has retained from the QS regulation, to ensure consistency and alignment with other requirements in the FD&C Act and its implementing regulations to ensure that the QMSR ensures the manufacturing of safe and effective devices. The requirements set forth at § 820.45(a)(2) through (5) are necessary to implement a QMS that is consistent with applicable FD&C Act requirements, but are not specified in ISO 13485. These requirements include the device labeling and packaging requirements, including an expiration date, storage instructions, handling instructions, and any additional processing instructions (see 21 CFR part 801).

FDA received a group of comments regarding the use of specific words in § 820.45.

(Comment 65) FDA received a group of comments regarding the use of specific words in § 820.45. One comment proposed removing the term "distribution,'' or clarifying the term in the portion of the rulemaking that requires manufacturers to document 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." The comment suggested that labeling generally informs users how to handle and store the product, and thus the use of the term "distribution'' is overbroad and unnecessary.

(Response) FDA agrees that it would be useful to clarify the term "distribution,'' but disagrees that it is appropriate to remove the term from the rulemaking. FDA will evaluate a firm's conformity to the requirements of the QMSR related to distribution through the initial consignee.

(Comment 66) The same comment suggested that FDA replace the word "where" with the word "as" in the portion of the requirement that states, ". . . 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" (emphasis added). The comment also asked that FDA clarify when controls (*e.g.,* inspection, storage) of labeling for use of the device would apply to the manufacturer.

(Response) FDA agrees with the suggestion, and we note that ISO 13485 uses the phrase "as appropriate" and clarifies how FDA interprets this phrase in clause 0.2. We have therefore changed the codified language to align with the comment, and the standard. In response to the request for additional clarification regarding which controls apply to certain activities, FDA reiterates that if a manufacturer engages in only some activities subject to the requirements in this part, and not in others, that manufacturer need only comply with those requirements applicable to the activities in which it is engaged.

(Comment 67) The same comment suggested that the term "operations'' as used in § 820.45 could refer to the application of labeling to the device as well as to the production of the label itself. The comment suggested that § 820.120(a) in the QS regulation required integrity of the label during use, where appropriate, and further suggested that the QMSR does not maintain this requirement.

(Response) FDA agrees that the term "operations'' as used in § 820.45 can refer to both the application of labeling to the device as well as to the production of the label itself. Further, we note that § 820.45(c) provides additional clarification regarding expectations for such operations. FDA, therefore, disagrees that it is necessary to retain § 820.120(a) to maintain the requirements regarding the integrity of the label, where appropriate. As FDA has noted, we have added additional requirements to ensure consistency and alignment with other requirements in the FD&C Act and its implementing regulations. Those additional requirements are intended to ensure that the device's label contains accurate information and is attached appropriately to the device in accordance with the applicable requirements of the FD&C Act and its implementing regulations.

H. Conforming Amendments and FDA Response

(Comment 68) FDA received a comment recommending that FDA create a harmonized approach for both the QMSR and part 4 to become effective 2 years after the date of publication in the **Federal Register**.

(Response) FDA agrees with the comment and has made the recommended modifications, as set forth in the Effective Date section of this rulemaking. FDA agrees with the comment that the effective date of the revisions to part 4 and the QMSR will be the same.

(Comment 69) FDA received a comment recommending that FDA clarify how MDSAP applies to combination products.

(Response) FDA notes that at this time, combination products are outside the scope of MDSAP. In amending part 4, FDA intends to achieve consistency with the QMSR and does not intend to imply that the MDSAP program is available for combination products.

(Comment 70) Commenters recommended that the Agency clarify

whether it intends to advance the mutual recognition of pharmaceutical CGMP for combination product manufacturers that have aligned their quality management systems to § 4.4(b)(2) to meet GMP requirements for the combination products.

(Response) While FDA supports the concepts of convergence and coordination with respect to CGMPs for combination products, pharmaceutical GMPs and mutual recognition agreements for combination products are outside the scope of this rulemaking.

(Comment 71) One commenter recommended that FDA delete specific text ("upon demonstration that these requirements have been satisfied, no additional showing of compliance with respect to the QMSR requirements need be made"), as the commenter suggested that the text implied that manufacturers of combination products need not comply with Clause 8.3, Clause 8.2.2, and/or Clause 8.2.3.

(Response) Compliance with the applicable provisions of the QMSR is required, and FDA disagrees that the text of the rulemaking implies otherwise. FDA agrees with the portion of the comment that recommends reiterating that manufacturers of combination products must also comply with Clause 8.2.2, and has added that provision. In addition, FDA notes that the other Clauses that the commenter lists are covered sufficiently in part 211 (21 CFR part 211). FDA notes that the language that the commenter recommends deleting previously existed in part 4.

(Comment 72) A commenter recommended that FDA add the terms "analysis of data" in § 4.4, as Corrective and Preventive Action has been replaced with the term "improvement," and has an expanded scope. To align with ISO 13485, the commenter proposed to add the phrase "analysis of data" in § 4.4(b)(1)(iv).

(Response) FDA agrees with the suggestion and has added the term "analysis of data" to the codified text at § 4.4(b)(1)(iv) to be consistent with the phrasing in the standard.

(Comment 73) A commenter recommended that FDA align terms with parts 210 (21 CFR part 210) and 211 by modifying the definition of the term "component'' in the QMSR consistent with the definition set forth in part 210.

(Response) FDA has considered the comment and declines to make the suggested change as we consider the term "component'' to be appropriately defined with respect to device CGMP requirements in the QMSR and to be appropriately defined with respect to drug CGMP requirements in parts 210 and 211. FDA does not consider the definition of "component'' set forth in § 210.3(b)(3) to be relevant to device CGMP requirements because that regulation defines the term within drug CGMP requirements. Introducing the definition in § 210.3(b)(3) in this rulemaking would lead to confusion and misinterpretation of device CGMP requirements.

(Comment 74) A commenter asked FDA to clarify whether the requirements set forth by this rulemaking will impact part 210 or part 211.

(Response) FDA clarifies that the requirements set forth by this rulemaking do not alter or change the requirements set forth at part 210 or part 211. This determination does not represent a change from the previous version of the QS regulation.

VI. Effective Date and Implementation Strategy

A. Effective Date

(Comment 75) FDA received many comments noting that the proposed effective date of 1 year was not enough time to implement this rulemaking. Some comments explained that 1 year would not be enough time to train staff, revise processes and/or procedures, and make necessary changes to current practices. Other comments explained that small firms, midsize firms, or firms who currently conduct business exclusively in the United States may need more than 1 year to become familiar with the QMSR and implement necessary changes. Several comments suggested that an effective date of 2 or 3 years after publication in the **Federal Register** would be appropriate, to allow firms adequate time to implement any such changes.

(Response) FDA has considered these comments and the testimony given during the Advisory Committee hearing. FDA agrees that firms will need to become familiar with the QMSR, and FDA appreciates that manufacturers will need to make appropriate changes within their organizations to align their QMSs, processes, and documents with the QMSR. FDA also agrees that domestic firms may find that ISO 13485 is new to them, although FDA also considers ISO 13485 to be substantially similar to the requirements of the QS regulation. Because ISO 13485 is substantially similar to the requirements of the QS regulation, FDA disagrees that small firms and/or midsize firms will need more time than larger firms to implement this rulemaking.

Therefore, to balance the concerns raised by comments and participants in the Advisory Committee Hearing and the Agency's interest in efficiently achieving global harmonization, streamlining regulatory requirements, reducing burdens on regulated industry, and providing patients more efficient access to necessary devices, FDA has reconsidered the proposed effective date of 1 year, and in this rulemaking, sets an effective date of 2 years after publication in the **Federal Register**. FDA believes 2 years is adequate time for firms to align internal processes and procedures, to make appropriate changes within their organizations, and to update their documentation with the QMSR.

(Comment 76) Some comments suggested that an appropriate effective date would be 2 years after FDA updates all guidance documents associated with this rulemaking and a subset of those comments reiterated the suggestion that FDA communicate its plan for updating associated guidance documents.

(Response) FDA disagrees with the comments. FDA does not believe guidance is needed before the effective date. For the reasons given in response to the other comments, FDA has set an effective date 2 years after publication in the **Federal Register**. FDA also disagrees with the suggestion that it is appropriate in this rulemaking to outline a schedule or plan for updating guidance documents. To help stakeholders better understand how existing policies will continue to apply within the QMSR, FDA intends to update existing guidance documents. Because we consider the QS regulation and the QMSR to be substantially similar, we expect to update guidance documents for consistency but do not expect there to be many differences in interpretation of these regulations or application of relevant policies.

(Comment 77) Some comments recommended that FDA phase in an effective date. Comments suggest that FDA either implement the effective date in phases, or allow firms to comply with either the QS regulation requirements or the requirements described in this QMSR rulemaking for a period of time following publication in the **Federal Register**. Another comment suggests that FDA use a risk-based approach to transition to the QMSR, taking into account the class of medical device.

(Response) FDA disagrees that a phased-in effective date is appropriate, because having two inspectional programs in operation at the same time would be inefficient and would result in significant potential for confusion. FDA believes that the 2-year effective date provides sufficient time to implement the QMSR, and that it meets FDA's goals

of efficiently achieving global harmonization, streamlining regulatory requirements, reducing burdens on regulated industry, and providing patients more efficient access to necessary devices. 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. FDA's inspections are risk based and will continue to be consistent with section 510(h) of the FD&C Act.

B. Implementation Strategy

FDA received many comments about FDA's anticipated inspection process, and the roles of certification and participation in MDSAP following this rulemaking. FDA responds to those comments as follows:

(Comment 78) One comment suggested that FDA will need to ensure that the MDSAP audit approach reflects the QMSR and that the auditing organizations are trained accordingly.

(Response) FDA, as a participating regulatory authority in MDSAP, will evaluate the MDSAP audit approach and training needs for auditing organizations and revise as appropriate to align with the QMSR.

(Comment 79) Comments recommended that FDA expand on how it will utilize, or not utilize, certification to ISO 13485 in the MDSAP program. Commenters noted that FDA has accepted certain MDSAP audit reports—which may discuss the manufacturer's certification to ISO 13485—as a substitute for FDA inspection, and suggested that not accepting certification would create a conflict with the MDSAP inspection process. One commenter asked specifically whether FDA intends to accept an ISO certificate as a substitute for an FDA Establishment Inspection Report (EIR).

(Response) FDA agrees that it will be useful to provide additional information on the manner in which FDA intends to consider certification to ISO 13485 and how certification relates to participation in the MDSAP program. FDA notes that MDSAP is a certification program that allows for a single QMS audit based on ISO 13485 in addition to other applicable FDA device regulatory requirements, which FDA may accept in lieu of routine surveillance inspections conducted by FDA investigators.

MDSAP audits are conducted by third-party auditing organizations that have applied for participation in MDSAP and who have been granted a status of "authorized'' or "recognized" by the MDSAP consortium after a prescribed assessment process conducted by the participating regulatory authorities. Participation in MDSAP is voluntary for device manufacturers regulated by FDA.

FDA utilizes the audit reports that are generated from MDSAP audits, rather than the certificate, as an additional tool for regulatory oversight of audited manufacturers. FDA conducts oversight activities of auditing organizations participating in MDSAP to ensure conformity to MDSAP and IMDRF policies and procedures. While both MDSAP and ISO 13485 audits cover the QMS requirements detailed in the standard, FDA cannot ensure that other FDA medical device requirements, such as parts 803, 806, 821, 830, are audited during independent ISO 13485 audits. Additionally, FDA does not conduct oversight of non-MDSAP auditing organizations and does not evaluate the content of audit reports issued outside of the MDSAP.

As such, FDA does not intend to require medical device manufacturers to obtain ISO 13485 certification and will not rely on ISO 13485 certificates to conduct its regulatory oversight of medical device manufacturers. For example, an ISO 13485 certificate will not be considered or accepted as a substitute for any oversight processes, including the performance of an inspection under section 704 of the FD&C Act or generation of an EIR. FDA inspections will not result in the issuance of a certificate of conformity to ISO 13485.

(Comment 80) Multiple comments recommended that FDA accept ISO 13485 certification in place of, or in combination with, FDA inspections. Some comments suggested that FDA clarify how a firm can achieve compliance with ISO 13485 if FDA does not accept certification to ISO 13485. A group of comments expressed a concern that entities that do not have certification will be unduly burdened by having to comply with the requirement to obtain certification where that is required by the regulatory authority, and also to comply with the requirements of the FD&C Act. Other comments recommended that FDA should allow entities that have obtained certification to utilize that certification to demonstrate compliance with the QMSR, in furtherance of global harmonization.

(Response) FDA disagrees with the comments that recommend the Agency accept certification to ISO 13485 in place of FDA inspections. In addition to the response to Comment 79 above, FDA also notes that ISO 13485 certificates are issued by organizations outside FDA. FDA's obligation remains to inspect medical device manufacturers to confirm compliance with the requirements of the FD&C Act and its implementing regulations, including not only the QMSR, but also other FDA medical device requirements, such as parts 803, 806, 821, and 830. Thus, FDA disagrees with the comments that it would be appropriate to accept certification to ISO 13485 in lieu of FDA inspection.

FDA also does not agree that it is unduly burdensome to comply with both certification to ISO 13485 (where that is required) and the QMSR. By way of this rulemaking, FDA is incorporating the requirements of ISO 13485 within the QMSR, which should simplify manufacturers' ability to comply with both ISO 13485 and requirements in the FD&C Act and its implementing regulations. Regardless of ISO 13485 certification, manufacturers must also comply with any additional and applicable requirements set forth in the FD&C Act.

(Comment 81) FDA received comments suggesting that because FDA's intent is to replace the QSIT approach with a new approach that follows the QMSR, FDA should outline and define the inspection procedures it intends to follow after the effective date of this rulemaking. Some commenters suggested that clarifying those procedures would provide manufacturers with more information on how to comply with the QMSR. Other comments recommended that FDA utilize the IMDRF to create the new inspection model, and that FDA utilize MDSAP techniques and consider multiple risk-based factors (including MDSAP enrollment and status, and ISO certification status) in developing its own inspection model.

(Response) Although this rule does not impact FDA's authority to conduct inspections under section 704 of the FD&C Act, FDA intends to replace its current inspection approach for medical devices, QSIT, with an inspection approach that will be consistent with the requirements of the QMSR. FDA understands that stakeholders are interested in knowing more details about FDA's inspection approach after this rule becomes effective and will determine in the future what details of our inspection model are appropriate to share. FDA notes that similar to the current QSIT inspection approach, these inspections will involve the collection of information to support observations

noted during the inspection and those included on a Form FDA 483, as appropriate and necessary. FDA inspections will not result in the issuance of certificates of conformance to ISO 13485 nor is FDA developing a certification program for ISO 13485. In addition, manufacturers with a certificate of conformance to ISO 13485 are not exempt from FDA inspections. FDA intends to engage in a variety of implementation activities, including, among other activities, updating information technology systems, training of personnel, finalizing the inspection approach, and assessing relevant regulations and other documents impacted by this rulemaking. FDA does not consider rulemaking to be the appropriate vehicle to describe any future implementation activities, including inspectional processes.

(Comment 82) Some comments recommended that FDA provide training and educational resources, and requested that FDA share its plan for updating appropriate guidance documents before the final rule becomes effective.

(Response) During this time, FDA intends to train FDA staff responsible for assessing compliance with medical device quality management system requirements, develop an inspection process, and assess relevant regulations and other documents impacted by this rulemaking, as appropriate. At this time, FDA considers the suggestion that it share a plan to be beyond the scope of this rulemaking.

(Comment 83) One comment recommended that after this rulemaking, FDA utilize the MDSAP inspection model in lieu of QSIT, for device-led combination products.

(Response) FDA disagrees with the recommendation, as combination products are currently outside the scope of the MDSAP program for FDA.

VII. Economic Analysis of Impacts

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, Executive Order 14094, the Regulatory Flexibility Act (5 U.S.C. 601–612), the Congressional Review Act/Small Business Regulatory Enforcement Fairness Act (5 U.S.C. 801, Pub. L. 104–121), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4).

Executive Orders 12866, 13563, and 14094 direct us to assess all benefits, costs, and transfers of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Rules are "significant'' under Executive Order 12866 Section 3(f)(1) (as amended by Executive Order 14094) if they "have an annual effect on the economy of $200 million or more (adjusted every 3 years by the Administrator of the Office of Information and Regulatory Affairs (OIRA) for changes in gross domestic product); or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, territorial, or tribal governments or communities." OIRA has determined that this final rule is a significant regulatory action under Executive Order 12866 section 3(f)(1).

Because this rule is likely to result in an annual effect on the economy of $100 million or more or meets other criteria specified in the Congressional Review Act/Small Business Regulatory Enforcement Fairness Act, OIRA has determined that this rule falls within the scope of 5 U.S.C. 804(2).

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Our small entities analysis (see Part III of the Final Regulatory Impact Analysis (Ref. 15)) indicates that the final rule would result in a net cost savings of over $500 million for medical device establishments deemed as small entities by the Small Business Administration. Therefore, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes estimates of anticipated impacts, before issuing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $177 million, using the most current (2022) Implicit Price Deflator for the Gross Domestic Product. This final rule will not result in an expenditure in any year that meets or exceeds this amount.

We estimate that the QMSR will result in an annualized net cost savings (benefits) of approximately $507 million at a 7 percent discount rate and approximately $528 million in cost savings at a 3 percent discount rate. In addition to the cost savings to the medical device industry, the qualitative benefits of the rule include quicker access to newly developed medical devices for patients leading to improved quality of life of the consumers. The rule will also align part 820 with other related programs potentially contributing to additional cost savings.

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule (Ref. 15) and at *https://www.fda.gov/about-fda/economics-staff/regulatory-impact-analyses-ria.*

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(j) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the one-time and annual recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Medical Devices; Quality Management System; OMB control number 0910–0073—Revision

Description: FDA is revising its device CGMP requirements as set forth in the QS regulation, codified in part 820. Through this rulemaking, FDA is converging its requirements with QMS requirements used by other regulatory authorities from other jurisdictions (*i.e.,* other countries). We are doing so by incorporating by reference the current 2016 version of ISO 13485 and the current 2015 version of Clause 3 of ISO 9000.

Through this rulemaking we also establish additional requirements that help connect and align ISO 13485 with existing requirements in the FD&C Act and its implementing regulations and make conforming edits to the portion of the CFR governing combination products (part 4) to clarify the device CGMP requirements for such products.

Description of Respondents: Respondents to this information

collection are any manufacturers engaged in the design, manufacture, packaging, labeling, storage, installation, or servicing of a finished device, including, but not limited to, organizations that perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, as well as initial distributors of foreign entities that perform these functions.

While the provisions of this part do not apply to manufacturers of components or parts of finished devices, such manufacturers are encouraged to consider provisions of this regulation as appropriate.

Respondents are also manufacturers of human cells, tissues, and cellular and tissue-based products, as defined in 21 CFR 1271.3(d), that are devices.

We estimate the burden of this collection of information as follows:

TABLE 1—ESTIMATED ONE-TIME RECORDKEEPING BURDEN [1]

Activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours	Total capital costs
Learn the rule	25,294	1	25,294	2.22	56,153	$9,858,780
Burden for those respondents whose processes do not already comply with ISO 13485	5,352	1	5,352	64	342,528	49,871,733
Total					398,681	59,730,513

[1] There are no operating and maintenance costs associated with this collection of information.

The number of establishments currently registered with FDA is 28,303. However, we excluded from the estimated one-time burden establishments registered as "initial importers" because we believe that compliance effort by initial importers would remain the same before and after the implementation of the final rule (see Ref. 15). Therefore, we assume 25,294 establishments will undergo a one-time burden to learn the rulemaking. We model the one-time learning cost as the time required by medical device establishments' regulatory affairs expert to access and read the rule, approximately 2.22 hours. The average total access and learning cost for all affected entities is $9,858,780 (see Ref. 15).

In addition to learning the rule requirements, medical device establishments that are not in compliance with ISO 13485 when the rulemaking is implemented would incur one-time initial costs related to training of a regulatory compliance expert, updating information technology, and updating documents related to policy and procedures. The additional estimated cost burden for medical device establishments that are not in compliance with ISO 13485 when the rulemaking is implemented is $49,871,733 (see Ref. 15).

The estimated hour burden of these additional one-time activities is included under "Burden for those respondents whose processes do not already comply with ISO 13485" in table 1. In the Regulatory Impact Analysis for this rulemaking, we estimate there are 5,352 respondents that do not currently comply with ISO 13485 and that the average burden per recordkeeping is approximately 64 hours (Ref. 15). Because we do not have robust data on the number of firms that currently comply with ISO 13485, we are using very small domestic medical device manufacturing establishments to represent those who will proportionately bear a greater burden of one-time costs by the final rule. As such, for this analysis, and as discussed in the Regulatory Impact Analysis, we assume that very small medical device manufacturing establishments currently do not sell their products abroad and do not comply with ISO 13485 (Ref. 15).

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1] [2]

Activity/21 CFR section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Quality Management System (§ 820.10 and ISO 13485)	28,303	1	28,303	348	9,849,444
Control of records (§ 820.35)	28,303	1	28,303	2	56,606
Total					9,906,050

[1] There are no capital costs or operating and maintenance costs associated with this annual collection of information.
[2] Numbers have been rounded.

The current burden associated with recordkeeping requirements in part 820 is 10,239,552 hours annually (as approved by OMB January 23, 2023). Assuming a commensurate level of burden for cumulative recordkeeping activities, we reduce our estimate to 9,906,050 to reflect a reduction of 333,502 hours annually. We believe this reduction will result from aligning our regulatory framework with that used by other regulatory authorities to promote consistency in the regulation of devices.

Quality management system (§ 820.10 and ISO 13485). Under § 820.10, an organization subject to part 820 must document a QMS that complies with the applicable requirements of ISO 13485, as incorporated by reference in § 820.7, and other applicable requirements of part 820.

Under § 820.10(c), manufacturers of class II, class III, and certain class I devices, as listed in § 820.10(c), must

comply with the requirements in Design and Development, Clause 7.3, and its subclauses in ISO 13485. This amendment does not substantively change the current recordkeeping requirement.

Under § 820.10(d), manufacturers of devices that support or sustain life, the failure of which to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in a significant injury, must comply with the requirements in Traceability for Implantable Devices, Clause 7.5.9.2 in ISO 13485, in addition to all other applicable requirements in this part. This amendment does not substantively change the current recordkeeping requirement.

Control of records (§ 820.35). Estimated burden for the recordkeeping requirements in § 820.35 is under "Control of records (§ 820.35)" in table 2. In addition to the requirements of Clause 4.2.5 in ISO 13485, Control of Records, the manufacturer must maintain certain records as provided for in § 820.35.

In addition to Clause 8.2.2 in ISO 13485, Complaint Handling, the manufacturer must maintain records of the review, evaluation, investigation, for any complaints involving the possible failure of a device, labeling, or packaging to meet any of its specifications. If an investigation has already been performed for a similar complaint, another investigation is not necessary, and the manufacturer shall maintain records documenting justification for not performing such investigation. For complaints that must be reported to FDA under part 803, complaints that a manufacturer determines must be investigated, and complaints that the manufacturer investigated regardless of those requirements the manufacturer must record the information listed in § 820.35(a). The reporting requirements of part 803 are approved under OMB control number 0910–0437 (title: Medical Device Reporting).

In adhering to Clause 7.5.4 in ISO 13485, Servicing Activities, the manufacturer must record the information listed in § 820.35(b), at a minimum, for servicing activities.

Under § 820.35(c), in addition to the requirements of Clauses 7.5.1, 7.5.8, and 7.5.9 of ISO 13485, the UDI must be recorded for each medical device or batch of medical devices.

Because the records required by § 820.35 should be readily available to the respondents, we estimate the average burden per response for § 820.35 to be no more than 2 hours. This estimate is in addition to the requirements of the applicable ISO 13485 Clauses, the burden for which is included under "Quality Management System (§ 820.10 and ISO 13485)" in table 2.

Device labeling and packaging controls (§ 820.45). In addition to the requirements of Clause 7.5.1 of ISO 13485, Control of production and service provision, manufacturers must document 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 as appropriate, use of the device, including requirements to ensure labeling and packaging have been examined for accuracy prior to release or storage (§ 820.45(a)), the release of the labeling for use must be documented in accordance with Clause 4.2.5 of ISO 13485 (§ 820.45(b)), and results of the labeling inspection in § 820.45(c) must be documented in accordance with Clause 4.2.5 of ISO 13485. The estimated recordkeeping burden for ISO 13485, Clause 4.2.5, is part of the estimate for "Quality Management System (§ 820.10 and ISO 13485)" in table 2. There is no additional hour burden associated with § 820.45.

We received several comments related to the proposed rule. Descriptions of the comments and our responses are provided in section V. of this document, Comments on the Proposed Rule and FDA Response. We have not made changes to the estimated burden as a result of the comments.

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995.

Before the effective date of this final rule, FDA will publish a notice in the **Federal Register** announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

X. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

XI. Consultation and Coordination With Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive order and, consequently, a tribal summary impact statement is not required.

XII. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov*. References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

1. ISO 13485:2016, "Medical devices—Quality management systems—Requirements for regulatory purposes," 3rd Ed., March 1, 2016.
* 2. FDA, "Regulations Establishing Good Manufacturing Practices for the Manufacture, Packing, Storage, and Installation of Medical Devices." **Federal Register**, 43: 31508–31532, July 21, 1978.
3. ISO 13485:1996, "Quality systems—Medical devices—Particular Requirements for the Application of ISO 9001," December 1996 (withdrawn). (Referenced at: *https://www.iso.org/standard/22098.html*.)
4. ISO 9001:1994, "Quality Systems—Model for Quality Assurance in Design, Development, Production, Installation, and Servicing," June 1994 (withdrawn).

(Referenced at: *https://www.iso.org/standard/16534.html*.)
* 5. FDA, "Medical Device Single Audit Program (MDSAP)." (Available at: *https://www.fda.gov/medical-devices/cdrh-international-affairs/medical-device-single-audit-program-mdsap#:~:text=The%20Medical%20Device%20Single%20Audit,authorities%20participating%20in%20the%20program.*)
6. Global Harmonization Task Force. Guidance document, "Implementation of Risk Management Principles and Activities Within a Quality Management System,'' May 20, 2005. (Available at: *https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n15r8-risk-management-principles-qms-050520.pdf*.)
7. ISO 14971, "Medical Devices—Application of Risk Management to Medical Devices." (Available at: *https://www.iso.org/standard/72704.html*.)
* 8. "Guidance for Industry, Third Parties and Food and Drug Administration Staff: Medical Device ISO 13485:2003 Voluntary Audit Report Submission Pilot Program," (77 FR 16036, March 19, 2012). (Available at: *https://www.federalregister.gov/citation/77-FR-16036*.)
9. International Medical Device Regulators Forum, *http://www.imdrf.org/*.
*10. Device Good Manufacturing Practice Advisory Committee Panel meeting on March 2, 2022, Panel Transcript: *https://www.fda.gov/advisory-committees/advisory-committee-calendar/march-2-2022-device-good-manufacturing-practice-advisory-committee-meeting-announcement-03022022*.
11. International Standard, ISO 9000 "Quality Management Systems—Fundamentals and Vocabulary," ISO 9000:2015; 4th Ed., September 15, 2015. (Available at: ISO 9000:2015(en), Quality management systems—Fundamentals and vocabulary.)
* 12. FDA, The Least Burdensome Provisions: Concept and Principles: Guidance for Industry and Food and Drug Administration Staff, February 5, 2019. (Available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles*.)
* 13. FDA, Medical Device Accessories—Describing Accessories and Classification Pathways: Guidance for Industry and Food and Drug Administration Staff, December 20, 2017. (Available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-accessories-describing-accessories-and-classification-pathways*.)
* 14. FDA, Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products, January 2017. (Available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/current-good-manufacturing-practice-requirements-combination-products*.)
* 15. FDA, "Final Regulatory Impact Analysis, Regulatory Flexibility Analysis, and Unfunded Mandates Reform Act Analysis; Medical Devices; Quality System Regulation Amendments.'' (Available at: *https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations*.)

List of Subjects

21 CFR Part 4

Biologics, Drugs, Human cells and tissue-based products, Incorporation by reference, Medical devices.

21 CFR Part 820

Incorporation by reference, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 4 and 820 are amended as follows:

PART 4—REGULATION OF COMBINATION PRODUCTS

■ 1. The authority citation for part 4 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360b–360f, 360h–360j, 360l, 360hh–360ss, 360aaa–360bbb, 371(a), 372–374, 379e, 381, 383, 394; 42 U.S.C. 216, 262, 263a, 264, 271.

■ 2. In § 4.2,

■ a. Revise the definition of "Device''; and

■ b. Remove the definition of ''QS regulation" and add in its place a definition for "QMSR".

The revision and addition read as follows:

§ 4.2 How does FDA define key terms and phrases in this subpart?

* * * * *

Device has the meaning set forth in § 3.2(f) of this chapter. A device that is a constituent part of a combination product is considered a finished device within the meaning of the Quality Management System Regulation (QMSR).

* * * * *

QMSR refers to the requirements under part 820 of this chapter.

* * * * *

■ 3. In § 4.4, revise paragraph (b)(1) and paragraph (b)(2) introductory text and add paragraph (f) to read as follows:

§ 4.4 How can I comply with these current good manufacturing practice requirements for a co-packaged or single-entity combination product?

* * * * *

(b) * * *

(1) If the combination product includes a device constituent part and a drug constituent part, and the current good manufacturing practice operating system has been shown to comply with the drug CGMP requirements, the following clauses of ISO 13485 (together with the definitions in Clause 3 of ISO 9000), which is incorporated by reference into the QMSR under § 820.7 of this chapter, and certain other provisions within the QMSR must also be shown to have been satisfied; upon demonstration that these requirements have been satisfied, no additional showing of compliance with respect to the QMSR need be made:

(i) *General requirements and management responsibility.* Clause 4.1, Clause 5 and its subclauses, Clause 6.1 of ISO 13485, and § 820.10 of this chapter;

(ii) *Design and development.* Clause 7.3 and its subclauses of ISO 13485. The organization shall document one or more processes for risk management in product realization. Records of risk management activities shall be maintained;

(iii) *Purchasing.* Clause 7.4. and its subclauses of ISO 13485;

(iv) *Analysis of data, improvement, and complaint handling.* Clause 8.2.2 and § 820.35(a) of this chapter, Clause 8.4, and Clause 8.5. and its subclauses of ISO 13485;

(v) *Installation activities.* Clause 7.5.3 of ISO 13485; and

(vi) *Servicing activities.* Clause 7.5.4 of ISO 13485 and § 820.35(b) of this chapter.

(2) If the combination product includes a device constituent part and a drug constituent part, and the current good manufacturing practice operating system has been shown to comply with the QMSR requirements for devices, the following provisions of the drug CGMP requirements must also be shown to have been satisfied; upon demonstration that these requirements have been satisfied, no additional showing of compliance with respect to the drug CGMP requirements need be made:

* * * * *

(f) The material listed in this paragraph (f) is incorporated by reference into this section with the approval of the Director of the Federal Register under 5 U.S.C. 552(a) and 1 CFR part 51. All approved incorporation by reference (IBR) material is available for inspection at the Food and Drug Administration (FDA) and at the National Archives and Records Administration (NARA). Contact FDA at Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852; 240–402–7500; *https://www.regulations.gov/document/FDA-*

2013-S-0610-0003. For information on the availability of this material at NARA, visit *www.archives.gov/federal-register/cfr/ibr-locations* or email *fr.inspection@nara.gov*. In addition, the terms and definitions given in ISO 9000:2015 are available for viewing, without cost, at *https://www.iso.org/obp/ui#iso:std:iso:9000:ed-4:v1:en.* This material is available from 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 9000:2015(E), ("ISO 9000"), *Quality Management systems – Fundamentals and vocabulary,* Clause 3—*Terms and definitions,* Fourth edition, September 15, 2015.

(2) ISO 13485:2016(E), ("ISO 13485"), *Medical devices – Quality management systems – Requirements for regulatory purposes,* Third edition, March 1, 2016.

■ 4. Revise part 820 to read as follows:

PART 820—QUALITY MANAGEMENT SYSTEM REGULATION

Subpart A—General Provisions

Subpart B—Supplemental Provisions

Subparts C–O [Reserved]

Authority: 21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, 383; 42 U.S.C. 216, 262, 263a, 264.

Subpart A—General Provisions

§ 820.1 Scope.

(a) *Applicability.* Current good manufacturing practice (CGMP) requirements are set forth in this quality management system regulation (QMSR). The requirements in this part govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use. The requirements in this part are intended to assure that finished devices will be safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act and that the use of other terminology, such as "safety and performance," in this part does not change this statutory standard or the requirements of this part. Any manufacturers engaged in the design, manufacture, packaging, labeling, storage, installation, or servicing of a finished device must establish and maintain a quality management system that is appropriate for its specific device(s). Manufacturers subject to this part include, but are not limited to, manufacturers that perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, as well as initial distributors of foreign entities that perform these functions. If a manufacturer engages in only some operations subject to the requirements in this part, and not in others, that manufacturer need only comply with those requirements applicable to the operations in which it is engaged.

(1) *Finished devices.* The provisions of this part shall apply to any finished device, as defined in this part, intended for human use, that is manufactured in any State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico, or that is imported or offered for import into the United States.

(2) *Components or parts.* The provisions of this part do not apply to manufacturers of components or parts of finished devices, but such manufacturers are encouraged to consider provisions of this regulation as appropriate.

(3) *Blood and blood components.* The provisions of this part do not apply to manufacturers of blood and blood components used for transfusion or for further manufacturing. Such manufacturers are subject to subchapter F of this chapter.

(4) *HCT/Ps.* The provisions of this part apply to manufacturers of human cells, tissues, and cellular and tissue-based products (HCT/Ps), as defined in § 1271.3(d) of this chapter, that are devices (subject to premarket review or notification, or exempt from notification, under an application submitted under the device provisions of the Federal Food, Drug, and Cosmetic Act or under a biological product license application under section 351 of the Public Health Service Act). HCT/Ps regulated as devices are also subject to the donor-eligibility requirements set forth in part 1271, subpart C of this chapter and applicable current good tissue practice requirements in part 1271, subpart D of this chapter. In the event of a conflict between applicable regulations in part 1271 and in other parts of this chapter, the regulation specifically applicable to the device in question shall supersede the more general regulation.

(b) *Conflicts with other requirements under the Federal Food, Drug, and Cosmetic Act.* The QMSR for devices in this part supplements regulations in other parts of this chapter except where explicitly stated otherwise. To the extent that any applicable requirements in this part conflict with requirements in other parts of this chapter, the requirements specifically applicable to the device in question shall supersede the more generally applicable requirements. Moreover, to the extent that any clauses of ISO 13485 (incorporated by reference, see § 820.7) conflict with any provisions of the Federal Food, Drug, and Cosmetic Act and/or its other implementing regulations, the Federal Food, Drug, and Cosmetic Act and/or its other implementing regulations will control.

(c) *Foreign manufacturers.* A device that is imported or offered for import into the United States is subject to refusal of admission to the United States under section 801(a) of the Federal Food, Drug, and Cosmetic Act if, among other things, it appears to be adulterated as set forth in the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

(d) *Exemptions or variances.* (1) A manufacturer subject to any requirement under section 520(f)(1) of the Federal Food, Drug, and Cosmetic Act, including any requirements under this part, may petition for an exemption or variance from such requirement in accordance with section 520(f)(2) of the Federal Food, Drug, and Cosmetic Act. Petitions for an exemption or variance shall be submitted in accordance with the procedures set forth in § 10.30 of this chapter.

(2) FDA may initiate and grant a variance from any requirement(s) in this part when the Agency determines that such variance is in the best interest of the public health, including that there is a public health need for the device and the device would not likely be made sufficiently available without the variance. Such variance will remain in effect only so long as there remains a public health need for the device and the device would not likely be made sufficiently available without the variance.

§ 820.3 Definitions.

The definitions in ISO 13485 and in Clause 3 of ISO 9000 (incorporated by reference, see § 820.7) apply to this part, except as specified in paragraph (b) of this section, and do not affect the meaning of similar terms defined in this title.

(a) The following terms, which are either not used or not defined in ISO 13485 or in Clause 3 of ISO 9000, also apply for the purposes of this part:

Component means any raw material, substance, piece, part, software, firmware, labeling, or assembly that is intended to be included as part of the finished, packaged, and labeled device.

Federal Food, Drug, and Cosmetic Act means the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321 *et seq.,* as amended.

Finished device means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized.

Human cell, tissue, or cellular or tissue-based product (HCT/P) regulated as a device means an HCT/P as defined in § 1271.3(d) of this chapter that does not meet the criteria in § 1271.10(a) of this chapter and that is also regulated as a device.

Remanufacturer means any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance or safety specifications, or intended use.

(b) All definitions in section 201 of the Federal Food, Drug, and Cosmetic Act shall apply to the regulation of quality management systems under this part and shall supersede the correlating terms and definitions in ISO 13485 (*e.g.,* the definitions of device and labeling in section 201(h) and (m) of the Federal Food, Drug, and Cosmetic Act apply to this part and supersede the definitions for the correlating terms in ISO 13485 (labelling and medical device)). In addition, the following terms and definitions apply to this part and supersede the definitions for the correlating terms in ISO 13485 or ISO 9000:

Implantable medical device shall have the meaning of "implant" as defined in section 860.3 of this chapter.

Manufacturer means any person who designs, manufactures, fabricates, assembles, or processes a finished device. Manufacturer includes, but is not limited to, those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.

Organization shall have the meaning of "manufacturer" as defined in this part.

Rework means action taken on a nonconforming product so that it will fulfill the specified requirements in the medical device file (MDF) before it is released for distribution.

Safety and Performance shall have the meaning of "safety and effectiveness'' in Clause 0.1 of ISO 13485. 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.

§ 820.5 [Reserved]

§ 820.7 Incorporation by reference.

Certain material is incorporated by reference into this part with the approval of the Director of the Federal Register under 5 U.S.C. 552(a) and 1 CFR part 51. All approved incorporation by reference (IBR) material is available for inspection at the Food and Drug Administration, and at the National Archives and Records Administration (NARA). Contact FDA at: Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852; 240–402–7500; *https://www.regulations.gov/document/FDA-2013-S-0610-0003.* For information on the availability of this material at NARA, visit *www.archives.gov/federal-register/cfr/ibr-locations* or email *fr.inspection@nara.gov.* This material may be obtained from 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.*

(a) ISO 9000:2015(E) ("ISO 9000"), *Quality Management systems – Fundamentals and vocabulary,* Clause 3—*Terms and definitions,* Fourth edition, September 15, 2015. IBR approved for § 820.3.

(b) ISO 13485:2016(E) ("ISO 13485"), *Medical devices – Quality management systems – Requirements for regulatory purposes,* Third edition, March 1, 2016; IBR approved for §§ 820.1, 820.3, 820.10, 820.35, and 820.45.

§ 820.10 Requirements for a quality management system.

A manufacturer subject to this part as described by § 820.1(a) must:

(a) *Document.* Document a quality management system that complies with the applicable requirements of ISO 13485 (incorporated by reference, see § 820.7) and other applicable requirements of this part; and

(b) *Applicable regulatory requirements.* Comply, as appropriate, with the other applicable regulatory requirements in this title, including, but not limited to the following, to fully comply with the listed ISO 13485 Clause:

(1) For Clause 7.5.8 in ISO 13485, Identification, the manufacturer must document a system to assign unique device identification to the medical device in accordance with the requirements of part 830 of this chapter.

(2) For Clause 7.5.9.1 in ISO 13485, Traceability—General, the manufacturer must document procedures for traceability in accordance with the requirements of part 821 of this chapter, if applicable.

(3) For Clause 8.2.3 in ISO 13485, Reporting to regulatory authorities, the manufacturer must notify FDA of complaints that meet the reporting criteria of part 803 of this chapter.

(4) For Clauses 7.2.3, 8.2.3, and 8.3.3, advisory notices shall be handled in accordance with the requirements of part 806 of this chapter.

(c) *Design and development.* Manufacturers of class II, class III, and those class I devices listed in paragraph (c)(1) of this section and table 1 to paragraph (c)(2) of this section must comply with the requirements in Design and Development, Clause 7.3 and its Subclauses in ISO 13485. The class I devices are as follows:

(1) Devices automated with computer software; and

(2) The devices listed in the following table:

TABLE 1 TO PARAGRAPH (c)(2)

Section	Device
868.6810 ..	Catheter, Tracheobronchial Suction.
878.4460 ..	Glove, Non-powdered Surgeon's.
880.6760 ..	Restraint, Protective.
892.5650 ..	System, Applicator, Radionuclide, Manual.
892.5740 ..	Source, Radionuclide Teletherapy.

(d) *Devices that support or sustain life.* Manufacturers of devices that support or sustain life, the failure of which to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in a significant injury, must comply with the requirements in Traceability for Implantable Devices, Clause 7.5.9.2 in ISO 13485, in addition to all other applicable requirements in this part, as appropriate.

(e) *Enforcement.* The failure to comply with any applicable requirement in this part renders a device adulterated under section 501(h) of the Federal Food, Drug, and Cosmetic Act. Such a device, as well as any person responsible for the failure to comply, is subject to regulatory action.

Subpart B—Supplemental Provisions

§ 820.20—§ 820.30 [Reserved]

§ 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 include the following information in certain records:

(a) *Records of complaints.* In addition to Clause 8.2.2 in ISO 13485, Complaint Handling, the manufacturer shall maintain records of the review, evaluation, and investigation for any complaints involving the possible failure of a device, labeling, or packaging to meet any of its specifications. If an investigation has already been performed for a similar complaint, another investigation is not necessary, and the manufacturer shall maintain records documenting justification for not performing such investigation. For complaints that must be reported to FDA under part 803 of this chapter, complaints that a manufacturer determines must be investigated, and complaints that the manufacturer investigated regardless of those requirements, the manufacturer must record the following information:

(1) The name of the device;

(2) The date the complaint was received;

(3) Any unique device identifier (UDI) or universal product code (UPC), and any other device identification(s);

(4) The name, address, and phone number of the complainant;

(5) The nature and details of the complaint;

(6) Any correction or corrective action taken; and

(7) Any reply to the complainant.

(b) *Records of servicing activities.* In adhering to Clause 7.5.4 in ISO 13485, Servicing Activities, the manufacturer must record the following information, at a minimum, for servicing activities:

(1) The name of the device serviced;

(2) Any UDI or UPC, and any other device identification(s);

(3) The date of service;

(4) The individual(s) who serviced the device;

(5) The service performed; and

(6) Any test and inspection data.

(c) *Unique Device Identification.* In addition to the requirements of Clauses 7.5.1, 7.5.8, and 7.5.9 in ISO 13485, the UDI must be recorded for each medical device or batch of medical devices.

(d) *Confidentiality.* Records deemed confidential by the manufacturer may be marked to aid FDA in determining whether information may be disclosed under the public information regulation in part 20 of this chapter.

§ 820.40 [Reserved]

§ 820.45 Device labeling and packaging controls.

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 document 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, as 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 mixups, including, but not limited to, inspection of the labeling and packaging 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.

Subparts C–O [Reserved]

Dated: January 22, 2024.

Robert M. Califf,

Commissioner of Food and Drugs.

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