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May 24, 2022

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2021-N-0507-0001– Proposed Rule: Medical Devices; Quality System Regulation Amendments

Dear Sir or Madam:

On behalf of the Advanced Medical Technology Association (AdvaMed), we provide these comments in response to the Food and Drug Administration (FDA or "Agency") "Proposed Rule: Medical Devices; Quality System Regulation Amendments" (hereinafter "proposed rule").

AdvaMed represents manufacturers of medical devices, digital health technologies, and diagnostic products that transform healthcare through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed has more than 400 member companies, ranging from the largest to the smallest medical technology innovators and manufacturers. Our member companies manufacture lifechanging technologies ranging from cardiovascular and orthopedic implants to cancer diagnostics, surgical instruments, and digital health products.

GENERAL COMMENTS

We strongly support FDA's proposal to amend the device current good manufacturing practice (CGMP) requirements of the Quality System (QS) Regulation to align more closely with the international consensus standard for devices by converging with the quality management system (QMS) requirements used by regulatory authorities from other jurisdictions. We support and agree with FDA's determination that the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the current part 820, 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 (FD&C) Act.

Additionally, we agree with FDA that globally harmonizing the regulation of devices will help consistently produce safe and effective devices, contributing to public health through timelier access for patients. Harmonizing differing regulations will remove unnecessary duplicative regulatory requirements and impediments to market access and remove barriers to patient access. The risk-management approach found within ISO 13485 offers appropriate flexibility and will meet the needs of patients to have access to quality devices in consonance with the progress of science and technology.

FDA Should Clarify Long-standing Policy of Protecting Internal Audits, Supplier Audits and Management Reviews to Encourage Robust Internal Audits

FDA has a long-standing policy, as outlined in its multiple documents, including the Quality System Inspection Technique (QSIT) Guide to Inspections, and Compliance Policy Guide (CPG) 130.300, that FDA will not review or copy reports or records that result from audits and inspections of a regulated entity's written quality assurance program. Moreover, FDA's regulation at 21 CFR § 820.180(c) lists the records not subject to FDA review during a routine inspection, including records of internal audits, management reviews, and certain supplier audits. The intent of this policy is to encourage firms to conduct management review and audits that are candid and meaningful.

FDA has explained in extensive detail in the past the policy importance of this exemption, including the preamble of the original GMP regulations and three FDA comments from the preamble to the current Quality System Regulation (QSR):

"The Commissioner shares the concerns of the comments and the Device GMP Advisory Committee that general FDA access to audit reports would tend to weaken the audit system." (FR 43(141):31515; July 21, 1978)

"FDA believes that refraining from routinely reviewing these reports may help ensure that the audits are complete and candid and of maximum use to the manufacturer." (FR 61(195):52613; October 7, 1996)

"FDA recognizes that quality audits of suppliers have a significant and demonstrated value as a management tool for corrective action, quality improvement, and overall assurance of component and service quality, and does not seek to undermine their value." (FR 61(195):52625)

"[FDA] believes that the disclosure of the audit reports themselves would be counterproductive to the intent of the quality system." (FR 61(195):52637)

We request that the exemption remain in effect in the proposed Quality Management System Regulation (QMSR) since it serves an important public health function of encouraging manufacturers to identify and address problems without the risk of compliance actions. Specifically, we request that FDA add language indicating that investigators will not review

management review and internal audit reports themselves, but upon request from FDA, a company employee in management with executive responsibility shall certify in writing that the required management reviews and quality audits, and applicable supplier audits, have been performed and documented, the dates on which they were performed, and that any required corrective action has been undertaken. This approach is consistent with the current regulations, QSIT Guide to Inspections, CPG, and policy goal of protecting the integrity of management reviews and internal audits.

FDA Should Provide a Three-Year Transition Period that Starts when All Needed Documents Finalized

All parties, including patients, industry and FDA want this transition to be a success. We greatly appreciate FDA's tremendous work to develop the proposed rule; however, substantial work remains for all involved. For instance, although this proposed rule does not impact FDA's authority to conduct inspections under section 704 of the FD&C Act, FDA states in the preamble that it intends to replace its current inspection approach for medical devices, QSIT, with an inspection approach that will be consistent with the requirements of the proposed part 820 as finalized.

Prior to enforcing this QMSR, FDA will need to: (i) finalize and make publicly available a revised QSIT that is adapted to part 820, as amended; (ii) ensure that investigators are trained with respect to the revised QSIT; (iii) ensure the revised QSIT is consistent with the inspectional approach of other ISO auditing organizations with the exception of those elements exempted from regulation, e.g., certifying to ISO 13485:2016; (iv) ensure through International Medical Device Regulators Forum (IMDRF) that the Medical Device Single Audit Program (MDSAP) inspectional approach reflects the amended QSR, and that the Auditing Organizations are trained accordingly, and; (v) develop and publish a work plan with anticipated timeframes for each of these milestones that communicates FDA's thinking and approach with respect to the revision of guidance documents and regulations impacted by the QSR Amendment.

The preamble to FDA's proposed rule outlined the Agency's intent to provide a one-year transition period from the date the final rule is issued in the *Federal Register*. During our testimony to the Devices Good Manufacturing Practice Advisory Committee, we stressed the need for a sufficiently long transition period to ensure success. We recommended at least two years based on our assessment of how long it would take a company to make the transition.

After further reviewing the details of the proposed rule, and considering the remaining work needed from not just industry but also FDA before implementation, we recommend a three-year transition period. We would recommend that the three-year period start when all needed supporting documents, such as the updated inspectional model, and training are complete. For instance, references to FDA's QSR and specific terminology, such as "device master record (DMR)" are embedded within several hundreds of quality system policies, procedures and other

documents. Sufficient time is needed to update these documents to remove old terminology and reflect the terminology in the final rule and to train layers of personnel on the updated documents.

Despite the need for sufficient time, we are excited about the end-goal and suggest that FDA consider the possibility of allowing companies that are ready to begin implementing earlier. Such a transition approach would resemble the transition approach used for standards, where a company may use the new or prior version during the transition period.

FDA Should Consider Multiple Risk-based Factors in Determining Scope and Frequency of Inspections under Revised Inspectional Model

In determining the frequency and scope of inspections in the revised inspectional model, FDA should consider a variety of risk-based factors, including MDSAP enrollment and status, and ISO 13485 certificate status, including the accrediting organization that issued the certificate. Such an approach will help ensure consistency of application of the standard amongst FDA, other global regulators, and accrediting organizations.

Further, consistent with our comments above, we encourage FDA to provide inspection criteria and any related guidance to industry well before the final rule is published to provide opportunity for notice and comment from manufacturers and to allow industry adequate time to prepare to be audited to the QMSR.

FDA Should Incorporate Third-Party Servicers and Refurbishers into the Rule

AdvaMed provides detailed comments below on incorporation of third-party servicers and refurbishers in our specific comments on the proposed rule. We also strongly urge FDA to reconsider its position of utilizing its discretionary enforcement powers vis-a-vis third-party servicers in light of the current geopolitical environment that is fraught with cybersecurity threats to our especially vulnerable healthcare sector.

On February 14, the Health and Human Services Cybersecurity and Infrastructure Security Agency (HHS CISA) issued a "Shields Up" Notice warning stating:

> Every organization in the United States is at risk from cyber threats that can disrupt essential services and potentially result in impacts to public safety. … we are mindful of the potential for the Russian government to consider escalating its destabilizing actions in ways that may impact others outside of Ukraine. Based on this situation, CISA has been working closely with its critical infrastructure partners over the past several months to ensure awareness of potential threats—part of a paradigm shift from being reactive to being proactive.

Given the current unregulated status of third-party servicing, the sheer number of third-party service entities,[1] and the important role medical devices play in the nation's medical infrastructure, it is not unreasonable to prepare for deliberate targeting of medical devices posed by unregulated third-party servicing entities.

FDA Should Strive to Incorporate Future Updates to the Standard in a Timely Manner

The 2016 version of ISO 13485 is specifically referenced in the proposed rule, and in the preamble to the proposed rule, FDA explains that future updates to the standard would need to be evaluated by FDA and the regulation amended. To the extent possible, we recommend that FDA incorporate future updates to ISO 13485 in a timely manner to ensure consistency and harmonization among regulators in different jurisdictions. We appreciate FDA's involvement and leadership in ISO TC210 and encourage other regulators to be similarly engaged to help ensure future standards are well-suited for regulatory purposes. See IMDRF Guidance: Optimizing Standards for Regulatory Use.

CONCLUSION

AdvaMed greatly appreciates the opportunity to provide comments. We thank FDA for its excellent work in development of the proposed rule. We are very supportive of this proposed change to align and consolidate our quality systems with common requirements and expectations. Our comments are intended to aid further clarity and promote an overall smooth transition. Detailed recommendations are included along with our specific comments to assist FDA as it works to develop the final rule. Please do not hesitate to contact me at 202-434-7230 or jwolszon@advamed.org if you have any questions.

Respectfully submitted,

/s/

Jamie Wolszon
Vice President
Technology & Regulatory Affairs

[1] In its May 2018 Report on the Quality, Safety, and Effectiveness of Servicing of Medical Devices, FDA estimated that there are between 16,520 and 20,830 firms performing device servicing. The volume of servicing activity has likely expanded greatly since FDA issued its report and these entities are unregistered and unknown to FDA.

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General	We request the Agency prioritize subsequent revisions to guidance documents that will be impacted by the final rule (e.g., Design Control Guidance, Current Good Manufacturing Practices for Combination Products, Applying Human Factors and Usability Engineering to Medical Devices).	
General	Based on harmonization with ISO 13485, we request that FDA and ISO also make available other consensus standards that are required to implement ISO 13485, such as ISO 14971.	
Throughout "incorporation by reference"	Please clarify	The parts incorporated by reference to ISO 13485:2016 include NOTEs. NOTEs in ISO standards are intended for promoting readers' understanding of the respective sections and not for compliance, but we are not certain how FDA intends to use the NOTEs. FDA should not use the NOTEs as requirements.
Part V, Table 1, page 17	Table 1 (High-level Summary of 21 CFR Part 820 Proposed Rule Differences and Additions) should include Clauses 0.1 (General), 0.2 (Clarification of Concepts), and 0.4 (Relationship With ISO 9001) of the Introduction of the ISO standard.	This will affirm that key elements of the standard's Introduction (such as the Clarification of Concepts clause, in which the term "as appropriate" is defined) are being incorporated into part 820. (Clause 0.5 of the standard is not relevant to part 820).

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Part V, Subpart A, page 19	Moreover, 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. It should be noted that incorporation of ISO 13485:2016 by reference includes Clauses 0.1 (General), 0.2 (Clarification of Concepts), and 0.4 (Relationship with ISO 9001) of the Introduction of the standard.	This will affirm that key elements of the standard's Introduction (such as the Clarification of Concepts clause, in which the term "as appropriate" is defined) are being incorporated into part 820. (Clause 0.5 of the standard is not relevant to part 820).
Page 10125	We recommend keeping the term "establish" in Part 820 for clarity. FDA explains in the preamble that it is proposing to remove the term from 820 as section 0.2 ISO 13485 states that when a requirement is required to be "documented", it is also required to be established, implemented, and maintained. FDA states that it believes the clarification of this concept within the standard is sufficient to convey the current requirement for manufacturers to establish and maintain the regulatory requirements of a QMS. We believe that, this explanation notwithstanding in the preamble, it still is helpful to retain establish for purposes of clarity.	We recommend keeping the term "establish" in Part 820 as it indicates to define, document, and implement. The term "document" alone does not necessarily capture this intent.

Line No	Proposed Change	Comment/Rationale
Page 10125	We propose to maintain the term management with executive responsibility in 820 along with the current definition.	We propose to maintain the term management with executive responsibility in 820 along with the current definition. We believe that FDA's current proposal to change the term, but keep the original definition, does not harmonize with ISO 13485 and manufacturers will still have to manage two different definitions. We also believe that "management with executive responsibility" conveys the intent of the term more clearly than top management (which is not as specific and is defined vaguely in ISO 9000:2015).
Page 10126	We recommend the following revision: "We also propose to clarify that Clause 7.3 Design and Development applies ~~only~~ to the manufacturers of the class I devices that are listed in this provision in addition to all manufacturers of class II and III devices."	Recommend removing the word "only" since it may cause confusion as to which class of device the clause applies.
Page 10126	"Additionally, FDA states that "[w]hen conducting a risk analysis, manufacturers are expected to identify possible hazards associated with the design in both normal and fault conditions. The risks associated with the hazards, including those resulting from user error, should then be calculated in both normal and fault conditions. If any risk is judged unacceptable, it should be reduced to acceptable levels by the appropriate means" (61 FR 52602 at 52620). FDA	We request that FDA clarify definitions for terms that are defined differently in FDA's guidance documents and ISO 13485 or the referenced standards in the final rule. For example, the term use error is defined differently in FDA's guidance on Applying Human Factors and Usability Engineering to Medical Device and IEC 62366-1, which is referenced in ISO 13485. Where terms/definitions may vary between FDA's guidance and now-referenced standards we would appreciate insight

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	has, therefore, expected risk management throughout a QMS and the total product lifecycle." Use error is defined as "User action or lack of action that was different from that expected by the manufacturer and caused a result that (1) was different from the result expected by the user and (2) was not caused solely by device failure and (3) did or could result in harm."	from FDA as to which should be used as a primary source. In this example, we recommend FDA's definition be referred to in the final rule.
Page 10131	"ISO 14971:2019, "Medical Devices— Application of Risk Management to Medical Devices." (Available at: https://www.iso.org/standard/72704.html.)"	We recommend adding which version of the 14971 will be recognized by FDA for purposes of this regulation.
820.45(c)	Recommend adding the term "medical device file," used below, to the list of definitions. (c) The manufacturer must ensure labeling and packaging operations have been established and maintained to prevent errors, including, but not limited to, inspection of the labeling and packaging immediately before use to assure that all devices have correct labeling and packaging, as specified in the medical device file. Results of such labeling inspection must be documented in accordance with Clause 4.2.5 of ISO 13485	There is no provision for a "medical device file" outlined within the quality records section. This term should be added to the list of definitions or the term should be changed to something more generic, e.g., "as per specification". This information is needed to ensure proper reference to, and implementation of, the harmonized QSR.

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72-73	(i) ISO 13485, "Medical devices—Quality management systems—Requirements for regulatory purposes," third edition, dated March 2016, in its entirety, including Clauses 0.1 (General), 0.2 (Clarification of Concepts) of the Introduction, and 0.4 (Relationship With ISO 9001) but excluding Clause 0.5 (Compatibility With Other Management Systems) and any other parts of the standard specified in this rule.	The text of the regulation should state that key parts of the Introduction of the ISO standard (preamble) are also being incorporated into part 820. This is because the Introduction includes important clarifications, such as those concerning the terms "risk" and "as appropriate" (Introduction, Clause 0.2). Additionally, the preamble includes reference to the concepts applied through ISO 9001. (Clause 0.5 of the Standard is not relevant to part 820).
Page 10131 (Lines 38-54)	Original text: "§ 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 CGMPs, the following clauses of ISO 13485 within the QMSR requirements for devices must also be shown to have been satisfied; upon demonstration that these requirements have been satisfied, no additional	Corrective and Preventive Action (CAPA) has been replaced with 'improvement' and has expanded scope (e.g., Analysis of Data, Statistical Techniques and CAPA) under ISO 13485. To align with 13485:2016, we propose to add Clause 8.4 under a different heading called "Analysis of data" and only reference Clause 8.5 under "Improvement".

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	showing of compliance with respect to the QMSR requirements for devices need be made: (i) Management responsibility. Clause 4.1, Clause 5 and its subclauses and Clause 6.1 of ISO 13485; (ii) Design and development. Clause 7.3 and its subclauses of ISO 13485; (iii) Purchasing. Clause 7.4 and its subclauses of ISO 13485; (iv) Improvement. Clause 8.4, 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)." We recommend the following revision: "(iv) Analysis of data, Clause 8.4, and Improvement, Clause 8.5, and its subclauses of ISO 13485."	
106 - 169	Add third-party servicers and third-party refurbishers to the Scope section.	In the proposed rule, FDA states that the "term 'organization' shall have the meaning of 'manufacturers' as defined in this part." See Line 273. FDA stated in the Preamble to the 1996 Medical Device; Current Good Manufacturing Practice (CGMP) Final Rule; Quality System Regulation:

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		FDA is not including the terms "servicer" or "refurbisher," as they relate to entities outside the control of the original equipment manufacturer, in this final regulation, even though it believes that persons who perform such functions meet the definition of manufacturer [emphasis added]. … FDA has elected to address application of the CGMP requirements to persons who perform servicing and refurbishing functions outside the control of the original manufacturer in a separate rulemaking later this year, with another opportunity for public comment. AdvaMed agrees with FDA that persons performing such servicing functions meet the definition of manufacturer, regardless of whether these persons are affiliated with the original equipment manufacturer. Although FDA has made clear that third-party servicers are manufacturers and subject to FDA's enforcement authority, to date the FDA has declined to apply any regulatory requirements to these entities, choosing instead to use its enforcement discretion toward these entities. We believe the FDA's failure to clearly include third-party servicers and third-party refurbishers in the proposed rule will be interpreted as the FDA relinquishing its right to exercise jurisdictional authority over third-party servicing and third-party refurbishing organizations now and in the future.

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		Therefore, to ensure that you retain this authority and to protect consumers and patients, we urge you to clearly include third-party servicers and third-party refurbishers within the scope of the proposed rule.
177	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. Raw material means the substance or commodity from which the component is made.	Separate definitions for *component* and *raw material* are needed because: (i) *components* are parts/subassemblies that are made of *raw materials*, and (ii) ISO 13485 views *components* and *raw materials* as separate. Section 0.1 of the ISO standard's Introduction states: "The requirements in this International Standard can also be used by suppliers or other external parties providing product (e.g., **raw materials, components**, subassemblies, medical devices, sterilization services, calibration services, distribution services, maintenance services) to such organizations."
170- 218	Add a definition of third-party servicer and third-party refurbisher to the definitions section.	To retain FDA authority over third-party servicers and third-party refurbishers. See also comment at lines 106-169.

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116 to 119	Add Servicing to the list of Manufacturer functions: Manufacturers subject to this part include, but are not limited to, manufacturers that perform the functions of contract sterilization, installation, servicing, relabeling, remanufacturing, repacking, or specification development, as well as initial distributors of foreign entities that perform these functions.	The requirements for the quality management system regulation (QMSR) were stated on lines 109-111 and included Servicing. The proposed addition is recommended to ensure organizations performing servicing activities are also subject to the QMSR.
213 to 216	Revise manufacturer definition to state: *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**, third-party servicing or refurbishing,** remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.	The QMSR will be applied inconsistently if service and repair provisions apply only to original equipment manufacturers but do not apply to third party service and repair entities. These entities should be subject to the same servicing quality requirements and recordkeeping requirements.

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179-181	"Customer means persons or organizations, including users, that could or do receive a product or a service that is intended for or required by this person or organization. ~~A customer can be internal or external to the organization.~~"	We believe that ISO 13485 does not intend to make the scope of customer applicable to the internal organization. Although customer is not defined in the standard, the standard does refer to customer processes, customer-owned product etc., which indicates that customer is a separate entity from the internal organization. Furthermore, the preamble of the proposed rule does not provide an explanation of internal customer. We therefore recommend striking the last sentence in this new definition for part 820.
192	~~Process agent~~ *Manufacturing material* means any material or substance used in or used to facilitate the manufacturing process, a concomitant constituent, or a byproduct constituent produced during the manufacturing process, which is present in or on the finished device as a residue or impurity not by design or intent of the manufacturer.	The proposed rule replaces *manufacturing material* (in the current part 820) with *process agent*, which creates a conflict with ISO 13485:2016. This is because the standard explicitly states that *process agents* are to be removed from product during manufacture (Clause 7.5.2). The definition for *process agent* in the proposed part 820, by contrast, suggests the process agent may be present in or on the finished device. We therefore recommend retaining the term *manufacturing material*, as in the current part 820.

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233-234	(1) ISO 13485, "Medical devices—Quality management systems—Requirements for regulatory purposes," third edition, dated March 2016; in its entirety, including Clauses 0.1 (General), 0.2 (Clarification of Concepts) of the Introduction, and 0.4 (Relationship With ISO 9001) but excluding Clause 0.5 (Compatibility With Other Management Systems) and any other parts of the standard specified in this rule.	The text of the regulation should state that key parts of the Introduction of the ISO standard (preamble) are also being incorporated into part 820. This is because the Introduction includes important clarifications, such as those concerning the terms "risk" and "as appropriate" (Introduction, Clause 0.2). Additionally, the preamble includes reference to the concepts applied through ISO 9001 (Clause 0.5 of the Standard is not relevant to part 820).
249-250	Please remove the reference to 21 CFR Part 821.	Reference to 21 CFR Part 821 in this provision is confusing. Current 21 CFR Part 820 makes no reference to 21 CFR Part 821. The requirements in Part 821 are not the same as the traceability requirements in Clause 7.5.9.1 in ISO 13485. 21 CFR § 821, which concerns tracking of devices after manufacture, is not the subject of amendment in this proposed rule and should remain intact without need to reference in the proposed rule.
246 – 248	Remove the reference to ISO 13485.	Per § 820.10 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. (Reference to 830: UDI: Subpart B - Requirements for a Unique Device Identifier).

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		We understand that 21 CFR § 820.10 (with reference to 21 CFR Part 830) is addressing UDI information/requirements for finished medical devices. In contrast, the ISO 13485 chapter 7.5.8 intends to identify devices by suitable means throughout the product realization process including processes before products become a finished product.
260-264	Please remove "life-sustaining and/or life-supporting" or revise this section to recognize the distinctions between 21 CFR Sec 820.65(a) and 7.5.9.2 in ISO 13485. FDA appears to interpret these two to be the same, but we believe those two are substantively different. The treatment of the two as the same is confusing to us, and we request that this provision is either deleted or revised to recognize the difference between the two.	In the proposal FDA indicates that it will add a requirement for devices that are life-sustaining and/or life-supporting to follow the traceability requirements in ISO 7.5.9.2 for implantable devices. Language in the preamble suggests that FDA believes that it is simply retaining existing 21 CFR § 820.65(a). We believe that FDA incorrectly conflates 21 CFR § 820.65(a) and 7.5.9.2 in ISO 13485 as we believe the two are substantively different. For instance, ISO 7.5.9.2 applies to only implantable devices, and not other life-sustaining and life-supporting devices. In this respect, this ISO section is narrower in scope than 21 CFR § 820.65. By contrast, the level of traceability for those devices that do fall within ISO 7.5.9.2 is more extensive than what is defined in 21 CFR § 820.65. ISO 7.5.9.2 has requirements

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		for tracking of devices after shipment that correlate in principle, but not in detail, with 21 CFR Part 821. We therefore find the provision to be very confusing, and request FDA either remove the language "life-supporting and/or life-sustaining" or revise this section to recognize the distinctions between 7.5.9.2 and 21 CFR § 820.65 and clarify the scope and requirements. As currently written, FDA has greatly expanded the applicability of 21 CFR §820.65. Specifically, ISO 7.5.9.2, which applies to implantables, requires that distributors maintain records of distribution and that distributors are subject to inspection, which is not a requirement in 820.65. Similarly, 7.5.9.2 requires maintenance of records of the names and addresses of consignees, which is not required by 820.65
284-287	**820.35 Control of records.** In addition to the requirements of Clause 4.2.5 in ISO 13485 (incorporated by reference, see § 820.7), Control of Records, the manufacturer must ~~obtain the signature for each individual who approved or re-approved the record, and the date of such approval, on that record and~~ As an alternative to the proposed deletion above, we would propose clarification that the records mentioned	We do not believe it is FDA's intent, but the current proposed language in section 820.35 appears to suggest that all records require signature. In Section V, Description of the proposed rule, FDA indicates "there are a few exceptions where we are proposing to clarify concepts or to augment specific clauses in ISO 13485, but overall we are not proposing to modify the clauses in ISO 13485." For example, current requirements under 21 CFR § 820.198 do not require such signature for complaint records. Therefore, industry is to understand that

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	here are "records required to provide evidence of conformity to requirements and of the effective operation of the quality management system" – in reference to ISO13485:2016 Clause 4.2.5	FDA is proposing a new, added requirement in addition to ISO 13485 and to the current version of part 820 which, as we understand from FDA's proposed rule, is not the intent. FDA should remove the requirement for signatures for the indicated records as drafted in the proposed rule. Doing so will ensure alignment with ISO 13485 and the current requirements, thereby supporting the goal of harmonization. It is not clear how a signature helps to provide clarity of information. The date of completion is relevant but is not required to pair with a signature to be meaningful. Electronic systems are validated with time and date stamping to be able to support the capturing of the completion date of the activity as well as the individual that completed the activity without a formal signature. If FDA does not remove the language, we recommend as an alternative adding language clarifying that the signature expectation would be limited to records required to demonstrate the effective operation of the QMS, per clause 4.2.5 in ISO 13485.

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284-287	Modify text to read as follows: The records may be kept electronically so long as the manufacturer has developed reasonable controls over documentation to limit system access to authorized individuals and maintain records that demonstrate traceability of electronic signatures. Such controls deem a manufacturer compliant with 21 CFR Part 11. The below information shall be maintained for certain records as follows:" An alternative approach would be: "~~on that~~ as part of the record and include the below information in certain records as follows:"	By streamlining such requirements while also acknowledging that electronic records are appropriate as part of Part 820, FDA can provide electronic record management requirements consistent with industry practice today and the development of more sophisticated record tracking technology. The term "on that record" implies that companies are restricted to adding a signature physically to the document and does not reflect document management systems that consider the application of a digital signature within the system to be part of the record. The change suggested also ensures that the regulation will continue to be appropriate in the future where more digital systems will be deployed and allows the evolution of digital signature applications. Note that the preamble to the proposed rule also states that: "Manufacturers can choose to develop electronic records and electronic methods for signing and dating such records, if that best suits their business practices" (Page 27 - Part V, Subpart F, Section 1 on Proposal for Control of Records).

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298-300	Remove 298-300. Records of complaints: ~~5. Nature and details of the complaint,~~ ~~6. Any corrective action taken; and 7. Any reply to the complainant.~~	Section 8.2.2 of ISO 13485 already addresses the referenced sections for complaint handling; therefore, U.S.-specific requirements for complaint records is not needed. We encourage FDA to limit U.S.-specific requirements to only those that would have a meaningful impact on a device's safety or efficacy. By taking this approach, industry and the Agency can reap the full benefits and efficiencies of the proposed rule.
312	(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/<u>included</u> for each medical device or batch of medical devices.	Current § 820.184 calls for inclusion or reference to the location of Unique Device Identifier (UDI). Current practice includes the labeling (with UDI) included in the batch records. Since the Device History Record (DHR) is no longer required, it is unclear how the UDI information should be recorded. Physically recording the UDI in the batch records will create risk for documentation errors and require process changes without adding additional value.
329-332	Remove 329-332; 820.45 (a)(2)-(5)	Clause 7.5.1 of ISO 13485 already establishes the need for labeling process controls. These additional requirements are thus duplicative and require uniformity where it is not necessary.

Line No	Proposed Change	Comment/Rationale
		AdvaMed agrees with FDA that "the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the current part 820, providing a similar level of assurance in a firms' quality management system and ability to consistently manufacture devices that are safe and effective…". The proposed addition of § 820.45 does not reflect such a position. When taken in totality, ISO 13485:2016, Section 7.5.1 is substantively similar to the current sections 820.120 and 820.130 requiring planning, implementation, monitoring and control of labeling and packaging operations, including release. In the course of implementing the requirements under ISO 13485, manufacturers will already meet these requirements. ISO 13485 references the GHTF/SG1/N70:20116 in defining labeling requirements. Therefore, inclusion of these aspects of proposed § 820.45 is unnecessary and represents additional, non-value added requirements for manufacturers, and should therefore be removed.

Line No	Proposed Change	Comment/Rationale
323 & 324	We propose removing "distribution" or clarifying what it means here. The labeling generally informs users how to handle and store the product. We recommend possibly rewording it to be the following: processing, storage, handling, distribution (if applicable), and where appropriate, use of the device In addition to the requirements of Clause 7.5.1 of ISO 13485 (incorporated by reference, see § 820.7), Control of production and service provision, each manufacturer must establish and maintain procedures that provide a detailed description of the activities to ensure the integrity, inspection, storage, and operations for labeling and packaging, during the customary conditions of processing, storage, handling, distribution, and ~~where~~ as appropriate, use of the device.	It is not clear if "operations" for labeling is referring to the application of labeling to the device or the production of the label itself. 820.120(a) *Label integrity* currently requires integrity of the label during use, where appropriate. This distinction is lost in the new verbiage. We wish to better understand when other controls (e.g., inspection, storage) of labeling for use of the device would apply to the manufacturer. The definition of the term "where appropriate" in section 820.1(a)(3) of the current QSR is absent from the proposed rule. We suggest using "as appropriate" in the proposed rule, as this is consistent with the ISO standard. The latter also defines the term "as appropriate" in the Introduction (0.2).
325	(c) The manufacturer must ensure labeling and packaging operations have been established and maintained to prevent errors, including, but not limited to, inspection of the labeling and packaging ~~immediately~~ before use to assure that all devices have correct labeling and packaging, as specified in the medical device file. Results of such labeling inspection must be documented in accordance with Clause 4.2.5 of ISO 13485.	This paragraph indicates a required inspection of labeling and packaging "immediately before use" It is not clear who is expected to be performing this inspection. If it is meant for the manufacturer, that cannot typically be done "immediately before use" as it is out of the control of the manufacturer. If it is meant for the end user, that inspection cannot be documented in accordance with Clause 4.2.5 of ISO 13485, as this would not be feasible.

Line No	Proposed Change	Comment/Rationale
		Propose removing ""immediately before use" or rewording to provide clarity Clarify that the inspection can be performed through system checks completed by non-QA employees. During production run set up: Operations confirms by scanning component part numbers into the production system that the label/package is appropriate per the MDF. If not correct, that component cannot be used in the manufacturing of that medical device (system will reject). Results of the confirmation are on the PHR - correct component line.
329-332	Remove 329-332; 820.45 (a)(2)-(5)	Clause 7.5.1 of ISO 13485 already establishes the need for labeling process controls. These additional requirements are thus duplicative and require uniformity where it is not necessary.
340	Reinstate or clarify 21 CFR 820.184	Section 820.184 was removed with the expectation it would be covered by ISO 13485 clause 4.2.3, Medical Device File. However, while the Medical Device file appears to cover the DMR and the DHF, it does not cover the production history of the device as required currently by the DHR.