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FDA's Shift from QSR to ISO 13485:2016: A Significant Change for Inspections?

TOPICS OF DISCUSSION: QSR VS. 13485:2016 REQUIREMENTS

- Why Harmonize?
- Potential Challenges to Harmonization
- A Big Change for the FDA
- Major Updates to 13485:2016
- Conceptual Differences between QSR and 13485:2016
- How do QS Subsystem Requirements Compare?
- Inspections vs Notified Body Audits

WHY HARMONIZE?

- Already ~ 95% harmonized
- Evolution of the intent and application of the regulation
- Similarities in terminology have become more apparent and aligned
- ISO 13485:2016 first harmonized with the QSR and now the QSR is being harmonized with 13485:2016
- ISO 13485:2016 is globally recognized and applied
- Serves as the regulatory base for Medical Device Single Audit Program (MDSAP)

POTENTIAL CHALLENGES TO HARMONIZING

LINKAGES NOT SPECIFICALLY COVERED BY 13485:2016

- Unique Device Identification (UDI)
- Part 803: Medical Device Reporting
- Part 806: Corrections and Removals
- Part 821: Device Tracking

These regulations are currently covered under 13485:2016 because country specific requirements that are not listed in 13485 can still be written as a nonconformance ("applicable requirements"). However, what happens when Part 820 is harmonized?

A BIG CHANGE FOR FDA

- Rulemaking Process
  - Notice and comment rulemaking
    - Proposed Rule
    - Public Comment
    - Final Rule in Federal Register
- Changes to internal guidance documents
  - QSIT
  - C.P. 7382.845
  - Many other inspection-related documents
- Timing of Roll-Out
  - Draft Rule by end of 2019?
  - Exercising Enforcement Discretion
    * Allowing industry (and FDA?) time to adjust
    * Series of town hall events planned
      - Educate industry on the draft rule
      - Collect feedback from stakeholders

PUBLIC COMMENTS IN RULE-MAKING

FROM THE FDA WEBSITE:

“The FDA encourages public comment on the agency's proposed rules because the public has a vested interest in the products it regulates, and because the input provides critical insight into the effects of the regulation on the public. The comments often present the "real world" concerns of those who use the products.”

The number of comments received for proposed rules varies. For example:

- Reporting procedures for problems with medical devices: 300 comments
- Regulation of tobacco: > 500,000 comments
- Change to generic drug approvals: 35 comments

Even the smallest number of comments still represented a wide range of companies, trade and consumer groups, and others.

MAJOR UPDATES IN 13485:2016

Clarification of Concepts (0.2)

- Not following country specific requirements that are not listed in 13485 can still be written as a nonconformance (“applicable requirements”)
- Risk pertains to safety and performance or compliance to regulatory requirements, not business risk
- “Documented” includes established, implemented and maintained
- When the term “product” is used, it can also mean “service”

CONCEPTUAL DIFFERENCES BETWEEN QSR AND13485:2016

Generally, 13485:2016 is more explicit than QSR (unless you read the preamble)

Definitions
For example, definition of "product" in QSR does not include services

Training and Competence
Education, skills, training and experience to perform their functions correctly more explicit in 13485:2016

Approvals vs. Signatures
QSR more explicit about requiring signature and date to meet legal precedence

Risk Management
Expectations for RM activities and risk-based approach to occur throughout the QMS (it is referenced 32 times throughout the standard vs. once in the QSR)

CAPA vs. Improvement Process
13485:2016 much clearer that when planned results are not achieved, timely corrections and corrective actions must be taken *at the appropriate level*

HOW DO QS REQUIREMENTS COMPARE?*
QSR VS. 13485:2016

SIGNIFICANT

- Management Controls
- Design Controls
- Purchasing Controls
- Production and Process Controls
- Corrective and Preventative Action

MINIMAL

- Document Controls
- Identification and Traceability
- Acceptance Activities
- Nonconforming Product

*Based on AAMI TIR102:2019 U.S. FDA 21 CFR mapping to applicable regulatory requirements in ISO 13485:2016 Quality Management Systems

MANAGEMENT CONTROLS

13485:2016 VS. QSR

- Management Review Inputs/Outputs more clearly defined
- Quality Manual is now required
- Emphasis on demonstrating and maintaining competence (appropriate education, training, skills, and experience)

13485:2016 IS MORE EXPLICIT
i.e. MANAGEMENT REVIEW

820.20 (C)

MANAGEMENT REVIEW.

Management with executive responsibility shall review the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system satisfies the requirements of this part and the manufacturer's established quality policy and objectives.

13485:2016 5.6.2

REVIEW INPUT.

A. Feedback

B. Complaint Handling

C. Reporting to Regulatory Authorities

D. Audits

E. Monitoring & Measurement of Processes

F. Monitoring & Measurement of Product

G. Corrective Action

H. Preventive Action

I. MR Follow Up Actions

J. Changes Impacting QMS

K. Recommendations for Improvement

L. Applicable New or Regulatory Requirements

13485:2016 IS MORE EXPLICIT
i.e. PERSONNEL

820.25(a) and (b)

(A) *General*. Each manufacturer shall have sufficient personnel with the necessary education, background, training, and experience to assure that all activities required by this part are correctly performed.

(B) *Training*. Each manufacturer shall establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities. Training shall be documented.

13485:2016 6.2

HUMAN RESOURCES.

A. Determine the necessary competence for personnel performing work affecting product quality
B. Provide training or take other actions to achieve or maintain the necessary competence
C. Evaluate the effectiveness of the actions taken (method is proportionate to risk of the work-related training)
D. Ensure personnel are aware of the relevance and importance of their activities and how they contribute to achievement of quality objectives
E. Maintain appropriate records of education, training, skills and experience

DESIGN CONTROLS

Design Inputs
- More specifically defined - Functional, performance, usability, and safety
- Direct link to risk management and usability

Design Reviews
- Do not specify a requirement for an independent reviewer (but still a good idea)

Design Verification and Validation
- Requires plans to specify methods, acceptance criteria, statistical techniques with rationale for sample sizes
- Confirmation of appropriate connectivity with other medical devices where applicable
- Risk management throughout entire product realization process
- Specifically requires clinical or performance evaluations of medical device

Design Transfer
- Design outputs verified as suitable for manufacturing prior to finalizing
- Production capability can meet product requirements

PURCHASING CONTROLS

- Service is included in the definition of product

- More explicit in purchasing process requirements
  - Supplier evaluation and selection
    - * Ability to provide product that meets requirements
    - * Performance of the supplier
    - * Effect of the purchased product on the quality of the device
    - * Proportionate to risk associated with the medical device
  - Non-fulfillment of purchasing requirements to be addressed with the supplier
    - * Proportionate to risk associated with purchased product

- Purchasing data more explicit
  - Product specifications
  - Requirements for product acceptance, procedures, processes, and equipment
  - Qualification of supplier personnel
  - QMS requirements

PRODUCTION AND PROCESS CONTROLS

- No significant differences
  * General
  * Production and Process Changes
  * Environmental Control
  * Personnel

- Differences
  * Contamination Controls - Requirements specific to sterile devices
  * Buildings and Equipment - Requirements specific to supporting services (transport, communication or information systems)
  * Manufacturing Material - Focus on cleaning rather than process for removing manufacturing material
  * Automated Processes - Level of SW validation is proportionate to risk, including effect on ability of product to conform to specifications and requires a procedure
  * Process Validation - Particular requirements for sterilization and sterile barrier systems

CORRECTIVE AND PREVENTIVE ACTION

- Separates out corrective and preventive actions
  * This has always been a source of confusion with the QSR
- Any necessary corrective action to be taken without *undue delay*
- Corrective actions to be proportionate to the effects of the nonconformities encountered
- Separates out verifying that the corrective actions does not adversely affect the product and reviewing the effectiveness of the corrective action taken
  * Clarifies the need for the VoE check

COMPLAINTS

Definition includes usability and service

Procedures must include:

- Handling of complaint-related product
- Determination of the need to initiate corrections or corrective actions
- Communication to external organizations (i.e., suppliers, contractors, etc.) if investigation determines they contributed to complaint

FDA INSPECTIONS VS. NOTIFIED BODY AUDITS

WHAT DO THEY HAVE IN COMMON?

- Observe the operation and the employees
- Ask questions and talk with personnel
- Determine the company's organization and structure
- Identify individuals responsible for key operations
- Review documents

HOW DO THEY DIFFER?

Top Down

- Determine if systems have been established
- Start with procedures
- Sample examples of implementation

Bottom Up

- Identify what is not working
- Start with complaints, non-conformances
- Audit upstream to find cause
- Sometimes product focused

Attitude

- "Partner" vs. Enforcer

Training

- Law and Evidence Development
- Investigative Interviewing

Duration

- Firm Schedule vs. As Long As Necessary

Scope

- Agenda vs. Following the Threads

SO WHAT CAN WE EXPECT?

SIMILAR BUT EXPANDED REGULATORY EXPECTATIONS

- Double-edged sword because easier to write up deficiencies against standard than the current QSR

STILL USING A BOTTOM UP APPROACH FOCUSING ON PROBLEM AREAS

- Starting with Measurement, Analysis and Improvement and following threads from there

ATTITUDE AND CONDUCT OF INSPECTIONS WILL REMAIN THE SAME

- FDA is still an enforcement agency

Guess the Observation!!

Observation #1:
The design review results, including the individual(s) performing the review, were not adequately documented in the design history file. Specifically, the name and function of the individual serving as the independent reviewer was not documented in the design review meeting minutes.

This is a violation of:

a) 21 CFR 820 b) 13485:2016 c) Both a and b d) None of the above

Guess the Observation!!

Observation #1 is a violation of:

a) 21 CFR 820 b) 13485:2016 c) Both a and b d) None of the above

21 CFR 820.30(e) requires "… participants at each design review include representatives of all functions concerned with the design stage being reviewed and an individual(s) who does not have direct responsibility for the design stage being reviewed…"

13485:2016 does not specify a requirement for an independent reviewer.

Guess the Observation!!

Observation #2:
An MDR report was not submitted within 30 days of receiving or otherwise becoming aware of information that reasonably suggests that a marketed device has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

This is a violation of:

a) 21 CFR 803 b) 13485:2016 c) Both a and b d) None of the above

Guess the Observation!!

Observation #2 is a violation of:

a) 21 CFR 803 b) 13485:2016 **c) Both a and b** d) None of the above

Although this is specifically a violation of 803.50(a)(1), it is also a violation of 13485:2016 8.2.3 Reporting to regulatory authorities, which states: “If applicable regulatory requirements require notification of complaints that meet specified reporting criteria of adverse events or issuance of advisory notices, the organization shall document procedures for providing notification to the appropriate regulatory authorities.”

“Documented” includes established, implemented and maintained.

Guess the Observation!!

Observation #3:
Procedures to ensure that purchased product conforms to specified purchasing information have not been adequately documented. Specifically, criteria for the evaluation and selection of suppliers based on the effect of the purchased product on the quality of the medical device and proportionate to the risk associated with the medical device have not been defined.

This is a violation of:

a) 21 CFR 820 b) 13485:2016 c) Both a and b d) None of the above

Guess the Observation!!

Observation #3 is a violation of:

a) 21 CFR 803 **b) 13485:2016** c) Both a and b d) None of the above

13485:2016 section 7.4.1 Purchasing process states: “The organization shall establish criteria for the evaluation and selection of suppliers…a) based on the supplier’s ability to provide product that meets the organization’s requirements; b) based on the performance of the supplier; c) based on the effect of the purchased product on the quality of the medical device; d) proportionate to the risk associated with the medical device.

Although the preamble specifies the expectation for risk-based decisions throughout the quality system, 21 CFR 820 has no explicitly stated requirement for the risk-based evaluations of suppliers.

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THANK YOU

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