FINAL DOCUMENT

Global Harmonization Task Force

Title: Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange

Authoring Group: Study Group 3 of the Global Harmonization Task Force

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This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide non-binding guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Preface

This document was produced by the Global Harmonization Task Force (GHTF), a voluntary group of representatives from medical device regulatory authorities and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development. It is expected that the reader is proficient with the requirements of ISO 13485:2003.

Introduction

This document is intended for regulatory authorities and auditing organizations. It introduces a standardized nonconformity grading system for regulatory purposes with a Regulatory Audit Information Exchange Form providing consistent audit information in order to enable exchange among regulatory authorities.

Currently, the significance of a nonconformity related to a medical device manufacturer's Quality Management System (QMS) may vary between regulatory authorities and auditing organizations. All parties will benefit from the use of a standardized and transparent grading system of QMS nonconformities. This will build the confidence necessary for the potential mutual acceptance of the results of a regulatory audit.

The major and minor classification of nonconformities commonly used does not provide enough detail for global information exchange. Therefore the terms major and minor nonconformity will not be defined nor utilized in this document. The intent of this new grading system for regulatory purposes is to support the exchange of audit results that go beyond the binary concept of major and minor to a 5 level grading system of nonconformities.

The regulatory authorities can determine how the audit information provided in the Regulatory Audit Information Exchange Form will be utilized within their jurisdiction. Regulatory authorities may also consider other data sources in addition to the outcome of the regulatory audits such as product evaluations, recalls, vigilance reports, etc. for regulatory oversight.

1.0 Scope

This document provides a method to present outcomes of regulatory audits that can be used by regulatory authorities for information exchange. It introduces a nonconformity grading system for regulatory purposes with a Regulatory Audit Information Exchange Form providing standardized results.

The following are not included in the scope of this document:

- How to perform audits and prepare associated reports (see GHTF SG4 documents)
- How the Regulatory Audit Information Exchange Form will be utilized by regulatory authorities

2.0 Definitions

2.1 Manufacturer

Any natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s). (GHTF SG1/N55:2009)

2.2 Nonconformity

Non fulfillment of a requirement. (ISO 9000:2005, 3.6.2)

2.3 Quality management system (QMS)

Management system to direct and control an organization with regard to quality. (ISO 9000:2005, 3.2.3)

3.0 References

GHTF SG4/N28R4:2008 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 1: General Requirements

GHTF SG4/N30:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy

GHTF SG4/N33R16:2007 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 3: Regulatory Audit Reports

GHTF SG4/N83:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 4: Multiple Site Auditing

GHTF SG4/N84:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 5: Audits of Manufacturer Control of Suppliers

ISO 13485:2003 – Medical Devices –Quality Management Systems - Requirements for Regulatory Purposes

ISO 9000:2005 - Quality Management Systems – Fundamentals and Vocabulary

ISO 17021:2011 – Conformity Assessment – Requirements for bodies providing audit and certification of management systems

ISO 19011:2011 – Guidelines for Auditing Management Systems

4.0 General

The following sections introduce a standardized nonconformity grading system for regulatory purposes. To enable consistent grading, guidance has been provided on how to write a nonconformity. The Regulatory Audit Information Exchange Form at the end of this document is a tool used to capture the grading so that it can be utilized in an exchange of information between interested regulatory bodies.

4.1 Writing Nonconformities

Regulatory audits should be performed in accordance with GHTF SG4 documents and other applicable regulatory references. The output of those audits may include nonconformities.

In order for the significance of nonconformities to be characterized utilizing the nonconformity grading system described in this document, it is essential that nonconformities are clearly worded with factual and precise language that enables the reader to comprehend the actual non-fulfillment that was detected during the audit. The information presented should be an accurate representation of the reviewed records, samples and procedures, as well as interviews conducted.

The nonconformity should[1]:

a) be a statement of nonconformity written in a clear, concise manner:
   - be self-explanatory and related to the issue, not just be a restatement of the audit evidence, or be used in lieu of audit evidence

b) be supported by objective evidence:
   - justify the extent of evidence (e.g. number of records) - what exactly was found or not found, with an example(s)
   - identify the location or basis (source document) for the evidence (e.g. in a record, procedure, interview, or visual observation)

c) identify the specific requirements which have not been met:
   - use the words of ISO 13485:2003
   - document the source of the requirement (e.g. medical device regulations, other applicable standards, procedures or requirements established by the organization, etc.)

Multiple instances of non-fulfillment of a requirement should be combined into a single nonconformity unless the instances originate or relate to different aspects of a clause (see Appendix A – "NC #2"). Examples of poorly and better worded nonconformities are provided in Appendix A.

[1] ISO & IAF 9001 Auditing Practices Group Guidance on: Documenting a Nonconformity (5 June 2009) www.iso.org/tc176/ISO9001AuditingPracticesGroup

4.2 Grading of Nonconformities

The nonconformity grading for regulatory purposes consists of a two-step approach that leads to calculation of a final grade for each nonconformity (Figure 1 – shaded area):

Step 1 - A Nonconformity Grading Matrix, which provides an initial grade

Step 2 - Additional escalation rules are applied, to determine a final grade

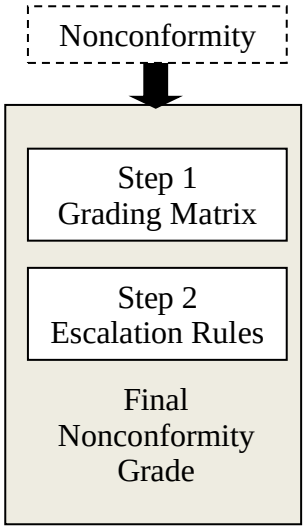

Figure 1: Grading Overview

4.2.1 Step 1 Grading Matrix

As illustrated in Figure 1 above, the Grading Matrix is the first step in grading a nonconformity.

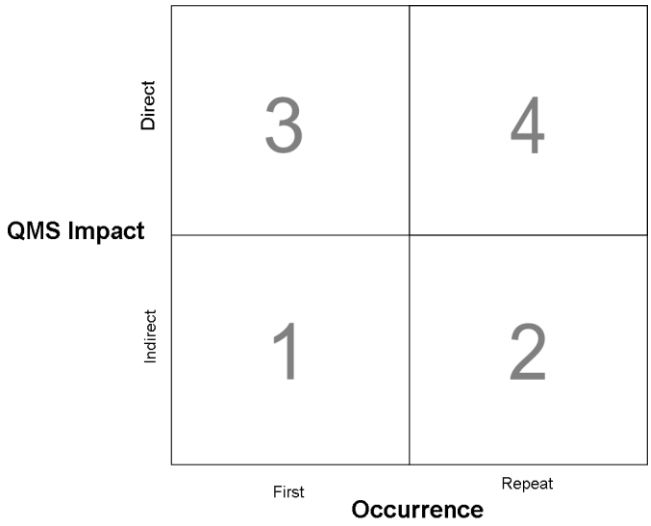

Figure 2: **Grading Matrix**

The Y-axis of the Grading Matrix (Figure 2) is **QMS Impact.** It is related to the influence of the QMS clause on medical device safety and performance. It is vitally important to highlight that all the clauses of the standard are equally required if applicable,[2] to effectively establish and maintain a quality management system that will meet regulatory purposes.

For the purpose of improved stratification in the grading system[3], the clauses of the standard are divided into two categories:

- **Indirect QMS Impact**: ISO 13485:2003 clauses 4.1 through 6.3, are seen as "enablers" (making it possible or feasible) for the QMS processes to operate. These clauses are therefore considered to have indirect influence on medical device safety and performance.

- **Direct QMS impact:** ISO 13485:2003 clauses 6.4 through 8.5, are seen as having direct influence on design, and manufacturing controls. These clauses are therefore considered to have direct influence on medical device safety and performance.

There are two basic principles that the auditors should follow when writing the nonconformity and assigning a clause number for purposes of utilizing this grading system.

[2] See ISO 13485:2003 clause 1.2

[3] Justification for approach: In order to assist the evaluation of QMS impact for this grading system, it was designed to categorize the QMS requirements contained within ISO 13485:2003 standard at a specific sub-clause level (e.g., 6 vs. 6.2 vs. 6.2.2).

- When the nonconformity has the potential to affect safety or performance, it should be written against the specific requirement in ISO 13485:2003 found in clauses 6.4 through 8.5, because it has direct QMS impact.

- When the nonconformity is against the manufacturer's quality manual, procedures or requirements, is not specifically required in ISO 13485:2003 or does not impact safety or performance, then the nonconformity should be assigned to clauses 4.1 through 6.3, because it has indirect QMS impact.

The X-axis of the Grading Matrix in Figure 2 is **Occurrence** and is divided into two categories:

- **First:** The first category addresses a nonconformity in a particular sub-clause (X.X.X)[4] of ISO 13485:2003 identified for the first time. The first time is defined as not observed in the two previous QMS audits which evaluated the same sub-clause.

- **Repeat:** The second category is a nonconformity that has been identified within either of two previous QMS audits which evaluated the same sub-clause (X.X.X). Such a nonconformity poses an increased risk because it is an indicator that a corrective action has not been adequately taken or implemented.

The "two previous QMS audits which evaluated the same sub-clause" was selected because:

- in order to assess the risk of repeat occurrence accurately, it is important to assess comparable nonconformities;
- historical data beyond the two previous QMS audits may not represent the current state; and
- review of more audit reports may be counterproductive for an efficient grading system.

However, it is important to ensure that the audits reviewed for the **Occurrence** assessment, have at a minimum evaluated the same sub-clause.

Occurrence in this document is directed at the frequency of a nonconformity cited from one audit to the next performed by the same auditing organization. It is not the occurrences of examples within a given sample size that the auditor may take to determine if a nonconformity exists during an audit.

Nonconformities can often be written up against more than one clause. Therefore, it is the auditor's obligation to determine the impact of the non-conformity on the QMS and assign the appropriate clause. The QMS impact of the nonconformity will determine whether the resulting clause will be **Direct** or **Indirect**. Some examples to help illustrate the grading process in Step 1 are provided below.

- ***Nonconformity where safety issues raise the grading to Direct Impact:*** A manufacturer distributes a product in the European Union, Canada and the US. The manufacturer has a documented procedure for notification of adverse events that meets the criteria of the European regulations, but has no references or requirements for adverse event reporting in the other jurisdictions. The medical device caused an adverse event and the manufacturer

[4] The system was assessed at several different tier levels and it was determined that the QMS impact should be started at the second sub-clause (X.X) level of standard, while the Occurrence should be started at the third sub-clause (X.X.X) level and to allow the subsequent rules to be added for further refinement of the grading system.

followed their procedures related to adverse event reporting. The manufacturer reported the event to the appropriate European Competent Authority and did not consider reporting it to the other jurisdictions. This nonconformity should therefore be assigned to clause 8.5 – Improvement and not to 4.2 Documentation Requirements.

- ***Nonconformity where safety is not an issue that is against a self imposed requirement in a procedure leads to a starting grade with an Indirect Impact*:** A manufacturer's procedure for a process revalidation of an injection molding process requires annual revalidation regardless of changes or process deviations. The annual revalidation was not performed, however there were no changes or process deviations noted. In this example, ISO 13485:2003 clause 7.5 does not require annual revalidation. There were no process changes or deviations and there does not appear to be a safety issue. This nonconformity should be assigned to clause 4.2 - Documentation Requirements for the manufacturer not following their own procedure and not against clause 7.5 – Production and Service provision.

- ***Nonconformity where safety is an issue, that is against a self imposed requirement based on a standard leads to a starting grade of a Direct Impact:*** A manufacturer is utilizing standard ISO 11137-1 for validating their radiation sterilization process and the standard requires quarterly dose audits. This was not performed as required by the standard. In this example, there is a safety issue since the standard requires quarterly dose audits to assure product sterility. Therefore this nonconformity should be assigned to clause 7.5 – Production and Service Provision.

- ***Nonconformity to illustrate a Repeat Occurrence*:** An initial nonconformity was found in 7.5.2.2 relating to a nonconformity in a sterilization process validation. A subsequent audit found a nonconformity in 7.5.2.1 in an injection molding process validation. Both nonconformities fall within 7.5.2 - Validation of Processes for Product and Service Provision. Therefore, the subsequent occurrence should be categorized as a Repeat Occurrence to the X.X.X level of the appropriate clause.

NOTE: If the scenarios are altered within the examples it must be recognized that the conclusions may change.

4.2.2 Step 2 Grading – Escalation Rules

The resultant grading from Step 1 is carried forward to Step 2, which is a rules-based escalation process to address areas of higher risk that have a potential to affect product safety and performance. Under this grading system the Step 1 grade is increased by 1 for each rule:

1. Absence of a documented process or procedure

The absence of a documented process or procedure will fundamentally affect consistency and effective implementation of any process.

The word "absent" (or "absence") should be used in the nonconformity statement when there is no documented process or procedure for the requirement. It is critical that this word be obvious within the nonconformity statement in order to consistently grade the nonconformity.

2. Release of a Nonconforming Medical Device

A nonconformity which resulted in the release of a nonconforming medical device to the market is direct evidence of a QMS failure. This rule in the grading system is assessing the QMS nonconformity at a higher risk, because nonconforming product is on the market and outside the control of the manufacturer's QMS. If a nonconforming medical device is released under concession with adequate technical and scientific justification, then the nonconformity has been resolved. It is no longer considered a nonconforming product and the escalation rule will not be applied.

4.3 Applying the Nonconformity Grading System

Step 1 – Using the Nonconformity Grading Matrix

A. Direct or Indirect Impact: When a nonconformity is written and the clause assigned, identify whether it is "direct impact" (score of 3) or "indirect impact" (score of 1), as defined above.

B. Repeat nonconformities against the same QMS sub-clause (X.X.X): The auditor should check the previous two audit reports which evaluated the same sub-clause to see if a nonconformity that is identified in the current audit was previously raised. The nonconformity does not have to be identical to the nonconformity in the previous audit, just cited to the same QMS sub-clause (X.X.X). If the nonconformity is a repeat, the grade increases by 1.

Step 2 – Application of Escalation Rules

In this step of grading, the Nonconformity Grading Matrix is no longer used. Each rule below is applied to determine the final grade of the nonconformity.

> **Rule 1 - Absence:** Absence of a documented process or procedure of any requirement, the grade increases by 1.
>
> **Rule 2 - Medical Device:** Release of a Nonconforming Medical Device outside of the controls of the manufacturer's QMS, the grade increases by 1.

The final grade for a nonconformity under this grading scheme will be a number between 1 and 6. However, the grade of "5" was determined to be the maximum, because this represents a significantly high enough risk that some intervention is required. The differentiation between 5 and 6 was not felt to be of benefit in the grading system. Therefore, if a grade of 6 is achieved, the final grade is documented as "5." Refer to Appendix B, example #8.

4.4 Regulatory Audit Information Exchange Form

To enable information exchange between regulators, the following Regulatory Audit Information Exchange Form (Form) is introduced.

List of Nonconformities			Nonconformity Grading						Medical Device Country Specific Regulatory Requirements					
NC#	Nonconformity		ISO 13485 :2003 Clause	Step 1 Grade	Absence	Medical Device	Grade		EU	CAN	USA	AUS	JPN	OTHER
1														
2														

Table 1 - Regulatory Audit Information Exchange Form

This Form consists of three sections (see Table 1):

1. **List of Nonconformities** - It is important to provide sufficient insight into the context and relevance of each nonconformity listed on the Form. The list of nonconformities provided in the Form should be identical to that provided in the audit report.

2. **Nonconformity Grading** - The details of how the final nonconformity grade was obtained for nonconformities specifically against ISO 13485:2003. The use of this section of the Form provides transparency in the calculation process.

3. **Medical Device Country Specific Regulatory Requirements** - Nonconformities that are within the manufacturer's QMS but are outside the specific requirements within the clauses of ISO 13485:2003 should be identified in the Medical Device Country Specific Regulatory Requirements section of the Form. This area is not graded, but the auditor should reference the specific section of the applicable Regulation or Legislation against which the nonconformity is cited.

4.5 Use of the Regulatory Audit Information Exchange Form

When the Form is exchanged between regulatory authorities, specific information about the audit should be included with the Form. Examples include: date of the audit, scope of the audit, sites audited, auditors' name(s), etc.

The Nonconformity Grading section of the Form is intended to capture the grade of nonconformities against ISO 13485:2003. If a nonconformity is against a ISO 13485:2003 clause, it should at minimum be captured under the Nonconformity Grading section of the Form and graded.

The intent of the Medical Device Country Specific Regulatory Requirements section is to capture additional issues outside the specific requirements of ISO 13485:2003. This section is not graded but the nonconformities are listed by regulatory jurisdictions (covered by the audit) and general regulatory requirements for that jurisdiction. Certain regulatory jurisdictions (such as Canada) may require that nonconformities against country specific regulatory requirements are written against a specific clause in the standard in the Nonconformity Grading section.

Below is a completed Form with some specific examples:

List of Nonconformities		Nonconformity Grading					Medical Device Country Specific Regulatory Requirements					
NC#	Nonconformity	ISO 13485 :2003 Clause	Step 1 Grade	Absence	Medical Device	Grade	EU	CAN	USA	AUS	JPN	OTHER
1	There is an absence of a Quality Policy in the organization.	5.3	1	+1		2						
2	Documented procedures for identifying training needs are not established.								21 CFR 820.25		Ord 169 (Article 23 subpart 2)	
3	The injection molding process has not been validated, as per procedure DOC12345 but has not resulted in nonconforming product being released to the market.	7.5.2	3			3	MDD (93/42/ EEC) (Annex II)					
4	The WIDGET™ device was sold in Canada without a medical device license. Procedure DOC12345 requires that all medical devices class II, III & IV are licensed prior to sale in Canada, according to section 26 of the CMDR. This type of NC was also cited in last year's audit.	4.1	2			2		CMDR section 26				

- Nonconformity #1 – An example of a nonconformity of the QMS from the requirements of ISO 13485:2003.

- Nonconformity #2 – An example of a country specific regulatory requirement that is a nonconformity within the manufacturer's QMS but more specific than the requirements of the clauses of ISO 13485:2003.

- Nonconformity #3 – An example of a nonconformity within the QMS that is also against a country specific regulatory requirement. In this case, the nonconformity could also be written against the EU Medical Device Directive.

- Nonconformity #4 – An example of a nonconformity to a country specific regulatory requirement that is also cited under section 4.1 of ISO 13485:2003. In this case, Canada requires all nonconformities be written against ISO 13485:2003.

The Form provides a transparent and standardized way of exchanging information between regulatory authorities on the outcome of medical device regulatory audits. The intent is that this Form will be provided to the medical device manufacturer after following standard auditing procedures where potential nonconformities are routinely discussed throughout the audit

and at the closing meeting of the audit (ISO 19011:2011, clause 6.4.9). It is recommended that a draft of the Form be provided at the closing meeting of the audit for sake of transparency.

The grade assigned to each nonconformity should not be changed as a result of any correction(s) or corrective action(s) taken by the manufacturer, but may be amended as a result of the auditing organization's documented appeals process (ISO 17021:2011, clause 9.7). After the auditing organization has completed the audit process, the final Form should be provided to the manufacturer. The intent is also that the grading and the Form be a method to accurately capture the assessment of the audit and to provide uniformity and consistency within the process of grading nonconformities.

The Form purposely does not provide a cumulative grade for the overall audit. How the Form is utilized is the decision of each regulatory authority for their appropriate assessment based on their own needs or requirements.

5.0 Appendix A: Examples of statements of nonconformities

	Nonconformity Statements		
NC #	**Poorly worded**	**Improved wording**	**ISO 13485:2003 Clause**
1	There was no evidence of training to the medical devices directive	The manufacturer did not follow their own training procedure (#14) requiring training on the medical devices directive (93/42/EEC) for internal auditors.	4.2.1
2	Document control was inadequate because of multiple occurrences of obsolete documents being utilized	The following obsolete documents were found to be in use: Obsolete version of procedure XYZ found to be in use in the calibration department Obsolete version of ABC in receiving area was found to be in use Obsolete version of design review procedure PQR was found to be in use in design department	4.2.3
3	The scheduled internal audit must be conducted and the report provided for review.	There was an absence of a documented procedure for conducting internal audits	8.2.2

6.0 Appendix B: Examples Illustrating Nonconformity Grading

	STEP 1				STEP 2			
Example of Nonconformity	**ISO 13485 Clause**	**Occurrence**	**STEP 1 Grade**	**Explanation of STEP 1 Grade**	**Absence**	**Medical Device**	**Final Grade**	**Explanation of Final Grade**
1. There is no objective evidence of the establishment of quality objectives for 2011, as required in the auditee's Quality Manual. The same non conformity was cited during the audit of 2010.	5.4.1 (indirect)	Repeat (2010, 2011)	2	This is a repeat NC. Therefore, it leads to a NC grade of 2.	NO	NO	2	This is not an absence of a QMS requirement. There is a documented procedure however the manufacturer could not provide objective evidence that it was being followed. As a result of this NC it is unlikely that a nonconforming product was placed on the market. Therefore the initial grade does not change.
2. Management reviews are held quarterly per procedure number DOC12345. However, there is no documentation of the third quarter management review meeting for 2010.	5.6.1 (indirect)	First NC	1	This is a first NC, leading to a NC grade of 1.	NO	NO	1	This is not an absence of a QMS requirement. As a result of this NC it is unlikely that a nonconforming product was placed on the market. Therefore the initial grade does not change
3. Competence, Awareness and Training processes are absent from the QMS. Documented evidence for training could not be provided. This NC was also raised in a previous QMS audit (2009, 2011).	6.2.2 (indirect)	Repeat NC	2	This is a repeat NC. Therefore, it leads to a NC grade of 2.	YES	NO	3	The absence of a QMS requirement increases the initial grade by 1, making the final grade as 3.
4. Suppliers are not adequately controlled as per procedure DOC1234. Supplier X of was replaced with Supplier Y on 1st May 2011 without approval. This is the second NC issued against the same subclause in a previous QMS audit (2010).	7.4.1 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	NO	NO	4	This is not an absence of a QMS requirement. There is no evidence of nonconforming product being placed on the market. Therefore the initial grade does not change.
5. Suppliers are not adequately controlled as per procedure DOC1234. Product XX was shipped on 2nd of September 2011 and was nonconforming due to an uncontrolled specification change made by the supplier. This is the second NC issued against the same subclause in a previous QMS audit (2010).	7.4.1 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	NO	YES	5	Non conforming product was placed on the market as a result of this QMS nonconformity. This increases the initial grading by 1, to a final grade of 5.

	STEP 1				STEP 2			
Example of Nonconformity	**ISO 13485 Clause**	**Occurrence**	**STEP 1 Grade**	**Explanation of STEP 1 Grade**	**Absence**	**Medical Device**	**Final Grade**	**Explanation of Final Grade**
6. There was no evidence of a record for control of storage conditions for a medical device with a 24 month shelf life that requires storage at 2-8^{0}C per procedure (#12345).	7.5.5 (direct)	First NC	3	This is a first NC, leading to a NC grade of 3.	NO	NO	3	The initial grade does not change.
7. There is an absence of a Quality Policy.	5.3 (indirect)	First NC	1	This is a first NC, leading to a grade of 1.	YES	NO	2	There is an absence of a QMS requirement. Therefore, the initial grade increases by 1 to a final grade of 2.
8. There was an absence of the requirement for Design verification in the manufacturer's QMS. As a result design changes to device model XXX were not verified prior to the product release to the market. This is the second NC issued against the same sub-clause in a previous QMS audit (2010).	7.3.5 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	YES	YES	5	This is an absence of a requirement and non conforming product was placed on the market. Therefore the grade would be 4+2=6. However, since the maximum grade can only be 5, it will be recorded as 5.
9. There was no evidence of design validation as per procedure DOC12 for device model XXX. The product was shipped to five customers.	7.3.6 (direct)	First NC	3	This is a first NC, leading to a grade of 3.	NO	YES	4	Non conforming product was placed on the market as a result of this QMS nonconformity. This increases the initial grade by 1, to a final grade of 4.

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1. Purpose

This document is intended for regulatory authorities and auditing organizations participating in or utilizing the results of the Medical Device Single Audit Program (MDSAP). It provides guidelines for the use of the document GHTF/SG3/N19:2012: *Quality management system - Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange* for grading nonconformities resulting from MDSAP audits.

2. Scope

The “major” and “minor” classification of nonconformities commonly used in medical device audit and certification schemes does not provide enough detail for global information exchange. However, the terms “major” and “minor” nonconformity are defined in ISO 17021-1:2015 clauses 3.12 and 3.13 and are often utilized in medical device certification programs, including those for regulatory purposes, to assign a priority to the implementation of corrective actions. While the terms “major” and “minor” are not the subject of this document, general correlation between “major” and “minor” nonconformities as defined in ISO 17021-1:2015 and the grading system defined in this document is discussed in section 5.2. The intent of this grading system for regulatory purposes is to support the exchange of information about nonconformities from audit findings that go beyond the binary concept of “major” and “minor” to a 5 level grading system of nonconformities.

The regulatory authorities can determine how the audit information provided in the Regulatory Audit Information Exchange Form will be utilized within their jurisdiction. Regulatory authorities may also choose to consider other data sources in addition to the outcome of the regulatory audits such as product evaluations, recalls, vigilance reports, etc. for regulatory oversight.

3. Definitions/Acronyms

AO: Auditing Organization

RA: Regulatory Authority

4. Authorities/Responsibilities

Auditing Organizations: responsible for oversight of audits that are conducted in accordance with MDSAP, including ensuring adherence to this procedure and all other relevant MDSAP policies and procedures.

Regulatory Authorities: responsible for evaluation of the graded nonconformities and MDSAP audit reports per their legislation.

5. Policy

5.0 General

The following sections introduce a standardized nonconformity grading system for regulatory purposes. To enable consistent grading, guidance has been provided on how to write a nonconformity.

Nonconformities identified during an MDSAP audit must be recorded on the Nonconformity Grading and Exchange (NGE) form (MDSAP AU F0019.2)

5.1 Writing Nonconformities

Regulatory audits conducted under the MDSAP should be performed in accordance with MDSAP AU documents and other applicable regulatory references. The output of those audits may include nonconformities.

In order for the significance of nonconformities to be characterized utilizing the nonconformity grading system described in this document, it is essential that the most specific requirement is correctly identified and used. Nonconformities are to be clearly worded with factual and precise language that enables the reader to comprehend the actual nonfulfillment that was detected during the audit. A nonconformity must assist the manufacturer to identify its cause. The

information presented should be an accurate representation of the reviewed records, samples and procedures, as well as interviews conducted.

The nonconformity should:

a) identify the specific requirements which have not been met:
- use the words of ISO 13485:2016 or of the applicable regulatory requirement
- document the source of the requirement (e.g. medical device regulations, other applicable standards, procedures or requirements established by the organization, etc.)

If several requirements may apply:
- choose the one which will result in the highest grade of nonconformity; and
- give preference to a requirement to implement over a requirement to just document.

b) be a statement of how a requirement is not being fulfilled and written using complete sentences in a clear, concise manner:
- be related to a requirement, not just be a restatement of the audit evidence, or be used in lieu of audit evidence
- be significant and relate to an observed or potential problem with the facility, equipment, processes, controls, products, employee practices, or records. “Potential problems” should have a reasonable likelihood of occurring based upon observed conditions or events.
- contain a statement regarding the product(s) related to the nonconformity using trade name(s) and generic name(s)
- be factual and avoid opinionated or subjective terms

c) be supported by objective evidence:
- the evidence must be directly related to the requirement
- be traceable so it should identify what (source procedure, record, interview, or visual observation), who (using job titles), when and where (location).
- justify the extent of evidence (e.g. number of records) - what exactly was found or not found, with an example(s)

Multiple instances (examples) of non-fulfillment of a requirement should be combined into a single nonconformity unless the instances originate or relate to different aspects of a clause.

5.2 Grading of Nonconformities

5.2.1 Step 1 Grading – Indirect or Direct QMS Impact

For the purpose of stratification in the grading system, the clauses of the standard are divided into two categories:

- ***Indirect QMS Impact:*** ISO 13485:2016 clauses 4.1 through 6.3 (with the exception of 4.2.3 – Medical device file, which is considered to have Direct QMS impact) are seen as “enablers” (making it possible or feasible) for the QMS processes to operate. These clauses are therefore considered to have indirect influence on medical device safety and performance and are generally analogous to “minor” nonconformities as defined in ISO 17021-1:2015 clause 3.13.

- ***Direct QMS impact:*** ISO 13485:2016 clauses 6.4 through 8.5 (with the exception of 8.2.4 – Internal audits, which is considered to have indirect QMS impact) are seen as having direct influence on design, and manufacturing controls. These clauses are therefore considered to have direct influence on medical device safety and performance and are more likely to be analogous to “major” nonconformities as defined in ISO 17021-1:2015 clause 3.12 when there is a significant doubt that effective process control is in place, or that products or services will meet specified requirements.

Clauses with Indirect QMS impact are graded at this step with a “1”.

Clauses with Direct QMS impact are graded at this step with a “3”.

There are two basic principles that the auditors should follow when writing the statement of nonconformity and assigning a clause number for purposes of utilizing this grading system.

- When an audit observation or audit evidence indicates that more than one applicable requirement has not been fulfilled, the nonconformity must be written against the specific requirement in ISO 13485:2016 found in clauses 4.2.3, 6.4 through 8.5, (if applicable), when the nonconformity does, or has the potential to, affect safety or performance; because it has direct QMS impact.

In general, nonconformities that have the potential to affect safety or performance are comparable to a "major" nonconformity per ISO 17021-1:2015 clause 3.12. These types of nonconformities would require the Auditing Organization to review, accept and verify the correction and corrective actions prior to granting a certification decision in accordance with ISO 17021-1:2015 clause 9.5.2(b).

- When an audit observation or audit evidence indicates that a requirement of the manufacturer's quality manual, procedures or requirements, or is not specifically required in ISO 13485:2016, or does not impact safety or performance, then the nonconformity should be assigned to clauses 4.1 through 6.3 (except 4.2.3, which is considered to have direct QMS impact), and 8.2.4; because it has indirect QMS impact.

Nonconformities can often be written up against more than one clause. Therefore, it is the auditor's obligation to determine the impact of the nonconformity on the QMS and assign the appropriate clause. The QMS impact of the nonconformity will determine whether the resulting clause will be Direct or Indirect. Some examples to help illustrate the grading process for direct versus indirect impact are provided below.

Example 1: Nonconformity where safety issues raise the grading to Direct Impact: A manufacturer distributes a product in Australia, Canada and the US. The manufacturer has a documented procedure for notification of adverse events that meets the criteria of Canada and the US, but has no references or requirements for adverse event reporting in Australia. The medical device caused an adverse event within Canada and the manufacturer followed their procedures related to adverse event reporting. The manufacturer reported the event to Health Canada and the US FDA, but did not consider reporting it to Australia. This nonconformity should therefore be assigned to clause 8.2.3 – Reporting to regulatory authorities and not to 4.2.5 Documentation Requirements.

Example 2: Nonconformity where safety is not an issue that is against a self-imposed requirement in a procedure leads to a starting grade with an Indirect Impact: A manufacturer's procedure for a process revalidation of an injection molding process requires annual revalidation regardless of changes or process deviations. The annual revalidation was not performed; however, there were no changes or process deviations noted. In this example, ISO 13485:2016 clause 7.5.6 does not require annual revalidation. There were no process changes or deviations and there does not appear to be a safety issue. This nonconformity should be assigned to clause 4.2.5 - Documentation

Requirements for the manufacturer not following their own procedure and not against clause 7.5.6 – Validation of processes for production and service provision.

Nonconformity where safety is an issue, that is against a self-imposed requirement based on a standard leads to a starting grade of a Direct Impact: A manufacturer is utilizing standard ISO 11137-1 for validating their radiation sterilization process and the standard requires quarterly dose audits. This was not performed as required by the standard. In this example, there is a safety issue since the standard requires quarterly dose audits to assure product sterility. Therefore, this nonconformity should be assigned to clause 7.5.7 – Particular requirements for validation of processes for sterilization and sterile barrier systems

Nonconformity to illustrate a Repeat Occurrence: An initial nonconformity was found in 7.5.6 relating to a nonconformity in a coating process validation. A subsequent audit found a nonconformity in 7.5.6 in an injection molding process validation. Both nonconformities fall within 7.5.6 - Validation of Processes for Product and Service Provision. Therefore, the subsequent occurrence should be categorized as a Repeat Occurrence to the X.X.X level of the appropriate clause.

NOTE: If the scenarios are altered within the examples it must be recognized that the conclusions may change.

5.2.2 Step 2 Grading – Escalation Rules

The resultant grading from Step 1 is carried forward to Step 2, which is a rules-based escalation process to address areas of higher risk that have a potential to affect product safety and performance. Under this grading system the Step 1 grade is increased by 1 for each rule:

The MDSAP form developed to record nonconformities (MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form) presents the grading as the result of 4 independent criteria:

- Impact on the QMS (direct: 3 or indirect: 1)
- Repeat nonconformity (yes: 1 or no: 0)
- Combination of the absence of a documented process or procedure and failure to implement (yes: 1 or no: 0)
- Release of nonconforming devices (yes: 1 or no: 0)

1. *Impact on the QMS*

See section 4.2.1 - Step 1 Grading – Indirect or Direct QMS Impact of this document.

2. *Repeat nonconformity*

This category is for a nonconformity that has been identified during any audits within the previous 3 years. Such a nonconformity poses an increased risk because it is an indicator that a corrective action has not been adequately taken or implemented.

The “two previous QMS audits which evaluated the same sub-clause” was selected because:

- in order to assess the risk of repeat occurrence accurately, it is important to assess comparable nonconformities;
- historical data beyond the two previous QMS audits may not represent the current state; and
- review of more audit reports may be counterproductive for an efficient grading system. However, it is important to ensure that the audits reviewed for the Occurrence assessment, have at a minimum evaluated the same sub-clause.

Occurrence in this document is directed at the frequency of a nonconformity cited from one audit to the next performed by the same auditing organization. It is not the occurrences of examples within a given sample size that the auditor may take to determine if a nonconformity exists during an audit.

Auditors should refrain from issuing a new (repeat) nonconformity for a similar finding that was observed at a previous audit if the device organization is implementing the timetabled actions that had been proposed by the device organization, and accepted by the AO. If an auditor can demonstrate that previously proposed actions are not effective, considering new occurrences of the nonconformities, then a nonconformity may be issued for an ineffective corrective action system.

Note: see also MDSAP AU P0019 on how to handle nonconformities previously recognized by the device organization and under process of remediation.

3. *Combination of the absence of a documented process or procedure and the failure to implement a requirement*

The absence of a documented process or procedure will fundamentally affect consistency and effective implementation of any process. The use of this escalation criteria should be limited to situations where there is a combined failure to document **and** implement a requirement.

Documenting a process or procedure aims at ensuring the consistent and effective implementation of the corresponding activities. However, failing to document a procedure or process does not systematically lead to noncompliant implementations of that activity, and conversely, documenting a procedure or process does not always ensures it will be implemented accordingly. However, where an organization fails to 1) document a procedure or process that ISO 13485:2016 or an applicable regulatory requirement require to be documented and 2) implement the corresponding activities in ways that comply with these same requirements, then the grading of the nonconformity shall be escalated.

This escalation rule applies even in case where the process is generally documented but entirely fails to address the requirements from a jurisdiction entirely and there is evidence that the implementation of the process failed to meet the requirements of that jurisdiction.

This escalation rule may be invoked in cases where the documented procedure entirely fails to address the topic, or only addresses an applicable regulatory requirement by referencing the regulation. However, it would not be invoked when a procedure addresses the topic but incompletely or lacking details.

4. *Release of a Nonconforming Medical Device*

A nonconformity which resulted in the release of a nonconforming medical device to the market is direct evidence of a QMS failure. This escalation criteria is grading the QMS nonconformity at a higher risk, because nonconforming product is on the market and outside the control of the manufacturer's QMS.

This type of direct evidence of QMS failure and release of nonconforming products to the market is analogous to a "major" nonconformity per ISO 17021-1:2015 clause 3.12 and would require that the Auditing Organization review, accept and verify the correction and corrective actions prior to granting a

certification decision in accordance with ISO 17021-1:2015 clause 9.5.2(b)..

If a nonconforming medical device is released under concession with adequate technical and scientific justification, then the nonconformity has been resolved. It is no longer considered a nonconforming product and the escalation rule will not be applied.

5.3 Applying the Nonconformity Grading System

While it is possible to have the sum of the steps in grading equal a “6” if the nonconformity is a direct QMS impact and all the escalation rules apply, the final grade for a nonconformity under this grading scheme will be a number between 1 and 5. A “5” will be the highest grade.

The grade assigned to each nonconformity should not be changed as a result of any correction(s) or corrective action(s) taken by the manufacturer, but may be amended as a result of the auditing organization’s documented appeals process (ISO 17021-1:2015, clause 9.7). After the auditing organization has completed the audit process, the final MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form should be provided to the manufacturer. The intent is also that the grading and the NGE form be a method to accurately capture the assessment of the audit and to provide uniformity and consistency within the process of grading nonconformities.

5.4 MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form

The MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form is used for information exchange between auditing organizations and regulatory authorities, as well as between regulatory authorities.

Form MDSAP AU F0019.2 can strictly be used as a tool to exchange information with the Regulatory Authorities about the nonconformities issued and their status at the time of the submission. In such case the response of the Audited Facility’s organization to the nonconformity is not recorded in the form. The Auditing Organization using this option needs to record the back and forth with the Audited Facility’s organization using their own tools. Otherwise, the form can also be used to also record the Audited Facility’s response to the nonconformity.

Nonconformity Reports and NGE forms should be actively updated until the effectiveness of the corrections and corrective actions proposed by the audited facility or organization has been verified.

Upon request from an MDSAP Regulatory Authority, the Auditing Organization is expected to provide updated nonconformity reports within 10 calendar days. It is not necessary for Nonconformity reports to be closed at the time they are shared with the Regulatory Authorities.

Form MDSAP AU F0019.2 purposely does not provide a cumulative grade for the overall audit. How the Form is utilized is the decision of each regulatory authority for their appropriate assessment based on their own needs or requirements.

MDSAP AU G0019.4 - Guidelines NC Grading Exchange Form explains the features of Form MDSAP AU F0019.2 - MDSAP Nonconformity Grading and Exchange Form and clarifies how the form is used.

6. Forms

MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form

7. Reference Documents

GHTF/SG3/Nl9:2012: Quality management system - Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange

MDSAP AU P0019 - Medical Device Regulatory Audit Reports Policy

MDSAP AU G0019.4 - Guidelines NC Grading Exchange Form

MDSAP AU P0027 - Post Audit Activities and Timeline Policy

8. Document History

VERSION NO.	VERSION DATE	DESCRIPTION OF CHANGE	AUTHOR NAME/PROJECT MANAGER
001	2021-09-01	Initial Release	Kimberly Lewandowski-Walker, US FDA

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MDSAP
MEDICAL DEVICE SINGLE AUDIT PROGRAM

AUDIT APPROACH

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Foreword

The intention of the Medical Device Single Audit Program (MDSAP) is to allow competent auditors from MDSAP recognized Auditing Organizations (AOs) to conduct a single audit of a medical device organization's quality management system that will satisfy the requirements of the medical device Regulatory Authorities (RAs) participating in the MDSAP program.

Audits performed under the MDSAP program will be process-based, focusing on several defined processes, a defined method for linking those processes, and built on a foundation of requirements for risk management.

Use of this document

This document contains specific instructions for performing audits under the MDSAP program. It incorporates an audit sequence, instructions for auditing each specific process and identifies links that highlight the interactions between the processes.

A red box emphasizes the interrelationships of specific processes and the relevant risk management activities; if viewing a color version of the document or are in gray boxes if viewing the black and white version. *"Blue"* font emphasizes the integration of risk management.

This revision of the document combines the formerly separate MDSAP Audit Model and Process Companion documents into a single document containing additional detail regarding each audited process; as well as guidance for assessing the conformity of each process. In electronic form, the navigation bar facilitates quick access to relevant Tasks. The user may create their own bookmarks to quickly navigate to various sections.

Overview

The design of the Medical Device Single Audit Program (MDSAP) audit process is to ensure a single audit will provide efficient yet thorough coverage of regulatory requirements. These requirements include; Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016), the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), the Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), the Canadian Medical Devices Regulations, the Japanese Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Reagents (MHLW Ministerial Ordinance No. 169), the Quality System Regulation (21 CFR Part 820), and specific requirements of the medical device regulatory authorities participating in the MDSAP program.

Audit Sequence

The design and development of the MDSAP audit sequence allows a logical, focused and efficient conduct of an audit. The MDSAP audit sequence follows a process approach and has four primary processes - Management process, Measurement, Analysis and Improvement process, Design and Development process and a Production and Service Controls process with links to the supporting process for Purchasing.

The definition of each process includes a purpose and an outcome that are indicators of process performance. Each participating Regulatory Authority expects that risk management to be the foundation for the five processes that are the requirements of a quality management system for medical device organizations.

The MDSAP audit process has two additional supporting processes: Device Marketing Authorization and Facility Registration and Medical Device Adverse Events and Advisory Notices Reporting. These processes are necessary to fulfill specific requirements of the participating MDSAP regulatory authorities.

The flowchart shown in Figure 1 illustrates the MDSAP audit sequence and interrelationships. The design of the MDSAP audit approach requires the audit of the primary MDSAP processes in the following sequence: (1) Management (2) Measurement, Analysis and Improvement (3) Design and Development, and (4) Production and Service Controls processes. The audit of the Purchasing process is in conjunction with the Measurement, Analysis and Improvement process, the Design and Development process, and the Production and Service Controls process.

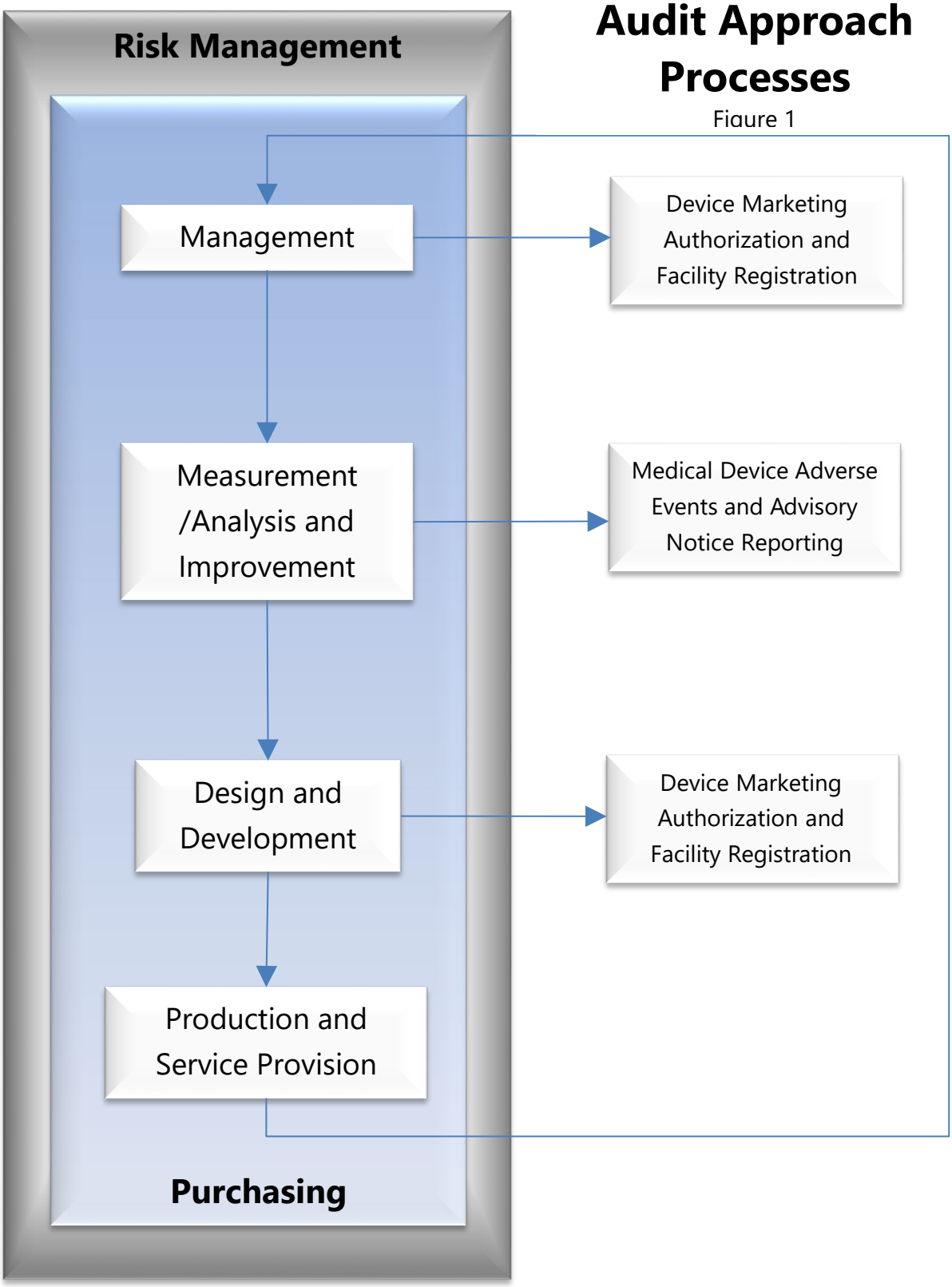
The design and implementation of a medical device organization’s quality management system is a strategic decision of the medical device organization. Through this system, it can meet the requirements of the participating regulatory jurisdictions in a way that is appropriate for the size of the

medical device organization, the processes employed and the products supplied. The medical device organization's quality management system does not need to implement certain processes (e.g. Design and Development) if regulation permits the exclusion or non-application of the process. Auditing Organizations are not required to audit such processes. However, if the medical device organization chooses to outsource any processes related to the design and/or manufacture of medical devices for which the medical device organization has responsibility, these processes remain the responsibility of the medical device organization. The medical device organization's quality management system must implement controls for monitoring and maintaining the quality of product from suppliers and outsourced processes.

The participating MDSAP jurisdictions intended to promote a single program of audits that takes into account all of their requirements for quality management systems. Hence, including the regulatory requirements of all MDSAP participating jurisdictions is a default requirement for a medical device organization's participation in the program. Marketing Authorization holders may have previously used an alternative source of evidence to demonstrate compliance with the regulatory requirements of a jurisdiction. The supply of a product into the jurisdiction of a participating MDSAP Regulatory Authority requires the auditor to include the relevant regulatory requirements in the scope of an audit.

However, in addition to the exclusions and non-applications permitted by ISO13485, the medical device organization may exclude the requirements of markets where the medical device organization does not intend to supply product. The audit scope and audit criteria must take into account any justified exclusions or non- applications. When a medical device organization claims an exclusion from the requirements of a target market, the auditor should use caution when applying the guidance provided in the MDSAP processes. Some requirements may not be applicable.

Medical devices regulated for use in pre-market clinical studies under special access programs, humanitarian use exemptions, and investigational device programs are outside of the scope of a typical MDSAP audit. The manufacture and distribution of a device supplied under a special access-type program may be subject to parts of the regulatory requirements included in the MDSAP. Auditing organizations are encouraged to contact the pertinent MDSAP-participating Regulatory Authority for any questions or clarifications.



Note: Whist there is a prescribed audit sequence for the MDSAP *processes,* auditors may audit *tasks*

within a given process in any sequence to allow for an efficient and effective audit.

The audit sequence should be followed as designed, however under certain circumstances, including the number and qualification of the auditors assigned to an audit, the inequal amount of information associated with specific client processes and the type of activity being conducted, the rigorous application of the audit sequence might prevent the efficient use of audit time and create problems with audit planning. In these cases, judicious exceptions to the audit sequence are allowed as long as there is sufficient justification and the core elements of the MDSAP Audit Approach, including linkages between processes are defined and risk-based sample selections, are respected.

Examples of reasonable exceptions:

- Auditing Measurement, Analysis and Improvement and Management at the same time to better allocate audit time for a multi-auditor activity.
- Starting the audit of a follow-on MDSAP process, such as Production or Design, when enough information had been gathered by the review of core elements in Measurement, Analysis and Improvement and Management and supporting processes, Device Marketing Authorization and Facility Registration and Medical Device Adverse Events and Advisory Notices Reporting, but prior to the full completion of these processes.
- Allowing an expert, such an expert in specific sterilization techniques, to commence the review of these specific client processes and areas.

In all cases of these adjustments, proper attention should be paid to intra-audit communication so that these decisions are re-evaluated as necessary as additional information is gathered throughout the audit, and appropriate actions taken if this information alters the viability of these changes.

Audit specific adjustments to the MDSAP audit sequence should be documented in the audit report along with appropriate justification.

Conducting the Audit

During the audit of the medical device organization's quality management system, as identified in the MDSAP processes, the audit team will be asked to be mindful of "linkages". In order for a medical device organization's quality management system to function effectively, it needs to identify and manage numerous interrelated (linked) processes in accordance with clause 4.1.2 (c) of ISO 13485:2016. The output of one process often directly forms the input of other processes, or the activities of a supporting process are relevant to other processes. The MDSAP audit sequence and audit tasks include linkages to remind the audit team of the interactions between the processes. For example, linkages assist auditors in making appropriate selections when moving to the next process (e.g. using information from the Measurement, Analysis and Improvement process to select a design project to review where appropriate).

Overview

An audit of the medical device organization's quality management system processes is to assess the extent to which the medical device organization is applying risk management principles when defining its activities. Implementing the risk-based approach to controls is an integral aspect of a medical device organization's quality management system and it is the responsibility of top management to provide the necessary commitment and resources for this effort. Effective implementation of the risk-based approach usually starts in conjunction with the design and development process, proceeds through product realization, including the selection of suppliers, considers feedback from post-market monitoring and continues until the time the product is decommissioned. Risk-based decisions occur throughout the various quality management system processes, and each medical device organization must implement the risk-based approach as well as risk management in product realization with a determination of how much residual risk is acceptable to ensure medical devices meet requirements for safety and performance and regulatory requirements.

Navigating the Audit Sequence

Each MDSAP audit process will require the audit team to accomplish audit tasks to determine if the process outcomes and the process purposes are achieved. Each audit process task includes *Clause and Regulation* references including; the applicable ISO 13485:2016 clause(s), the corresponding section(s) of the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Canadian Medical Devices Regulations, Japan Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Reagents (MHLW Ministerial Ordinance No. 169), the Quality System Regulation (21 CFR 820), and any unique requirements that pertain to a participating MDSAP regulatory authority. These references have been provided to assist the auditors in assuring that the requirements of all MDSAP participating regulatory authorities are addressed during the audit.

Many audit tasks require verification of the availability and control of MDSAP regulator specific documentation and records. These tasks have a *Clause and Regulation* reference to ISO 13485:2016 clause 4.2.1, as the quality management system documentation is to include documentation specified by applicable regulatory requirements (regulations, administrative practices and policies) [4.2.1(e)]. Where a regulatory requirement relates to the documentation required by other, more specific, clauses of ISO 13485:2016 the auditing organization is to reference the more specific clause when recording findings of nonconformity (refer to MDSAP AU P0037 - **Guidelines on the use of GHTF/SG3/N19:2012 for MDSAP purposes**). To be consistent with ISO 13485:2016 the audit team is

also reminded to apply the concept that "when a requirement is required to be documented, it is also required to be established, implemented and maintained."[1]

The medical device organization needs to demonstrate its ability to provide medical devices that consistently meet customer and regulatory requirements. During the audit, it is important that the auditors are mindful of any instances where the medical device organization demonstrates failure to fulfill any of the requirements in ISO 13485:2016, or portion of the requirements listed in the audit activities and tasks, and that these nonconformities are recorded in appropriate detail. Particular attention should be paid to the potential interrelationship of the nonconformities observed. For example, audit findings in both purchasing controls and acceptance activities may indicate a significant nonconformity because control over suppliers, and the products they supply, depends on an effective mix of both these activities, and deficiencies in one or the other may affect the quality of the finished device.

Whenever a MDSAP Audit Task requires an auditor to verify the identification and documentation of a requirement in QMS documentation, this verification should be performed as part of the pre-audit preparation and documentation review, as practical, to minimize on-site audit time and to increase the auditor's familiarity with the medical device organization's QMS.

Terminology

The term "device" is used throughout the MDSAP processes. For the purpose of applying the MDSAP processes, and to accommodate nuances in the regulatory systems of the participating Regulatory Authorities, the use of the term "device" is to refer to any product that is capable of functioning as a medical device, whether or not it is packaged, labeled, or sterilized. In some jurisdictions, such a product is defined as a "finished device". In other jurisdictions, a finished device is one that is intended to be used as a medical device and is at a stage where the product is ready to be placed on the market, or put into service, by the medical device organization whose name appears on the labelling.

The term medical device organization in this document is intended to be a reference to the definition in ISO 9000:2016- Cl 3.2.1 and as used in ISO 13485:2016. A "manufacturer" is a specific kind of a medical device organization that is variously defined in the regulations of the participating regulatory authorities.

[1] ISO 13485:2016 – Clause 0.2

Overview

A purchased or otherwise obtained "product" or "service" [2] is an outsourced product or service. In addition, a "supplier" is anyone that is independent from the medical device organization's quality management system. This includes a supplier that may be part of the same corporation as the medical device organization but operates under a separate quality management system from the audited medical device organization. For further clarification, if a supplier is not a part of the medical device organization's internal audit scope, then the supplier is under a separate quality management system. Corporations or companies that have corporate quality policies and procedures do not necessarily place all divisions or groups under the same quality management system. Therefore, one division or group can be a supplier to another division or group within the same corporation/company when not within the scope of the same quality management system. The control of suppliers that are part of the same corporation and not part of the QMS of the audited medical device organization is similar to the way external suppliers are controlled. Therefore, for the purposes of MDSAP and as necessary, an Auditing Organization has the discretion to audit external suppliers of a medical device organization, including corporate suppliers. The medical device organization must have proper controls over outsourced processes that provide medical devices and related services that consistently meet customer and applicable regulatory requirements.

Critical Suppliers:

For the purposes of MDSAP, "critical suppliers" include, but are not limited to;

- those entities that supply the organization with finished devices, i.e. a device, or accessory to any device, that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized;
- suppliers of products, including services, that impact design outputs that are essential for the proper functioning of the device; and
- suppliers of products and services that require process validation.

Annexes

Annex 1 contains country specific information as to the expectations for the audit of product / process related technologies (other than sterilization – See Annex 2) and the audit of technical documentation as part of the execution of the Audit Tasks.

Annex 2 contains information as to the expectation for the audit of requirements for sterile medical devices.

[2] GHTF/SG3/N17:2008 - Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers

Annex 3 contains a table showing a summary of timeframes for reporting advisory notices and individual adverse event reports in the participating MDSAP jurisdictions.

Annex4 contains country specific guidance on expectations for various types of written agreements for regulatory purposes.

Annex 5 contains tables showing comparisons between Japan's new and old QMS ordinance. See **footnote 3** in Management.

Annex 6 contains a table for acceptable exclusions from a manufacturer's scope of certification.

MDSAP Audit Cycle

The Medical Device Single Audit Program is based on a three (3) year audit cycle. The Initial Audit, also referred to as the "Initial Certification Audit" is a complete audit of a medical device organization's quality management system (QMS) consisting of a Stage 1 Audit (17021-1:2015 – Cl 9.3.1.2) and a Stage 2 Audit (17021-1:2015 – Cl 9.3.1.3). The initial Audit is followed by a partial Surveillance Audit (17021-1:2015 – Cl 9.6.2.2) in each of the following two (2) years and a complete Re-audit, also referred to as a "Recertification Audit" (17021-1:2015 – Cl 9.6.3.2) in the third (3rd) year. A recertification audit may also include a Stage 1 audit if there have been significant changes to the QMS that have not been otherwise adequately assessed.

Special Audits (17021-1:2015 – Cl 9.6.4.2), Audits Conducted by Regulatory Authorities, and Unannounced Audits are potential extraordinary audits that may occur at any time within the audit cycle.

Note: Not all MDSAP participating regulatory authorities require, or make use of, certification documents that relate to a medical device organization's QMS. The terms "certification" and "recertification" appear within this document to maintain consistency with the terminology used within ISO/IEC 17021-1:2015 Conformity assessment – Requirements for bodies providing audit and certification of management systems.

The audit cycle of a quality management system for sterile medical device should include a comprehensive assessment of the control of the device sterility, generally during the initial/recertification audit. The surveillance audit, in the absence of changes significantly affecting the control of sterility, may be limited to the verification of the appropriate implementation of the validated process parameters; control and monitoring activities; and final product release. While some auditing activities can be conducted remotely (e.g. review of the sterilization process validation report), remote activities alone cannot effectively ensure the comprehensive control of the device sterilization processes. The outcome of such remote review activities must serve as input to the on-site audit and be incorporated or attached to the MDSAP audit report. The off-site assessment of the controls of the

product sterility should not prevent the on-site audit team from following audit trails, including audit trails necessitating the review of documents that had previously been assessed remotely.

During the course of the audit cycle, all product families and significant processes should be assessed when possible.

The selection of samples during audits in order to obtain evidence of conformity or nonconformity with MDSAP audit criteria can be either statistically based or judgement based. Judgement based sampling using audit trails from one task or process to inform the selection of samples in other tasks or processes is preferred. Where possible, auditors should select samples of records representing all participating MDSAP jurisdictions applicable to the audit.

Initial Audit (Initial Certification Audit)

The "Initial" also known as "Initial Certification" audit consists of a Stage 1 and a Stage 2 audit.

Stage 1 – Documentation review, evaluation of preparedness for Stage 2 audit, etc.

A Stage 1 audit shall be conducted in accordance with Clause 9.3.1.2 of ISO/IEC 17021-1:2015 and all applicable MDSAP Audit Process tasks and regulatory requirements.

From an MDSAP perspective, the primary purposes of a Stage 1 audit are (1) to determine if QMS documentation required by ISO 13485:2016 - Clauses 4.2.1 and other applicable MDSAP documentation requirements have been adequately defined, and documented; (2) to assess the medical device organization's preparedness for a Stage 2 audit; (3) to provide a focus for planning a Stage 2 audit; and, (4) to collect information regarding the scope of the quality management system and other aspects of the medical device organization.

Portions of a Stage 1 audit (e.g. documentation review) may be performed at a site other than the site(s) of the medical device organization seeking initial certification.

The outcome of the Stage 1 audit will assist the MDSAP recognized Auditing Organization in its determination of the readiness of the medical device organization to undergo a Stage 2 audit. The Auditing Organization shall determine how best to accomplish tasks of Stage 1 and Stage 2 with regards to off-site documentation and record review and on-site verifications. Hence portions of a Stage 1 audit (e.g. documentation review) may be performed at a site other than the site(s) of the medical device organization seeking initial certification. In practice it is intended that the Auditing Organization may combine elements of Stage 1 and Stage 2 to allow for a single on-site visit for the initial audit or re-audit of the medical device organization.

Stage 2 – Evaluation of QMS Implementation and Effectiveness

Overview

A Stage 2 audit shall be conducted in accordance with Clause 9.3.1.3 of ISO/IEC 17021-1:2015 and using all applicable MDSAP Audit Process tasks.

The purpose of a Stage 2 audit is to determine if all applicable requirements of ISO 13485:2016 and the relevant regulatory requirements from participating regulatory authorities have been implemented. Stage 2 audit objectives shall specifically include an evaluation of:

- the effectiveness of the medical device organization's QMS incorporating the applicable regulatory requirements;
- product/process related technologies (e.g. injection molding, sterilization);
- adequate product technical documentation in relation to relevant regulatory requirements; and,
- the medical device organization's ability to comply with these requirements.

As part of achieving these objectives, the auditor is to verify that the medical device organization maintains sufficient and reliable objective evidence to demonstrate its devices meet essential principles of safety, performance, and effectiveness and any other regulatory requirement identified in the audit tasks. This verification is to ensure that documentation and records required by the national regulations of the participating Regulatory Authorities are present, current, and complete. The auditor should expect that the documentation and records are maintained to demonstrate continued compliance with regulatory requirements during the post-market phase of the device life-cycle.

A Stage 2 audit shall be performed at all sites that will be recorded on the certificate. (Hence, any sites which are relevant to the medical device organization's quality management system but audited off-site, should not be recorded on the certificate.)

Surveillance Audits

(1st and 2nd Surveillance Audits):

A Surveillance Audit shall be conducted in accordance with Clause 9.6.2.2 of ISO/IEC 17021-1:2015 and clause 9.6.2 of IMDRF/MDSAP WG/N3:2016 and using applicable MDSAP Audit Process tasks.

The purpose of a series of surveillance audits is to assure that all applicable requirements of ISO 13485:2016 and the relevant regulatory requirements from participating regulatory authorities are audited during the cycle of a three year audit program for the medical device organization. Surveillance audit objectives during the audit cycle shall specifically include evaluation of:

- the effectiveness of the medical device organization's QMS incorporating the applicable regulatory requirements.
- the medical device organization's ability to comply with these requirements; and
- new or changed product/process related technologies; and,

- new or amended product technical documentation in relation to relevant regulatory requirements.

In addition, surveillance audits shall include a review of issues related to medical device safety and effectiveness since the last audit such as complaints, problem reports, vigilance reports, and recalls/field corrections/advisory notices.

These objectives allow the MDSAP recognized Auditing Organization to maintain confidence that the QMS continues to meet requirements between re-audits (re-certification audits). The auditor should again expect that the documentation and records are maintained to demonstrate continued compliance with regulatory requirements during the post-market phase of the device life-cycle.

Surveillance audits do not require a Stage 1 audit unless significant changes have occurred since the last audit. For example, where there are QMS changes associated with new legislation, or legislative changes, or if otherwise deemed necessary by the Auditing Organization.

Each *individual* surveillance audit in the cycle need not cover all MDSAP requirements. However, as a minimum, each surveillance audit must address the following (as applicable):

a) A review of changes to the medical device organization, their QMS, or their products, since the previous audit

Note: changes may necessitate regulatory submissions

b) The MDSAP Audit Process tasks as listed in the table in Appendix 1 of MDSAP AU P0008 – Audit Time Determination Procedure.

Note: Where there are indicators of existing or potential nonconformities in the data, or other information observed during a surveillance audit that suggest that such nonconformities have not been adequately addressed by the medical device organization's QMS, an audit of the Design and Development Process and/or the Production and Service Controls Process should focus on those indicators of existing or potential nonconformities.

Note: If the first surveillance audit includes the Design and Development Process, the second surveillance should include the Production and Service Controls Process (or vice-versa) unless further indicators of existing or potential nonconformities dictate otherwise.

c) Confirmation that the medical device organization has arrangements in place to maintain the currency of the technical documentation for all devices (see **Annex 1**).

d) The use of marks and references to certification.

Guidance on the selection of samples of data for the audit of the processes in a) and b) above is provided within the relevant tasks of those MDSAP Audit Processes. The selection should be limited to the data that is relevant to the processes in a) and b) above.

Re-audit (Recertification Audits)

A Re-audit (Recertification Audit) shall be conducted in accordance with Clause 9.6.3 of ISO/IEC 17021-1:2015 and using all applicable MDSAP Audit Process tasks.

The purpose of a re-audit is to confirm the continued relevance, applicability and suitability of the medical device organization's QMS (as a whole), to satisfy all applicable requirements of ISO 13485:2016 and the relevant regulatory requirements from participating regulatory authorities, with respect to the scope of certification. Recertification audit objectives shall specifically include evaluation of:

- the effectiveness of the medical device organization's QMS incorporating the applicable regulatory requirements
- product/process related technologies (e.g. injection molding, sterilization)
- adequate product technical documentation in relation to relevant regulatory requirements
- the medical device organization's continued fulfillment of these requirements.

Re-audits do not require a Stage 1 audit unless significant changes have occurred since the last audit. For example, where there are QMS changes associated with new legislation or legislative changes, or if otherwise deemed necessary by the Auditing Organization. If there have been significant changes to the QMS, Auditing Organizations shall review the documentation that implements those changes in accordance with Clause 9.6.3.1.3 of 17021-1:2015. Re-audits may be shorter than initial audits through selective and focused sampling.

As part of achieving the objectives for a Re-Audit, an auditor shall verify the requirements of ISO/IEC 17021-1:2015 Clause 9.6.3.2.1, and the following, where applicable:

- A review of the MDSAP audit reports for the current audit cycle. That is, those prepared since the initial audit or previous re-audit
- A review of changes to the medical device organization, QMS, or products since the previous surveillance audit
- A follow-up of corrections and/or corrective actions stemming from the findings of the previous MDSAP audit, of any kind
- A review of the effectiveness and suitability of the medical device organization's QMS over the current audit cycle
- All applicable MDSAP Audit Process tasks.

The audit of the processes and the sampling should focus on the following (based on risk):

- new or modified designs and new products
- previously identified potential and existing nonconformities
- new or modified processes
- areas not sufficiently covered during the surveillance period.

During a recertification audit, the Auditing Organization shall audit all sites that are recorded on the certificate. (Hence any sites which are relevant to the medical device organization's quality management system but audited off-site, should not be recorded on the certificate)

Special Audits

Special audits are extraordinary audits in that they are not part of the planned audit cycle. These audits should only be used when necessary and should focus on specific elements of the medical device organization's QMS.

Special audits may include audits conducted in response to an application for the extension to the scope of an existing certification, to determine whether or not the extension can be granted or as short-notice audits conducted to investigate potentially significant complaints, or if specific information provides reasons to suspect serious non-conformities of the devices, or for other reasons.

Short-notice audits may be conducted at the request, and under the direction, of the MDSAP participating regulatory authorities or at the discretion of the Auditing Organization.

Special audits should be conducted in accordance with the applicable requirements of ISO/IEC 17021-1:2015 Clause 9.6.4 as well as any additional requirements of the MDSAP recognized Auditing Organization and/or the MDSAP participating regulatory authorities (where applicable).

Special audits should be used to address, as applicable:

- The need to extend the scope of the audit or certification of the medical device organization to include new or modified products between regularly programmed audits
- A shortfall in oversight by the MDSAP recognized Auditing Organization. For example, due to insufficient audit time, inappropriate audit team constitution, etc.
- To follow up on specific post-market issues. For example, for potentially significant complaint.
- To follow up on significant findings from a previous MDSAP audit
- At the request of an MDSAP participating regulatory authority (based on a specific assignment)
- To conduct supplier audits as dictated by regulatory authority or Auditing Organization policy.

Overview

An Auditing Organization that performs a special audit at the request of the recognizing Regulatory Authority(s) shall submit the audit report to the recognizing Regulatory Authority(s) within 15 days from the last day of the audit.

Unannounced Audits

Another type of Special Audit is the unannounced audit. The MDSAP participating regulatory authorities require Auditing Organizations to conduct unannounced audits in circumstances where high grade non-conformities have been detected. See IMDRF/MDSAP WG/N3 Final: 2016 (2nd Ed) for criteria.

Audits Conducted by Regulatory Authorities

Audits may also be conducted by MDSAP participating regulatory authorities at any time and for a range of reasons *including* (1) "For Cause" due to information obtained by the regulatory authority, (2) as follow up to the findings of a previous audit, and (3) to confirm the effective implementation of MDSAP requirements by MDSAP recognized auditing organizations.

The purpose of audits conducted by regulatory authorities is to ensure appropriate oversight of a recognized MDSAP Auditing Organization's audit activities, as an alternative means of assessing medical device organizations that have been identified as undertaking high risk manufacturing processes and have not been adequately audited, where sufficient detail regarding audited processes has not been included in an audit report, or where there is a history of low compliance with QMS or regulatory requirements.

Chapter 1 - Management

The intent of the Management Process is to provide adequate resources for device design, manufacturing, quality assurance, distribution, installation, and servicing activities; to assure the quality management system is functioning properly and effectively; and to monitor the quality management system and make necessary adjustments. A quality management system that has been implemented effectively and is monitored to identify and address existing and potential problems is more likely to produce medical devices that function as intended.

The management representative is responsible for ensuring that the requirements of the quality management system have been effectively defined, documented, implemented, and maintained. Prior to the audit of a process, it may be helpful to interview the management representative (or designee) to obtain an overview of the process and a feel for management's knowledge and understanding of the process.

The Management process is the first process to be audited per the MDSAP audit sequence.

Auditing the Management Process

Purpose: The purpose of auditing the Management process is to verify top management ensures an adequate and effective quality management system has been established and maintained. The management processes should be re-evaluated at the end of the audit to determine whether top management has demonstrated the necessary commitment for an effective quality management system that has been communicated to personnel.

Outcomes: As a result of the audit of the Management process, objective evidence will show whether the medical device organization has:

A) Identified processes needed for the quality management system, their application throughout the medical device organization, and their sequence and interaction
B) Defined, documented, and implemented procedures and instructions to ensure the development and maintenance of an effective quality management system
C) Established quality objectives at relevant functions and levels within the medical device organization consistent with the quality policy and ensured that these are periodically reviewed for continued suitability
D) Determined the criteria and methods needed to ensure the operation and control of quality management system processes, including the identification and management of interrelated processes
E) Committed the appropriate personnel and resources for infrastructure to the quality management system
F) Assigned responsibility and authority to personnel and established the organizational structure to ensure processes assuring quality are not compromised

G) Performed risk management planning and ongoing review of the effectiveness of risk management activities to ensure that policies, procedures and practices are established for analyzing, evaluating and controlling risk
H) Ensured the continued effectiveness of the quality management system and its processes
I) Established a quality management system which is capable of producing devices that are safe, effective and suitable for their intended use.

Links to Other Processes:

Measurement, Analysis and Improvement; **Design and Development**; **Purchasing**; **Production and Service Controls**; **Device Marketing Authorization and Facility Registration**

Task 1 – QMS Planning, Implementation, Changes and Quality Manual

Confirm that quality management system planning is performed to ensure that all required processes are identified, documented, implemented, monitored and maintained in order to conform to the applicable requirements and meet quality objectives.

Verify that changes to the quality management system are managed to maintain the conformity of the quality management system and of the devices produced.

Verify that a quality manual has been documented.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.1.2, 4.1.3, 4.2.2, 4.1.4, 5.4.2;

TGA: TG(MD)R Sch3 P1 1.4(4);

ANVISA: RDC ANVISA 665/2022: Art. 4º, Art. 106

MHLW/PMDA: MHLW MO169: 5-1, 5-2, 5-3, 5-4, 7-1, 14; [Old[3]: 5, 7, 14]

FDA: 21 CFR 820.20

[3] The MHLW MO169 was initially established in order to harmonize the Japanese medical device QMS to ISO13485:2003. The ordinance was revised to be aligned to ISO13485:2016 in 2021 and the transition period is set as 3 years. "Old" in this context means the clause numbers of the old ordinance which is aligned to ISO13485:2003. The MDSAP auditors are required to audit against the old ordinance, when the organization selects it as audit criteria during the transition period.

Additional country-specific requirements

None

Assessing conformity

Quality management system

Medical device organizations are required to establish a quality management system (including quality system procedures and instructions) that is tailored to the regulatory roles assumed by the medical device organization and the medical devices they are manufacturing or designing. The medical device organization's quality management system must properly implement all applicable requirements of Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016), the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Japanese QMS Ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820) and specific requirements of medical device regulatory authorities participating in the MDSAP program, as well as other necessary controls to assure its finished devices, the design and manufacturing processes, and all related activities conform to approved specifications.

Quality system procedures and instructions

The medical device organization may refer to these as Level 1 documents. They are typically high-level, non- product and non-process specific documents and can usually be found in the Quality Manual. These procedures and instructions may contain information on the sequence and interaction of various quality management system processes. It is expected that when the standard specifies that a certain process is required to be documented, it is also required to be established, implemented and maintained. [4] The Quality Manual is to outline the structure of the documentation and to describe the interaction of processes (e.g. the processes for identifying nonconformities and corrections, and the processes for investigating nonconformities to determine root cause and corrective actions).

Quality Management System Planning

Quality planning is concerned with the design and implementation of the quality management system. Such planning typically occurs during the initial development and implementation of a quality system, but also occurs when there are changes in quality policy, quality objectives, QMS and regulatory requirements, or when changes are necessary to for the QMS to continue to be effective. Quality

[4] ISO13485:2016 – Clause 0.2

planning at this level shouldn't be confounded with quality planning as described in clause 7.1 of ISO 13485:2016.

Evidence of quality system planning should at least include documents that identify and record the inputs and outputs of quality system planning. A procedure for quality system planning may also be available.

The inputs to quality planning can include:

- quality policy
- quality objectives
- quality management system standards (e.g. ISO 13485:2016)
- regulatory requirements
- product-specific requirements (e.g. servicing, installation, etc.)
- risk mitigation strategies (e.g. user training)
- required changes (e.g. identified during audits or management review)

The outputs of quality planning can include, amongst others:

- a description of the QMS processes and their inputs, outputs, sequence, and interactions
- the quality manual and associated procedures
- a gap analysis
- identification or resources needed to implement the QMS
- identification of competences and training needed to implement the QMS
- implementation and action plans.

Quality management system planning should also be used when changes to the quality management system are contemplated or required in order to ensure the continuing conformity of the QMS.

Links

Measurement, Analysis and Improvement; **Design and Development**; **Purchasing**; **Production and Service Controls**; **Device Marketing Authorization and Facility Registration**

During the audit, whenever a change is identified, verify that the medical device organization has implemented appropriate change controls.

Task 2 – Management Representative

Confirm top management has documented the appointment of a management representative.

Verify the responsibilities of the management representative include ensuring that quality management system requirements are effectively established and maintained, reporting to top management on the performance of the quality management system, and ensuring the promotion of awareness of regulatory requirements throughout the medical device organization.

Clause and Regulation

ISO: ISO 13485:2016: 5.5.2

TGA: TG(MD)R Sch3 P1 1.4(5)(b)(ii)

ANVISA: RDC ANVISA 665/2022: Art. 9º

MHLW/PMDA: MHLW MO169: 16

FDA: 21 CFR 820.20(b)]

Additional country-specific requirements

None

Assessing conformity

Management representative

It is important to confirm that top management has appointed a management representative and that the responsibilities and authorities of the management representative have been defined, documented, and implemented. The appointment of the management representative must be documented.

Confirm appointment

The medical device organization may document the appointment of a management representative in an organizational chart, Quality Manual, memorandum to file, position description, or other appropriate manner. The appointment of the management representative may be made by name or title.

Evaluate responsibility and authority

Confirm that management has established the management representative's responsibility and authority for ensuring that the quality management system is effectively defined, documented, implemented, and maintained. The management representative must also have responsibility and authority for reporting to top management on the performance of the quality management system.

Confirmation can be accomplished by interviewing the management representative and top management and reviewing the Quality Manual, the management representative's position description, or similar documents.

Other examples

Additional examples of evidence of the management representative's responsibilities and authorities may include:

- Sign-off authority for changes to procedures, processes, designs, etc.
- Authority to act on behalf of top management during the audit
- Authority to place products or processes on hold
- Responsibility for managing quality audit functions
- Responsibility for contributing to corrective and preventive action activities, complaint handling and the handling of nonconforming product, etc.

Training

Where the activities performed personally by the management representative result in a determination of whether product meets requirements, including regulatory requirements, the management representative must be competent to perform such activities. In such cases, verify that training and experience includes the relevant regulatory requirements.

Links

None

Task 3 – Quality Policy and Quality Objectives

Verify that a quality policy and objectives have been set at relevant functions and levels within the medical device organization.

Ensure the quality objectives are measurable and consistent with the quality policy.

Confirm appropriate measures are taken to achieve the quality objectives.

Clause and Regulation

ISO: ISO 13485:2016: 5.3, 5.4.1

TGA: TG(MD)R Sch3 P1 1.4(5)(a)

ANVISA: RDC ANVISA 665/2022: Art. 5º, Art. 6º, Art. 7º

MHLW/PMDA: MHLW MO169: 12, 13

FDA: 21CFR 820.20(a)]

Additional country-specific requirements
None

Assessing conformity
Quality policy
A quality policy is comprised of one or more statements of the medical device organization's intentions and direction with respect to meeting agreed requirements. Top management must establish the quality policy and ensure quality objectives are established that are consistent with the quality policy. Top management must ensure that the quality policy is understood and communicated at all levels of the medical device organization. An assessment of whether the medical device organization's quality system is satisfying the established quality policy and objectives should be a topic addressed during management reviews.

Quality objectives
An effective way of determining whether quality objectives have been implemented is to ask for examples of quality objectives and the status of these objectives. Typically, a quality objective is expressed as a measurable target or goal. An example of a medical device organization's quality objective could be "to have all essential components meet specifications at a defined reliability rate or better."

To accomplish this objective, the medical device organization will have to identify, evaluate, and approve reliable suppliers or bring the manufacturing of that component in-house.

Links
None

Task 4 – Organizational Structure, Responsibility, Authority, Resources
Review the medical device organization's organizational structure and related documents to verify that they include provisions for responsibilities, authorities (e.g., management representative), personnel, resources for infrastructure, competencies, and training to ensure that personnel have the necessary competence to design and manufacture devices in accordance with the planned arrangements and applicable regulatory requirements.

Clause and Regulation
ISO: ISO 13485:2016: 5.1, 5.5.1, 5.5.2, 6.1, 6.2

TGA: TG(MD)R Sch3 P1 1.4(5)(b)

ANVISA: RDC ANVISA 665/2022: Art. 8º, Art. 13, Art. 14, Art. 15; Art. 16, Art. 17

MHLW/PMDA: MHLW MO169: 10, 15, 16, 21, 22, 23

FDA: 21 CFR 820.20(b), 820.25]

Additional country-specific requirements

None

Assessing conformity

Responsibility and authority

Methods for completing this audit task include reviewing the organizational chart(s) and asking authority and responsibility questions. The responsibilities and authorities of various individuals within the medical device organization are also typically described within the Quality Manual, position descriptions, and job postings.

Resources

Top management is responsible for ensuring that resources necessary to maintain an effective quality management system are provided. Resources include money, equipment, supplies, and personnel. One method for confirming that adequate resources are made available is to ask the management representative to provide several examples of recent requests for different types of resources and describe the outcomes of these requests.

Links

None

Task 5 - Extent of Outsourcing

Determine the extent of outsourcing of processes that may affect the conformity of product with specified requirements and verify the proper documentation of controls in the quality management system.

Verify the list of critical suppliers is current and accurate.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.5, 4.2.1

TGA: TG (MD)R Sch3 P1 1.4(5) (b)(iii), (d)(ii)

ANVISA: RDC ANVISA 665/2022: Art. 21, Art. 22, Art. 23, Art. 24

MHLW/PMDA: MHLW MO169: 5-5, 6; [Old: 5, 6]

FDA: 21 CFR 820.50

Additional country-specific requirements

Australia (TGA):
The conditions of marketing authorization (ARTG inclusion) require that Australian Sponsors undertake some regulatory activities including; customer complaint handling (Act s 41FN, Reg 5.8), the management and communication of technical files /technical documentation (Act s 41FN(3)), adverse event reporting (Act s 41FN, Reg 5.7), conducting recalls (Part 4-9), ensuring that the name and address of the Sponsor is provided with the device (Reg 10.2), the storage of devices (Act s 41FN,Reg 5.9), the keeping of complaint and distribution records (Act s 41FN,Reg 5.10), annual reporting for an initial period of three years, of specified information to the TGA (ACT s41FN, Reg 5.11) for Class AIMD, Class III and Class IIb devices that are implantable, information about supply of specified IVDs (Act s41FN, Reg 5.12), ensuring that some devices that would contravene Part 2 of the Poisons standards are not supplied.

Some Sponsors also provide services for the installation and servicing of a device on behalf of the Manufacturer and consequently are to be treated as a supplier to the Manufacturer.

Where a regulatory requirement for a Sponsor intersects with a regulatory requirement or a requirement of ISO13485 for the Manufacturer, the activity is to be treated as an outsourced activity and documented in the Manufacturer's QMS. See also Task 5 Purchasing.

The requirement of Regulation 10.2 for "ensuring that the name and address of the Sponsor is provided with the device in such a way that the user of the device can readily identify the Sponsor" is only an obligation on the Sponsor. This activity does not need to be included in the Manufacturer's QMS documentation however the arrangements for the provision of this information should be disclosed in the written agreement between the Manufacturer and the Sponsor. In cases where an activity performed by the Sponsor also includes the provision of information required by Essential Principle 13 (Labels and IFU), or 13A (patient implant cards and leaflets), the Manufacturer must treat the Sponsor as supplier for that activity.

The Sponsor does not need to be treated as a supplier if the scope of the Manufacturer's quality management system includes the site and activities of the Sponsor. The oversight of activities that are required by legislation to be conducted by the Sponsors are to be clearly documented in the QMS and included in plans for internal audit.

Canada (HC):
Verify that the roles and responsibilities of any regulatory correspondents, importers, distributors, or providers of a service are clearly documented in the medical device organization's quality management system and are qualified as suppliers and controlled, as appropriate.

Assessing conformity

Outsourcing
Most organizations outsource at least some products (including services) that affect the ability of the medical device to conform to specified requirements. Some organizations outsource the majority of products. During interview of the management representative, ascertain the extent to which the medical device organization outsources processes essential for the proper functioning of the finished medical device. Process performance and product conformity, including the performance of supplied product, must be included in management review. The medical device organization must ensure control over outsourced products and processes that affect product conformance with specified requirements.

Links

Purchasing

During audit of the medical device organization's purchasing process, ensure that management has assured the appropriate level of control over suppliers, including an assessment of the relationship between supplied products and product risk.

Task 6 – Personnel Competency and Training

Confirm the medical device organization has determined the necessary competencies for personnel performing work affecting product quality, provided appropriate training, and made personnel aware of the relevance and importance of their activities on product quality and achievement of the quality objectives.

Ensure records of training and competencies are maintained.

Clause and Regulation
ISO: ISO 13485:2016: 4.2.1, 6.2

ANVISA: RDC ANVISA 665/2022: Art. 8°, Art. 13, Art. 14, Art. 15

MHLW/PMDA: MO169: 6, 22, 23

FDA: 21 CFR 820.20(b)(2), 820.25

Additional country-specific requirements

Brazil (ANVISA):
Confirm that the manufacturer ensures that any consultant who gives advice regarding design, purchasing, manufacturing, packaging, labeling, storage, installation, or servicing of medical devices has proper qualification to perform such tasks. Those consultants shall be contracted as a formal service supplier, according to purchasing controls defined by the manufacturer [RDC ANVISA 665/2022: Art. 16, Art. 17].

Assessing conformity

Training
A review of employee training records can be performed to ensure that employees have been trained regarding the medical device organization's quality policy and objectives. In particular, this should be done for employees involved in key operations that affect product realization and product quality.

During the audit of the Production and Service Controls process, ensure that employees who are involved in key operations that affect product realization and product quality have been trained in their specific job tasks, as well as the quality policy and objectives.

When appropriate, review the training records for those employees whose activities have contributed to process nonconformities.

Links

Production and Service Controls

Task 7 – Risk Management Planning and Review

Verify that management has committed to and has responsibility for overall risk management planning, including ongoing review of the effectiveness of risk management activities ensuring that policies, procedures and practices are established and documented for analyzing, evaluating and controlling product risk throughout product realization.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.2 (b), 7.1

TGA: TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20

MHLW/PMDA: MO169: 5-2.1.2, 26; [Old: 26]

FDA: 21 CFR 820.30(g)

Additional country-specific requirements

None

Assessing conformity

Commitment to risk management

Confirm that top management has shown commitment to the risk management process by ensuring the provision of adequate resources and the assignment of qualified personnel for risk management activities. Risk-based decisions occur throughout the various quality management system processes. Top management is responsible for defining and documenting the policy for determining criteria for risk acceptability. Additionally, ensure top management reviews the suitability of the risk management process. This review may be part of the management review. Previously unidentified risks discovered during production and post-production of the medical device may indicate a need to improve the risk management process. Each medical device organization must decide how much risk is acceptable.

When appropriate, assess the role of top management when risk-based decisions are made that appear to justify levels of risk that do not meet the medical device organization's previously established risk- acceptance criteria.

Risk management usually starts in conjunction with the design and development planning process, at a point in the development when the results of risk analysis can affect the design process. During audit of the Design and Development process, evaluate top management's commitment to risk management activities. Evidence of commitment to risk management may include the implementation of new or more stringent controls in response to changes in the likelihood or severity of a hazard occurring, external controls (e.g. additional supplier-related controls), or design changes to maintain an acceptable level of product risk.

Links

Design and Development

Task 8 – Document and Record Controls

Verify that procedures have been defined, documented, and implemented for the control of documents and records of both internal and external origin required by the quality management system.

Confirm the medical device organization retains records and at least one obsolete copy of controlled documents for a period of time at least equivalent to the lifetime of the device, but not less than two years from the date of product release.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.4, 4.2.1, 4.2.4, 4.2.5

TGA: TG(MD)R Sch3 P1 1.4(4)

ANVISA: RDC ANVISA 665/2022: Art. 28, Art. 29, Art. 30, Art. 31, Art. 34, Art. 36, Art. 37

MHLW/PMDA: MO169: 5-4, 6, 8, 9; [Old: 5, 6, 8, 9]

FDA: 21 CFR 820.40, 820.180]

Additional country-specific requirements

Australia (TGA):

Confirm that Quality Management System documentation and records in relation to a device described in TG(MD)R Sch3 P1 1.9 are retained by the Manufacturer for at least 5 years.

Note that the conditions of marketing authorization (ARTG inclusion) require Australian sponsors of Class III/AIMD, implantable Class IIb or Class 4 IVDs to keep records of distribution, and records of information relating to; any malfunction or deterioration in the characteristics or performance of a device, or any inadequacy in the design, manufacture, labelling, instructions for use or advertising materials of a device, or any use in accordance with, or contrary to, the use intended by the manufacturer of a device, that has led to any complaint or problem in relation to the device, for a period of up to 10 years. (Reg 5.10)

These requirements should be reflected in the written agreement between the Australian Sponsor and Manufacturer and may also be identified in the Manufacturer's procedures.

Brazil (ANVISA):

Verify that change records include a description of the change, identification of the affected documents, the signature of the approving individual(s), the approval date, and when the change becomes effective [RDC ANVISA 665/2022: Art. 32].

Confirm that the manufacturer maintains a master list of the approved and effective documents [RDC ANVISA 665/2022: Art. 33].

Verify that electronic records and documents have backups [RDC ANVISA 665/2022: Art. 35].

Japan (MHLW):
Confirm that Quality Management System documentation and records in relation to a device are retained for the following periods (5 years for training records and documentation). [MHLW MO169: 8, 9, 67, 68]. (1) 15 years for 'specially designated maintenance control required medical devices' [or one year plus the shelf life for products when the shelf life or the expiry date (hereinafter simply referred to as the "shelf life") plus one year exceeds 15 years]. (2) 5 years for the products other than the 'specially designated maintenance control required medical devices' (or one year plus the shelf life for the products of which the shelf life plus one year exceeds 5 years).

> **Note:** The 'specially designated maintenance control required medical device' is defined as below in PMD Act 2.8:

A medical device designated by the Minister of Health, Labour and Welfare after hearing the opinion of the Pharmaceutical Affairs and Food Sanitation Council as those whose potential risk to the diagnosis, treatment or prevention of disease is significant without proper control since this kind of equipment requires expert knowledge and skill in examination for maintenance and inspection, repair and other management.

United States (FDA):
Verify that electronic records and documents have backups [21 CFR 820.180].

Assessing conformity

Implementation of document and record control procedures
Confirm that the medical device organization has defined, documented, and implemented procedures for control of quality management system documents and records. Evidence that these controls are effective can be ascertained through the audit of the other quality management system processes. For example, evidence that the document controls process is ineffective might be the observation of obsolete procedures being used or required records being unavailable.

Ensure at least one copy of obsolete controlled documents is maintained.

Links
None

Task 9 – Management Reviews

Verify that procedures for management review have been documented, management reviews are being conducted at planned intervals and that they include a review of the suitability and effectiveness of the quality policy, quality objectives, and quality management system to assure that the quality management system meets all applicable regulatory requirements.

Clause and Regulation

ISO: ISO 13485:2016: 5.6

TGA: TG(MD)R Sch3 P1 1.4(5)(b)(iii)(f)

ANVISA: RDC ANVISA 665/2022: Art. 10, Art. 11, Art. 12

MHLW/PMDA: MO169: 18, 19, 20

21 CFR820.20(c)]

Additional country-specific requirements

None

Assessing conformity

Verify implementation of management review procedures

It is important to verify that the medical device organization has documented and implemented effective management review procedures. Top management must review the suitability, adequacy and effectiveness of the medical device organization's quality management system at defined intervals and with sufficient frequency to ensure that the quality management system satisfies applicable requirements of Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Japanese QMS Ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820) and specific requirements of medical device regulatory authorities participating in the MDSAP program, in addition to the medical device organization's own established quality policy and objectives. The dates and results of the management reviews must be documented. These documentation requirements must be included in the management review procedure.

Other requirements commonly seen in management review procedures include a fixed agenda of topics to be discussed (with flexibility for unique agenda items to be added), the necessary attendees who are to participate in the management review, and how action items resulting from the management review are to be addressed and input into the Measurement, Analysis and Improvement process when necessary. Ensure that the quality policy and objectives have been reviewed for

continued suitability and that any changes to regulatory requirements have been identified. Other inputs to management review include results of internal and external audits, customer feedback, process performance and product conformity, status of preventive and corrective actions, follow-up actions from previous management reviews, changes that could affect the quality management system, and recommendations for improvement.

During audit of the Measurement, Analysis and Improvement process, confirm when necessary that action items resulting from Management review are considered for corrective or preventive action.

Links

Measurement, Analysis and Improvement

Task 10 – Distribution of Devices with Appropriate Marketing Authorization

Confirm that the medical device organization has defined and implemented controls to ensure that only devices that have received the appropriate marketing authorization are distributed or otherwise offered for commercial distribution into the applicable markets.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.2.1, 5.2, 7.2.1, 7.2.3

Additional country-specific requirements

None

Assessing conformity

Responsibilities and authorities of personnel

During the audit of the Management process, verify that the medical device organization has identified and documented the responsibilities of employees and personnel for ensuring proper registration, listing, licensing, notification and approval information is accurately submitted to regulatory authorities or authorized representatives (e.g. Australian Sponsor) participating in the MDSAP.

Verify that the medical device organization has identified and documented the responsibilities and authorities of personnel who are responsible for implementing controls to ensure that devices are only distributed in participating MDSAP jurisdictions where market authorizations have been obtained.

Verify that these obligations are being carried out by competent personnel.

Controls to ensure appropriate market authorization

Verify that the medical device organization has identified, documented, and implemented controls to ensure that only devices that have received market authorization are released for distribution, or otherwise offered for commercial distribution, into participating MDSAP jurisdictions where the medical device organization intends to supply the product.

Controls can include, but are not limited to:

- Change control processes that ensure that changes are assessed for their impact on existing marketing authorizations
- Procedures and/or work instructions that clearly identify the jurisdictions in which products can be sold
- Separate part numbers for devices, by jurisdictions
- Review of purchase orders to assure the customer requests and receives only product with the appropriate market clearance
- Review of sales and marketing practices and materials (including internet pages) to assure product is promoted only for markets where the product maintains appropriate market clearance
- Segregation of finished devices in warehousing and shipping areas, by jurisdictions
- Business rules in software to prevent the acceptance of purchase orders where marketing authorization is absent
- Specific language in distribution agreements limiting devices that can be distributed in certain jurisdictions
- Jurisdiction-specific marketing materials (catalogues, websites, etc.)
- The availability of accurate information on marketing authorizations obtained by jurisdiction.

The effectiveness of these controls can be verified by, for example:

- Interviewing sales and customer-support personnel
- Interviewing personnel in shipping and distribution
- Challenging sales / ERP software
- Reviewing distribution agreements
- Reviewing marketing material
- Reviewing distribution records and/or DHR records against lists of valid market authorizations.

The verification of the effectiveness of these controls should be specific to the device identifier(s) (e.g. model number) as listed in the marketing authorization(s). A broad sample covering many products and jurisdictions should be selected, particularly when reviewing distribution records.

In order to prepare for this audit task, audit teams should ensure that they have current lists of market authorizations held by the medical device organization as well as the names of all authorized representatives in the MDSAP jurisdictions prior to coming on site.

The appropriate application of registration, listing, licensing, notification and approval processes, and the accuracy of information for Device Marketing Authorization for submission to Regulatory Authorities or authorized representatives (e.g. Australian Sponsor) participating in the MDSAP will be verified under the Device Marketing Authorization and Facility Registration process. A preliminary review of device marketing authorization and facility registration may be made during the audit of the Management process, followed by comprehensive coverage for specific medical devices selected for review under the Design and Development process.

Links

Device Marketing Authorization and Facility Registration

Task 11 – Top Management Commitment to Quality

At the conclusion of the audit, a decision should be made as to whether top management has demonstrated the necessary commitment to ensure a suitable and effective quality management system is in place and being maintained and whether the effectiveness of the system has been communicated to personnel.

Clause and Regulation

ISO: ISO 13485:2016:4.1.1, 4.1.4, 5.1, 5.5.3

ANVISA: RDC ANVISA 665/2022: Art. 4°, Art. 5°, Art. 6°, Art. 7°

MHLW/PMDA: MO169: 5-1, 5-4, 10, 17; [Old: 5, 10, 17]

FDA: 21 CFR 820.20(a), 820.5]

Additional country-specific requirements

None

Assessing conformity

Audit the other processes

During the audit of the other MDSAP processes, the audit team will have the opportunity to assess whether management is appropriately carrying out its responsibilities; whether the quality policy is understood, implemented, and maintained at all levels of the medical device organization; if the

necessary resources are being provided to maintain an effective quality management system; if the management representative has the necessary responsibilities and authorities; the adequacy of the organizational structure; and whether management reviews and quality audits are effective, etc.

Remember that a quality management system that has been implemented effectively, monitored to identify and address existing and potential problems, and has an integrated risk management process utilizing risk-based decision-making is more likely to produce medical devices that function as intended.

Links

None

Chapter 2 - Device Marketing Authorization and Facility Registration

The Device Marketing Authorization and Facility Registration process may be audited as a linkage from the Management process and/or the Design and Development process.

Auditing the Device Marketing Authorization and Facility Registration Process

Purpose: The purpose of auditing the Device Marketing Authorization and Facility Registration process is to verify that the medical device organization has performed the appropriate activities regarding device marketing authorization and facility registration with regulatory authorities participating in the MDSAP.

Outcomes: As a result of the audit of the Device Marketing Authorization and Facility Registration process, objective evidence will show whether the medical device organization has:

A) Complied with requirements to register and/or license device facilities
B) Submitted device listing information to regulatory authorities when applicable
C) Obtained device marketing authorization in the appropriate jurisdictions
D) Arranged for assessment of changes (where applicable) and obtained marketing authorization for changes to devices or the quality management system which require amendment to existing marketing authorization

Links to Other Processes:

Management; **Design and Development**

Task 1 – Submission for Device Marketing Authorization and Facility Registration

Verify the medical device organization has complied with regulatory requirements to register and/or license device facilities and submit device listing information in the appropriate jurisdictions where the medical device organization markets or distributes their devices.

Assessing conformity

In some jurisdictions, Device Market Authorization is the responsibility of the importer / Marketing Authorization Holder / Sponsor. Market Authorization however may only be appropriate if the medical

device organization and importer fulfil obligations that have been placed upon them by the relevant legislation, including obligations to each other (e.g. communications concerning feedback, adverse event reporting and the management of advisory notices and recalls).

Prior to an audit, an Auditing Organization shall independently investigate the identity and range of products, facilities and importers (e.g. Importer, MAH, Sponsor, etc.) that are known to the Regulatory Authority of each jurisdiction where the medical device organization intends to supply product.

Verify at audit, or prior to audit, that the regulatory requirements to register and/or license device facilities and submit device listing information have been appropriately applied by the Medical Device Organization for **each** Medical Device Organization / Importer arrangement. Note that some importers / MAHs / Sponsors may have provided information to Regulatory Authorities indicating that a medical device organization is the "legal manufacturer" even though the medical device organization inappropriately considers themselves to be an Original Equipment Manufacturer or an Original Device Manufacturer. A review of labelling for product being supplied to a particular jurisdiction may assist with determining if appropriate market authorization processes have been applied.

Special attention should be paid to instances where products are being marketed to MDSAP jurisdictions that marketing authorization has not been granted. This may be evident through audit of other processes, such as Design and Development.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.2.1, 5.2, 7.2.1, 7.2.3

Country specific requirements

Australia (TGA):

Manufacturer of a medical device is the person who is responsible for the design, production, packaging and labeling of the device before it is supplied under the person's name, whether or not it is the person, or another person acting on the person's behalf, who carries out those operations. A manufacturer of a medical device is also the person who, with a view to supplying the device under a person's name, does one or more of the following using ready made products: assembles, packages, processes, refurbishes, labels the device, or assigns a different intended purpose through the use of labels, instructions for use, advertising, or technical documentation (TG Act s41BG).

Australian importers (Sponsors) are required to include (register) medical devices from non-Australian Manufacturers in the Australian Register of Therapeutic Goods (ARTG). Sponsors are required to register the Manufacturers that they represent and to obtain a Client ID and Location ID for the manufacturer from the TGA.

Chapter 2 - Device Marketing Authorization and Facility Registration

Task 1 – Submission for Device Marketing Authorization and Facility Registration

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To assist the Australian Sponsor, Manufacturers, who are supplying product to the Australian market and choose to participate in the MDSAP, must undertake the following to demonstrate that they have met the obligations on Manufacturers [TG Act s41DA(1)] who wish to supply to Australia;

- Classify the device using the Australian classification rules
- Identify from the Therapeutic Goods (Medical Devices) Regulation 2002, an Australian conformity assessment procedure that is to be applied in accordance with the classification of the device
- Select a relevant GMDN term and advise the Sponsor.
- Obtain an MDSAP audit of their QMS and their device technical documentation in accordance with this Audit Approach, for demonstrating that the QMS requirements of the selected conformity assessment procedure have been applied.
- Prepare an Australian Declaration of Conformity in accordance with the requirements of the Conformity Assessment Procedure that has been applied [TG(MD)R Sch 3 P1 Cl1.8].
- Enter into a written agreement with the Sponsor. See **Annex 4** for guidance on the roles and responsibilities of the Australian Sponsor and an Overseas Manufacturer

  Note: If the manufacturer chooses to participate in the MDSAP for any reason, and product is supplied to the Australian market, the requirements for QMS in a relevant conformity assessment procedure must be included with the scope of the audit performed by a recognized MDSAP auditing organization.

  Note: Sponsors are required to provide the Manufacturer with information in relation to the Manufacturer's obligations under a conformity assessment procedure and information in relation to whether the devices comply with the Essential Principles [TG Act 41FN(3)(e)].

Refer to following:

Therapeutic Goods Act 1989

- Part 4-2 – Essential Principles and medical device standards
- Part 4-3 – Conformity Assessment Procedures
- Part 4-5 – Including medical devices in the Register
- Part 4-9 – Public Notification and recall of medical devices
- Chapter 5 - Advertising

Therapeutic Goods (Medical Devices) Regulations 2002

- Part 5 – Division 5.2 - Conditions
- Schedule 1 – Essential Principles
- Schedule 2 – Classification Rules
- Schedule 3 – Conformity Assessment Procedures

Brazil (ANVISA):
Manufacturer means any person who designs, manufactures, assembles or processes finished devices, including those who only perform sterilization process, labeling and packaging [RDC ANVISA 665/2022: Art. 3°, section IX].

For a domestic manufacturer, confirm that the establishment has ANVISA's authorization to manufacture medical devices (AFE - Autorização de Funcionamento da Empresa). For domestic and international manufacturers, verify that the products already distributed in the Brazilian market are registered/notified with ANVISA [Brazilian Federal Law nº 6360/76].

According to Brazilian Legislation, the Good Manufacturing Practice (GMP) certification is a prerequisite for medical device registration. Therefore, the facility site inspection precedes the device registration request. Medical devices subject to notification do not need the GMP certificate, but even not being certified, their manufacturers shall comply with the GMP requirements.

Medical devices registration/notification

Device marketing authorization shall be requested to ANVISA by the domestic manufacturer or importer (legal representative) formally established in Brazil. Registration is a comprehensive process for market authorization, applied to medical devices in classes III and IV. [ANVISA RDC nº 36/2015, RDC nº 40/2015]

Notification is a simplified market authorization process, applied to all medical device classes I and II. [ANVISA RDC nº 36/2015, RDC nº 40/2015]. Registration is valid for 10 years, while notification has no expiry date. Renewal of the registration shall be requested upon time defined at Brazilian Law 6360/1976.

Establishment license

Domestic manufacturer: shall be authorized by ANVISA, at a minimum, as a manufacturer of medical devices. This license includes authorization to store and distribute medical devices.

Importer: the importer is considered the legal representative of the international manufacturer in Brazil and shall be authorized by ANVISA to import, store, and distribute medical devices. In the case of outsourcing the storage, the importer does not need authorization for this activity.

Canada (HC):
Manufacturer means a person who sells a medical device under their own name, or under a trade-mark, design, trade name or other name or mark owned or controlled by the person, and who is responsible for designing, manufacturing, assembling, processing, labeling, packaging, refurbishing or

modifying the device, or for assigning to it a purpose, whether those tasks are performed by that person or on their behalf [CMDR 1].

No person shall import or sell a Class II, III or IV medical device unless the manufacturer of the device holds a license in respect of that device or, if the medical device has been subjected to a change described in section 34, an amended medical device license [CMDR 26].

An application for a medical device license shall be submitted to the Minister by the manufacturer of the medical device in a format established by the Minister [CMDR 32].

An application for a medical device license shall include a copy of a quality management system certificate certifying that the quality management system under which the medical device is manufactured (class II) or designed and manufacturer (class III or IV) satisfies National Standard of Canada CAN/CSA-ISO 13485:2016. [CMDR 32(2)(f); 32(3)(j); 32(4)(p)].

Japan (MHLW):
"Marketing Authorization Holder" means a person who resides in Japan and is granted a license for marketing from a prefectural government [PMD Act 23-2.1].

Application or Notification for marketing

Class 2, class 3, and class 4 medical devices except for the ones specified by the requirement of PMD Act 23-2-23.1.

An" Application for Marketing Approval" shall be submitted to PMDA by the Marketing Authorization Holder to get authorization for marketing a medical device in Japan. [PMD Act 23-2-5.1]

An "Application for QMS Audit" shall also be submitted to PMDA by the Marketing Authorization Holder, when they do not have an effective QMS Certificate for the device. [PMD Act 23-2-5.6, 7]

Class 2 and class 3 medical devices which are specified by the requirement of PMD Act 23-2-23.1

An" Application for Marketing Certification" shall be submitted to a Registered Certification Body (RCB) by the Marketing Authorization Holder to get authorization for marketing a medical device in Japan. [PMD Act 23-2-23.1].

An "Application for QMS Audit" shall also be submitted to an RCB by the person, when the person does not have a valid QMS Certificate for the device. [PMD Act 23-2-23.3, 4].

Class 1 medical device

A "Notification for Marketing" shall be submitted to PMDA by the Marketing Authorization Holder for marketing a class 1 device in Japan [PMD Act 23-2-12].

A class 1 medical device doesn't need any QMS Certificate for marketing.

Facility Registration (Registered Manufacturing Site)

A medical device manufacturing site which conducts one of the designated manufacturing processes listed below shall be registered:

- Main Designing
- Main assembly
- Sterilization
- Domestic storage before final release.

The site is called "Registered Manufacturing Site". It has to submit an application to PMDA for registration by itself [PMD Act 23-2-3.1, 23-2-4].

United States (FDA):
21 CFR 807 - Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices.

Establishment means a place of business under one management at one general physical location at which a device is manufactured, assembled, or otherwise processed.

Owner or operator means the corporation, subsidiary, affiliated company, partnership, or proprietor directly responsible for the activities of the registering establishment.

Owner or operator must register the establishment and submit listing information to Food and Drug Administration (FDA) for those devices in commercial distribution, regardless of classification.

The registration and listing requirements must pertain to any person who:

- Initiates or develops specifications for a device that is to be manufactured by a second party for commercial distribution by the person initiating specifications
- Manufactures for commercial distribution a device either for itself or for another person; regardless of whether the manufacturer places the device into commercial distribution or returns the device to the customer
- Repackages or relabels a device
- Acts as an initial importer, except that initial importers may fulfill their listing obligation for any device for which they did not initiate or develop the specifications for the device or repackage or relabel the device by submitting the name and address of the manufacturer
- Manufactures components or accessories which are ready to be used for any intended health-related purpose and are packaged or labeled for commercial distribution for such purpose

- Sterilizes or otherwise makes a device for or on behalf of a specification developer or any other person
- Acts as a complaint file establishment
- Is a device establishment located in a foreign trade zone.

Links

Management

During audit of the Management process, confirm that management is aware of and has made arrangements for device marketing authorization and facility registration.

Task 2 – Evidence of Marketing Clearance or Approval

Confirm the medical device organization has received appropriate marketing clearance or approval in the regulatory jurisdictions where the medical device organization markets their devices.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.2.1, 5.2, 7.2.1, 7.2.3

Country specific requirements

Australia (TGA):

Marketing authorization (inclusion in the Australian Register of Therapeutic Goods [ARTG]) is granted to the Australian Sponsor. The Sponsor cannot apply for marketing authorization until the Manufacturer has completed a conformity assessment procedure that is relevant for the Class of the device. Non-Australian Manufacturers will need to assist the Sponsor through the provision of information to support an application for marketing authorization and to meet the relevant conditions for on-going supply. A Sponsor is provided with a Certificate of Inclusion in the ARTG to identify the products that have been granted marketing authorization. Products with marketing authorization may be identified from the public facing ARTG database.

A Sponsor is not normally permitted to import, supply, export, or manufacture (in Australia) a medical device unless; the device complies with the essential principles, the Manufacturer has applied a relevant conformity assessment procedure, and the Sponsor has included the device in the ARTG. An exemption to allow importation and supply may be approved and granted to the Sponsor by the TGA, in cases where the TGA is satisfied that the device is to be used under a clinical trial scheme or the special access or authorized prescriber schemes. An exemption approval may contain conditions in

relation to the manufacture of the product. The Manufacturer should verify with the Australian Sponsor if any such conditions have been applied to the exemption approval.

A Manufacturer must maintain a list of their Australian Sponsors and the products those Sponsors have included in the Australian Register of Therapeutic Goods.

A Manufacturer's procedures should ensure that product is not released for supply to the Australian market unless the Sponsor has been issued with a "Certificate of Inclusion in the Australian Register of Therapeutic Goods", that identifies each kind of medical device that has been approved for supply to the Australian market [TG Act s41FJ], or the Sponsor holds a relevant exemption (TG Act Part 4-7).

As part of an application for marketing authorization a Sponsor commits to certain requirements that are identified in s41FD - "Matters to be certified". These matters include establishing a written agreement with the manufacturer about the provision of information and establishing effective communication channels for post-market activities. See **Annex 4** for further guidance.

Brazil (ANVISA):
In Brazil there are two kinds of marketing clearance, registration and notification:

- Device market clearance shall be requested to ANVISA by the domestic manufacturer or importer (legal representative) formally established in Brazil. Registration is a comprehensive process for market authorization, applied to medical devices in classes III and IV. [ANVISA RDC nº 36/2015, RDC nº 40/2015].
- Notification is a simplified market authorization process, applied to all medical devices classes I and II. [ANVISA RDC nº 36/2015, RDC nº 40/2015] Registration is valid for 10 years, while notifications have no expiry date - renewal of the registration shall be requested upon time defined at Brazilian Law 6360/1976.

Canada (HC):
No person shall import or sell a Class II, III or IV medical device unless the Manufacturer of the device holds a license in respect of that device or, if the medical device has been subjected to a change described in section 34 - an amended medical device license [CMDR 26].

Japan (MHLW):
Any person who intends to market a medical device for business in Japan shall have a license for marketing granted by the prefectural government. This person is called a "Marketing Authorization Holder" (MAH) and shall reside in Japan [PMD Act 23-2.1]. The person has to submit an Application for Marketing Approval/Certification (class 2, 3 or 4 medical device) or a Notification for Marketing (class 1 medical device) to get marketing clearance for the medical device. No person shall market a

medical device in Japan, unless the Marketing Authorization Holder of the device has been granted the marketing clearance [PMD Act 23-2-5.1, 23-2-23.1, 23-2-12].

United States (FDA):

21 CFR 807.81- Premarket Notification:

Each person who is required to register his establishment pursuant to 807.20 must submit a premarket notification submission to the Food and Drug Administration at least 90 days before he proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use which meets any of the following criteria:

- The device is being introduced into commercial distribution for the first time; that is, the device is not of the same type as, or is not substantially equivalent to, (i) a device in commercial distribution before May 28, 1976, or (ii) a device introduced for commercial distribution after May 28, 1976, that has subsequently been reclassified into class I or II.
- The device is being introduced into commercial distribution for the first time by a person required to register.

21 CFR 814 – Premarket Approval

A Premarket approval is required for any FDA class III device that was not on the market (introduced or delivered for introduction into commerce for commercial distribution) before May 28, 1976, and is not substantially equivalent to a device on the market before May 28, 1976, or to a device first marketed on, or after that date, which has been classified into class I or class II.

Links

Management, **Design and Development**

During the audit of the Management and Design and Development processes, ensure that management is aware of requirements for device marketing authorization and facility registration, and that these are considered when designing the device.

Confirm that management obtains marketing authorization in the appropriate jurisdictions prior to commercial distribution of the device.

Task 3 – Notification of Changes to Marketed Devices or to the QMS

Verify the medical device organization has identified changes to marketed devices or the quality management system which require notification to regulatory authorities.

The audit team should pay special attention to situations observed in the audit of the Design and Development process (specifically design changes) that may require notification to the jurisdictions to which the changed devices are marketed.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.2.1, 5.2, 7.2.1, 7.2.3, 7.3.9

Country specific requirements

Australia (TGA):

The Manufacturer is required to notify their auditing organization body of:

- A proposed change to their QMS, including the name of location of the manufacturer
- A proposed change to critical suppliers or the goods and services they provide
- A proposed change to a validated manufacturing process
- A proposed change to the kinds of medical devices to which the system is to be applied
- For Class III or AIMD, a proposed change to the design, intended performance, intended user, packaging, storage or transport conditions of a device.

Changes are to be evaluated by the Auditing Organization to determine whether a special audit is required to verify the continuing integrity of the quality management system, or whether verification of the change may occur at the next routine audit. The Auditing Organization should also verify the continuing adequacy of technical documentation as a result of the change (**see Annex 1**)

If the Manufacturer is a holder of a TGA Conformity Assessment Certificate, then the Manufacturer is also required to notify the TGA of these changes, prior to implementation. For changes that are not considered substantial by the Manufacturer or applicant, they should be notified to the TGA at the time of recertification of an existing conformity assessment certificate, included within the scope of another conformity assessment application, or made available for the auditor during the next on site audit; whichever occurs earlier.

Examples of substantial changes that may require notification to the TGA include, but are not limited to, the following:

- Name and/or address of the Manufacturer
- Scope of existing manufacturing facilities, including manufacturing steps
- Addition or removal of a manufacturing facility along with associated activities
- Critical manufacturing process (e.g. a drug coating process, a sterilization method etc.)
- Critical supplier and/or relevant scope
- Type of conformity assessment procedure
- Device category

- Product design (e.g. materials for medical devices, storage, shelf-life, and packaging)
- Information to be provided with a medical device (e.g. intended purpose of the device in the IFU, removal of warnings, contraindications, or other information regarding safety etc.)

Refer to:

Therapeutic Goods (Medical Devices) Regulations 2002

- Regulation 3.5 – Medical devices manufactured outside Australia
- Schedule 3 - The relevant conformity assessment procedure chosen by the Manufacturer

Note: An entry in the Australian Register of Therapeutic Goods (inclusion) in the name of the Australian Sponsor is in effect until cancelled.

Brazil (ANVISA):
Changes involving medical devices already approved by ANVISA, shall be submitted for a new approval [Brazilian Law nº 6360/76 - Art. 13]. Changes/modifications that shall be submitted are those ones classified as significant change, which affects:

- features of safety and effectiveness, including measures to communicate information (ex. residual risk)
- identification of the device or its manufacturer or manufacturing site
- indication for use, including its purpose, patient type (adult, pediatric, newborn)or environment to be used (domestic, hospital, ambulance, etc.)
- device classification
- technical specification of the device, including composition and other operational/technical/physical features
- manufacturing method.

Examples of modifications that may require a submission include, but are not limited to, the following:

- Sterilization method
- Structural material / composition
- New or additional manufacturer
- Manufacturing method
- Manufacturing site
- Operating parameters or conditions for use
- Patient or user safety features
- Sterile barrier packaging material
- Stability or expiration claims
- Design

- Labels and instructions of use (if modification is regarding information)
- Commercial name
- Indication for use
- New software version
- Commercial presentation
- Inclusion of a new device in a family of medical devices already approved
- Inclusion of new accessories.

Canada (HC):
If the Manufacturer proposes to make one or more changes, the Manufacturer shall submit to the Minister, in a format established by the Minister, an application for a medical device license amendment including the information and documents set out in section 32 that are relevant to the change [CMDR 34].

Every Manufacturer of a licensed medical device shall, annually before November 1 and in a form authorized by the Minister, furnish the Minister with a statement signed by the Manufacturer or by a person authorized to sign on the Manufacturer's behalf describing any change to the information and documents supplied by the Manufacturer with respect to the device, other than those to be submitted under section 34 or 43.1 [CMDR 43].

If the holder of a medical device license discontinues the sale of the medical device in Canada, the licensee shall inform the Minister within 30 days after the discontinuance, and the license shall be cancelled at the time that the Minister is informed [CMDR 43(3)].

Subject to section 34, if a new or modified quality management system certificate is issued in respect of a licensed medical device, the Manufacturer of the device shall submit a copy of the certificate to the Minister within 30 days after it is issued [CMDR 43.1].

Japan (MHLW):
A change to a medical device which is approved/certified by PMDA/a Registered Certification Body may require the Marketing Authorization Holder to submit a new application, a change application, or a change notification [PMD Act 23-2-5.1, 23-2-5.11, 23-2-5.12, 23-2-23.1, 23-2-23.6, 23-2-23.7].

Changes that require the application or the notification are those ones which directly impact the safety and efficacy of the device and/or the substantial identity of the fact approved during marketing approval / certification.

The Registered Manufacturing Site shall communicate with the Marketing Authorization Holder about the change when the Registered Manufacturing Site plans such changes, so that the Marketing

Authorization Holder could take any necessary regulatory actions mentioned above [MHLW MO169: 29].

Examples of changes that may require an application or a notification include, but are not limited to, the following:

- Design
- Composition
- Raw material
- Sterilization method
- Manufacturing method
- Manufacturing site
- Patient or user safety features
- Operating Parameters or conditions for use
- Indication for use
- Shelf life
- Performance Specification.

United States (FDA):
21 CFR 807 - Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices.
Update the device listing information during each June and December or, at its discretion, at the time the change occurs. Conditions that require updating and information to be submitted for each of these updates are as follows:

- If an owner or operator introduces into commercial distribution a device identified with a classification name not currently listed by the owner or operator
- If an owner or operator discontinues commercial distribution of all devices in the same device class

Update registration if changes in individual ownership, corporate or partnership structure, or location of at the time of annual registration, or by letter if the changes occur at other times. This information must be submitted within 30 days of such changes. Changes in the names of officers and/or directors of the corporation(s) must be filed with the establishment's official correspondent and must be provided to the Food and Drug Administration upon receipt of a written request for this information.

21 CFR 807.81- Premarket Notification:
A new complete 510(k) application is usually required for changes or modifications to an existing device, where the modifications could significantly affect the safety or effectiveness of the device, or

the device is to be marketed for a new or different indication. Most changes in indications for use require the submission of a 510(k).

Examples of modifications that may require a 510(k) submission include, but are not limited to, the following:

- Sterilization method
- Structural material
- Manufacturing method
- Operating parameters or conditions for use
- Patient or user safety features
- Sterile barrier packaging material
- Stability or expiration claims
- Design.

21 CFR 814.39 – PMA Supplements

After FDA's approval of a PMA, an applicant must submit a PMA supplement for review and approval by FDA before making a change affecting the safety or effectiveness of the device for which the applicant has an approved PMA. While the burden for determining whether a supplement is required is primarily on the PMA holder, changes for which an applicant shall submit a PMA supplement include, but are not limited to, the following types of changes if they affect the safety or effectiveness of the device:

- New indications for use of the device
- Labeling changes
- The use of a different facility or establishment to manufacture, process, or package the device
- Changes in sterilization procedures
- Changes in packaging
- Changes in the performance or design specifications, circuits, components, ingredients, principle of operation, or physical layout of the device
- Extension of the expiration date of the device based on data obtained under a new or revised stability or sterility testing protocol that has not been approved by FDA
- An applicant may make a change in a device after FDA's approval of a PMA for the device without submitting a PMA supplement if the change does not affect the device's safety or effectiveness and the change is reported to FDA in post approval periodic reports required as a condition to approval of the device, e.g., an editorial change in labeling which does not affect the safety or effectiveness of the device.

Links

Design and Development

During the audit of the Design and Development process, the audit team should confirm the medical device organization has considered regulatory requirements for device marketing authorization and facility registration; and has complied with these requirements prior to marketing the changed device in the applicable regulatory jurisdictions.

Chapter 3 - Measurement, Analysis and Improvement

One of the most important activities in the quality management system is the identification of existing and potential causes of product and quality problems. Such causes must be identified so that appropriate and effective corrective or preventive actions can take place. These activities are carried out under the Measurement, Analysis and Improvement process.

The purpose of a medical device organization's Measurement, Analysis and Improvement process is to collect and analyze information, identify and investigate existing and potential causes of product and quality problems, and take appropriate and effective corrective or preventive action to prevent recurrence or occurrence. It is essential that a medical device organization verify or validate these actions, communicate corrective and preventive action activities to responsible people, provide relevant information for management review, and document these activities. These activities will help the medical device organization deal effectively with existing or potential product and quality problems, prevent their recurrence and/or occurrence, and prevent or minimize device failures or other quality problems.

The **management representative** is responsible for ensuring that the requirements of the quality management system have been effectively defined, documented, implemented, and maintained. Prior to the audit of a process, it may be helpful to interview the management representative (or designee) to obtain an overview of the process and a feel for management's knowledge and understanding of the process.

The Measurement, Analysis and Improvement process is the second primary process to be audited per the MDSAP audit sequence. When applicable, information regarding device or identified quality management system nonconformities observed during the audit of the Measurement, Analysis and Improvement process should be used to make decisions as to design projects or design changes to assess during audit of the Design and Development process, suppliers to evaluate during audit of the Purchasing process, and processes to review during audit of the Production and Service Controls process.

Auditing the Measurement, Analysis and Improvement Process

Purpose: The purpose of auditing the Measurement, Analysis and Improvement process is to verify that the medical device organization's processes ensure that information related to products, process/es, or the quality management system is collected and analyzed to identify actual and potential product, process, or quality system nonconformities, that problems and potential problems are investigated, and that appropriate and effective corrective actions and preventive actions are taken.

Chapter 3 - Measurement, Analysis and Improvement

Task 1 – Procedures for Measurement, Analysis, and Improvement of QMS Effectiveness and Product Conformity

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Outcomes: As a result of the audit of the Measurement, Analysis and Improvement process, objective evidence will show whether the medical device organization has:

A) Defined, documented, and implemented procedures for measurement, analysis and improvement that address the requirements of the quality management system standard and participating MDSAP regulatory authorities
B) Identified, analyzed, and monitored appropriate sources of quality data to identify nonconformities or potential nonconformities and determined the need for corrective or preventive action
C) Ensured investigations are conducted to identify the underlying cause(s) of nonconformities and potential nonconformities, where possible
D) Implemented appropriate corrective action to eliminate the recurrence or preventive action to prevent the occurrence of product or quality system nonconformities, commensurate with the risks associated with the nonconformities or potential nonconformities encountered
E) Reviewed the effectiveness of corrective action and preventive action
F) Utilized information from the analysis of production and post-production quality data to amend the analysis of product risk, as appropriate

Links to Other Processes:

Design and Development; **Production and Service Controls**; **Purchasing**; Medical Device Adverse Events and Advisory Notices Reporting; Management

Task 1 – Procedures for Measurement, Analysis, and Improvement of QMS Effectiveness and Product Conformity

Verify that procedures for measurement, analysis and improvement which address the requirements of the quality management system standard and regulatory authorities have been established and documented.

Confirm the medical device organization maintains and implements procedures to monitor and measure product conformity throughout product realization, as well as procedures that provide for mechanisms for feedback to provide early warnings of quality problems and the implementation of corrective action and preventive action.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 8.1, 8.2.1, 8.2.6, 8.5

TGA: TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii), (f)

Chapter 3 - Measurement, Analysis and Improvement

Task 1 – Procedures for Measurement, Analysis, and Improvement of QMS Effectiveness and Product Conformity

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ANVISA: RDC ANVISA 665/2022: Art. 88, Art. 120, Art. 121

MHLW/PMDA: MO169: 6, 54, 55-1, 58, 59, 62, 63, 64; [Old: 6, 54, 55, 58, 59, 62, 63, 64]

FDA: 21 CFR 820.100(a)]

Additional country-specific requirements:

Brazil (ANVISA):

Verify that the manufacturer has ensured that information about quality problems or nonconforming products are properly disseminated to those directly involved in the maintenance of product quality and to prevent occurrence of such problems [RDC ANVISA 665/2022: Art. 120 section VI].

United States (FDA):

Verify procedures 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 problems [21 CFR 820.100(a)(6)].

Confirm procedures provide for the submission of relevant information on identified quality problems, as well as corrective and preventive actions, for management review [21 CFR 820.100(a)(7)].

Assessing conformity

Procedures

Each medical device organization must establish and maintain procedures for analyzing data and implementing corrective action and preventive action. The procedures must include requirements for:

- Analyzing feedback, conformity to product requirements, characteristics and trends of processes and products (including opportunities for preventive action), and conformity of suppliers
- Reviewing nonconformities, including customer complaints
- Evaluating the need for action to prevent recurrence or occurrence of nonconformities
- Recording the results of any investigations and of actions taken
- Identifying the action(s) needed to correct and prevent recurrence or occurrence of nonconforming product and other quality problems
- Ensure that action is effective and does not adversely affect the finished device
- Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems
- Ensuring 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

Task 2 – Sources of quality data

Determine if appropriate sources of quality data have been identified and analyzed according to a documented procedure for use the use of valid statistical methods (where appropriate) for input into the measurement, analysis and improvement process, including customer complaints, feedback, service records, returned product, internal and external audit findings, nonconformities from regulatory audits and inspections, and data from the monitoring of products, processes, nonconforming products, and suppliers.

Information from the organization's analysis of quality data should be used to inform the audit team's decision as to specific complaint records to review in Task 12, and products and processes to audit during the Design and Development, Production and Service Controls, and Purchasing processes.

Clause and Regulation

ISO: ISO 13485:2016: 7.5.4, 8.1, 8.2.1, 8.2.6, 8.4

TGA: TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii), (f)

ANVISA: RDC ANVISA 665/2022: Art. 120 section I, Art. 131

MHLW/PMDA: MO169: 43, 54, 55-1, 58, 59, 61; [Old: 43, 54, 55, 58, 59, 61]

FDA: 21 CFR 820.100(a)]

Additional country-specific requirements

None

Assessing conformity

Quality data sources

Complaints, records of acceptance activities and concessions, nonconformities identified in internal audits, service records, acceptability of supplied product and supplier performance, and data presented in management review are common quality data sources that are useful in identifying quality problems, among others.

Some sources of quality data that may be useful in identifying potential problems are acceptance activities, such as component, in-process, or finished device testing; environmental monitoring, and statistical process control (SPC). Results of acceptance activities may indicate an unfavorable trend that left unattended may result in product nonconformity.

During the audit of the Measurement, Analysis and Improvement process, it is recommended that the auditor(s) review the previous audit report if there is one for the medical device organization. If this information is available, the audit team should use the information in the report when selecting some quality data sources to review during the audit. For example, if service records were reviewed during the previous audit and the medical device organization handled the data appropriately, the audit team may wish to select a different data source for review during the audit.

However, if the previous audit documented that the data from service records were not being entered into the Measurement, Analysis and Improvement process appropriately, the audit team should consider reviewing service records again to determine whether the previous deficiency was effectively addressed:

- Select some sources of quality data
- Determine if the data from these sources were entered into the medical device organization's Measurement, Analysis and Improvement process for analysis and whether the information was complete, accurate, and entered in a timely fashion
- Be mindful of quality problems that appear in more than one data source. For example, device nonconformities noted in complaints should be compared with similar nonconformities noted during the medical device organization's analysis of data from other data sources such as product reject reports, or nonconforming product or process reports.

This comparison will help the medical device organization and the audit teams understand the full extent of the quality problem.

Analysis of data

A medical device organization should use data from a variety of quality data sources to identify the causes of existing product and quality problems. Not all organizations will have the same sources of quality data. For example, service records and installation reports are quality data sources that may not be found at every medical device organization.

As the audit team is conducting the audit, determine what sources of quality data the medical device organization has identified. The audit team will also determine whether the sources identified by the medical device organization are appropriate and if the medical device organization is analyzing quality data from these sources to identify existing product problems as well as existing problems within its quality system.

Later in the evaluation of the Measurement, Analysis and Improvement process, the audit team will be sampling raw quality data to determine how the medical device organization analyzed the quality data and responded to the results of its analysis.

A medical device organization should also use data from a variety of quality data sources to identify the causes of potential product and quality problems. The medical device organization should be looking for trends or other indications of potential problems before the problems actually occur. The medical device organization may choose to perform analysis of competing devices, including reviewing advisory notices related to competing devices, to determine whether similar nonconformities could occur in the medical device organization's devices.

Determine whether the medical device organization can identify potential product and quality problems that may require preventive action.

A medical device organization has the flexibility to use whatever methods of analysis are appropriate to identify existing and potential causes of nonconforming product or other quality problems. However, a medical device organization must use appropriate statistical methodology where necessary to detect recurring quality problems.

A medical device organization must also use appropriate statistical tools when it is necessary to use statistical methodology. It should not misuse statistics in an effort to minimize the problem or avoid addressing the problem.

Links

Purchasing

During the audit of the Measurement, Analysis and Improvement process, the audit team may encounter data involving product nonconformities, including complaints involving finished devices, where the underlying cause of the quality problem has been traced to supplied product.

During the audit of the Purchasing process, the audit team should consider selecting suppliers to audit that have corrective action indicators of nonconformities with supplied components or processes.

Task 3 – Investigation of Nonconformity

Determine if investigations are conducted to identify the underlying cause(s) of detected nonconformities, where possible.

Confirm investigations are commensurate with the risk of the nonconformity.

Clause and Regulation

ISO: ISO 13485:2016: 8.5.2

TGA: TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii),(f), TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 116, Art. 120 section II

MHLW/PMDA: MO169: 63

FDA: 21 CFR 820.100 (a)(2)]

Additional country-specific requirements
None

Assessing conformity

Investigations of nonconformities
Organizations must define and implement a process for investigations. The process should consist of a structured, risk-based approach (in a mature QS) intended to determine the root or underlying cause(s) of a quality problem. Criteria should be defined to determine when an investigation is necessary and the extent of the investigation. The investigation should be based on a pre-approved plan or other defined approach, timelines should be defined, roles and responsibilities should be assigned, and the course of action should be assessed when the underlying cause cannot be determined. The results of the investigation must be recorded. The depth of the medical device organization's investigation of a process, product, or other quality system nonconformity should be commensurate with the significance and risk of the nonconformity. The process for determining the extent of an investigation may be linked to the medical device organization's risk management system and the design outputs essential to the proper functioning of the device.

A correction is not the same as a corrective action.

In order for a medical device organization to take a corrective action (i.e., action taken to prevent recurrence of an existing nonconformity), an investigation must be conducted to determine the cause of the nonconformity. Often a medical device organization will only make a correction to handle the immediate problem (e.g. relabeling a lot of mislabeled finished devices). Determining the cause of the lot of mislabeled finished devices is more difficult and may be overlooked. Where possible, the medical device organization should identify the underlying cause or causes of the nonconformity so that appropriate corrective action can be taken.

Selecting records
When selecting records of investigations to review, be mindful of the risk of the nonconformity to the product or process. Select records of investigations where the nonconformity has a higher risk of adversely affecting the ability of the finished device to meet its essential design outputs or the nonconformity affects the safety and efficacy of the product.

Links
None

Task 4 – Investigation of Potential Nonconformity

Determine if investigations are conducted to identify the underlying cause(s) of potential nonconformities, where possible.

Confirm investigations are commensurate with the risk of the potential nonconformity.

Clause and Regulation
ISO: ISO 13485:2016: 8.5.3

TGA: TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii),(f),TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 120 section I

MHLW/PMDA: MO169: 64

FDA: 21 CFR 820.100(a)(2)]

Additional country-specific requirements
None

Assessing conformity

Investigations of potential nonconformities
The depth of the medical device organization's investigation into potential process, product, or other quality system nonconformities should be commensurate with the risk of the nonconformity if it were to occur. The process for determining the extent of an investigation may be linked to the medical device organization's risk management system and outputs essential to the proper functioning of the device.

Selecting records
When selecting records of investigations to review, be mindful of the risk of the potential nonconformity to the product or process. Select records of investigations where the potential nonconformity has a higher risk of adversely affecting the ability of the finished device to meet its essential design outputs or the potential nonconformity could affect the safety and efficacy of the product.

Links

None

Task 5 – Correction, Corrective Action, and Preventive Action

Confirm that corrections, corrective actions, and preventive actions were determined, implemented, documented, effective, and did not adversely affect finished devices.

Ensure corrective action and preventive action is appropriate to the risk of the nonconformities or potential nonconformities encountered.

Clause and Regulation

ISO: ISO 13485:2016: 8.2.1, 8.2.5, 8.3.1, 8.5.2, 8.5.3

TGA: TG(MD)R Sch1 P1 2, TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii), (f)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 116, Art. 120 sections II, II, IV, V

MHLW/PMDA: MO169: 55-1, 57, 60-1, 63, 64; [Old: 55, 57, 60, 63, 64]

FDA: 21 CFR 820.100(a)(3), 820.100 (a)(4),820.100(a)(6), 820.100(b)]

Additional country-specific requirements

None

Assessing conformity

Determining the extent of actions

Corrective actions taken by a medical device organization can vary depending on the situation. Corrective actions are intended to correct and also prevent recurrence of not only nonconforming product but also poor practices, such as inadequate training.

In developing corrective action addressing nonconforming product, the medical device organization should consider corrections to be taken regarding the affected products, whether distributed or not. Corrections and corrective actions must be commensurate with the risk associated with the nonconformity.

The audit team may encounter situations where a quality problem has been identified, but the medical device organization's management has decided not to undertake corrective actions. Confirm that the medical device organization's decision not to take corrective action has been made using appropriate risk-based decision making, including a determination that the finished device meets risk acceptability criteria.

Determining the effectiveness of actions

During the audit of the Measurement, Analysis and Improvement process, review the mechanisms by which the medical device organization assessed effectiveness of the corrective and preventive actions. Compare the records of significant and/or higher risk corrective actions and preventive actions to the medical device organization's product and quality data analyses, such as trend results. Look for product or quality problems or trends that continued or began after the actions were implemented. This may indicate that the corrective actions or preventive actions were not effective.

Review how the medical device organization has determined that the actions do not adversely affect the finished device(s).

Links

Medical Device Adverse Events and Advisory Notices Reporting

Determine whether any of the medical device organization's corrective actions require reporting to participating MDSAP authorities.

Task 6 – Assessment of Design Change resulting from Corrective or Preventive Action

When a corrective or preventive action results in a design change, verify that any new hazard(s) and any new risks are evaluated under the risk management process.

Clause and Regulation

ISO: ISO 13485:2016: 7.1, 7.3.9

TGA: TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 60

MHLW/PMDA: MO169: 26, 36-1; [Old: 26, 36]

FDA: 21 CFR 820.30(i), 820.30(g)

Additional country-specific requirements

None

Assessing conformity

Design change

Completing this audit task may involve linkages to other subsystems. Verification and validation are important elements in assuring that corrective actions and preventive actions that result in design changes are effective and do not introduce new hazards.

Links

Design and Development

If the corrective action or preventive action involves changing the design, design controls should be applied to the change where applicable.

When necessary, confirm that design controls were applied to the change according to the medical device organization's procedures.

In addition, design changes should be evaluated under the medical device organization's risk management process to ensure that changes do not introduce new hazards.

Task 7 – Assessment of Process Change resulting from Corrective or Preventive Action

When a corrective or preventive action results in a process change, confirm that the process change is assessed to determine if any new risks to the product are introduced.

Verify the medical device organization has performed revalidation of processes where appropriate.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.2, 4.1.4, 4.1.6, 4.2.1, 7.1, 7.5.2, 7.5.6, 7.5.7

TGA: TG(MD)R Sch1 P1 2; Sch3 P1 1.5(4)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 106, Art. 120

MHLW/PMDA: MO169: 5-2, 5-4, 5-6, 6, 26, 41, 45, 46; [Old: 5, 6, 26, 41, 45, 46]

FDA: 21 CFR 820.100(a)(4), 820.100(a)(5), 820.70(b), 820.75(c)

Additional country-specific requirements

Australia (TGA):
Confirm that the Manufacturer's procedure for dealing with substantial changes to a critical process (e.g. sterilization, processing materials of animal origin, processing materials of microbial or recombinant origin, or processes that incorporate a medicinal substance in a medical device), requires the Manufacturer to notify the Auditing Organization of their plans before implementing a change to a critical process. The Auditing Organization is to assess the proposed change before implementation by the Manufacturer, to determine if the requirements of the relevant conformity assessment procedure will still be met after the change. [TG(MD)R Sch3 P1 1.5(2)].

If the Manufacturer is also a holder of a TGA Conformity Assessment Certificate, then the Manufacturer is also required to notify the TGA of these changes, prior to implementation.

Canada (HC):
Verify that the Manufacturer has a process or procedure for identifying a "significant change" to a class III or IV device. Verify that information about "significant changes" is submitted in a medical device license amendment application [CMDR 1, 34].

Japan (MHLW):
Confirm that when the Registered Manufacturing Site plans to make a significant change to a manufacturing processes (e.g. sterilization site change, manufacturing site change), the Registered Manufacturing Site notifies the Marketing Authorization Holder so as the Marketing Authorization Holder can take appropriate regulatory actions [MHLW MO169: 29].

Assessing conformity

Process changes
Completing this audit task may involve linkages to other quality management system processes. Production processes require at least some degree of qualification, verification, or validation. If the change involves a validated process, review the medical device organization's evaluation of the process change to determine if revalidation is needed.

For changes to production processes that are performed by suppliers, the audit team should consider selecting those suppliers for evaluation during audit of the Purchasing process. In cases where the medical device organization makes a change to a validated process performed by a supplier, the audit team should evaluate whether re-validation is required. If re-validation of production processes is required, confirm the results show the process meets the planned result.

Links

Production and Service Controls, **Purchasing**

If the corrective action or preventive action involves changing a production process, the audit team should consider selecting this change for evaluation during audit of Production and Service Controls.

Task 8 – Identification and Control of Nonconforming Product

Verify that controls are in place to ensure that product which does not conform to product requirements is identified and controlled to prevent its unintended use or delivery.

Confirm that an appropriate disposition was made, justified, and documented and that any external party responsible for the nonconformity was notified.

Clause and Regulation

ISO: ISO 13485:2016: 8.3.1, 8.3.2

TGA: TG(MD)R Sch3 P1 1.4(5)(b)(iii)

ANVISA: RDC ANVISA 665/2022: Art. 117, Art. 118, Art. 120 section VI

MHLW/PMDA: MO169: 60-1, 60-2; [Old: 60]

FDA: 21CFR 820.90(a)

Additional country-specific requirements

None

Assessing conformity

Nonconforming product

The audit team should review procedures and controls for preventing the unintended distribution of nonconforming product. The auditor(s) may choose to select a sample of records involving nonconforming product that was in stock or returned to review how the procedures and controls were applied to control the nonconforming product.

Confirm the medical device organization has established and maintained procedures that define the responsibility for review and the authority for the disposition of nonconforming product, as well as the

execution of the review and disposition process. Disposition of nonconforming product must be documented.

The audit team may encounter situations where the medical device organization's management has decided to authorize the use of nonconforming product under concession. Documentation must include the justification for use of nonconforming product and the signature of the individual(s) authorizing the use. Confirm that the medical device organization's decision to use nonconforming product under concession has been made using appropriate risk-based decision making, including a determination that the finished device meets specified requirements. Be mindful of instances where the use of nonconforming product under concession has led to devices not meeting specifications.

Selecting records

When selecting records of nonconforming products to review, be mindful of the risk of the nonconformity to the finished device and the patient or user. Select records of nonconforming products to review where the nonconformity has a higher risk of adversely affecting the ability of the finished device to meet its essential design outputs or the nonconformity affects the safety and efficacy of the product.

Links

None

Task 9 – Action Regarding Nonconforming Product Detected After Delivery

Confirm that when nonconforming product is detected after delivery or use, *appropriate action is taken commensurate with the risk,* or potential risks, of the nonconformity.

Clause and Regulation

ISO: ISO 13485:2016: 8.3.3, 8.5.2

TGA: TG(MD)R Sch1 P1 2, TG(MD)R Sch3 P1 1.4(3)(a),(b), (5)(b)(iii), (f)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 120 section VIII

MHLW/PMDA: MO169: 60-3, 63; [Old: 60, 63]

FDA: 21 CFR 820.100(a)]

Additional country-specific requirements

None

Assessing conformity

Control and action based on risk

During this audit task, confirm that the medical device organization has determined the control and actions to be taken on nonconforming products detected after delivery or use, commensurate with the risk associated with a product failure.

While it may not be necessary for the medical device organization to recall nonconforming product from distribution as part of its identified actions needed to correct and prevent recurrence of the problem, confirm that the decision is made using an adequate risk justification.

Links

Medical Device Adverse Events and Advisory Notices Reporting

If the medical device organization has taken field action on products already distributed, confirm that the appropriate MDSAP regulatory authorities have been notified, as necessary.

Task 10 – Internal Audit

Verify that internal audits of the quality management system are being conducted according to planned arrangements and documented procedures to ensure the quality management system is in compliance with the established quality management system requirements and applicable regulatory requirements, and to determine the effectiveness of the quality system.

Confirm that the internal audits include provisions for auditor training and independence over the areas being audited, corrections, corrective actions, follow-up activities, and the verification of corrective actions.

Clause and Regulation

ISO: ISO 13485:2016: 6.2, 8.2.4

TGA: TG(MD)R Sch3 P1 1.4(5)(b)(iii)

ANVISA: RDC ANVISA 665/2022: Art. 122, Art. 123, Art. 124

MHLW/PMDA: MO169: 22, 23, 56

FDA: 21 CFR 820.22, 820.100

Additional country-specific requirements

None

Assessing conformity

Internal audits

Internal audits are systematic, independent examinations of a medical device organization's quality management system that are performed at defined intervals and at sufficient frequency to determine whether both quality management system activities and the results of such activities comply with quality management system procedures. Internal audits should also determine whether these procedures are implemented effectively and whether they are suitable to achieve quality management system objectives.

Auditors

Internal audits are to be conducted according to established procedures by appropriately trained individuals not having direct responsibility for the matters being audited. If possible, interview auditors and ask how audits are conducted, how long audits typically last, what documents are typically reviewed, etc.

Requirements

Internal audit procedures typically include requirements for auditor qualifications, requirements for the frequency of audits, specified functional areas to be audited, and audit plans (or the requirement to establish audit plans prior to the audit). Procedures should also include requirements for:

- How audit activities and results are to be communicated, addressed, and followed up (including re-audit, if necessary) and,
- How audit activities are to be documented.

Review and documentation

Management having responsibility for the matters audited must review the report of the quality audit. The dates and results of all quality audits (and subsequent re-audits, if necessary) must be documented, as well as any corrective or preventive actions resulting from the internal audits.

Links

Management

During the audit of the Management process, the audit team should confirm that the output of internal audits is an input to management review.

Task 11 – Information Supplied for Management Review

Determine if relevant information regarding nonconforming product, quality management system nonconformities, corrections, corrective actions, and preventive actions has been supplied to management for management review.

Clause and Regulation

ISO: ISO 13485:2016: 5.6.2

TGA: TG(MD)R Sch3 P1 1.4(5)(b)(iii)

ANVISA: RDC ANVISA 665/2022: Art. 12, Art. 120 section VII

MHLW/PMDA: MO169: 19

FDA: 21 CFR 820.100 (a)(7)]

Additional country-specific requirements

None

Assessing conformity

Management review

During the performance of this audit task, the auditor(s) may choose to select a recent, significant corrective or preventive action and determine which records or information regarding the event was submitted for management review.

Links

Management

During the audit of the Management process, the audit team should have confirmed that the status of corrective and preventive actions is an input to the management review.

During the audit of the Measurement, Analysis and Improvement process, determine if top management is aware of higher-risk quality problems, as well as significant corrective and preventive actions, when necessary.

Task 12 – Evaluation of Information from Post-Production Phase, Including Complaints

Confirm that the medical device organization has made effective arrangements for gaining experience from the post-production phase, including postmarket surveillance, handling complaints, and investigating the cause of nonconformities related to advisory notices with provision for feedback into the Measurement, Analysis and Improvement process.

Select records of complaints for review that represent the highest risk to the user or have the largest impact on the ability of the device to meet its essential design outputs.

Verify that information from the analysis of production and post-production quality data was considered for amending the analysis of product risk, as appropriate.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.2.3, 7.5.4 (a), 8.2.1, 8.2.2, 8.5.1

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 1.4(3), 1.4(5)(b)(iii) &1.4(5)(f)

ANVISA: RDC ANVISA 665/2022: Art. 121

HC: CMDR 57-58, 61.4-61.6

MHLW/PMDA: MO169: 6, 29, 43, 55-1, 55-2, 62; [Old: 6, 29, 43, 55, 62]

FDA: 21 CFR 820.198]

Additional country-specific requirements

Australia (TGA):

Verify that the medical device organization has procedures for a post-marketing system that includes a systematic review of post-production experience (e.g. from; expert user groups, customer surveys, customer complaints and warranty claims, service and repair information, literature reviews, post-production clinical trials, user feedback other than complaints, device tracking and registration schemes, user reactions during training, adverse event reports). Investigation should take place in a timely manner to ensure that reporting timeframes for adverse events or the implementation of advisory notices (recalls) may be met by the Australian Sponsor [TG(MD)R Sch3 P1 1.4(3)(a)].

Note: In Australia the conduct of a recall is the responsibility of the Australian Sponsor in accordance with the Australian Uniform Recall Procedure for Therapeutic Goods.

Brazil (ANVISA):

Verify that each manufacturer has established and maintains procedures to receive, examine, evaluate, investigate and document complaints. Such procedures must ensure that:

- Complaints are received, documented, analyzed, evaluated, investigated and documented by a formally designated unit
- Where applicable, complaints must be reported to the competent health authority
- Complaints must be examined to determine whether an investigation is necessary. When an investigation is not done, the unit must maintain a record that includes the reason that the investigation was not performed and the name of the persons responsible for the decision.
- Each manufacturer must examine, evaluate and investigate all complaints involving possible nonconformities of the product. Any claim for death, injury or threat to public health must be immediately reviewed, evaluated and investigated.
- The records of the investigation must include:
- Product name
- Date of receipt of the complaint
- Any control number used
- Name, address and telephone number of the complainant
- Nature of complaint
- Data and research results including actions taken [RDC ANVISA 665/2022: Art. 121].

Canada (HC):

Verify that the Manufacturer maintains records of reported problems related to the performance characteristics or safety of a device, including any consumer complaints received by the Manufacturer after the device was first sold in Canada, and all actions taken by the Manufacturer in response to the problems referred to in the complaints [CMDR Section 57].

Verify that the Manufacturer has established and implemented documented procedures that will enable it to carry out an effective and timely investigation of the problem reports through the customer complaints, and to carry out an effective and timely recall of the device [CMDR Section 58].

Verify that the Manufacturer has established and implemented documented procedures for preparing summary reports with respect to information received or of which they became aware:

- During the previous 24 months for class II medical devices; and

During the previous 12 months for class III and IV medical devices. CMDR 61.4(1)]

Verify that summary reports cover:

- Adverse effects;
- Reported problems and complaints;
- Reportable incidents in accordance with section 59(1);

Serious risks of injury to human health that are relevant to the safety of the medical device in accordance with section 61.2(2). [CMDR 61.4(2)]

Verify that the summary report includes a concise critical analysis of the information required in section 61.4(2)

[CMDR 61.4(3)]

Verify that the manufacturer has determined, based on the analysis of data, whether what is known about the benefits and risks associated with the medical device has changed as follows:

- Any of the benefits that may be obtained by patients through the use of the medical device could be less;
- In respect of any of the risks:
  - the risk is more likely to occur; or,
  - if the risk occurs, the consequences for the health and safety of patients, users or other persons could be more serious.
- a new risk has been identified.

Verify that the manufacturer has included the conclusions drawn from the above-mentioned analysis in the summary report.

[CMDR 61.4(4)&(5)]

Verify that the manufacturer has notified the Minister in writing within 72 hours after concluding that what is known about the benefits and risks associated with the medical device has changed. [Note: Refer to the guidance document "**Guidance on summary reports and issue-related analyses for medical devices: Summary reports**" for instructions for reporting to the Minister.]

[CMDR 61.4(6)]

Verify that the manufacturer retains records of the summary reports, the information used in the preparation of the reports, and any associated notification to the Minister for seven years after the day on which they are created.

[CMDR 61.6]

Japan (MHLW/PMDA):
Confirm that the person operating the Registered Manufacturing Site has determined and implemented effective arrangement for communicating with the Japanese Marketing Authorization Holder in relation to customer feedback, including customer complaints, and advisory notices [MHLW MO169: 29].

United States (FDA):
Verify procedures have been defined, documented, and implemented for receiving, reviewing, and evaluating complaints by a formally designated unit. Procedures must ensure that:

- All complaints are processed in a uniform and timely manner
- Oral complaints are documented upon receipt
- Complaints are evaluated to determine whether the complaint represents an event which is required to be reported to FDA

Each manufacturer must review and evaluate all complaints to determine whether an investigation is necessary. When no investigation is made, the manufacturer must maintain a record that includes the reason no investigation was made and the name of the individual responsible for the decision not to investigate.

Any complaint of the failure of the device, labeling, or packaging to meet any of its specifications must be reviewed, evaluated, and investigated, unless such investigation has already been made for a similar complaint and another investigation is not necessary.

Any complaint that represents an event which must be reported to FDA must be promptly reviewed, evaluated, and investigated by a designated individual(s) and must be maintained in a separate portion of the complaint files or otherwise clearly identified. Records of investigation must include a determination of:

- Whether the device failed to meet specifications
- Whether the device was being used for treatment or diagnosis
- The relationship, if any, of the device to the reported incident or adverse event

When an investigation is made, a record of the investigation must be maintained by the formally designated unit. The record of investigation must include:

- The name of the device
- The date the complaint was received
- Any unique identifier (UDI), or Universal Product Code (UPC) or any other device identification(s) and control number(s) used
- The name, address, and telephone number of the complainant
- The nature and details of the complaint
- The dates and results of investigation
- Any corrective action taken

When the manufacturer's formally designated unit is located at a site separate from the manufacturing establishment, the investigated complaint(s) and the record(s) of investigation must be reasonably accessible to the manufacturing establishment [21 CFR 820.198].

Assessing conformity

Evaluation of post-production data

During the review of quality data sources that serve as inputs to the Measurement, Analysis and Improvement process, the audit team may choose to review complaints and customer feedback. Confirm that complaints are handled as required by the MDSAP participating regulatory authorities. Complaints can be an important source of information regarding quality problems and are often indicative that distributed devices (or their packaging or labeling) did not meet specified requirements.

Selecting records

One method to analyze complaints and customer feedback is to review the analysis of complaint data and postmarket surveillance activities and select one or more complaint failure modes, **preferably failure modes associated with higher risk to the patient or user**. Once the audit team has selected complaint failure modes, the auditor(s) can select a sample of complaints from those failure modes and confirm the complaints are handled appropriately, including investigation and implementation of corrective action when necessary.

Risk management

Information from post-production sources, including complaints, customer feedback, and postmarket surveillance can provide important information for the risk management activities for the device. In particular, previously unidentified risks discovered during the post-production monitoring may indicate a need for improving the risk management process or may indicate a need for design

changes. Additionally, on the basis of post-production quality data, the medical device organization may choose to enact new or more stringent controls to maintain an acceptable level of product risk.

Links

Medical Device Adverse Events and Advisory Notices Reporting; **Design and Development**; **Production and Service Controls**

During the review of complaints and feedback, confirm that individual medical device reports were made to the appropriate regulatory authorities when necessary.

Information from reviewing post-production sources, including complaints and postmarket surveillance reports, should guide the audit team in selecting designs to review and production processes to audit.

Task 13 – Communications with External Parties Involved on Complaints

Where investigation determines that activities outside the medical device organization, contributed to a customer complaint, verify that records show that relevant information was exchanged between the organizations involved.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.5, 7.4.1, 8.3.1

ANVISA: RDC ANVISA 665/2022: Art. 120 section VI

MHLW/PMDA: MO169: 5-5, 37, 60-1; [Old: 5, 37, 60]

FDA: 21 CFR 820.100(a)(6)

Additional country-specific requirements

None

Assessing conformity

Complaints and nonconformities attributed to supplied product

Confirm that information related to quality problems or nonconforming product, including complaints, is disseminated to those directly responsible for assuring the quality of product. This includes instances where investigation reveals the underlying cause of the complaint or nonconforming product to be related to the supplied product. The medical device organization should notify the supplier of the quality problem and appropriate corrective action must be taken when necessary. Failure of an

outside medical device organization to provide products that meet specified requirements may disqualify them as an acceptable or approved supplier.

Links

Purchasing

During the audit of the Measurement, Analysis and Improvement process, if significant nonconformities are related to the supplied product, the audit team should consider selecting those suppliers for evaluation during the audit of the medical device organization's Purchasing process.

Task 14 – Evaluation of Complaints for Adverse Event Reporting

Verify that the medical device organization has defined and documented procedures for the evaluation of complaints for adverse event reporting.

Confirm that decisions to not report complaints were made according to established procedures and a documented rationale.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.2.3, 8.2.3

TGA: TG(MD)R Sch3 P1 1.4(3)(c)

ANVISA: RDC ANVISA 665/2022: Art. 120 section VIII, RDC ANVISA 67/2009

HC: CMDR 59-61.1

MHLW/PMDA: MO169: 6, 29, 55-3; [Old; 6, 29, 62]

FDA: 21 CFR 803

Additional country-specific requirements

Refer to MDSAP process Medical Device Adverse Events and Advisory Notices Reporting

Assessing conformity

Individual adverse event reports

An output of the activities associated with the Measurement, Analysis and Improvement process, such as complaint handling, is the evaluation of individual adverse events to determine whether individual adverse event reports are required to be submitted to the regulatory authorities. During review of complaint records, assess whether the complaint was evaluated to determine whether the criteria for

reporting was met and confirm the appropriate reports and information was provided to the regulatory authority when appropriate. Ensure the individual adverse event reports contain accurate information by comparing the submitted reports to the associated complaint and complaint investigation.

Reportable events are often an important Measurement, Analysis and Improvement process quality data source since these events are indicative that the finished device has caused death, serious injury, or has malfunctioned in a manner such that if the malfunction were to recur, the result could be death or serious injury. Any death, even if the medical device organization attributes it to user error, is considered to have potentially high risk associated with it. Confirm that reportable events were evaluated for corrective action when necessary.

Links
None

Task 15 – Evaluation of Quality Problems for Advisory Notices

Confirm that the manufacturer has made effective arrangements for the timely evaluation of quality problems involving distributed product for potential issuance and implementation of advisory notices.

Select records for review of quality problems that were evaluated for potential issuance of advisory notices (include records where a decision was made not to issue an advisory notice as well as records of decision to issue advisory notices) and assess whether the organization has taken actions appropriately based on risk and documented the rationale.

Clause and Regulation
ISO: ISO 13485:2016: 4.2.1, 7.2.3, 8.3.3

TGA: TG(MD)R Sch3 P1 1.4(3)(c)

ANVISA: RDC ANVISA 665/2022: Art. 120 section VIII, RDC ANVISA 551/2021

HC: CMDR 63-65.1

MHLW/PMDA: MO169: 6, 29, 60-3; [Old: 6, 29, 60]

FDA: 21 CFR 806, 820.100(a)]

Additional country-specific requirements
Refer to MDSAP process Medical Device Adverse Events and Advisory Notices Reporting

Assessing conformity

Advisory notices

An output of the activities associated with the Measurement, Analysis and Improvement process, including complaint handling and the discovery of nonconforming product that has been distributed, may be the determination of whether an advisory action is necessary. When applicable, select quality issues that were evaluated for potential advisory actions and assess whether appropriate actions were taken and the organization's decisions were justified, based on the risk of the quality problem to device users. This may include assessing whether the organization appropriately determined the scope of the quality issue. For example, if the organization determined that a product is distributed in three MDSAP jurisdictions, but the advisory notice was only issued in one MDSAP jurisdiction, the audit team should determine whether the organization has an appropriate documented justification for the scope of the advisory action.

The quality problems that led to an advisory notice is often an important quality data source for the corrective actions process since these events are indicative that the finished device does not meet specified requirements and has the potential for unreasonable risk to the user. Confirm that quality problems that were evaluated by the organization for potential advisory actions were evaluated for corrective action. If corrective action was taken, evaluate the mechanism by which the medical device organization assured the action is effective and does not adversely affect the ability of the device to meet specified requirements. If corrective action was not taken for quality problems associated with a correction, removal, or advisory notice; or action appears unduly delayed considering the risk of the quality problem, review the medical device organization's rationale for not undertaking corrective action and confirm that the decision is appropriate using a risk-based decision making process.

Decisions to not report a correction, removal, or advisory notice

The audit team may encounter instances where the medical device organization has performed activities involving issuance of advisory notices without notifying regulatory authorities in the markets in which the device is marketed. In these situations, review the medical device organization's rationale for not reporting these actions and ensure that the rationale is appropriate. Verify that records of the action are maintained.

Links

None

Task 16 – Top Management Commitment to Measurement, Analysis, and Improvement Process

Determine, based on the assessment of the Measurement, Analysis and Improvement process overall, whether management provides the necessary commitment to detect and address product and quality management system nonconformities, and ensure the continued suitability and effectiveness of the quality management system.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.3, 5.2, 8.1, 8.5.1

ANVISA: RDC ANVISA 665/2022: Art. 5°, Art. 6°, Art. 7°

MHLW/PMDA: MO169: 5-3, 11, 54, 62; [Old: 5, 11, 54, 62]

Additional country-specific requirements

None

Links

None

Chapter 4 - Medical Device Adverse Events and Advisory Notices Reporting

The Medical Device Adverse Events and Advisory Notices Reporting process may be audited as a linkage from the Measurement, Analysis and Improvement process.

Auditing the Medical Device Adverse Events and Advisory Notices Reporting

Purpose: The purpose of auditing the Medical Device Adverse Events and Advisory Notices Reporting is; to verify that the medical device organization's processes ensure that individual device-related adverse events and, advisory notices involving medical devices are reported to regulatory authorities within required timeframes.

Outcomes: As a result of the audit of the Medical Device Adverse Events and Advisory Notices Reporting process, objective evidence will show whether the medical device organization has:

A) Defined processes to ensure individual device-related adverse events are reported to regulatory authorities as required
B) Ensured that advisory notices are reported to regulatory authorities and authorized representatives when necessary
C) Maintained appropriate records of individual device-related adverse events and advisory notices

Links to Other Processes:

Measurement, Analysis and Improvement

Task 1 – Notification of Adverse Events

Verify that the medical device organization has a process in place for identifying device-related events that may meet reporting criteria as defined by participating regulatory authorities.

Verify that the complaint process has a mechanism for reviewing each complaint to determine if a report to a regulatory authority is required.

Confirm that the medical device organization's processes meet the timeframes required by each regulatory authority where the product is marketed.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.2.3, 8.2.2, 8.2.3

Country-specific requirements

Australia (TGA):

Manufacturers are required to implement a post-marketing system that includes provisions for adverse event reporting – e.g. *Therapeutic Goods (Medical Devices) Regulations 2002* Schedule 3 Part 1 Clause 1.4(3)(c)(i). In view of the written agreement between Manufacturers and the Australian Sponsor [TG Act 41FD], events must be reported by the Manufacturer to the TGA, or to the Sponsor, in a timely manner to ensure that a Sponsor can meet their reporting obligations under the *Therapeutic Goods (Medical Devices) Regulation* 5.7:

- Verify that the Manufacturer or other person becoming aware of an event that represents a serious threat to public health provides information as soon as practicable. The Sponsor is to report the event within 48 hours.
- Verify that the Manufacturer or other person becoming aware of an event that led to the death or serious deterioration in the state of health of a patient, a user, or other person provides information as soon as practicable. The Sponsor is to report the event within 10 days.
- Verify that the manufacturer or other person becoming aware of an event that the recurrence of which might lead to the death or serious deterioration in the state of health of a patient, a user, or other person provides information as soon as practicable. The Sponsor is to report the event within 30 days.

Note: An event that leads to a serious threat to human health is a hazard arising from a systematic failure of the devices or an event or other occurrence that may lead to death or serious injury.

Note: Adverse events may be reported on-line to the TGA, by the Manufacturer or Sponsor, at **https://www.tga.gov.au/reporting-problems**.

Note: It is a condition on Australian Sponsors of Class AIMD, Class III and Implantable Class IIb devices that they provide three consecutive annual reports to the TGA following inclusion of the device in the ARTG. Annual reports are due 1 October each year. Reports should be for the period 1 July to 30 June. The report is to include:

- ARTG no.
- Product name
- Model no(s)
- Number supplied in Australia
- Number supplied worldwide (Numbers should include devices that are the same but supplied under a different name in another jurisdiction)
- Number of complaints in Australia
- Number of complaints worldwide

- Number of adverse events and incident rates in Australia (Rate= No. of events/ No. Supplied x 100 = Rate%)
- Number of adverse events and incident rates worldwide
- A list of the more common complaints and all of the adverse events
- Device Incident Report (DIR) number of those adverse events reported to the TGA
- Regulatory/corrective action/notification by Manufacturer

Note: Australian Sponsors are required to provide Manufacturers with any information that will assist the Manufacturer to comply with the obligations of a conformity assessment procedure (e.g. information in relation to adverse events) [TG(MD)R Reg 5.8].

Brazil (ANVISA):

Verify that a post-market surveillance system is established and implemented in the medical device organization and integrated into the Quality System, with procedures and workflows established to ensure the correct and the prompt identification of adverse events, the performance of investigations and use of the results to improve the safety and effectiveness of the device when necessary [RDC ANVISA 67/2009 – Art. 6º].

For domestic manufacturers (also applies to legal representatives in Brazil) - verify that top management has designated a professional to be responsible for the post-market surveillance system. This designation shall be documented [RDC ANVISA 67/2009 – Art. 5º].

Verify that the medical device organization has mechanisms for processing and recording complaints, conducting investigations, and providing feedback directly to the complainant, or in the case of an international manufacturer, to their legal representative in Brazil, as necessary [RDC ANVISA 67/2009 – Art. 6º, Art. 7º, Art. 9º].

Verify that the medical device organization has notified the regulatory authority about problems associated with their devices, including adverse events (critical or non-critical), any technical defect that was identified regarding products already marketed, anything that can cause a serious hazard to public health, or cases of counterfeit [RDC ANVISA 67/2009 – Art. 8º].

For international manufacturer, verify that the legal representative in Brazil is aware about the occurrence of possibility of death, serious hazard to public health or cases of counterfeit, associated with their products exported to Brazil [RDC ANVISA 67/2009 – Art. 8º].

Canada (HC):

CMDR 59-61.1, 61.2-61.3

Verify that the Manufacturer and the importer of a medical device make a preliminary and final report to the minister concerning any incident occurring inside Canada involving a device sold (authorized for sale) in Canada that:

- Is related to the failure of the device or deterioration in its effectiveness or any inadequacy in its labeling or in its directions for use; and
- Has led to death or serious deterioration in the state of health of a patient, user, or other person, or could do so if it were to recur [CMDR 59(1)].

[Note: the requirement to report incidents occurring outside of Canada no longer applies to class II-IV devices authorized for sale in Canada. The requirement nonetheless still applies for class I devices.[CMDR 59(1.1)]]

Verify that the Manufacturer or other person becoming aware of an event that led to the death or serious deterioration in the state of health of a patient, a user, or other person provides information in a preliminary report within 10 days after the person becomes aware of the event or occurrence [CMDR 60 (1)(a)(i)].

Verify that the Manufacturer or other person becoming aware of an event that the recurrence of which might lead to the death or serious deterioration in the state of health of a patient, a user, or other person provides information in a preliminary report within 30 days after the person becomes aware of the event or occurrence [CMDR 60 (1)(a)(ii)].

Verify that Manufacturer has made effective arrangements to submit preliminary reports to the Minister and that the reports contain [CMDR 60 (2)]:

- the identifier of any medical device that is part of a system, test kit, medical device group,
- medical device family or medical device group family
- if the report is made by:
    - the Manufacturer:
        - the name and address of that Manufacturer and of any known importer, and
        - the name, title and telephone and facsimile numbers of a representative of the Manufacturer to contact for any information concerning the incident, or
    - the importer of the device:
        - the name and address of the importer and of the Manufacturer, and
        - the name, title and telephone and facsimile numbers of a representative of the importer to contact for any information concerning the incident.
- the date on which the incident came to the attention of the Manufacturer or importer
- the details known in respect of the incident, including the date on which the incident occurred
- and the consequences for the patient, user or other person
- the name, address and telephone number, if known, of the person who reported the incident to the Manufacturer or importer
- the identity of any other medical devices or accessories involved in the incident, if known
- the Manufacturer's or importer's preliminary comments with respect to the incident

- the course of action, including an investigation, that the Manufacturer or importer proposes to follow in respect of the incident and a timetable for carrying out any proposed action and for submitting a final report
- a statement indicating whether a previous report has been made to the Minister with respect to the device and, if so, the date of the report.

If a preliminary report required by section 60 is submitted to the Minister and/or Importer, verify that the Manufacturer has submitted a final report to the Minister in writing in accordance with the timetable established under CMDR 60(2)(h) and the final report contains [CMDR 61(1)(2)]:

- a description of the incident, including the number of persons who have experienced a serious deterioration in the state of their health or who have died
- a detailed explanation of the cause of the incident and a justification for the actions taken in respect of the incident
- any actions taken as a result of the investigation, which may include:
    - increased post-market surveillance of the device
    - corrective and preventive action respecting the design and manufacture of the device, and
    - recall of the device.

Manufacturers and Importers can use the **"Mandatory Medical Device Problem Reporting Form for Industry**" to submit preliminary and final incident report.

If the reports required by section 60 and 61 are submitted to the Minister just by the Importer, verify that the Manufacturer has advised the Minister in writing that the reports the Manufacturer and importer would have submitted were identical and that the Manufacturer has permitted the importer to prepare and submit reports to the Minister on the Manufacturer's behalf [CMDR 61.1]. This notification is to be done using **Health Canada form "FRM-0090"**.

[Note: additional guidance on Mandatory Problem Reporting, including these modified requirements, is available in the associated **Guidance Document**.]

Verify that the Manufacturer of a medical device submits to the Minister information regarding serious risk of injury to human health related to the safety of the device that it becomes aware of or receives, regarding:

(a) Risks that have been communicated by any Regulatory Agency that is set out in the **List of Regulatory Agencies for the Purposes of Section 61.2 of the Medical Devices Regulations**, or by any person who is authorized to manufacture or sell a medical device within the jurisdiction of such a Regulatory Agency, and the manner of the communication;
(b) changes that have been made to the labelling of any medical device and that have been communicated to or requested by any Regulatory Agency that is set out in the list referred to in paragraph (a); and

(c) recalls, reassessments and suspensions or revocations of authorizations, including licences, in respect of any medical device, that have taken place within the jurisdiction of any Regulatory Agency that is set out in the list referred to in paragraph (a). [CMDR 61.2(2)]

For greater clarity, serious risk of injury to human health is defined as a hazard associated with the medical device that is relevant to the safety of the medical device and that, without risk mitigation, would likely:

- be life-threatening
- result in persistent or significant disability or incapacity
- require inpatient hospitalization or prolonged hospitalization
- result in a serious health consequence such as loss of function or debilitating chronic pain
- result in death

Verify that manufacturers submit notifications of foreign risks within 72 hours after receiving or becoming aware that a notifiable action has been taken in response to a serious risk, whichever comes first. [CMDR 61.2(3)]

Foreign Risk Notifications can be submitted using the "**Medical Device Foreign Risk Notification Form for Industry**".

If the notification required by section 61.2 is submitted to the Minister just by the Importer, verify that the Manufacturer has advised the Minister in writing that the report the Manufacturer and importer would have submitted were identical and that the Manufacturer has permitted the importer to prepare and submit reports to the Minister on the Manufacturer's behalf [CMDR 61.3(2)]. This notification is to be done using **Health Canada form "FRM-0090"**.

Additional information and guidance on Foreign Risk Notification can be found in the associated **Guidance Document**.

Japan (MHLW):

Marketing Authorization Holders are required to implement post market safety activities in accordance with domestic (Japanese) regulatory requirements in addition to the QMS requirements.

The persons operating the Registered Manufacturing Sites are not required to report any adverse event directly to a Regulatory Authority but shall report any adverse event which meets the criteria specified by the Ordinance for Enforcement of PMD Act Article 228-20 to the Marketing Authorization Holder [MHLW MO169: 55-3; (Old: 62.6)].

Verify that the person operating the Registered Manufacturing Site provides events which meets the following criteria defined by the Ordinance for Enforcement of PMD Act Article 228-20.2 (see below), to the Marketing Authorization Holder in a timely manner.

- The following malfunction events which may cause or may have caused health damage:

- Serious event (domestic and foreign)
- Unlabeled non-Serious event (domestic)
- The following Adverse Reaction events which was caused or might have been caused by the malfunction of a medical device:
- Serious event (domestic and foreign)
- Unlabeled non-Serious event (domestic)
- Any action taken for preventing the occurrence or expansion of public health hazard in relation to a medical device which is marketed in foreign countries and is equivalent to the one marketed in Japan. The action includes but not limited to:
- Suspension of manufacturing, importing or selling
- Recall and
- Abolishment.
- Study report that indicates:
- Possibility of event of cancer and other serious illness, injury or death caused by malfunction of a medical device (domestic and foreign), or by infectious disease arising from usage of a device (domestic and foreign)
- Significant occurrence rate change of event etc. caused by malfunction of a medical device (domestic and foreign)
- Significant occurrence rate change of infectious disease caused by usage of a medical device (domestic and foreign)
- The fact that a medical device is less effective than claimed when approved.

United States (FDA):
21 CFR 803: Medical Device Reporting

Determine whether the manufacturer has developed a process for reporting to FDA incidents involving device-related deaths, serious injuries, and reportable malfunctions that occur within and outside the United States if the same or similar device is marketed to the United States.

Confirm that the manufacturer has developed, maintained, and implemented written medical device reporting (MDR) procedures for the following:

- Internal processes that provide for:
- Timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements
- A standardized review process or procedure for determining when an event meets the criteria for reporting
- Timely transmission of complete medical device reports to FDA
- Documentation and recordkeeping requirements for:

- Information that was evaluated to determine if an event was reportable;
- All medical device reports and information submitted to FDA
- Processes that ensure access to information that facilitates timely follow-up and audit.

Verify that reports are made within 30 calendar days after the day that the manufacturer receives or otherwise becomes aware of information, from any source, that reasonably suggests that a device that is marketed may have caused or contributed to a death or serious injury:

- Confirm the manufacturer's MDR files contain the following:
- Information (or references to information) related to the adverse event, including all documentation of deliberations and decision-making processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable to FDA
- Copies of all MDR forms and other information related to the event submitted to FDA.

If a device has malfunctioned and this device or a similar device that is marketed would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur, quarterly summary reporting is acceptable for most device product codes.

If the manufacturer maintains MDR event files as part of the complaint file, ensure that the manufacturer has prominently identified these records as MDR reportable events. FDA will not consider a submitted MDR report to comply with 21 CFR 803 unless the manufacturer evaluates an event in accordance with the quality management system requirements. Confirm that the manufacturer has documented and maintained in the MDR event files an explanation of why the manufacturer did not submit or could not obtain any information required by 21 CFR 803, as well as the results of the evaluation of each event.

Compare the information submitted on the individual medical device report to the information contained in the associated complaint and confirm the medical device report contains all information related to the event that is reasonably known to the manufacturer.

Verify the manufacturer has submitted reports to FDA no later than 5 work days after the day that the manufacturer becomes aware that:

- An MDR reportable event necessitates remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer may become aware of the need for remedial action from any information, including any trend analysis; or
- FDA has made a written request for the submission of a 5-day report. If the manufacturer receives such a written request from FDA, the manufacturer must submit, without further requests, a 5-day report for all subsequent events of the same nature that involve substantially similar devices for the time period specified in the written request. FDA may extend the time

period stated in the original written request if FDA determines it is in the interest of the public health.

Verify the manufacturer submitted supplemental reports within one month of obtaining information that was not submitted in an initial report.

Confirm that medical device reports include the unique device identifier (UDI) that appears on the device label or on the device package.

Medical device reports submitted to FDA must be submitted electronically via the Electronic Submissions Gateway (ESG) using eSubmitter or the AS2 Gateway-to-Gateway using HL7 ICSR XML software.

Links

Measurement, Analysis and Improvement

Reports of individual adverse events are a form of feedback and must be analyzed as appropriate for trends requiring improvement or corrective action.

During the audit of the Measurement, Analysis and Improvement process, confirm that the medical device organization has considered individual adverse events and trends of adverse events in the analysis of data.

Task 2 – Notification of advisory notices

Verify that advisory notices are reported to regulatory authorities when necessary and comply with the timeframes and recordkeeping requirements established by participating regulatory authorities.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.2.3, 8.2.3, 8.3.3

Country specific requirements

Australia (TGA):

Manufacturers are required to implement a post-marketing system that includes provisions for the recall of devices – e.g. *Therapeutic Goods (Medical Devices) Regulations 2002* Schedule 3 Part 1 Clause 1.4 (3A). Under the MDSAP, and in view of the written agreement between Manufacturers and the Australian Sponsor [TG Act 41FD] (see **Annex 4**), proposed recalls must be reported by the Manufacturer to the MDSAP AO, and to the TGA or Sponsor in a timely manner to ensure that a

Sponsor can meet their reporting obligations [*Therapeutic Goods (Medical Devices)* Regulation 5.7 and 5.8, *Therapeutic Goods Act* Part 4-9 and the Uniform Recall Procedure for Therapeutic Goods (URPTG)].

Note: Further information concerning the Australian requirements for advisory notices and the recovery of devices is available at **https://www.tga.gov.au/recalls**

Note: Australian Sponsors are required to provide Manufacturers with any information that will assist the Manufacturer to comply with the obligations of a conformity assessment procedure (e.g. information in relation to the recovery of devices) [TG(MD)R Reg 5.8].

Brazil (ANVISA):
Verify that procedures and work flows were established in order to identify when field actions (recalls and corrections) are necessary, in accordance with the medical device organization's post-market surveillance system and quality system [RDC ANVISA 67/2009 - Art. 6º, RDC ANVISA 551/2021 – Art. 1º, Art. 5º].

Verify that the medical device organization keeps records regarding field actions performed, including those that do not need to be reported to regulatory authorities [RDC ANVISA 551/2021 – Art. 4º; Art. 6º, Art. 10, Art. 11, Art. 16].

For domestic manufacturers (also applies to legal representatives in Brazil) - verify that the medical device organization has sent to the regulatory authority the reports requested, according to Brazilian regulation [RDC ANVISA 551/2021– Art. 10, Art. 11].

Verify that the medical device organization has performed field actions based on potential or concrete evidence that their product does not comply with essential requirements of safety and effectiveness [RDC ANVISA 551/2021 – Art. 4º, Art. 6º, Art. 7º, Art. 13, Art. 14, Art. 15].

For domestic manufacturers (also applies to legal representatives in Brazil) - verify that the medical device organization has performed field actions when required by the regulatory authority [RDC ANVISA 551/2021 – Art. 6º].

For domestic manufacturers (also applies to legal representatives in Brazil) - verify that the medical device organization notified the regulatory authority regarding field actions, in accordance with requirements and deadlines established per Brazilian regulation [RDC ANVISA 551/2021 – Art. 7º, Art. 8º].

For international manufacturers, verify that the legal representative in Brazil was aware about the occurrence of field actions performed on products exported to Brazil [RDC ANVISA 67/2009 – Art. 8º].

Canada (HC):
Medical Device Regulations SOR/98-282, Section 63 – 65.1:

Verify that the Manufacturer and the importer of a medical device, on or before undertaking a recall of a device provide the minister with the following information [CMDR 64]:

- the name of the device and its identifier, including the identifier of any medical device that is part of a system, test kit, medical device group, medical device family or medical device group family
- the name and address of the Manufacturer and importer, and the name and address of the establishment where the device was manufactured, if different from that of the Manufacturer
- the reason for the recall, the nature of the defectiveness or possible defectiveness and the date on and circumstances under which the defectiveness or possible defectiveness was discovered
- an evaluation of the risk associated with the defectiveness or possible defectiveness
- the number of affected units of the device that the Manufacturer or importer:
- manufactured in Canada,
- imported into Canada,
- sold in Canada.
- the period during which the affected units of the device were distributed in Canada by the Manufacturer or importer
- the name of each person to whom the affected device was sold by the Manufacturer or importer and the number of units of the device sold to each person
- a copy of any communication issued with respect to the recall
- the proposed strategy for conducting the recall, including the date for beginning the recall, information as to how and when the Minister will be informed of the progress of the recall and the proposed date for its completion
- the proposed action to prevent a recurrence of the problem
- the name, title and telephone number of the representative of the Manufacturer or importer to contact for any information concerning the recall.

Verify that as soon as possible after the completion of the recall the Manufacturer and the importer reports to the minister the results of the recall and the action taken to prevent a recurrence of the problem [CMDR 65].

If the reports required by section 64 and 65 are submitted to the Minister just by the Importer, verify that the Manufacturer has advised the Minister in writing that the reports the Manufacturer and importer would have submitted were identical and that the Manufacturer has permitted the importer to prepare and submit reports to the Minister on the Manufacturer's behalf [CMDR 65.1].

For greater clarity and consistency with **section 4.1.1 of Health Canada's Recall Policy for Health Products (POL-0016)**, AOs and auditors are advised of the following interpretations of the timelines in sections 64 and 65 of the *Medical Devices Regulations*:

*Section 64 of the Medical Devices Regulations requires the manufacturer and importer of a medical device to provide Health Canada with information concerning a recall "**on or before undertaking a recall**". This is interpreted to mean that the manufacturer and importer must submit to Health Canada as much recall information as is known **within 24 hours of having made the decision to recall**. This initial notification may be made verbally or in writing. This must be followed by a written report containing full information as required by section 64 **within three business days of starting the recall**. As per section 65 of the Medical Devices Regulations, a report on the results of the recall and the action taken to prevent a recurrence of the problem must be submitted **as soon as possible after the completion of a recall**.*

Japan (MHLW):
Marketing Authorization Holders are required to report advisory notices to Regulatory Authorities [PMD Act 68-11].

Confirm that the person operating the Registered Manufacturing Site has determined and implemented effective arrangement for communicating with the Marketing Authorization Holder in relation to advisory notices [MHLW MO169: 29].

Note: Persons operating Registered Manufacturing Sites are not required to report any advisory notice directly to regulatory authority, but shall communicate with the Marketing Authorization Holder, so they can take necessary regulatory actions.

United States (FDA):
21 CFR 806: Medical Devices; Reports of Corrections and Removals

Verify that the manufacturer has a process in place to notify FDA in the event of actions concerning device corrections and removals and to maintain records of those corrections and removals.

Verify that the written report to FDA of any correction or removal initiated to reduce a risk to health or remedy a violation of the U.S. Food, Drug and Cosmetic Act is reported within 10 working days of initiating the correction or removal. Confirm that the report contains the unique device identifier (UDI) that appears on the device label or on the device package, or the device identifier, Universal Product Code (UPC), model, catalog, or code number of the device and the manufacturing lot or serial number of the device or other identification number.

Confirm that the manufacturer maintains records of any correction and removal not required to be reported to FDA (e.g. corrections and removals conducted to correct a minor violation of the U.S. Food, Drug and Cosmetic Act or no risk to health). Confirm that records of corrections and removals not required to be reported contain the unique device identifier (UDI) that appears on the device label

or on the device package, or the device identifier, Universal Product Code (UPC), model, catalog, or code number of the device and the manufacturing lot or serial number of the device or other identification number.

Links

Measurement, Analysis and Improvement

Corrections and removals are indicative that the product or process does not meet specified requirements or planned results and the nonconformity was not detected prior to distribution. When specified requirements or planned results are not achieved, correction and corrective action must be taken as necessary.

During the audit of the Measurement, Analysis and Improvement process, confirm the medical device organization has taken appropriate correction regarding devices already distributed, and taken appropriate corrective action to prevent recurrence of the condition(s) that caused the nonconformity.

Chapter 5 - Design and Development

The purpose of the Design and Development process is to control the design of a medical device and to assure that the device meets user needs, intended use, and its specified requirements. Attention to design and development planning, identifying design inputs, developing design outputs, verifying that design outputs meet design inputs, validating the design, controlling design changes, reviewing design results, transferring the design to production, and compiling the appropriate records will help a medical device organization assure that resulting designs will meet user needs, intended uses, and requirements.

The **management representative** is responsible for ensuring that the requirements of the quality management system have been effectively defined, documented, implemented, and maintained. Prior to the audit of a process, it may be helpful to interview the management representative (or designee) to obtain an overview of the process and a feel for management's knowledge and understanding of the process.

Audit of the Design and Development process will follow audit of the Measurement, Analysis and Improvement process per the MDSAP audit sequence. Information regarding product or quality system nonconformities noted during audit of the Measurement, Analysis and Improvement process should be considered when making decisions as to the design and development projects, including design changes resulting from corrective actions, to be reviewed during the audit of the Design and Development process.

Review of the Design and Development process will also provide an opportunity to evaluate how the medical device organization has utilized risk management activities to ensure design inputs are comprehensive and meet user needs, to confirm that risk control measures that were planned have been implemented in the design, and to verify that risk control measures are effective in controlling or reducing risk.

Additionally, review of design and development activities will assist the audit team during the audit of the medical device organization's Purchasing process because the auditor(s) has an opportunity to select suppliers for review whose activities are associated with higher risk to the product or whose activities are critical to the essential design outputs. The review of design and development activities also provides information to assist the audit team in performing a final evaluation of the Management process at the conclusion of the audit.

Auditing the Design and Development Process

Purpose: The purpose of auditing the Design and Development process is to verify that the medical device organization establishes, documents, implements, and maintains controls to ensure that medical devices meet user needs, intended uses, and specified requirements.

Outcomes: As a result of the audit of the Design and Development process, objective evidence will show whether the medical device organization has:

A) Defined, documented and implemented procedures to ensure medical devices are designed according to specified requirements
B) Effectively planned the design and development of a device

C) Established mechanisms, including systematic review, for addressing incomplete, ambiguous or conflicting requirements
D) Determined the internally or externally imposed requirements for safety, function, and performance for the intended use, including regulatory requirements, risk management, and human factors requirements
E) Verified that design outputs satisfy design input requirements
F) Identified and mitigated, to the extent practical, the risks associated with the device, including the device software
G) Ensured that changes to the device design are controlled, the risks associated with the design change are identified and mitigated, to the extent practical, and that the device will continue to perform as intended
H) Performed design validation to ensure devices conform to user needs and intended use
I) Confirmed that the design is correctly translated into production methods and procedures

Links to Other Processes:

Purchasing; **Production and Service Controls**; **Measurement, Analysis and Improvement**; **Device Marketing Authorization and Facility Registration**

Task 1 – Identification of devices subject to design and development procedures; technical documentation

Verify that those devices that are, by regulation, subject to design and development procedures have been identified. (See Annex 1)

Clause and Regulation

ISO: ISO 13485:2016: 4.1.1, 4.2.1, 7.1, 7.3.10

TGA: TG(MD)R Division 3.2

MHLW/PMDA: MO169: 5-1, 6, 26, 36-2; [Old: 5, 6, 26]

FDA: 21 CFR 820.30(a)]

Additional country-specific requirements

Australia (TGA):

When a Manufacturer applies TG(MD)R Division 3.2 and selects the Full Quality Assurance conformity assessment procedures [TG(MR)R Schedule 3, Part1, (excluding or including clause 1.6)], quality management system procedures for design and development must be available.

In addition, for all classes of devices, the guidance provided for the audit of technical documentation in **Annex 1** is to be followed to ensure the availability of objective evidence that demonstrates compliance with the Essential Principles of Safety and Performance.

Brazil (ANVISA):
According to Brazilian legislations, there is no exception to design control.

If design activities are outsourced, verify that the manufacturer has a complete device master record for the device and records of the design transfer to production [RDC ANVISA 665/2022: Art. 52, Art. 63].

Canada (HC):
With respect to Class II devices that are not subject to Design and Development controls, verify that the manufacturer has objective evidence to establish that Class II devices meet the safety and effectiveness requirements of section 10 to 20 [CMDR 9, 10 to 20].

Japan (MHLW):
Class 1 devices are not required to comply with the requirements of MHLW MO169:30-36-2, which are equivalent to the requirements of design and development in ISO13485 [MHLW MO169: 4.1].

Assessing conformity

Absence of design activity

The audit team may encounter situations where the medical device organization has not completed any design projects, has no ongoing or planned design projects, and has not made any design changes (i.e., there has been no design activity). At the minimum, verify that the medical device organization maintains a defined and documented design change procedure. A medical device organization may also have defined and documented other design control procedures. For that type of medical device organization — a medical device organization with no design activity, including no design changes — assess the procedures the medical device organization has in place. The audit team can then proceed to the audit of the next process.

Outsourced design activities

In cases where design activities (development and changes) are completely outsourced by the medical device organization, the audit team must verify (at a minimum) that the controls and records related to the design transfer to production have been determined and that the production line, implemented in the medical device organization's site, meets the production requirements established during the design and development of the device.

In these cases, the medical device organization shall ensure that the supplier complies with the requirements of design and development, established by Medical devices – Quality management systems – Requirements for

regulatory purposes (ISO 13485:2016), the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Japanese QMS Ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820), and any other specific requirements of medical device regulatory authorities participating in the MDSAP program.

Links

Purchasing

If the medical device organization outsources design and development activities, or any portion of the design and development, confirm that the medical device organization treats the outsourced medical device organization as a supplier, has appropriately qualified and maintains control over the supplier, communicates requirements to the supplier, including regulatory requirements, and has arrangements to verify that the design and development activities satisfy those requirements.

Task 2 – Selection of a completed design and development project

Select a completed (where applicable) design and development project for review.

Priority criteria for selection:

1. complaints or known problems with a particular device
2. product risk
3. recent design changes, particularly design changes made to correct quality problems associated with the device design
4. age of design (prefer most recent)
5. designs that have not been recently audited

Links

Measurement, Analysis and Improvement

At this point in the audit, the audit team will have already reviewed the Measurement, Analysis and Improvement process. If the auditors noted corrective actions that resulted in design changes, or noted product nonconformities that have been attributed to the design of the device, the audit team should consider selecting those designs for review.

The audit team should be particularly mindful of how the identified quality problems from the Measurement, Analysis and Improvement process are related to specific aspects of the design and development of the device. For example, if the auditors review complaints related to a safety feature of the device that is not performing as intended, the audit team should consider selecting for review the design verification of that safety feature and determine whether appropriate risk control methods were confirmed to be effective.

Task 3 – Design and development planning

Verify that the design and development process is planned and controlled.

Review the design plan for the selected design and development project to understand the design and development activities; including the design and development stages, the review, verification, validation, and design transfer activities that are appropriate at each stage; and the assignment of responsibilities, authorities, and interfaces between different groups involved in design and development.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.1, 7.3.2

TGA: TG(MD)R Sch3 P1 Cl 1.4(4)&(5)(c)

ANVISA: RDC ANVISA 665/2022: Art. 44, Art. 61

MHLW/PMDA: MO169: 6, 26, 30

FDA: 21 CFR 820.30(b), 820.30(j)]

Additional country-specific requirements

Australia (TGA):

Verify that effective planning for design and development is documented, typically as part of a Quality Plan [TG(MD)R Sch3 P1 Cl 1.4(4)].

Canada (HC):
Verify that Manufacturers of Class IV devices maintain a quality plan that sets out the specific quality practices, resources, and sequence of activities relevant to the device [CMDR 32].

Assessing conformity

Reviewing the design plan
Review the design plan for the selected project to understand the layout of the design and development activities, including assigned responsibilities and interfaces.

The design plan for the selected project can be used by the audit team as a roadmap for the review of the project.

Plans may vary depending on the type or size of the project. Some design plans may be expressed as simple flowcharts, or for larger projects, Gantt or Program Evaluation Review Technique (PERT) charts may be used. Plans do not have to show starting or completion dates for activities covered. However, plans must define responsibility for implementation of the design and development activities and describe the interfaces with different groups or activities.

Expect to see interfacing between research and development, marketing, regulatory, manufacturing, and quality departments. The audit team might also see interfacing with purchasing, installers, and servicers. When external institutions (e.g. universities or research and development centers) are involved in the design and development activities, the interfaces between the medical device organization and those external institutions must also be defined.

Design and development plans may change while the design and development process evolves; however, all changes on the plan must be documented and approved.

Links
None

Task 4 – Implementation of the design and development process

For the device design and development record(s) selected, verify that design and development procedures have been established and applied.

Confirm the design and development procedures address the design and development stages, review, verification, validation, design transfer, and design changes.

Clause and Regulation
ISO: ISO 13485:2016: 4.2.1, 7.3.1, 7.3.10

TGA: TG(MD)R Sch3 P1 Cl 1.4(4)&(5)(c)

ANVISA: RDC ANVISA 665/2022: Art. 43

MHLW/PMDA: MO169: 6, 30, 36-2; [Old: 6, 30]

FDA: 21 CFR 820.30(a), 820.30(j)]

Additional country-specific requirements

United States (FDA):
Verify that the design input procedures contain a mechanism for addressing incomplete, ambiguous, or conflicting requirements [21 CFR 820.30(c)].

Assessing conformity

Review of procedures

Design and development procedures set the structure, provide the framework, and support the medical device organization's Design and Development process. The purpose of auditing the procedures is to determine if the medical device organization has that framework in place. If procedures have not been defined and documented, or are deficient, the medical device organization's devices may not meet user needs and intended use.

In accomplishing this audit task, the audit team is to review the medical device organization's procedures and verify that the procedures address the requirements of the Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016), the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Japanese QMS Ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820), and specific requirements of medical device regulatory authorities participating in the MDSAP program. For example:

- verify that the design input procedure includes a mechanism for addressing incomplete, ambiguous, or conflicting requirements
- Verify that the output procedure ensures that essential outputs are identified
- Verify that the design review procedure ensures that each design review includes an individual who does not have responsibility for the design stage being reviewed.

Minimum requirement

If the medical device organization has no ongoing or planned design projects, has not made any design changes, then ensure that, at a minimum, the medical device organization maintains defined and documented design change procedures.

Links

None

Task 5 – Design and development input

Verify that design and development inputs were established, reviewed and approved; and that they address customer functional, performance and safety requirements, intended use, applicable regulatory requirements, and other requirements including those arising from human factors issues, essential for design and development.

Verify that any risks and risk mitigation measures identified during the risk management process are used as an input in the design and development process.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 5.2, 7.2.1, 7.3.3, 8.2.1

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl 1.4(2)&(5)(c), Sch 3 P1 1.4(3)(a)&(b)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 46, Art. 61

HC: CMDR 10-20, 21-23, 66, 67, 68

MHLW/PMDA: MO169: 6, 11, 27, 31, 55-1; [Old: 6, 11, 27, 31, 55]

FDA: 21 CFR820.30(c), 820.30(g)]

Additional country-specific requirements

Australia (TGA):

Verify that the Manufacturer has identified the relevant Essential Principles that apply to the medical device [TG(MD)R Sch1 Essential Principles].

Verify that Manufacturer has taken into account post-production feedback as an input to monitoring and maintaining product requirements and improving product realization processes.

United States (FDA):

For the selected device(s), verify that the medical device organization has the appropriate marketing clearance [510(k)] or pre-market approval (PMA) if distributing the devices in the United States [21 CFR 807].

Assessing conformity

Design inputs

Inputs are the physical and performance requirements of a device that are used as a basis for device design. Inputs must be documented and approved by appropriate personnel. The audit team should review the sources used to develop the inputs and determine that relevant aspects of the requirements for the device were covered. These sources must include the relevant regulations where safety and performance criteria have been defined (e.g. safety and efficacy requirements or Essential Principles of Safety and Performance). Examples of relevant aspects include:

- intended use, performance characteristics
- intended user
- risk mitigation
- biocompatibility
- compatibility with the environment of intended use (including electromagnetic compatibility)
- software
- radiation protection
- human factors
- sterility.

Organizations must take into account the current thinking of experts where published information is available (e.g. Standards).

Design inputs may also relate to manufacturing processes particularly where validation, revalidation, the periodic monitoring of critical process parameters, or the implementation of specified controls, is required to assure the quality of product (e.g. sterilization, injection molding, control on the source, or inactivation of transmissible agents in, materials of animal origin, or GMP controls on the handling, processing or incorporation of a medicinal substance in a medical device).

Design inputs are the basis of the design verification and validation; therefore, design inputs need to be defined and recorded as formal requirements that allow for confirmation to the design outputs.

Relevant information for design input can also come from post-production data or experience from similar devices. Complaints, adverse events, feedback, and post-market surveillance form a feedback system that can help drive quality improvements in new designs and changes to current designs.

Links

Device Marketing Authorization and Facility Registration

Confirm the medical device organization has considered regulatory requirements for registration, listing, notification and licensing; and has complied with these requirements prior to marketing the device in the applicable regulatory jurisdictions.

Task 6 – Completeness, coherence, and unambiguity of design and development input

Confirm that the design and development inputs are complete, unambiguous, and not in conflict with each other.

Clause and Regulation

ISO: ISO 13485:2016: 7.3.3

TGA: TG(MD)R Sch 3 Part 1.4(4)

ANVISA: RDC ANVISA 665/2022: Art. 46

MHLW/PMDA: MO169: 31

FDA: 21 CFR820.30(c)]

Additional country-specific requirements

Australia (TGA):

Confirm that design inputs include the relevant Essential Principles [TG(MD)R – Schedule 1].

Solutions adopted by the Manufacturer for the design and construction of a medical device are to conform to safety principles that are derived from the generally acknowledged state of the art. [TG(MD)R – Sch 1 – EP2] Safety principles are usually identified in internationally recognized standards.

Compliance with any given standard is not mandatory under Australian legislation however it is one way to demonstrate compliance with the Essential Principles.

The TGA is to presume compliance with the relevant Essential Principles if the Manufacturer has applied, in full, a relevant standard that is identified in a Medical Device Standards Order. (See TGA website - For example, ISO 10993).

If relevant standards have not been identified as design inputs, ensure that the Manufacturer has documented a rationale to explain why alternatives have been applied to demonstrate compliance with the Essential Principles [TG(MD)R Sch3 Part 1.4(5)(c)(iii)(C)].

Assessing conformity

Design inputs

Design inputs must be defined and recorded as verifiable requirements, approved by the appropriate personnel. If the medical device organization does not have accurate and complete design inputs, the final design may not meet user needs and intended use.

A common method for a medical device organization to confirm the design inputs for a design and development project are complete, unambiguous, and not in conflict with each other is to perform a design review after the initial requirements are determined.

Links

None

Task 7 – Design and development output and design verification

Review medical device specifications to confirm that design and development outputs are traceable to and satisfy design input requirements.

Verify that the design and development outputs essential for the proper functioning of the medical device have been identified.

Outputs include, but are not limited to:

- device specifications
- specifications for the manufacturing process
- specifications for the sterilization process (if applicable)
- the quality assurance testing
- device labeling and packaging.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 4.2.3, 7.3.4

TGA: TG(MD)R Sch3 P1 Cl 1.4(5)(c)

ANVISA: RDC ANVISA 665/2022: Art. 48, Art. 49, Art. 61

MHLW/PMDA: MO169: 6, 7-2, 32; [Old: 6, 32]

FDA: 21 CFR 820.30(d), 820.30(f)]

Additional country-specific requirements

Australia (TGA):
If relevant standards have not been applied, or not been applied in full, ensure that the Manufacturer has documented a rationale to explain why alternative methods have been applied to demonstrate compliance with the Essential Principles [TG(MD)R Sch3 Part 1.4(5)(c)(iii)(C)].

For devices incorporating a medicinal substance, verify that documentation also identifies the data to be derived from tests conducted in relation to the substance, and its interaction with the device [TG(MD)R Sch 3 Part 1.4(5)(c)(v)].

Assessing conformity

Design outputs
Design outputs are the work products or deliverables of a design stage. Design outputs can include documents such as diagrams, drawings, specifications, and procedures for both products and processes. The outputs from one stage may become inputs to the next stage. The total finished design output consists of the specifications for the device, its packaging and labeling (including implant cards and leaflets, where applicable), quality management system requirements, the manufacturing process, and if applicable, installation and servicing requirements.

During this design stage, a tremendous number of records, or outputs, can be produced. Only the approved outputs need to be retained. However, if a medical device organization chooses to retain other records, for historical or other purposes, they may do so.

Essential outputs
Outputs that are essential for the proper functioning of the device must be identified. Typically, a medical device organization can use a risk management tool to determine the essential outputs. To verify that this has been done, the auditor(s) may review the medical device organization's process for determining how the essential outputs were identified and if it was done in accordance with their design output procedures.

The identification of essential outputs may influence other quality system activities. For example, the establishment of manufacturing process controls and tolerances, the degree of purchasing controls and acceptance activities applied to a supplier or the priority and depth of a failure investigation may be influenced by whether or not the component (assembly, material, etc.) is considered an output essential for the proper functioning of the device.

Design outputs for sterile devices

Design and development of medical devices that are intended to be sterile should ensure compatibility of the sterilization process with the device, compatibility of the device packaging and the sterilization process, ability of the device to be sterilized or re-sterilized, and (if applicable), rationale for adding the device to a product family covered by a validated sterilization process.

Design verification

In design verification, the medical device organization obtains objective evidence (i.e., data) that design outputs meet design inputs. A medical device organization generates this objective evidence by conducting verification activities such as tests, measurements, and analyses. These activities should be explicit and thorough in their execution. A medical device organization's verification activities should be predictive, not empiric. In other words, acceptance criteria need to be stated in advance of the verification activity. The establishment of pre-determined acceptance criteria should be documented in a verification protocol or similar document. During the review of design verification activities, the auditor(s) will determine if the design verification data confirms that design outputs met the design input requirements.

Verification techniques

Complex designs will require more and different types of verifications than simple designs. Sometimes a medical device organization has to use its own expertise to develop (in-house) a way to verify a particular aspect of a design. Any approach selected by a medical device organization is acceptable as long as it provides reliable objective evidence that the output met the input.

Choosing verification activities for review

In accomplishing this audit task, select records generated from design verification activities associated with a number of design inputs and design outputs. The review of these records will determine whether design outputs met design input requirements. When possible, select documentation of design verification activities that are associated with outputs that are considered essential for the proper functioning of the device or are associated with the highest risk to the user or patient.

Links

Purchasing, **Production and Service Controls**

During the review of a design project, the audit team should be mindful of production processes and supplied products that are essential to the proper functioning of the device. Production processes can include not only the manufacturing instructions, but also internal controls, such as the type and extent of acceptance activities, equipment calibration and maintenance intervals, environmental controls, and personnel controls. For suppliers that provide products and services related to the essential design outputs, the degree of purchasing controls necessary is commensurate with the effect of the supplied product on the proper functioning of the finished device.

During the audits of the Purchasing process and Production and Service Controls process, the audit team should consider reviewing production processes and supplied products that have the highest risk or greatest effect on the essential design outputs.

Task 8 – Risk management activities applied throughout the design and development project

Verify that risk management activities are defined and implemented for product and process design and development.

Confirm that risk acceptability criteria are established and met throughout the design and development process.

Verify that any residual risk is evaluated and, where appropriate, communicated to the customer (e.g., labeling, service documents, advisory notices, etc.).

Note: In some instances, it may be necessary for the medical device organization to conduct a risk/benefit analysis to justify a risk that cannot be mitigated to an acceptable level. ***Additionally, it may be necessary to audit other processes (e.g. Production and Service Controls, Purchasing) to verify that risk acceptability criteria are met, risk is controlled or reduced, and residual risk is communicated if necessary.***

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.1, 7.3.3, 7.3.4

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl 1.4(5)(c)(iii)

Chapter 5 - Design and Development

Task 8 – Risk management activities applied throughout the design and development project

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ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 61, RDC ANVISA 56/2001

HC: CMDR 10, 11, 15, 16

MHLW/PMDA: MO169: 6, 26, 31, 32

FDA: 21 CFR 820.30(g)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that the manufacturer has established and maintains a continuous process of risk management which covers the entire life cycle of the product. Possible hazards must be identified in both normal and fault conditions, including those arising from human factors issues. The risk associated with those hazards, shall be calculated. Risks must be analyzed, evaluated and controlled, as necessary. Effectiveness of risk controls implemented shall be evaluated [RDC ANVISA 56/2001, RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20].

United States (FDA):

Confirm that the manufacturer has identified the possible hazards associated with the device in both normal and fault conditions. The risks associated with the hazards, including those resulting from user error, should be calculated in both normal and fault conditions. If any risk is judged to be unacceptable, it should be reduced to acceptable levels by the appropriate means. Ensure changes to the device to eliminate or minimize hazards do not introduce new hazards [21 CFR 820.30(g); preamble comment 83].

Assessing conformity

Risk management

Each medical device organization must determine and document how much risk is acceptable. The actual use of any medical device includes some measure of risk to users or patients. Determining an acceptable level of risk depends on the intended use of the device, including the particular health concern of the patient population, the training of the users involved, and the use environment. For example, pediatric patients may have less ability to detect a device malfunction. A device used by consumers generally has less medical oversight than a device used in a hospital setting. The goal of a risk management program is to ensure the device is as safe as practical and the safety of the device is acceptable for the intended use.

Effective risk management usually starts in conjunction with the design and development process, proceeds through product realization, including the selection of suppliers, and continues until the time the product is decommissioned. Risk management should be initiated at a point early in the design and development process. This includes defining the intended use of the device, considering risk under normal use and reasonably foreseen misuse. Starting the risk management process after the design has progressed beyond a point where reasonable risk mitigation features can be included in the design can lead to devices that do not

meet customer needs and the medical device organization's requirements for safety. Records of risk management should demonstrate that risks that have been identified as unacceptable have been mitigated to an acceptable level.

Mitigation of risks

There are a number of mechanisms that can be used to mitigate product risk. These risk mitigation mechanisms, in descending order of effectiveness, include safety features inherent in the device design, protective measures in the design (e.g. alarms), and user notifications (e.g. labeled warnings).

Review of risk management activities

During the review of the design project selected, verify that risk management is initiated early in the design and development process. Confirm that the medical device organization's risk management process involves the proactive evaluation, control, and monitoring of product risk, followed by the reactive response to quality data that indicates new or changing product risk.

Links

None

Task 9 – Design verification or design validation to confirm effectiveness of risk control measures

Confirm that design verification and/or design validation includes assurances that risk control measures are effective in controlling or reducing risk.

Clause and Regulation

ISO: ISO 13485:2016: 7.1, 7.3.6, 7.3.7

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl 1.4(5)(c)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 48

HC: CMDR 10,11, 15, 16

MHLW/PMDA: MO169: 26, 34, 35-1, [Old: 26, 34, 35]

FDA: 21 CFR 820.30(f), 820.30(g)]

Additional country-specific requirements

None

Assessing conformity

Verification of risk control measures

During the review of design verification activities for the chosen design project, confirm that the identified risk control measures are actually effective in reducing or controlling risk. For example, a design for an enteral feeding tube may have a unique connector to prevent the potential for misconnection to other types of devices, such as suction catheters. Design verification should show that it is difficult or impossible to connect non-related devices to the enteral feeding tube.

Links

None

Task 10 – Design validation

Verify that design and development validation data show that the approved design meets the requirements for the specified application or intended use(s).

Verify that design validation testing is adjusted according to the nature and risk of the product and element being validated.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.3.7

TGA: TG(MD)R Sch1 P1 2; Sch3 P1 Cl1.4(5)(d)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 49, Art. 53, Art. 54, Art. 55, Art. 56, Art. 57, Art. 58, Art. 61

HC: CMDR 12, 18, 19

MHLW/PMDA: MO169: 6, 35-1; [6, 35]

FDA: 21 CFR 820.30(g)]

Additional country-specific requirements

Australia (TGA):

For devices contain temperature sensitive material, environmental conditions should be considered for country specific requirement. For example, test samples should be conditioned as per ISTA 2A to cover Australian climate zone (extreme temperature range -29C-50C) for packaging validation.

Assessing conformity

Design validation

Design validation is performed to provide objective evidence that design specifications (outputs) conform to user needs and intended uses. Design validation must be completed before commercial distribution of the product. The design validation activities should be predictive, not empiric. In other words, acceptance criteria need to be stated in advance of the validation activity. The establishment of pre- determined acceptance criteria may be found in a validation protocol or similar document.

Design validation must be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. Design validation shall ensure that devices conform to defined user needs and intended uses and includes testing of production units under actual or simulated use conditions. The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, must be recorded.

Needs, environment and uses

Design validation must address the needs of all relevant parties, such as the patient, healthcare worker, biomedical engineer, and storage clerk. Consideration must be given to the environment in which the device will be stored, transported, and used.

Design validation needs to be performed for each intended use. Design validation must also confirm that user needs and intended uses associated with the device's packaging and labeling are met. These outputs have human factors implications and unless they are adequately considered during design validation, they may adversely affect the device and its use. Confirm that design validation data show that the approved design met the predetermined user needs and intended uses. The intended uses must include the purpose of the device, patient type (adults, pediatrics or newborn) and the environment in which the device is to be transported and used (domestic use, hospitals, ambulances, etc.).

Links

None

Task 11 – Clinical evaluation and/or evaluation of medical device safety and performance

Verify that clinical evaluations and/or evaluation of the medical device safety and performance were performed as part of design validation if required by national or regional regulations.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.3.7

TGA: TG(MD)R Reg 3.11, Sch1 EP14, Sch3 P1 Cl 1.4(5)(c)(vii), Sch3 P8

ANVISA: RDC ANVISA 665/2022: Art. 53, Art. 54, Art. 55, Art. 56, Art. 57, Art. 58, Art. 61, RDC ANVISA 56/2001

HC: CMDR 12, 18, 19

MHLW/PMDA: MO169: 6, 35-1; [Old: 6, 35]

FDA: 21 CFR 820.30(g)]

Additional country-specific requirements

Australia (TGA):
Verify that records of the validation include clinical evidence as required by the clinical evidence procedures [TG(MD) Sch3 P1 Cl 1.4(5)(c)(vii) and TG(MD) Sch3 P8].

For more information about the sources and types of clinical evidence and how they may be used to demonstrate compliance with the Australian EPs, auditors may refer to the clinical evidence guidelines (medical devices)

Assessing conformity

Clinical evaluations and testing
Design validation may involve the performance of some sort of clinical evaluation, including testing under actual or simulated use conditions. Clinical evaluations may involve full clinical studies. Clinical evaluations may also consist of other evaluations in a clinical or non-clinical setting, provision of historical evidence that similar designs are clinically safe, or reviews of scientific literature.

The audit team should limit their review of clinical evaluations to verifying whether clinical evaluations have been performed as part of design validation, when necessary, and whether the medical device organization has established acceptance criteria for the results in order to validate the device and that the results obtained meet the defined acceptance criteria.

When applicable, review the clinical evaluations, if performed, to validate the design. The audit team should confirm that the data from clinical evaluations demonstrates that the user needs and intended uses for the device and its packaging and labeling were met.

Links
None

Task 12 – Software design and development

If the medical device contains software, verify that the software was subject to the design and development process.

Confirm that the software was included within the risk management process.

Clause and Regulation

ISO: ISO 13485:2016: 7.3.2, 7.3.10

TGA: TG(MD)R Sch1 P1 2, Sch1 EP12.1

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 53, Art. 54, Art. 55, Art. 56, Art. 57, Art. 58, Art. 61

HC: CMDR 20

MHLW/PMDA: MO169: 30, 36-2; [Old: 30]

FDA: 21 CFR 820.30(g)]

Additional country-specific requirements

None

Assessing conformity

Software development

Many devices are at least partially controlled by software. Some devices consist almost entirely of software. For the device software, confirm that the software is part of the design and development plan for the device. The life cycle requirements for medical device software must be defined, including the intended use.

Software verification

"Software verification" is a term often used to describe the testing of the software. During the review of the software development, confirm that the medical device organization has conducted appropriate verification activities. Verification is often accomplished by performing test cases at the unit, subsystem, and integration levels; as well as system functional testing.

Software verification can include the testing of the software product installed on the target hardware. As with other types of design verification, verification of software is a predictive activity. The acceptance criteria must be determined prior to performing the testing.

The predetermined acceptance criteria are often found in a verification protocol or similar document. Confirm that the predetermined acceptance criteria have been met by reviewing the actual results of the selected software tests. The risk management activities for the device and software can help guide the audit team as to which verification tests involve the essential design outputs of the device and software.

Software validation

Software validation is a "confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through software can be consistently fulfilled." It involves checking for proper operation of the software in its actual or simulated use environment, including integration into the final device where appropriate. Testing of device software functionality in a simulated use environment, and user site testing are typically included as components of an overall design validation program for a software automated device.

The audit team may encounter times when the software has been installed at user sites as part of validation, often referred to as "beta testing". Beta testing can be a method to confirm the device, including the software, meets the user needs and intended uses.

Links

None

Task 13 – Design and development change

Verify that design and development changes were controlled, verified (or where appropriate validated), and approved prior to implementation.

Confirm that any new risks associated with the design change have been identified and mitigated to the extent practical.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 4.2.3, 7.1, 7.3.9, 7.3.10, 8.2.1

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl 1.4(5)(f), Sch3 P1Cl1.5(4), Sch3 P1 1.4(3)(a)&(b)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 49, Art. 53, Art. 54, Art. 55, Art. 56, Art. 57, Art. 58, Art. 60, Art. 61, Brazilian Law 6360/76 - Art. 13

HC: CMDR 1, 34

MHLW/PMDA: MO169: 6, 7-2, 26, 36-1, 36-2, 55-1; [Old: 6, 26, 36]

FDA: 21 CFR 820.30(i)]

Additional country-specific requirements

Australia (TGA):

Verify that the Manufacturer has a process or procedure for notifying the Auditing Organization of a substantial change to the design process or the range of products to be manufactured [TG(MD)R Sch3 Cl1.5].

Verify that the Manufacturer has a process or procedure for identifying a proposed substantial change to the design, or the intended performance, of a Class AIMD or Class III device, and to notify the assessment body prior to implementing the change [TG(MD)R Sch3 P1 Cl 1.6(4)].

If the Manufacturer is also a holder of a TGA Conformity Assessment Certificate, then the Manufacturer is also required to notify the TGA of these changes.

Verify that Manufacturer has taken into account post-production feedback as an input to monitoring and maintaining product requirements and improving product realization processes.

Brazil (ANVISA):
If the medical device evaluated is already registered/notified with ANVISA, verify that the design change was correctly and promptly submitted to ANVISA for approval, when applicable [Brazilian Law 6360/76 - Art. 13].

Canada (HC):
Verify that the manufacturer has a process or procedure for identifying a "significant change" to a Class III or IV medical device. Verify that information about "significant changes" is submitted in a medical device license amendment application [CMDR 1, 34].

Japan (MHLW):
For the Marketing Authorization Holder, confirm if the Marketing Authorization Holder has submitted a new application, a change application, or a change notification to PMDA/ a Registered Certification Body, when applicable [PMD Act 23-2-5.1, 23-2-5.11, 23-2-5.12, 23-2-23.1, 23-2-23.6, 23-2-23.7].

For the Registered Manufacturing Site, confirm if the site has a mechanism to communicate with the Marketing Authorization Holder about device modifications, so the Marketing Authorization Holder can take appropriate actions. If a critical medical device modification has happened in the Registered Manufacturing Site, confirm if the Registered Manufacturing Site has communicated with Marketing Authorization Holder about the change [MHLW MO169: 29].

United States (FDA):
Verify that the medical device organization obtained a new 510(k) or supplement to the pre-market approval if required [21 CFR 807].

Assessing conformity

Procedures
A medical device organization may have separate change control procedures to handle the post-production and pre-production changes, or a medical device organization may have one procedure that handles both.

Nature of change

The documentation and control of changes begins when the initial design inputs are approved and continues for the life of the product. Design change control applies to changes to inputs or outputs as a result of design verification or design validation, changes to labeling or packaging, changes to enhance a product's performance, changes of production process/es, and changes that result from product complaints. Change can be acceptable as long as it is controlled.

Records

The control of changes is not complete until the results of the review of changes and any updates to product specifications or changed processes are documented or amended.

Communication and consequential actions

Changes need to be effectively communicated and requirements for any consequential actions should be defined (e.g. training or communication to design or production staff

Links

Measurement, Analysis and Improvement process (if a design change was made to correct a quality problem with the device); **Device Marketing Authorization and Facility Registration**

During the audit of the Measurement, Analysis and Improvement process, the auditors may encounter corrective actions or preventive actions that resulted in design changes. When corrective action or preventive action involves changing the design, confirm that design controls have been applied to the change, in accordance with the medical device organization's procedures. Confirm these design changes were effective in addressing the quality issues or potential quality issues identified in corrective or preventive action. In addition, the design change should be evaluated under the medical device organization's risk management process to ensure that changes do not introduce new hazards. Some changes may require revalidation where it is not possible to verify that requirements have been met after the change has been implemented.

The audit team should also confirm the medical device organization has considered regulatory requirements for registration, listing, notification and licensing; and has complied with these requirements prior to marketing the changed device in the applicable regulatory jurisdictions.

Task 14 – Design review

Verify that design reviews were conducted at suitable stages as required by the design and development plan.

Confirm that the participants in the reviews include representatives of functions concerned with the design and development stage being reviewed, as well as any specialist personnel needed.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.3.2, 7.3.5

TGA: TG(MD)R Sch3 P1 C1.4(5)(c)(i)

ANVISA: RDC ANVISA 665/2022: Art. 50, Art. 61

MHLW/PMDA: MO169: 6, 30, 33

FDA: 21 CFR 820.30(e)]

Additional country-specific requirements

United States (FDA):

Verify that procedures ensure that participants 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, as well as any specialists needed [21 CFR 820.30(e)].

Assessing conformity

Design reviews

Design reviews typically occur at the end of each design stage or phase or after the completion of project milestones. The number of design reviews can vary, but at a minimum, one formal review must be conducted. Reviews should provide feedback to the design team on emerging problems, assess the progress of the design and development project, and confirm that the design is ready to move to the next phase of development or for transfer to the manufacturing phase.

It is not necessary to have fully convened meetings for all design reviews. For simple designs or minor changes, desk reviews and sign-offs may be adequate. Design reviews must include an individual who does not have direct responsibility for the design stage being reviewed and representation from manufacturing to ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications.

During the review of design review activities for the selected design project, confirm that the reviews included an individual who did not have direct responsibility for the design stage being reviewed. The audit team should also confirm that outstanding action items are being resolved or have been resolved.

Links

None

Task 15 – Impact review of design and development changes on previously made and distributed devices

Verify that design changes have been reviewed for the effect on products previously made and delivered, and that records of review results are maintained.

Clause and Regulation

ISO: ISO 13485:2016: 7.3.9

ANVISA: RDC ANVISA 665/2022: Art. 60

MHLW/PMDA: MO169: 36-1; [Old: 36]

FDA: 21 CFR 820.30(i)]

Additional country-specific requirements

None

Assessing conformity

Effects on constituent parts and products already delivered

There are situations where a design change can affect constituent parts. For example, a change to a disposable portion of an aspiration system might affect the ability of the disposable to connect to the console. When necessary, ensure the design change does not negatively impact products in distribution.

Links

None

Task 16 – Design transfer

Determine if the design was correctly transferred to production.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 4.2.3, 7.3.8

ANVISA: RDC ANVISA 665/2022: Art. 52, Art. 54, Art. 55, Art. 56, Art. 57, Art. 58, Art. 61

MHLW/PMDA: MO169: 6, 7-2, 35-2; [Old: 6, 30]

FDA: 21 CFR 830.30(h)]

Additional country-specific requirements

Brazil (ANVISA):

Confirm that the manufacture ensures that the design is not released for production until its approval by the persons assigned by the manufacturer and that the person/s assigned review all records required to the design history file in order to ensure it is complete and the final design is compatible with the approved plans, prior to its release. Confirm that this release, including date and manual or electronic signature of the responsible is documented [RDC ANVISA 665/2022: Art. 58, Art. 61].

Assessing conformity

Transferring the design to production

During this phase, the design is translated into production specifications. This can take place in steps or phases. The audit team should review how the design for the selected project was transferred into production specifications. Based on the medical device organization's identification of essential outputs and risk management activities, review significant elements of the manufacturing processes, including products from suppliers and the established tolerances for processes, and compare them with the approved design outputs contained within the design records. These activities can confirm whether or not the design was correctly transferred.

Design transfer is a process that may be initiated not only at the end of the design and development process, but may also be initiated immediately before validation stages and may continue as design and development evolves. This early initiation of design transfer is helpful in order to have production processes and device validations conducted properly and allow for corrections during the process. At the end, design and development process is "finalized" by a "final design transfer."

Links

Production and Service Controls, **Purchasing**

Verify that production processes for the device, including process validation (if required) have been defined, documented, and implemented. Confirm that potential hazards that could be introduced or exacerbated by the production process have been identified, and production controls have been established. Production processes include not only the manufacturing instructions, but also internal controls, such as the type and extent of acceptance activities, equipment calibration and maintenance intervals, environmental controls, and personnel controls.

Confirm that the medical device organization has determined the type and extent of supplier controls based on the relationship between the supplied products and services and product risk.

Task 17 – Top management commitment to design and development process

Determine, based on the assessment of the design and development process overall, whether management provides the necessary commitment to the design and development process.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.3, 5.1, 5.5.1

TGA: TG(MD)R Sch3 P1 Cl 1.4(5)(b)(ii)

ANVISA: RDC ANVISA 665/2022: Art. 5°, Art. 6°, Art. 7°

MHLW/PMDA: MO169: 5-3, 10, 15

Additional country-specific requirements

None

Links

None

Chapter 6 - Production and Service Controls

The purpose of the Production and Service Controls process is to manufacture products that meet specifications. Developing processes that are adequate to produce devices that meet specifications, validating (or fully verifying the results of) those processes, and monitoring and controlling those processes are all steps that help assure the result will be devices that meet specified requirements. After completing the audit of the medical device organization's Production and Service Controls process, the audit team will return to the Management process to make a final decision of whether top management ensures that an adequate and effective quality management system has been established and maintained at the medical device organization.

In order to meet the Production and Service Controls requirements of Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016), the Quality Management System requirements of the Conformity Assessment Procedures of the Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3), Brazilian Good Manufacturing Practices (RDC ANVISA 665/2022), Japanese QMS Ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820), and specific requirements of medical device regulatory authorities participating in the MDSAP program, the medical device organization must understand when deviations from device specifications could occur as a result of the production process or environment.

The **management representative** is responsible for ensuring that the requirements of the quality management system have been effectively defined, documented, implemented, and maintained. Prior to the audit of a process, it may be helpful to interview the management representative (or designee) to obtain an overview of the process and a feel for management's knowledge and understanding of the process.

Audit of the Production and Service Controls process will follow audit of the Measurement, Analysis and Improvement process and the Design and Development process per the MDSAP audit sequence. Information the audit team has learned about device and quality management system nonconformities during audit of the Measurement, Analysis and Improvement process, as well as higher risk elements and essential design outputs from the design projects reviewed during audit of the Design and Development process, should be used to make decisions as to the production processes to be reviewed during the audit of the Production and Service Controls process.

Auditing the Production and Service Controls Process

Purpose: The purpose of auditing the production and service controls process (including testing, infrastructure, facilities, equipment, and servicing) is to verify that the medical device organization's process/es are capable of ensuring that products will meet specifications.

Outcomes: As a result of the audit of the Production and Service Controls process, objective evidence will show whether the medical device organization has:

A) Defined, documented and implemented procedures to ensure production and service processes are planned, developed, conducted, controlled, and monitored to ensure conformity to specified requirements
B) Developed production and service process controls commensurate with the potential effect of the process on product risk
C) Ensured that when the results of a process cannot be verified by subsequent monitoring or measurement, the process is validated with a high degree of assurance that the process will consistently achieve the planned result
D) Implemented procedures for the validation of the application of computer software for production and service processes that affect the ability of the product to conform to specified requirements, including validation of computer software used in the quality management system
E) Maintained records for each batch of medical devices that provides information for traceability and confirmation that the batch meets specified requirements
F) Implemented controls to protect customer property, including intellectual property, confidential health information, and other forms of customer property that is used or incorporated into products

Links to Other Processes:

Management; **Design and Development**; **Measurement, Analysis and Improvement**; **Purchasing**

Task 1 – Planning of production and service process

Verify that the product realization processes are planned, including any necessary controls, controlled conditions, and risk management activities required for the product to meet the specified or intended uses, the statutory and regulatory requirements related to the product, and (when applicable) unique device identifier requirements.

Confirm that the planning of product realization is consistent with the requirements of the other processes of the quality management system and performed in consideration of the quality objectives.

Clause and Regulation

ISO: ISO 13485:2016: 7.1, 7.2.1, 7.5.1

TGA: TG(MD)R Sch 1 P1 2, Sch3 P1 Cl1.4(4), Sch3 P1 Cl1.4(5)(d)&(e)

ANVISA: RDC ANVISA 665/2022: Art. 5°, Art. 6°, Art. 7°, Art. 44, Art. 52, Art. 64, Art. 65, Art. 66

MHLW/PMDA: MO169: 26, 27, 40

FDA: 21 CFR 801, 820.30(b), 820.20(a), 820.30(h), 820.70(a), 830]

Additional country-specific requirements

United States (FDA):
Confirm that the medical device organization has determined the applicability of unique device identifier requirements per 21 CFR 801 and 21 CFR 830, has obtained the unique device identifiers from an FDA-accredited UDI-issuing agency, and the required data elements have been entered in the Global Unique Device Identification Database (GUDID) [21 CFR 801, 830].

Assessing conformity

Planning

In planning product realization, the medical device organization must determine as appropriate the quality objectives and requirements for the product, the processes, documents, and resources specific to the product, the criteria for product acceptance, and the required verification, monitoring, inspection, and test activities specific to the product. Planning of product realization often begins in the design and development of the product, including the translation of the design into production specifications.

The planning of product realization should be consistent with the risk control and mitigation strategies identified by the medical device organization during risk management activities.

During the audit, be mindful of requirements for the product that relate to statutory and regulatory requirements, requirements necessary for the product to meet specified or intended uses, and requirements for safe and efficacious use of the product. The medical device organization must ensure their processes, and the monitoring of processes, inspection, and test activities are planned and developed to ensure these requirements are met.

Unique Device Identifier (UDI)

A UDI is a coded representation of specified information. It appears on the device label, packaging, or in some cases on the device itself. The UDI should be presented in two forms: easily readable plain text, and Automated Identification and Data Capture (or AIDC) format. Many types of AIDC compliant codings are available and are permissible provided they can be entered into an electronic patient record or other computer system via an automated process.

The requirements of the rule are generally directed at labelers. Labeler is defined in 21 CFR 801.3.

Two main factors determine if a party is a labeler: (1) a labeler causes a label to be applied to a device with the intent that the device will be commercially distributed without any intended subsequent replacement or modification of the label, or (2) a labeler causes a label to be replaced or modified with the intent that the device will be commercially distributed.

Manufacturers, contract manufacturers, private label distributors, and convenience kit assemblers are the most common types of organizations that are considered labelers. Some small exceptions apply, such as adding a name or contact information to the already existing label.

The UDI program requires labelers to work with an FDA accredited issuing agency to produce their UDIs. The issuing agency provides a portion of the UDI to identify the labeler, as well as providing a standards compliant format for the display of the UDI in easily readable plain text and AIDC code.

The UDI rule requires device labelers to meet two basic requirements: (1) the devices must bear a UDI in the appropriate location, (2) and certain data elements must be entered in the Global Unique Device Identification Database (GUDID). The GUDID is a database maintained by the UDI team at FDA that serves as a public facing repository for UDI related device information.

Under the UDI rule, all medical devices, regardless of class (and including unclassified devices) must comply with the requirements of the rule, unless covered by an exemption or enforcement discretion.

Quality objectives

Quality objectives are typically expressed as a measurable target or goal. The planning of product realization should include consideration of how the production processes, the criteria for product acceptance, and the required verification, validation, monitoring, inspection, and test activities specific to the product will achieve the quality objectives. Confirm that the medical device organization has defined quality objectives for the device.

Links

Management

Confirm when necessary that the quality objectives related to the product were considered for inclusion in management review.

Task 2 – Selection of production and service process(es)

Review production processes considering the following criteria.

Select one or more production processes to audit.

Reminder: Information the audit team has learned about device and quality management system nonconformities during audit of the Measurement, Analysis and Improvement process, as well as higher risk elements and essential design outputs from the design projects reviewed during audit of the Design and Development process should be used to make decisions as to the production processes to be reviewed.

Priority criteria for selection:

1. Corrective and preventive action indicators of process problems or potential problems
2. Use of the production process for higher risk products
3. Use of production processes that directly impact the ability of the device to meet its Essential design outputs
4. New production processes or new technologies
5. Use of the process in manufacturing multiple products
6. Processes that operate over multiple shifts
7. Processes not covered during previous audits

Links

None

Task 3 – Controls for the implementation of selected production and service process(es)

For each selected process, determine if the production and service provision processes are planned and conducted under controlled conditions that include the following:

- the availability of information describing product characteristics
- the availability of documented procedures, requirements, work instructions, and reference materials, reference measurements, and criteria for workmanship
- the use of suitable equipment
- the availability and use of monitoring and measuring devices
- the implementation of monitoring and measurement of process parameters and product characteristics during production
- the implementation of release, delivery and post-delivery activities
- the implementation of defined operations for labeling and packaging
- the establishment of documented requirements for changes to methods and processes

Clause and Regulation

ISO: ISO 13485:2016: 7.5.1, 8.2.5, 8.2.6

TGA: TG(MD)R Sch3 P1 Cl1.4(5)(d)&(e)

ANVISA: RDC ANVISA 665/2022: Art. 30, Art. 63, Art. 62, Art. 64, Art. 65, Art. 66, Art. 84, Art. 88

MHLW/PMDA: MO169: 40, 57, 58, 59

FDA: 21 CFR 820.70(a), 820.70(b), 820.75, 820.120, 820.130]

Additional country-specific requirements
None

Assessing conformity

Establishment of work instructions, procedures, and production processes
Production processes that may cause a deviation to a device specification and all validated processes must be controlled and monitored. The planning of production includes the establishment of procedures and work instructions for the control and monitoring of the production processes, including service controls when necessary. Control and monitoring procedures may include in-process and finished device acceptance activities as well as environmental and contamination control measures. The establishment of procedures and work instructions to control the production of the device should provide the controls and tolerances necessary to ensure finished devices conform to product specifications.

Links
None

Task 4 – Control of product cleanliness

Determine if the medical device organization has established documented requirements for product cleanliness including any cleaning prior to sterilization, cleanliness requirements if provided non-sterile, and assuring that process agents are removed from the product if required.

Clause and Regulation
ISO: ISO 13485:2016: 4.2.1, 4.2.3, 6.4.2, 7.5.2

TGA: TG(MD)R Sch3 P1 Cl1.4(5)(d)

ANVISA: RDC ANVISA 665/2022: Art. 69, Art. 75, Art. 79

MHLW/PMDA: MO169: 6, 7-2, 25-2, 41; [Old: 6, 25, 41]

FDA: 21 CFR 820.70(c), 820.70(d), 820.70(e), 820.70(h)]

Additional country-specific requirements:

Brazil (ANVISA):
Confirm that a pest control program has been established and where chemicals are used as part of the pest control program, the company must ensure that they do not affect product quality [RDC ANVISA 665/2022: Art. 74].

Verify that the manufacturer has established and maintains housekeeping procedures and schedules for production areas and warehouses, in conformance with production specifications [RDC ANVISA 665/2022: Art. 69].

Assessing conformity

Cleanliness requirements

The goal of establishing requirements for product cleanliness is to minimize contamination of the finished device and the manufacturing environment. Sterile devices may require a higher level of control in terms of minimizing the bioburden and particulate contamination in order to assure the desired sterility assurance level is met.

Each medical device organization must evaluate the extent of cleanliness required for the proper functioning and intended use of the finished device and implement the necessary control measures. Examples of control measures include, but are not limited to, cleaning procedures, environmental controls (e.g. cleanrooms, or other controlled environments), requirements for attire, and training of personnel. When necessary, confirm the medical device organization has identified the cleanliness requirements for the finished device and the proper controls to achieve the required level of cleanliness.

Process agents

Process agents, also known as manufacturing materials, are generally defined as materials or substances used to facilitate the manufacturing process, which are present in or on the finished devices as a residue or impurity. Examples of process agents include cleaning agents, mold- release agents, lubricating oils, latex proteins, sterilant residues, etc. The medical device organization must evaluate process agents used during the manufacturing process when the process agent could potentially have an adverse effect on the product. During the design of the product and the development of the manufacturing process, the potential effect of process agents should be considered.

If the audit team encounters situations where process agents are being utilized in the manufacturing of the product, and the process agent could potentially have an adverse effect on the product, confirm that the medical device organization has made effective arrangements to control the process agent in a manner commensurate with the risk the agent poses to the finished device. For example, the medical device organization may need to validate a cleaning process to ensure cutting oil is removed from an orthopedic implant prior to packaging and sterilization.

Links

None

Task 5 – Infrastructure

Verify that the medical device organization has determined and documented the infrastructure requirements to achieve product conformity, including buildings, workspace, process equipment, and supporting services.

Confirm that buildings, workspaces, and supporting services allow product to meet requirements.

Verify that there are documented and implemented requirements for maintenance of process equipment where important for product quality, and that records of maintenance are maintained.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 6.3, 7.5.1

ANVISA: RDC ANVISA 665/2022: Art. 67, Art. 78

HC: CMDR 14

MHLW/PMDA: MO169: 6, 24, 40

FDA: 21 CFR 820.70(g), 820.70(f)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that manufacturing facilities are configured in order to provide adequate means for people flow [RDC ANVISA 665/2022: Art. 67].

Assessing conformity

Infrastructure requirements

The medical device organization is responsible for evaluating the manufacturing facility to ensure that the buildings, utilities, and space allow for the achievement of product conformity. The medical device organization is responsible for ensuring adequate space to prevent mix-ups and ensure orderly handling of products.

Equipment maintenance

The medical device organization must consider whether maintenance of production equipment may affect product quality. Procedures, including the frequency of maintenance and the records of maintenance must be available for these items of equipment.

Links

None

Task 6 – Work environment

Verify documented requirements have been established, implemented and maintained for:

- health, cleanliness, and clothing of personnel that could have an adverse effect on product quality
- monitoring and controlling work environment conditions that can have an adverse effect on product quality
- training or supervision of personnel who are required to work under special environmental conditions
- controlling contaminated or potentially contaminated product (including returned products) in order to prevent contamination of other product, the work environment, or personnel

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 6.4

TGA: TG(MD)R Sch1 P2 7.2, 8

ANVISA: RDC ANVISA 665/2022: Art. 68

MHLW/PMDA: MO169: 6, 25-1, 25-2; [Old: 6, 25]

FDA: 21 CFR 820.70(c), 820.70(d), 820.70(e)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that biosafety standards are used, when applicable [RDC ANVISA 665/2022: Art. 76].

Assessing conformity

Contamination control

The medical device organization is responsible for establishing and maintaining procedures to prevent contamination of products, equipment, and personnel by substances that could adversely affect the device. If contamination control measures are necessary to meet specified requirements, cleaning and sanitation procedures and schedules may be required to ensure the contamination control measures are properly functioning. The medical device organization should consider the segregation and decontamination of returned product.

Personnel practices

Personnel practices must address personnel health, cleanliness, and attire if these could adversely affect product quality or the work environment. In the event that maintenance or other personnel are required to work temporarily under special environmental conditions, these individuals must be appropriately trained or supervised by a trained individual.

Links

None

Task 7 – Identification of processes subject to validation

Determine if the selected process(es) and sub-process(es) have been reviewed, including any outsourced processes, to determine if validation of these processes is required.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 4.1.6, 7.5.6

TGA: TG(MD)R Sch1 P2 8.2, 8.3; Sch3 P1 1.4(5)(d)

ANVISA: RDC ANVISA665/2022: Art. 103, Art. 104, Art. 105, Art. 106

MHLW/PMDA: MO169: 6, 5-6, 45; [Old: 6, 45]

FDA: 21 CFR 820.75(a)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that analytical methods, supporting auxiliary systems for production and environmental control that can adversely affect product quality or the quality system are validated, periodically reviewed and, when necessary, revalidated according to documented procedures [RDC ANVISA 665/2022: Art. 103, Art. 104, Art. 105, Art. 106].

United States (FDA):

Process validation is required for sterilization, aseptic processing, injection molding, and welding [21 CFR 820.75; preamble comment 143].

Assessing conformity

Process validation

During the planning of product realization, the medical device organization must determine which production processes require validation and which processes can be verified. Process validation may apply to processes that generate components, subassemblies, or finished devices. Process validation is required for processes

where the results of the process cannot be fully verified. Processes that cannot be fully verified include processes where clinical or destructive testing is necessary to show that the process produced the desired result, where routine inspection and/or testing does not examine quality attributes essential to the proper functioning of the finished device, or where routine testing has insufficient sensitivity to verify the desired safety and efficacy of the finished product.

Examples of processes that require validation include, but are not limited to sterilization, aseptic processing, welding, and injection molding. When applicable, confirm that the medical device organization has identified processes which require validation, including validation requirements for any outsourced processes.

When validating processes, organizations must take into account the current thinking of experts where published information is available (e.g. though the application of ISO standards for sterilization validation).

Links

Purchasing

The audit team may encounter situations where the medical device organization outsources processes that require validation.

During the review of the Purchasing process, review the controls the medical device organization has instituted over suppliers that perform validated processes. This can be particularly important for higher risk validated processes performed by suppliers, since the finished device manufacturer does not have immediate control over those processes.

Task 8 – Process validation

Verify that the selected process(es) have been validated according to documented procedures if the result of the process cannot be fully verified or can be verified, but is not.

Confirm that the validation demonstrates the ability of the process/es to consistently achieve the planned result.

In the event changes have occurred to a previously validated process, confirm that the process was reviewed and evaluated, and re-validation was performed where appropriate.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.5.6

TGA: TG(MD)R Sch1 P1 2(1), Sch3 P1 1.4(5)(d)

ANVISA: RDC ANVISA 665/2022: Art. 3° section 31, Art. 103

MHLW/PMDA: MO169: 6, 45

FDA: 21 CFR 820.75(a), 820.75(c)]

Additional country-specific requirements

Australia (TGA):
Confirm that methods of validation have regard to the generally acknowledged state of the art (e.g. current Medical Device Standard Orders - MDSO, ISO/IEC Standards, BP, EP, USP etc.) [TG Act s41CB, TG(MD)R Sch 1 P1 2(1)].

Assessing conformity

Process validation
Process validation means establishing by objective evidence (i.e. data) that a process ***consistently*** produces a ***result*** (e.g., sterility assurance level) or ***product*** meeting predetermined specifications. Remember that the term "***product***" applies to components and in-process devices as well as finished devices. Therefore, process validation may apply to processes that generate components, in-process devices, or finished devices.

Process validation procedures
Some organizations have general process validation procedures. Other organizations establish separate procedures for each individual process validation study. Both methods for establishing process validation procedures are acceptable.

Reviewing a validation
During review of a validation study, determine when applicable whether:

- The instruments used to generate the data were properly calibrated and maintained
- Predetermined product and process specifications were established
- Sampling plans used to collect test samples are based on a statistically valid rationale
- Data demonstrates predetermined specifications were met consistently
- Process tolerance limits were challenged
- Process equipment was properly installed, adjusted, and maintained
- Process monitoring instruments were properly calibrated and maintained
- Changes to the validated process were appropriately challenged (if applicable)
- Process operators were appropriately qualified.

Achieving the planned result
Process validation activities are predictive, rather than empiric. In order for a process validation study to show the process achieves the planned result, the acceptance criteria must be stated in advance of performing the

validation. The data from the process validation study must show the predetermined acceptance criteria have been met.

Evidence of nonconformities

Process validation studies may also provide valuable insight into process or product nonconformities. For example, the process validation study must demonstrate not only that the process can produce a result or product meeting predetermined specifications but also that the process will consistently produce a result or product meeting predetermined specifications. If process or product nonconformities related to a validated process are encountered at a higher than anticipated rate, it may indicate the process validation study did not confirm that the process could consistently produce a result or product meeting predetermined specifications. Unless the medical device organization recognized this during the process validation study, they may not have investigated the cause of the process inconsistency.

Links

None

Task 9 – Validation of sterilization process

If product is supplied sterile (see Annex 2):

Verify the sterilization process is validated, periodically re-validated, and records of the validation are available.

Verify that devices sold in a sterile state are manufactured and sterilized under appropriately controlled conditions.

Determine if the sterilization process and results are documented and traceable to each batch of product.

Clause and Regulation

ISO: ISO 13485:2016: 4.2.1, 7.5.5, 7.5.6, 7.5.7

TGA: TG(MD)R Sch1 2(1) & 8.3, Sch3 P1 1.4(5)(d)

ANVISA: RDC ANVISA 665/2022: Art. 83, Art. 103, Art. 104, Art. 105, Art. 106

HC: CMDR 17

MHLW/PMDA: MO169: 6, 44, 45, 46

FDA: 21 CFR 820.75, 820.184(d)]

Additional country-specific requirements

Australia (TGA):
Verify that methods of sterilization validation have regard to the generally acknowledged state of the art (e.g. Australian Medical Device Standard Orders – MDSO e.g. **Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018**) or Australian Conformity Assessment Standard Orders - **Conformity Assessment Standards Order (Quality Management Systems) 2019** that refer to the use of ISO 11135, ISO 11137 and other standards). [TG(MD)R Sch1 P1 2(1)].

Assessing conformity

Validation of sterilization processes
Sterilization processes include terminal sterilization methods (such as radiation and ethylene oxide) as well as aseptic processing methods. Sterilization processes must be validated, with periodic revalidation as required by established standards or requirements established by the medical device organization.

Control of the manufacturing processes for devices intended to be sterile
In addition to ensuring the cleaning, packaging, and sterilization processes are validated, auditors should ensure the medical device organization maintains appropriate controls over the following:

- routine monitoring and measurement of the cleaning, packaging and sterilization processes
- routine acceptance criteria of the cleaning, packaging and sterilization processes
- (re-)qualification, (re-)verification, (re-)calibration and maintenance of the cleaning, packaging and sterilization equipment
- environmental control of production areas (cleanroom design and monitoring)
- storage of device parts, components, and packaging material
- storage of finished sterile product and management of shelf life
- handling processes for non-sterile devices for re-sterilization.

Links
None

Task 10 – Monitoring and measurement of product conformity

Verify that the system for monitoring and measuring of product characteristics is capable of demonstrating the conformity of products to specified requirements.

Confirm that product risk is considered in the type and extent of product monitoring activities.

Chapter 6 - Production and Service Controls

Task 11 – Control, operation, and monitoring of the production and service process; risk controls

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Clause and Regulation

ISO: ISO 13485:2016: 7.1, 7.5.1, 8.1, 8.2.6

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 1.4(5)(b)&(e)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 64, Art. 131

MHLW/PMDA: MO169: 26, 40, 54, 58, 59

FDA: 21 CFR 820.70(a), 820.250(a)]

Additional country-specific requirements

None

Assessing conformity

Monitoring systems

The general goal of monitoring processes and product characteristics during production is to ensure that products conform to the specified requirements defined and approved during the design and development of the device. The medical device organization has the flexibility to determine the controls that are necessary, commensurate with the risk to the finished device if processes or product characteristics do not meet specified requirements. During the audit of production processes, confirm that the control measures are suitable for detecting process or product nonconformities.

Links

None

Task 11 – Control, operation, and monitoring of the production and service process; risk controls

Verify that the processes used in production and service are appropriately controlled, monitored, operated within specified limits and documented in the product realization records.

In addition, verify that risk control measures identified by the medical device organization for production processes are implemented, monitored and evaluated.

Clause and Regulation

ISO: ISO 13485:2016: 7.1, 7.5.1, 8.1, 8.2.5

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 1.4(5)(b)&(e)

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 64, Art. 83, Art. 128, Art. 131

MHLW/PMDA: MO169: 26, 40, 54, 57

FDA: 21 CFR 820.70(a), 820.75(b), 820.250]

Additional country-specific requirements

Australia (TGA):
See **Annex 1**

Assessing conformity

Process control and monitoring

Processes that may cause a deviation to device specifications and validated processes must be controlled and monitored. Control and monitoring procedures may include in-process and finished device acceptance activities as well as environmental and contamination control measures.

Compare the process monitoring and acceptance procedures contained or referenced within the records of production specifications with those available to the production personnel. Confirm that the procedures available to the production personnel are the most current approved revisions.

While in the production area, verify that the building is of suitable design and contains sufficient space to perform necessary operations. Also, verify that the results of control and monitoring activities demonstrate that the process is currently operating in accordance with applicable procedures. This can be done by comparing work instructions with what is actually being done, comparing product acceptance criteria with acceptance activity results, reviewing control charts against specified requirements, etc.

Links

Design and Development

The design outputs for a device include documents such as diagrams, drawings, specifications, procedures, and the production processes that are essential to the proper manufacturing of the device. Production processes can include not only the manufacturing instructions, but also internal controls, such as the type and extent of acceptance activities, equipment calibration and maintenance intervals, environmental controls, and personnel controls.

During the audit of the Production and Service Controls process, consider reviewing production processes that have the highest risk or greatest effect on the essential design outputs.

Task 12 – Competence of personnel

Verify that personnel are competent to implement and maintain the processes in accordance with the requirements identified by the medical device organization.

Clause and Regulation

ISO: ISO 13485:2016: 6.2

ANVISA: RDC ANVISA 665/2022: Art. 15

MHLW/PMDA: MO169: 22

FDA: 21 CFR 820.25, 820.70(d), 820.75(b)]

Additional country-specific requirements

None

Assessing conformity

Personnel training and qualification

Production processes must be performed by adequately trained personnel. The medical device organization must establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities.

This training must be documented. In addition, personnel who perform validated processes must be qualified.

It is management's responsibility to determine what qualifications are necessary for personnel who perform validated processes.

Links

Management

During the audit of the Production and Service Controls process, ensure that employees who are involved in key operations that affect product realization and product quality have been trained in their specific job tasks, as well as the quality policy and objectives.

When appropriate, review the training records for those employees whose activities have contributed to process nonconformities.

Task 13 – Control of monitoring and measuring device

Confirm that the medical device organization has determined the monitoring and measuring devices needed to provide evidence of conformity to specified requirements.

Verify that the monitoring and measuring equipment used in production and service control has been identified, adjusted, calibrated and maintained, and capable of producing valid results.

Clause and Regulation

ISO: ISO 13485:2016: 7.5.1, 7.6

TGA: TG(MD)R Sch3 P1 1.4(5)(e)

ANVISA: RDC ANVISA 665/2022: Art. 93, Art. 94, Art. 95

MHLW/PMDA: MO169: 40, 53

FDA: 21 CFR 820.70(g), 820.72]

Additional country-specific requirements

None

Assessing conformity

Maintenance and calibration

While reviewing the selected production process, make note of significant pieces of process equipment and significant pieces of measuring or test equipment. Consider selecting process and test equipment that, if not properly controlled, could cause devices to not meet specified requirements; or produce inaccurate results that could lead to unrecognized nonconformities. Confirm that the production and test equipment selected for review is suitable for its intended purpose and capable of giving valid results.

Review the maintenance, control, and calibration procedures (and records) for the equipment selected for review. The initial frequency with which measuring and test equipment is calibrated and maintained is usually based on the equipment manufacturer's recommendations. As the medical device organization gains experience with the piece of equipment, the frequency of calibration and maintenance may be adjusted, based on a documented rationale.

Accuracy and precision

When accuracy and precision is a factor in the validity of the result of the measuring equipment, the required accuracy and precision should be defined during the planning of product realization to ensure the equipment is suitable and capable of providing valid results.

Reviewing records

If production equipment or test equipment is found to be outside of its maintenance or calibration requirements, verify that the medical device organization made an assessment of the effect of the out-of-tolerance situation on in-process, finished, or released devices, based on risk. Equipment adjustment, calibration, and maintenance procedures and records may provide insight into nonconformities. Review these procedures and records to determine whether inadequate procedures or the medical device organization's failure to comply with adequate procedures contributed to the nonconformity. For example, determine whether the lack of specified equipment adjustment or maintenance contributed to the production of nonconforming product.

Links

None

Task 14 – Impact analysis of monitoring and measuring device found out of specifications

Confirm that the medical device organization assesses and records, the validity of previous measurements when equipment is found not to conform to specified requirements and takes appropriate action on the equipment and any product affected.

Verify that the control of the monitoring and measuring devices is adequate to ensure valid results. Confirm that monitoring and measuring devices are protected from damage or deterioration.

Clause and Regulation

ISO: ISO 13485:2016: 7.6

TGA: TG(MD)R Sch3 P1 1.4(5)(e)

ANVISA: RDC ANVISA 665/2022: Art. 102

MHLW/PMDA: MO169: 53

FDA: 21 CFR 820.72(a)]

Additional country-specific requirements

None

Assessing conformity

Control of monitoring and measuring devices

Organizations must maintain proper calibration, storage, and handling controls for measuring, monitoring, and test equipment used in the development, production, installation, and servicing of product. Calibration must be traceable to a national or international measurement standard if one is available. If calibration services are provided by a supplier, the supplier controls are to be applied to ensure calibration is performed competently. Proper controls will help instill confidence in results obtained from the use of the equipment.

Procedures

Organizations must define, implement, and maintain procedures for the control of monitoring and measuring devices. The medical device organization may choose to develop general policies for the control of monitoring and measuring devices, along with separate, more specific procedures for the actual calibration and control of each piece of equipment.

Procedures must account for any environmental controls necessary for the equipment to produce valid results, as well as any specific storage or handling requirements when necessary. For example, a set of calibrated calipers may require storage in a padded case to maintain the required accuracy and precision. Confirm that the medical device organization has the proper procedures and controls in place to preserve the proper functioning of monitoring, measuring, and test equipment.

When equipment is found to be out-of-tolerance

The medical device organization may discover that monitoring or measuring equipment is no longer within its adjustment or calibration tolerance. In these situations, the medical device organization must assess and record the validity of previous measuring results and take appropriate action on the equipment and any product affected.

Links

None

Task 15 – Validation of software used for the control of the production and service process

If the selected process is software controlled, or if software is used in production equipment or the quality management system, verify that the software is validated for its intended use.

Software validation may be part of equipment qualification.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.6, 7.5.6, 7.6

Chapter 6 - Production and Service Controls

Task 15 – Validation of software used for the control of the production and service process

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ANVISA: RDC ANVISA 665/2022: Art. 104

MHLW/PMDA: MO169: 5-6, 45, 53; [Old: 45, 53]

FDA: 21 CFR 820.70(i)]

Additional country-specific requirements

None

Assessing conformity

Validation of production and quality system software

Production process control software (and any other software used in the medical device organization's quality system) must be validated for its intended use according to an established protocol. If the production process the audit team selected for review is controlled with software, review the software validation documents and records.

Software validation documents and records should include:

- A software requirements document describing the intended use(s) and user needs associated with the software.
- An established validation protocol or similar document describing the activities necessary to demonstrate that the software requirements can be met.
- Records of the results of the software validation activities described in the software validation protocol or similar document.
- Records that software changes are appropriately controlled (where applicable).

For off-the-shelf quality management system software and software-controlled production or test equipment, it may not be possible, practical, or necessary for the medical device organization to review the software code or the various software verification test cases that are typically performed by the software or equipment manufacturer. However, the medical device organization must still ensure the software is capable of functioning according to the device medical device organization's needs. The validation to confirm the software meets the medical device organization's needs must be performed according to a protocol or similar document with predetermined acceptance criteria.

If multiple software driven systems are used in the production process, be sure to assess the system(s) most likely to have an impact on the finished device's ability to meet specified requirements. Not all software driven systems used in a production process will need to be audited during each audit.

Links

None

Task 16 – Device master file

Determine if the medical device organization has established and maintained a file for each type of device that includes or refers to the location of device specifications, production process specifications, quality assurance procedures, traceability requirements, and packaging, labeling specifications, and when applicable requirements for installation and servicing.

Confirm that the medical device organization determined the extent of traceability based on the risk posed by the device in the event the device does not meet specified requirements.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 4.2.3, 7.1, 7.5.8, 7.5.9.1

TGA: TG(MD)R, Sch1 EP13, Sch3 P1 1.4(5) (c),(d),(e) & 1.9

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20, Art. 63, Art. 64, Art. 84, Art. 85, Art. 86, Art. 87

HC: CMDR 9(2), 21-23, 52-56, 66-68

MHLW/PMDA: MO169: 6, 7-2, 26, 47, 48; [Old: 6, 26, 47, 48]

FDA: 21 CFR 820.65, 820.181]

Additional country-specific requirements:

Australia (TGA):
Verify that the design and location of information to be provided with a medical device, including labelling and instructions for use, comply with Essential Principle 13 and implant cards and leaflets with Essential principle 13A.

Brazil (ANVISA):
Verify that the manufacturer has established and maintains procedures to ensure integrity and to prevent accidental mixing of labels, instructions, and packaging materials [RDC ANVISA 665/2022: Art. 85].

Confirm that the manufacturer has ensured that labels are designed, printed and, where applicable, applied so that they remain legible and attached to the product during processing, storage, handling and use [RDC ANVISA 665/2022: Art. 86].

Canada (HC):
Verify that the Manufacturer maintains objective evidence that devices meet the safety and effectiveness requirements. [CMDR 9(2)].

Verify that devices sold in Canada have labeling that conforms to Canadian English and French language requirements and contains the Manufacturer's name and address, device identifier, control number (for Class III

and IV devices), contents of packaging, sterility, expiry, intended use, directions for use and any special storage conditions [CMDR 21-23].

Verify that the Manufacturer maintains distribution records in respect of a device that will permit a complete and rapid withdrawal of the device from the market [CMDR 52-56].

United States (FDA):
If a control number is required for traceability, confirm that a control number is on, or accompanies the device throughout distribution [21 CFR 820.120(e)].

Assessing conformity

Records
The required records for each type or model of device include documents such as diagrams, drawings, specifications, and procedures associated with the device, its packaging and labeling; as well as, quality management system and production process requirements; and if applicable, installation and servicing requirements. Documents and records associated with production processes can include not only the manufacturing instructions, but also internal controls, such as the type and extent of acceptance activities, equipment calibration and maintenance intervals, environmental controls, and personnel controls.

These documents and records provide the requirements and instructions for the proper manufacturing, labeling, packaging, and testing of the device to assure specified requirements are met during the production of each batch of devices. For the device(s) the audit team has selected to review, confirm that the required records have been established.

General traceability
It is the responsibility of the medical device organization to establish procedures for traceability. For devices that are not implanted and are not life-supporting or life-sustaining, the medical device organization has the flexibility to determine which raw materials and components are required to be traceable, commensurate with the risk posed by the device in the event the component does not meet specified requirements.

Traceability systems commonly include elements such as written procedures describing the control numbering system to be used, as well as the documentation of lot numbers, control numbers, or serial numbers identifying the batch of components, subassemblies, finished devices, packaging, and labeling in order to aid their identification in the manufacturing process.

Links

Design and Development

During the design and development of the device, the essential design outputs for the proper functioning of the device should have been identified. Raw materials, components, and subassemblies should have been considered for traceability if their nonconformity could result in the finished device not meeting its specified requirements and essential functions.

Task 17 – Production record; evidence of compliance of released devices

Determine if the medical device organization has established and maintained a record of the amount manufactured and approved for distribution for each batch of medical devices, the record is verified and approved, the device is manufactured according to the file referenced in Task 16, and the requirements for product release were met and documented.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.5.1, 7.5.8, 7.5.9.1, 8.2.6

ANVISA: RDC ANVISA 665/2022: Art. 39, Art. 113, Art. 114

MHLW/PMDA: MO169: 6, 40, 47, 48, 58, 59

FDA: 21 CFR 820.120, 820.184]

Additional country-specific requirements

Brazil (ANVISA):

Verify that the device history record of the product includes or refers to the following information: date of manufacture; components used; quantity manufactured; results of inspections and tests; parameters of special processes; quantity released for distribution; labeling; identification of the serial number or batch of production; and final release of the product [RDC ANVISA 665/2022: Art. 40].

Verify that labeling has not been released for storage or use until a designated individual has examined the labeling for accuracy. The approval, including the date, name, and physical or electronic signature of the person responsible, must be documented in the device history record [RDC ANVISA 665/2022: Art. 87].

United States (FDA):

Verify that labeling is not released for storage or use until a designated individual has examined the labeling for accuracy including, where applicable, the correct unique device identifier (UDI) or Universal Product Code

(UPC), expiration date, control number, storage instructions, handling instructions, and any additional processing instructions [21 CFR 820.120(b)].

Confirm that labeling is stored in a manner that provides proper identification and prevents mix-ups. Verify labeling and packaging operations are controlled to prevent labeling mix-ups [21 CFR 820.120(c) and (d)].

Verify that the label and labeling used for each production unit, lot, or batch are documented in the batch record, as well as any control numbers used [21 CFR 820.120(e), 820.184(e)].

Assessing conformity

Verify manufacturing of the device

Verify that each batch of devices was manufactured in accordance with product and production specifications, being mindful that in some instances, a batch can be a single device. This verification should include a review of the purchasing controls and receiving acceptance activities applied to at least one significant component or raw material, in-process and final finished device acceptance activities and results, environmental and contamination control records (if applicable), and sampling plans for process and environmental controls and monitoring.

The record for each batch of devices must include, or refer to the location of, the following information:

- The dates of manufacture
- The quantity manufactured
- The quantity released for distribution
- The acceptance records which demonstrate the device has been manufactured in accordance with the planned arrangements and defined product specifications
- The primary identification label and labeling used for each production unit
- Any device identification(s) and control number(s) used, including unique device identifiers when applicable
- A provision to indicate that the record has been verified and approved.

Determine if there are problems

If, during the accomplishment of this audit task, the audit team observes evidence that the process is outside the medical device organization's acceptance range for operating parameters or that product nonconformities exist, confirm that the nonconformities were handled appropriately, with input into the Measurement, Analysis and Improvement process when appropriate.

Links

None

Task 18 – Traceability applied to implantable, life-supporting or life-sustaining medical devices

If the medical device organization manufactures active or non-active implantable medical devices, life-supporting or life-sustaining devices, confirm that the medical device organization maintains traceability records of all components, materials, and work environment conditions (if these could cause the medical device to not satisfy its specified requirements) in addition to records of the identity of personnel performing any inspection or testing of these devices.

Confirm that the medical device organization requires that agents or distributors of these devices maintain distribution records and makes them available for inspection.

Verify that the medical device organization records the name and address of shipping consignees for these devices.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.5.9.2, 8.2.6

MHLW/PMDA: MO169: 6, 49, 59

FDA: 21 CFR 820.65]

Additional country-specific requirements

Canada (HC):

Verify that the Manufacturer has identified Schedule 2 implants and provides implant registration cards with devices or employs another suitable system approved by Health Canada [CMDR 66-68].

Verify that the Manufacturer of devices that are listed on Schedule 2 of the Medical Devices Regulations maintains distribution records of these devices as well as any information received on implant registration cards related to these Schedule 2 devices [CMDR 54].

United States (FDA):

Verify that the manufacturer has implemented a tracking system for devices for which the manufacturer has received a tracking order from FDA. The tracking system must ensure the manufacturer is able to track the device to the end-user. The manufacturer must conduct periodic audits of the tracking system [21 CFR 821].

Assessing conformity

Traceability of implantable, life-supporting or life-sustaining devices

Medical device organizations that produce finished devices whose failure could result in serious injury or harm to the user must implement a traceability system. The traceability system must allow for each batch of finished

devices to be traced by a control number or similar mechanism throughout the distribution chain. Organizations must also provide for the control and traceability of components and materials used in the manufacture of the device, as well as documentation of the manufacturing conditions when manufacturing conditions could cause the finished device to not meet specified requirements (e.g. cleanroom conditions).

The determination of which components and raw materials may be required to be traceable may be made by the medical device organization using risk management tools, such as risk analysis, or by identification of the components and processes used to fulfill the essential design outputs.

Medical Device Tracking

Some regulatory authorities participating in the MDSAP have requirements for tracking certain types of devices to the end-user. For regulatory authorities that have tracking requirements, these requirements generally apply to a small subset of devices that are life-sustaining or life supporting, intended for implant longer than one year, or are considered by the regulatory authority to be high risk.

If the medical device organization manufactures or distributes a device that falls under a tracking requirement, confirm that the medical device organization has the necessary systems in place to provide for tracking each device to the end-user.

The medical device organization's tracking system must be periodically reviewed and audited by the medical device organization to confirm that the tracking system is effective. The tracking system must contain the unique device identifier (UDI), lot number, batch number, model number, or serial number of the device or other identifier necessary to provide for effective tracking of the devices.

Links

None

Task 19 – Identification of product status

Verify that product status identification is adequate to ensure that only product which has passed the required inspections and tests is dispatched, used, or installed.

Clause and Regulation

ISO: ISO: 13485:2016: 7.5.8

ANVISA: RDC ANVISA 665/2022: Art. 108, Art. 113

MHLW/PMDA: MO169: 47; [Old: 47, 50]

FDA: 21 CFR 820.86]

Additional country-specific requirements

None

Assessing conformity

Identification

Identification is generally defined as the description of the product that distinguishes it from other product. Organizations must define, document, and implement processes for the identification and control of product, including components, process agents, subassemblies, finished devices, packaging, and labeling. This can be accomplished through the use of part numbers, lot numbers, batch numbers, work order numbers, quantities, supplier name, as well as other means. The extent of identification activities should be based on the complexity and risk of the product.

Links

None

Task 20 – Customer property

Verify that the medical device organization has implemented controls to identify, verify, protect, and safeguard customer property provided for use or incorporation into the product.

Verify that the medical device organization treats patient information and confidential health information as customer property.

Clause and Regulation

ISO: ISO: 13485:2016: 7.5.10

MHLW/PMDA: MO169: 51

Additional country-specific requirements

None

Assessing conformity

Safeguarding customer property

The medical device organization is responsible for safeguarding customer property while it is under the medical device organization's control. If any customer property is lost, damaged, or otherwise unsuitable for use, this must be reported to the customer and records maintained.

Links

None

Task 21 – Acceptance activities

Verify that acceptance activities assure conformity with specifications and are documented.

Confirm that the extent of acceptance activities is commensurate with the risk posed by the device.

Note: Acceptance activities apply to any incoming component, subassembly, or service, regardless of the medical device organization's financial or business arrangement with the supplier.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.4.3, 7.5.8, 8.2.6

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl1.4(5)(d)

ANVISA: RDC ANVISA 665/2022: Art. 88, Art. 89, Art. 90, Art. 131

MHLW/PMDA: MO169: 6, 39, 47, 58, 59

FDA: 21 CFR 820.80, 820.250(b)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that sampling plans are defined and based on valid statistical rationale. Each manufacturer must establish and maintain procedures to ensure that sampling methods are suitable for their intended use and are reviewed regularly. A review of sampling plans should consider the occurrence of nonconforming product, quality audit reports, complaints and other indicators [RDC ANVISA 665/2022: Art. 132, Art. 133, Art.134].

United States (FDA):

Verify that the manufacturer establishes and maintains procedures to ensure that sampling methods are adequate for their intended use and ensure that when changes occur, the sampling plans are reviewed [21 CFR 820.250(b)].

Assessing conformity

Recognized acceptance activities

Organizations are expected to define, document, and implement systems and procedures for acceptance activities to verify that products, including finished devices, in-process devices, components, packaging, and labeling conform to specified requirements. Recognized acceptance activities include, but are not limited to, inspections, tests, review of certificates of analysis, and supplier audits. Effective acceptance procedures and systems directly affect the ability of a medical device organization to demonstrate that the process and product meets specifications.

During the audit of acceptance activities for the devices selected for audit, confirm that the medical device organization has defined processes for receiving, in-process, and final acceptance activities. Determine if the acceptance activities have been implemented. One way to accomplish this audit task is to review a sample of batch records and confirm that the acceptance activities have been documented and that the acceptance activities show specified requirements have been met. Records should identify who conducted acceptance activities.

The acceptance status of incoming, in-process, and finished devices must be identified. The identification of acceptance status must be maintained throughout manufacturing, packaging, labeling, and where applicable, installation and servicing to ensure that only product which has passed the required acceptance activities is distributed, used, or installed.

Acceptance activities involving related firms
The audit team may encounter situations where the medical device organization receives incoming product from a financial or corporate affiliate. It is the receiving medical device organization's responsibility to perform and record the necessary acceptance activities to ensure the received product conforms to specified requirements, as well as applying the necessary purchasing controls to the supplier. Acceptance activities and purchasing controls apply to all product received from suppliers outside of the scope of the medical device organizations quality management system, whether a payment occurs or not, and regardless of the corporate or financial relationship of the supplier to the medical device organization.

Sampling
The audit team may encounter the use of sampling during acceptance activities. For example, a medical device organization might choose to use sampling to perform receiving acceptance on a large lot of incoming components. When used, sampling plans must be written and based on a valid statistical rationale and a risk-based methodology.

Combination of controls
An important concept to remember is that quality cannot be inspected or tested into products. Organizations must establish an appropriate mix of acceptance activities and purchasing controls to ensure products will meet specified requirements. The type and extent of acceptance activities can be based in part on the amount of purchasing controls applied to the supplier, the demonstrated capability of the supplier to provide quality products, and the potential impact of the product on the finished device, including the risk the device poses to the patient or user if specified requirements are not met. Organizations that conduct quality control solely in-house must still assess the capability of suppliers to provide acceptable products.

Evidence of inadequate acceptance activities
The audit team may encounter instances where product has been deemed acceptable by the successful completion of acceptance activities but the product is later shown to not meet specified requirements (i.e. failure of the device leading to product complaint). This can be an indication that the acceptance activities are

not sufficient to identify nonconformities. Confirm that the medical device organization has taken the appropriate action to determine the suitability of the acceptance activities.

Links

Purchasing, **Design and Development**

The audit team should consider reviewing the purchasing controls and requirements for suppliers of higher risk products. The audit team should also consider reviewing the purchasing controls and requirements for suppliers of products that undergo minimal acceptance activities at the medical device organization, particularly if the supplied product is manufactured using a process that requires validation. During the review of acceptance activities, if the audit team encounters situations where records of acceptance activities for supplied product reveal products that do not meet specified requirements, consider selecting those suppliers for review during the audit of the medical device organization's Purchasing process.

The establishment of the necessary purchasing controls and required acceptance activities is a design output. The degree of the purchasing controls necessary and extent of acceptance activities should be based on the risk posed by the product not meeting its specified requirements and essential design outputs.

Task 22 – Identification, control, and disposition of nonconforming products

Verify that the identification, control, and disposition of nonconforming products is adequate, *based on the risk the nonconformity poses to the device meeting its specified requirements*.

Clause and Regulation

ISO: ISO: 13485:2016: 7.5.8, 8.3

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl1.4(5)(b)

ANVISA: RDC ANVISA 665/2022: Art. 115, Art. 116

MHLW/PMDA: MO169: 47, 60-1, 60-2, 60-3, 60-4; [Old: 47, 50, 60]

FDA: 21 CFR 820.60, 820.90(a), 820.86, 820.100(a)]

Additional country-specific requirements

None

Assessing conformity

Procedures

The purpose of controlling nonconforming product is to prevent the unintended use and distribution of nonconforming product, including components, processing agents, in-process devices, and finished devices. Confirm that the medical device organization has defined and implemented procedures for the identification, control, segregation, evaluation, and disposition of nonconforming product.

Handling nonconforming product

The medical device organization can address nonconforming product by taking action to eliminate the detected nonconformity (e.g. sorting an incoming lot of components to remove components that do not meet specifications), authorizing its use, release, or acceptance under concession, or by taking action to prevent its original intended use (e.g. allowing the components or devices to be used as demonstration units at marketing conferences).

Until a disposition can be made, the medical device organization must have a process to properly identify nonconforming product to prevent its accidental or unauthorized use. One example is tagging and moving the nonconforming product to a controlled enclosure away from the production area.

If nonconforming product is accepted under concession, the records of the identity of the person authorizing the concession must be maintained.

If nonconforming product has been detected after a product has been released and put into use the medical device organization must consider the risks associated with the device and may need to consider an advisory notice or recall.

Evaluation of nonconforming product

The evaluation of nonconformity must include a determination of the need for an investigation and notification of the persons or organizations responsible for the nonconformity, such as a supplier. Ensure that the medical device organization has adequately established an interface / interaction between the processes for the identification of non-conforming product and the processes for corrective action. These interactions should be evident in the quality manual.

Links

Measurement, Analysis and Improvement

The audit team should be mindful of any instances where the acceptance of nonconforming product has led to finished devices not meeting specified requirements. This information can often be found in records of acceptance activities and complaint records.

During the review of the medical device organization's corrective and preventive actions, the auditors may have noted instances where nonconforming products were found to be the underlying cause of quality problems and complaints. The audit team should consider reviewing the medical device organization's handling and evaluation of nonconforming products that were determined to be the underlying cause of quality problems.

Ensure that the analysis of data regarding nonconforming product is considered as an input to the medical device organization's Measurement, Analysis and Improvement process and that corrective or preventive actions have been implemented when necessary.

Task 23 – Rework of nonconforming products

If a product needs to be reworked, confirm that the medical device organization has made a determination of any adverse effect of the rework upon the product.

Verify that the rework process has been performed according to an approved procedure, that the results of the rework have been documented, and that the reworked product has been re-verified to demonstrate conformity to requirements.

Clause and Regulation

ISO: ISO: 13485:2016: 8.3.4

ANVISA: RDC ANVISA 665/2022: Art. 119

MHLW/PMDA: MO169: 60-4; [Old: 60]

FDA: 21 CFR 820.90(b)]

Additional country-specific requirements

None

Assessing conformity

Reworking nonconforming product

The audit team may encounter instances where the medical device organization has chosen to address nonconforming product by means of reworking the component, subassembly or finished device. The medical device organization must have suitable approved procedures in place to address nonconforming product destined for rework. Reworked product must be re-evaluated or re-tested to ensure it meets its original specified requirements. Rework must be documented.

Be mindful of instances where the underlying cause of quality problems, such as complaints that finished devices do not meet specified requirements, are traced to devices that have been reworked. This can be an indication that the rework process was not adequate to ensure the finished device meets specifications.

Additionally, rework of products manufactured using validated processes can be an indication that the process cannot consistently produce product that meets specified requirements. If the audit team notes a pattern of reworking products that are manufactured using a validated process, consider reviewing the process validation to confirm that the medical device organization has data to show the process is effective, reproducible, and stable; and that the medical device organization is operating the process within the validated parameters.

Links

None

Task 24 – Preservation of the product

Verify that procedures are established and maintained for preserving the conformity of product and constituent parts of a product during internal processing, storage, and transport to the intended destination. This preservation encompasses identification, handling, packaging, storage, and protection, including those products with limited shelf-life or requiring special storage conditions.

Clause and Regulation

ISO: ISO: 13485:2016: 7.5.8, 7.5.11

TGA: TG(MD)R Sch1 P1 4&5

ANVISA: RDC ANVISA 665/2022: Art. 84, Art. 107, Art. 111

HC: CMDR 14

MHLW/PMDA: MO169: 47, 52

FDA: 21 CFR 820.130, 820.140, 820.150, 820.160(a)]

Additional country-specific requirements

None

Assessing conformity

Ensuring proper handling

The medical device organization must have a documented system that defines product handling requirements at all stages of manufacturing to prevent mix-ups, damage, and deterioration. This can include specified requirements for storage and shipping to ensure the preservation of the product to its destination. For example, an in-vitro diagnostic device may need to be stored and shipped in a frozen state to maintain proper shelf-life of the reagents. or test samples may need to be conditioned as per ISTA 2A to cover Australian climate zone (extreme temperature range -29C-50C) for packaging validation These handling requirements should have been considered during the planning of product realization for the device. When necessary, confirm that the needed control measures are implemented to ensure the conformity of product to its specified requirements.

Links

None

Task 25 – Review of customer requirements, distribution records

Confirm that the medical device organization performs a review of the customer's requirements, including the purchase order requirements, prior to the medical device organization's commitment to supply a product to a customer.

Verify that the medical device organization maintains documentation required by regulatory authorities regarding maintenance of distribution records.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 5.2, 7.2.2, 7.5.9

ANVISA: RDC ANVISA 665/2022: Art. 112

MHLW/PMDA: MO169: 6, 11, 28, 48, 49

FDA: 21 CFR 820.160(a)]

Additional country-specific requirements

Brazil (ANVISA):
Verify that the manufacturer maintains distribution records which include or make reference to: the name and address of the consignee, the identification and quantity of products shipped, the date of dispatch, and any numerical control used for traceability [ANVISA RDC 6.3].

Canada (HC):
Verify that the Manufacturer maintains distribution records that contain sufficient information to permit complete and rapid withdrawal of the medical device from the market [CMDR 52-53].

Verify that distribution records of a device are retained by the Manufacturer in a manner that will allow for timely retrieval, for the longer of (a) the projected useful life of the device; and (b) two years after the date the device was shipped [CMDR 55-56].

United States (FDA):
Verify that the Manufacturer maintains distribution records which include or refer to the location of the name and address of the initial consignee, the identification and quantity of devices shipped; and any control numbers used [21 CFR 820.160(b)].

Assessing conformity

Distribution records
The medical device organization must maintain distribution records which include or refer to the location of the initial consignee, the identification and quantity of devices shipped, the date shipped, and any control numbers used.

Links
None

Task 26 – Installation activities

If installation activities are required, confirm that records of installation and verification activities are maintained.

Clause and Regulation
ISO: ISO: 13485:2016: 7.5.3

ANVISA: RDC ANVISA 665/2022: Art. 125, Art. 126

MHLW/PMDA: MO169: 42

FDA: 21 CFR 820.170]

Additional country-specific requirements

None

Assessing conformity

Installation activities

When a device must be installed for suitable functioning, the medical device organization must establish procedures and instructions to ensure proper installation. These instructions must be made available to personnel performing the installation. Installation activities must be documented.

Determining the extent of review

In the absence of identified quality problems related to the installation of the selected device, the audit team may choose to limit the review of the installation process to confirming the necessary procedures are in place.

Links

None

Task 27 – Servicing activities

Determine if servicing activities are conducted and documented in accordance with defined and implemented instructions and procedures.

Confirm that service records are used as a source of quality data in the Measurement, Analysis and Improvement process.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.5.4, 8.4

ANVISA: RDC ANVISA 665/2022: Art. 130

MHLW/PMDA: MO169: 6, 43, 61

FDA: 21 CFR 820.200]

Additional country-specific requirements

Brazil (ANVISA):

Confirm that the manufacturer has established and maintains procedures to ensure that records of servicing activities are kept with the following information:

- the product serviced
- the control number of the product serviced

- the date of completion of service
- identification of the service provider
- description of service performed
- results of inspections and tests performed [RDC ANVISA 665/2022: Art. 129].

Verify that the manufacturer periodically reviews the records of servicing activities. In cases where the analysis identifies trends that pose danger or records involving death or serious injury, a corrective or preventive action must be initiated [RDC ANVISA 665/2022: Art. 130].

United States (FDA):
Verify that each manufacturer who receives a service report that represents an event that must be reported to FDA as a medical device report automatically considers the report a complaint [21 CFR 820.200(c)].

Confirm that service reports are documented and include the name of the device serviced, any unique device identifier (UDI) or universal product code (UPC), and any other device identification(s) and control number(s) used; and the date of service [21 CFR 820.200(d)].

Assessing conformity

Procedures
When servicing is a specified requirement, the medical device organization must define and maintain procedures, instructions, and processes for performing and verifying that servicing activities meet specified requirements.

Servicing process
When organizations implement servicing programs, the medical device organization must ensure components used for repair are acceptable for the intended use, inspection and test procedures are available, and test equipment is properly maintained to ensure serviced devices will perform as intended after servicing. Personnel performing service activities must have the appropriate training.

The audit team may observe instances where nonconformities occurred and/or complaints were received after the servicing of the device. This can be an indication that the service activity was not properly controlled or that service personnel do not have the proper equipment, instructions, or training to perform the required service.

Analysis of service reports
Service reports can be an important source of quality data for input into the medical device organization's Measurement, Analysis and Improvement process. When necessary, confirm data regarding service reports is analyzed for possible corrective action or preventive action. Service reports must also be analyzed to determine if the service event represents an adverse event that is reportable to regulatory authorities.

In some instances, product complaints may be initially recorded by the medical device organization as a service report. For example, a user may report to the medical device organization that a patient blood parameter monitoring device is not working correctly and requires service. Upon receipt of the device from the user by the medical device organization's service function, the service function notes the reason the monitoring device is not working is that an essential component within the device failed prematurely. This service report should be considered by the medical device organization to be a complaint and analyzed by the medical device organization to determine if an adverse event report needs to be submitted to regulatory authorities.

Links

Measurement, Analysis and Improvement

During the audit of the medical device organization's Measurement, Analysis and Improvement process, the audit team may have already confirmed that quality data from the analysis of servicing activities is analyzed for possible corrective or preventive action. When reviewing the medical device organization's service reports, the audit team should be mindful of service reports that appear to be product complaints. Ensure that service reports that appear to be complaints have been appropriately addressed.

In some instances, a similar quality problem for a particular device may be found in the service reports and the complaint records. In these instances, confirm that the medical device organization is taking appropriate corrections and/or corrective actions considering a similar quality problem is observed in multiple data sources.

Task 28 – Risk controls applied to transport, installation, and servicing

When appropriate, verify that risk control and mitigation measures are applied to transport, installation and servicing, in accordance with the medical device organization's risk management practices.

Clause and Regulation

ISO: ISO: ISO 13485:2016: 7.1, 7.5.1, 7.5.3, 7.5.4, 7.5.11

TGA: TG(MD)R Sch1 P1 2&5

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 19, Art. 20

MHLW/PMDA: MO169: 26, 40, 42, 43, 52

FDA: 21 CFR 820.160(a), 820.170(a), 820.200(a)]

Additional country-specific requirements
None

Assessing conformity

Risk control
The requirements for delivery, installation, and servicing of a particular device should have already been evaluated and addressed by the medical device organization during design and development and planning for product realization.

If risk control measures were identified involving the delivery, installation, and servicing for a particular device, confirm that the necessary processes have been implemented to ensure the risk control measures are in place. For example, a medical device organization may have identified that in order for a medical imaging device to give accurate images, servicing must be performed by trained personnel according to specific instructions.

Risk control measures might include warnings on the imaging device that only authorized personnel should service the device and the design of a unique tool to access the inside of the device that is only provided to authorized service personnel.

Links
None

Task 29 – Top management commitment to the production and service process

Determine, based on the assessment of the production and service control process overall, whether management provides the necessary commitment to the production and service control process to ensure devices meet specified requirements and quality objectives.

Clause and Regulation
ISO: ISO: 13485:2016: 5.1, 5.2

ANVISA: RDC ANVISA 665/2022: Art. 5°, Art. 6°, Art. 7°

MHLW/PMDA: MO169: 10, 11

Additional country-specific requirements
None

Links
None

Chapter 7 - Purchasing

The intent of the Purchasing process is to ensure that purchased, subcontracted, or otherwise received products and services conform to specified requirements. The medical device organization is expected to establish and maintain documented controls for planning and performing purchasing activities.

The controls necessary depend on the effect of the product on the quality, safety, and effectiveness of the finished device. Effective purchasing processes incorporate purchasing requirements and specifications, the selection of acceptable suppliers based on the capability of the suppliers to provide acceptable product, the performance of necessary acceptance activities, and maintenance of the required quality records.

The **management representative** is responsible for ensuring that the requirements of the quality management system have been effectively defined, documented, implemented, and maintained. Prior to the audit of a process, it may be helpful to interview the management representative (or designee) to obtain an overview of the process and a feel for management's knowledge and understanding of the process.

The Purchasing process is integral to the other processes of the MDSAP audit sequence. As the audit is being performed of the medical device organization's Measurement, Analysis and Improvement process, Design and Development process, and Production and Service Controls process, the audit team should be assessing the affect purchased product has on the quality of the finished device. The audit team should be using information learned about actual and potential product and process nonconformities during the audit of the Measurement, Analysis and Improvement process, higher risk elements and essential design outputs from the design projects reviewed during audit of the Design and Development process, in addition to significant outsourced product and production processes identified during the audit of the Production and Service Controls process to make decisions as to supplier evaluation files to be reviewed during the audit of the Purchasing process.

The medical device organization's purchasing process may be reviewed in conjunction with the Measurement, Analysis and Improvement process, the Design and Development process, and the Production and Service Controls process, being mindful of the MSDAP process linkages. The Purchasing process should be considered a critical process for those organizations that outsource essential activities such as design and development and/or production to one or more suppliers.

Auditing the Purchasing Process

Purpose: The purpose of auditing the Purchasing process is to verify that the medical device organization's processes ensure that products (e.g. components, materials and services provided by suppliers, including contractors and consultants) are in conformance with specified purchase requirements, including quality management system requirements. This is particularly important for those organizations who outsource activities such as design and development and/or production to one or more suppliers, and when the supplied product or service cannot be verified by inspection (e.g. sterilization services). Suppliers include those providers of any product received from outside the medical device organization, including corporate or financial affiliates, where the product has an effect on subsequent product realization or the final product.

Chapter 7 - Purchasing

Task 1 – Planning activities regarding purchased products and outsourced processes

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Outcomes: As a result of the audit of the Purchasing process, objective evidence will show whether the medical device organization has:

A) Defined, documented and implemented procedures to ensure purchased or otherwise supplied products conform to specified purchase requirements
B) Established criteria for the selection, evaluation and re-evaluation of suppliers based on the type and significance of the product purchased and the impact of the supplied product on subsequent product realization or the quality of the finished device
C) Performed the evaluation and selection of suppliers based on the capability of the supplier to meet specified requirements
D) Ensured the continued capability of suppliers to provide quality products that meet specified purchase requirements through re-evaluation
E) Determined and implemented an appropriate combination of controls applied to suppliers in conjunction with acceptance verification activities to ensure conformity to product and quality management system requirements, based on the impact of the supplied product on the finished device.

Links to Other Processes:

Management; **Design and Development**; **Measurement, Analysis and Improvement**; **Production and Service Controls**

Task 1 – Planning activities regarding purchased products and outsourced processes

Verify that planning activities describe or identify products to purchase and processes to outsource, the specified requirements for purchased products, the requirements for purchasing documentation and records, purchasing resources, the activities for purchased product acceptance, and *risk management* in supplier selection and purchasing.

Clause and Regulation

ISO: ISO: 13485:2016: 4.1.2, 4.1.3, 4.1.5, 7.1, 7.4.1, 7.4.2, 7.4.3

TGA: TG(MD)R Sch1 P1 2, Sch3 P1 Cl1.4(5)(d)(ii)

ANVISA: RDC ANVISA665/2022: Art. 18, Art. 21

MHLW/PMDA: MO169: 5-2, 5-3, 5-5, 26, 37, 38, 39; [Old: 5, 26, 37, 38, 39]

FDA: 21 CFR 820.20, 820.50]

Additional country-specific requirements

None

Assessing conformity

Planning

In planning product realization, the medical device organization must determine as appropriate the quality objectives and requirements for the purchased products, the processes, documents, and resources specific to the purchased products, the criteria for purchased product acceptance, and the required verification, monitoring, inspection, and test activities specific to the purchased products. Planning of product realization often begins in the design and development of the product, including the translation of the design into production specifications. The translation of the design into production specifications includes the establishment of specified requirements for purchased product.

Quality objectives

Quality objectives are typically expressed as a measurable target or goal. The planning of product realization should include consideration of how the purchased product, the criteria for purchased product acceptance, and the required verification, monitoring, inspection, and test activities specific to the purchased product will achieve the quality objectives.

Links

Design and Development, **Management**

During the review of a design project, confirm that the medical device organization has considered the effect of purchased product on the essential design outputs. For suppliers that provide product and services related to the essential design outputs, the degree of purchasing controls necessary is commensurate with the effect of the supplied product on the proper functioning of the finished device.

During the audit of the Purchasing process, confirm when necessary that the degree of control over suppliers of purchased product has been made based on the risk the supplied product poses to the ability of the finished device to meet specified requirements.

Additionally, confirm when necessary that the quality objectives related to the purchased product were considered for inclusion in management review.

Task 2 – Selection of supplier file to audit

Select one or more supplier evaluation files to audit.

Priority criteria for selection:

1. Indications of problems with supplied products or processes from audit of the Measurement, Analysis and Improvement process
2. *Suppliers of higher risk products or processes*
3. Suppliers who provide products or services that directly impact the design outputs required for proper functioning of the device
4. Suppliers of processes that require validation or revalidation
5. Newly approved suppliers of products or services
6. Suppliers of products or services used in the manufacturing of multiple products
7. Suppliers of components or services not covered during previous audits

Links

None

Task 3 – Procedure for the control of purchased products and outsourced processes

Verify that procedures for ensuring purchased product conforms to purchasing requirements have been established and documented.

Clause and Regulation

ISO: ISO: 13485:2016: 7.4.1

TGA: TG(MD)R Sch3 P1 Cl1.4(5)(d)(ii)

ANVISA: RDC ANVISA 665/2022: Art. 21

MHLW/PMDA: MO169: 37

FDA: 21 CFR 820.50]

Additional country-specific requirements

None

Assessing conformity

Procedures

The medical device organization must define, document, and implement procedures to ensure that purchased product conforms to specified requirements. These procedures commonly contain information as to the mechanisms by which the medical device organization is going to categorize suppliers based on the risk the supplied product has on the ability of the finished device to meet specified requirements, the criteria the medical device organization intends to use to evaluate the suppliers, the means of determination that a

supplier is acceptable, the methods for supplier monitoring, the requirements for re-evaluating suppliers, and the means by which a supplier might be determined to be unacceptable.

It is important to remember that the requirements for purchasing controls apply to all product received from a supplier by the medical device organization that have an impact on product realization, whether a payment occurs or not, and regardless of the corporate or financial affiliation between the supplier and the medical device organization.

Links

None

Task 4 – Extent of controls applied to the supplier and the purchased product; criteria for selection, evaluation, and re-evaluation of the supplier

Verify that the procedures assure the type and extent of control applied to the supplier and the purchased product is dependent upon the effect of the purchased product on subsequent product realization or the final product.

Verify that criteria for the selection, evaluation and re-evaluation of suppliers have been established and documented.

Clause and Regulation

ISO: ISO: 13485:2016: 7.4.1

ANVISA: RDC ANVISA 665/2022: Art. 22, Art. 23

MHLW/PMDA: MO169: 37

FDA: 21 CFR 820.50]

Additional country-specific requirements

None

Assessing conformity

Extent of control

The type and extent of control applied to the supplier must take into consideration the affect the supplied product has on the finished device. Procedures commonly contain methods to categorize suppliers, based on the importance of the supplied product to the proper functioning of the finished device and the past history (if applicable) of the supplier.

Be mindful of organizations that use a "one-size-fits-all" approach to managing their suppliers, as these systems may not provide the necessary amount of evaluation and oversight over suppliers of products essential for the proper functioning of the finished device.

Evaluation criteria
The medical device organization must define, document, and implement procedures outlining the criteria for the selection, evaluation and re-evaluation of suppliers. The procedures for supplier evaluation and selection typically include such items as the methods by which suppliers will be evaluated and the means and frequency by which supplier performance will be monitored.

The evaluation of suppliers must provide a means to assess the capability of the supplier to supply products that meet specified requirements. The medical device organization can assess a supplier's capability to supply quality product in a number of ways, including but not limited to performing supplier audits, first-article inspections, supplier surveys, and reviewing the supplier's past history in supplying a similar product or service if applicable.

The medical device organization may also choose to consider the supplier's conformity with quality management system requirements through third party certifications; however, third party certification should not be relied on exclusively in initially evaluating a supplier.

Controls over suppliers of sterilization processes
For devices intended to be sterile, the medical device organization must determine the criteria the supplier must meet to be selected, with regards to the control of the sterility of the device and perform selection and monitoring of suppliers considering the identified criteria.

Links
None

Task 5 – Selection of supplier based on ability of the supplier to satisfy the specified purchase requirements

Verify that suppliers are selected based on their ability to supply product or services in accordance with the medical device organization's specified requirements.

Confirm that the degree of control applied to the supplier is commensurate with the significance of the supplied product or service on the quality of the finished device, based on risk.

Verify that records of supplier evaluations are maintained.

Chapter 7 - Purchasing

Task 5 – Selection of supplier based on ability of the supplier to satisfy the specified purchase requirements

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Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.1, 7.4.1

TGA: TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 16, Art. 17, Art. Art. 18, Art. 23

MHLW/PMDA: MO169: 6, 26, 37; [Old: 6, 26, 37, 65]

FDA: 21 CFR 820.50(a)]

Additional country-specific requirements

Australia (TGA):

The conformity assessment procedures require that a Manufacturer demonstrates compliance with the Essential Principles through application of a QMS. Hence a Manufacturer must show how risk management principles have been applied during design and construction, including purchasing, to mitigate risk. (EP 2 - TG(MD)R Sch1 P1 2).

The conditions of marketing authorization (ARTG inclusion) require that Australian Sponsors undertake some regulatory activities including; customer complaint handling (Act s 41FN, Reg 5.8), the management and communication of technical files /technical documentation (Act s 41FN(3)), adverse event reporting (Act s 41FN, Reg 5.7), conducting recalls (Part 4-9), ensuring that the name and address of the Sponsor is provided with the device (Reg 10.2), the storage of devices (Act s 41FN,Reg 5.9) and the keeping of complaint and distribution records (Act s 41FN,Reg 5.10). Some Sponsors also provide services for the installation and servicing of a device on behalf of the Manufacturer.

Where a regulatory requirement for a Sponsor intersects with a regulatory requirement or a requirement of ISO13485 for the Manufacturer, the activity is to be treated as an outsourced activity and documented in the Manufacturer's QMS. Verify that the Manufacturer has adequate supplier controls to mitigate risk and ensure the Sponsor fulfils the outsourced activities included in a written agreement [TG Act 41FN] for those activities.

Other activities that may be outsourced to the Sponsor include making applications on behalf of the Manufacturer to the TGA [TG Act s41EB], representing the Manufacturer in interactions with the TGA [TG Act s41FN(3)], as an intermediary in recalls of products [TG(MD)R Sch 3 - Part 1:1.4(3)], in the notification of substantial changes to a kind of medical device (TG Act s41BE) that may require a variation to an entry in the Australian Register of Therapeutic Goods (TG Act s9D), for the provision of records [TG(MD)R Schedule 3 - Part 1:1.5, 1.9], or other matters that may be required to allow the Sponsor to fulfill market authorization conditions [TG Act Part 4-5 Div 2].

The requirement of Regulation 10.2 for "ensuring that the name and address of the Sponsor is provided with the device in such a way that the user of the device can readily identify the Sponsor" is only an obligation on the Sponsor. This activity does not need to be included in the Manufacturer's QMS documentation however the arrangements for the provision of this information should be disclosed in the written agreement between the Manufacturer and the Sponsor. In cases where an activity performed by the Sponsor also includes the provision of information required by Essential Principle 13 (Labels and IFU) or 13A (implant cards and leaflets) the Manufacturer must treat the Sponsor as supplier for that activity.

The Sponsor does not need to be treated as a supplier if the scope of the Manufacturer's quality management system includes the site and activities of the Sponsor. The oversight of the Sponsors activities should be clearly documented in the QMS and be included in plans for internal audit.

Canada (HC):
Verify that any regulatory correspondent used by the Manufacturer is treated as a supplier and is adequately qualified.

Assessing conformity

Supplier selection
The selection of suppliers must be based on defined criteria. An important concept to remember is that quality cannot be inspected or tested into products. Medical device organizations that choose to conduct product quality control solely in-house must still assess the capability of suppliers to provide acceptable product.

Some organizations require suppliers to maintain various types of certifications or registrations. While registrations and third-party certifications may be considered in supplier evaluations, the medical device organization should not exclusively rely on these methods to perform the initial evaluation of suppliers.

For the supplier(s) the audit team has chosen to review, confirm that the medical device organization's selection of the supplier was based on defined criteria commensurate with the risk posed if the supplied product causes the finished device to not meet specified requirements.

Records of supplier evaluations
The medical device organization must maintain records of the evaluation of the capability of the supplier to meet specified requirements. The records should include the mechanism by which the supplier was evaluated, the results of the evaluation, and the determination of whether the supplier was deemed to be acceptable.

For the supplier(s) the audit team has selected, review the medical device organization's evaluation of the supplier(s). Confirm that the evaluation was made according to defined criteria and is commensurate with the effect the supplied product has on the essential design outputs.

Links

Design and Development, **Production and Service Controls**

The establishment of the necessary purchasing controls and required acceptance activities is a design output. The degree of the purchasing controls necessary and extent of acceptance activities should be based on the risk posed by the product not meeting its specified requirements and essential design outputs.

Auditors may encounter situations where the medical device organization outsources processes that require validation.

During the review of the Purchasing process, review the controls the medical device organization has instituted over suppliers that perform validated processes. This typically includes confirming that the medical device organization has reviewed the process validation data generated by the supplier to ensure the process is effective, reproducible, and stable. This can be particularly important for higher risk validated processes performed by suppliers, since the medical device organization does not have immediate control over those processes.

The audit team should also consider reviewing the purchasing controls and requirements for suppliers of products that undergo minimal acceptance activities by the medical device organization.

Task 6 – Records of supplier evaluation

Verify that the medical device organization maintains effective controls over suppliers and product, so that specified requirements continue to be met.

Clause and Regulation

ISO: ISO: 13485:2016: 7.4.1

ANVISA: RDC ANVISA 665/2022: Art. 23

MHLW/PMDA: MO169: 37

FDA: 21 CFR 820.50(a)]

Additional country-specific requirements

None

Assessing conformity

Monitoring supplier performance

The medical device organization must define and implement processes to monitor the performance of suppliers. The monitoring of supplier performance should not be based solely on cost considerations or on-time deliveries. The monitoring of suppliers should take into consideration the actual performance of the supplier in terms of providing products that meet specified requirements. Examples of supplier monitoring activities may include, but are not limited to supplier re-audits, statistical analysis of incoming acceptance results, monitoring of complaints and nonconformities related to supplied product, independent confirmation of certificate of conformance data, and consideration of the supplier's responses to requests for corrective action.

In order for the supplier to maintain a status as an acceptable supplier, the supplier must be capable of supplying product that consistently meets the medical device organization's specified requirements. If supplier monitoring does not demonstrate that the supplier has the capability to provide acceptable products, the medical device organization must have a means to undertake appropriate action, including such activities as requesting corrective action from the supplier, and in some cases, removing the supplier from records of acceptable suppliers.

For the supplier(s) the audit team has chosen to review, confirm that the supplier monitoring is documented and reviewed by the appropriate individuals responsible for supplier selection. Be particularly mindful of instances where supplied product has caused complaints and/or product nonconformities. Verify that the medical device organization has performed the appropriate monitoring of the supplier and taken actions when necessary, such as requesting the supplier undertake a corrective action.

Links

Production and Service Controls, **Measurement, Analysis and Improvement**

Organizations are expected to define, document, and implement systems and procedures for acceptance activities to verify that supplied products conform to specified requirements. Effective acceptance procedures and systems directly affect the ability of a medical device organization to demonstrate that supplied products meets specifications. During the audit of the Production and Service Controls process, confirm that the appropriate acceptance activities have been implemented and monitored to ensure the received product meets specified requirements.

Additionally, organizations are required to determine, collect, and analyze appropriate data to demonstrate the ability of suppliers to provide acceptable product. During the audit of the Measurement, Analysis and Improvement process, confirm that analysis of supplier performance data has been performed and considered for corrective or preventive action when necessary.

Task 7 – Effective controls over supplier and products

Confirm that the re-evaluation of the capability of suppliers to meet specified requirements is performed at intervals consistent with the significance of the product on the finished device.

Clause and Regulation

ISO: ISO: ISO 13485:2016: 7.4.1

TGA: TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 22

MHLW/PMDA: MO169: 37

FDA: 21 CFR820.50(a)]

Additional country-specific requirements

None

Assessing conformity

Supplier re-evaluation intervals

Organizations must implement the appropriate combination of supplier evaluation, supplier monitoring, and acceptance activities to provide the necessary confidence in the acceptability of supplied product. However, supplier evaluation is not a "one-time" assessment. The medical device organization must ensure the continued capability of the supplier to provide product that meets specified requirements. The frequency of re-evaluation must be performed according to the medical device organization's procedures and at intervals consistent with the significance of the product or service on the finished device. The frequency of re-evaluation may change based on identified quality problems with the supplied product.

For the supplier(s) the audit team has chosen to review, confirm that the re-revaluation of the supplier was performed commensurate with the risk the supplied product poses to the ability of the finished device to meet specifications.

Links

Measurement, Analysis and Improvement

The frequency and extent of supplier re-evaluation activities may be based, in part, on the performance of the supplier as demonstrated by such activities as statistical monitoring of the supplier, monitoring of complaints and nonconformities related to supplied product, and corrective or preventive actions related to the supplier.

Task 8 – Verification of the adequacy of purchasing information, specified purchase requirements, and written agreement to notify changes, before their communication to the supplier

Verify that the medical device organization assures the adequacy of purchasing requirements for products and services that suppliers are to provide, and defines risk management activities and any necessary risk control measures.

Confirm that the medical device organization ensures the adequacy of specified purchase requirements prior to their communication to the supplier and that a written agreement with the supplier is established in which suppliers has to notify the medical device organization about changes in the product.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.4.2, TG(MD)R Sch1 P1 2

ANVISA: RDC ANVISA 665/2022: Art. 18, Art. 24, Art. 26

MHLW/PMDA: MO169: 6, 38

FDA: 21 CFR 820.50(b)

Additional country-specific requirements

Brazil (ANVISA):

Confirm that purchase orders are approved by a designated person. This approval, including date and signature, shall be documented [RDC ANVISA 665/2022: Art. 27].

Assessing conformity

Adequacy of purchasing information

Purchasing information is commonly provided to suppliers in documents such as, but not limited to, specification sheets, drawings, contracts, purchase orders, and quality agreements. The amount of detail required in the purchasing information must be commensurate with the effect of the supplied product on the performance of the finished device.

Risk control measures

The medical device organization is responsible for the quality and performance of the finished device. The specified requirements for the finished device cannot be met unless the individual parts of the finished device meet specifications. While the medical device manufacturer may require certain risk management activities to be adopted by the supplier to help ensure acceptability of incoming product, the ultimate responsibility for the

finished device is borne by the medical device organization. The medical device organization is responsible for identifying any risk control measures that are required for the supplied product. For suppliers that provide product and services related to the essential design outputs, the degree of necessary risk control measures is commensurate with the effect of the supplied product on the proper functioning of the finished device.

Some examples of risk control measures related to supplied product include, but are not limited to, requiring the supplier to use quality assurance procedures approved by the medical device organization, the establishment of inspections or testing of supplied product before shipment to the medical device organization, requiring each incoming shipment be accompanied by a certificate of conformance, periodic verification of the certificate of conformance by third-party laboratory analysis, implementation of acceptance activities at the medical device organization based on the risk the supplied product poses to the ability of the finished device to meet specifications, and the verification of validation data by the medical device organization for validated processes performed by a supplier.

For the supplier(s) files the audit team has selected for review, confirm that risk control measures have been identified when appropriate and the risk control measures have been implemented and are effective. If the auditor(s) observe that supplied product has been identified as an underlying cause of complaints and nonconformities, this can be an indication that the risk control measures are inadequate or ineffective.

Links

None

Task 9 – Documented purchasing information and specified purchase requirements

Verify that the medical device organization documents purchasing information, including where appropriate the requirements for approval of product, procedures, processes, equipment, qualification of personnel, sterilization services, and other quality management system requirements.

Confirm that documents and records for purchasing are consistent with traceability requirements where applicable.

Clause and Regulation

ISO: ISO 13485:2016: 7.4.2, 7.5.9

ANVISA: RDC ANVISA 665/2022: Art. 24, Art. 25, Art. 113

MHLW/PMDA: MO169: 38, 48, 49

FDA: 21 CFR 820.50(b), 820.65, 820.160]

Additional country-specific requirements

None

Assessing conformity

Documenting purchasing information

Purchasing information must describe the product to be purchased, including (when appropriate) the requirements for approval of product, procedures, processes, and equipment, the requirements for qualification of personnel, and quality management system requirements related to the purchased product.

Where possible, the purchasing information must contain an agreement that the supplier agrees to notify the medical device organization of changes in products or services that may affect the quality of the finished device. The medical device organization should approve or reject these changes, based on the impact of the change on the essential design outputs of the finished device.

Purchasing information may be recorded in written or electronic format, but must be documented.

Traceability

It is the responsibility of the medical device organization to establish procedures for traceability. For devices that are not implanted and are not life-supporting or life-sustaining, the medical device organization has the flexibility to determine which raw materials and components are required to be traceable, commensurate with the risk posed by the device in the event the component does not meet specified requirements.

Medical device organizations that produce finished devices whose failure could result in serious injury or harm to the user, or are implanted or life-supporting or life-sustaining must implement a traceability system. The traceability system must allow for each batch of finished devices to be traced by a control number or similar mechanism throughout the distribution chain. Organizations must provide for the control and traceability of components and materials used in the manufacture of the device when these could cause the finished device to not meet specified requirements.

The determination of which components and raw materials may be required to be traceable may be made by the medical device organization using risk management tools, such as risk analysis, or by the identification of the components and processes used to fulfill the essential design outputs.

Links

None

Task 10 – Verification of purchased products

Confirm that the verification (inspection or other activities) of purchased products is adequate to ensure specified requirements are met.

Confirm that the medical device organization has implemented an appropriate combination of controls applied to the supplier, the specification of purchase requirements, and acceptance verification activities that are commensurate with the risk of the supplied product upon the finished device.

Verify that records of verification activities are maintained.

Clause and Regulation

ISO: ISO: 13485:2016: 4.2.1, 7.1, 7.4.3

TGA: TG(MD)R Sch1 P1 2, Sch3 1.4(5)(e)

ANVISA: RDC ANVISA 665/2022: Art. 22, Art. 41, Art. 42, Art. 89

MHLW/PMDA: MO169: 6, 26, 39

FDA: 21 CFR 820.50, 820.80(b)]

Additional country-specific requirements

Brazil (ANVISA):

Verify that the manufacturer has established and maintains procedures to ensure the retention of components, raw materials, in-process products and returned products until inspections, tests or other specified verifications have been performed and documented [RDC ANVISA 665/2022: Art. 91].

Assessing conformity

Establishment of acceptance activities

The medical device organization must establish an appropriate combination of supplier assessment and receiving acceptance activities to ensure products and services, including sterilization services are acceptable for their intended use. After a supplier has been approved, the necessary acceptance activities for the supplied product must be implemented. The degree of acceptance activities may vary with the type and significance of the product or service on the quality of the finished device and the extent of measures performed by the supplier to ensure product acceptability.

Organizations are expected to define, document, and implement processes and procedures for acceptance activities to verify that supplied products conform to specified requirements. Recognized acceptance activities include, but are not limited to, inspections, tests, reviews of certificates of analysis, and supplier audits.

Effective acceptance procedures and systems directly affect the ability of a medical device organization to demonstrate the process and product meet specifications.

It is important to remember that acceptance activities apply to any incoming component, subassembly, or service, whether a payment occurs or not, and regardless of the medical device organization's financial or business arrangement with the supplier.

Records of verification activities
The records of verification activities must show the supplied product is in conformity with specified requirements. If nonconformities are found by the medical device organization, confirm the medical device organization has appropriately handled the nonconformity according to the medical device organization's established procedures.

The medical device organization can address nonconforming product by taking action to eliminate the detected nonconformity (e.g. sorting an incoming lot of components to remove components that do not meet specifications), authorizing its use, release, or acceptance under concession, or by taking action to prevent its original intended use (e.g. allowing the components to be used as training aids to show production personnel the difference between an acceptable and unacceptable component).

For the supplied product(s) the audit team has chosen to review, confirm the records of verification activities have been maintained. One way to perform this task is to request a sample of verification records for the chosen product and confirm the acceptance activities have been documented, including the documentation and appropriate disposition of nonconforming product.

Links

Production and Service Controls

The audit team may encounter instances where product has been deemed acceptable by the successful completion of acceptance activities but the product is later shown to not meet specified requirements (e.g. failure of the device due to nonconforming component leading to product complaint). This can be an indication that the acceptance activities are not sufficient to identify nonconformities; or were not appropriately conducted.

Confirm that the medical device organization has taken the appropriate action to determine the suitability of the acceptance activities. For example, the medical device organization may need to validate the test method used for incoming acceptance to ensure the test method is actually capable of identifying nonconforming product.

Task 11 – Purchasing control activities as source of quality data for the measurement, analysis, and improvement process

Verify that data from the evaluation of suppliers, verification activities, and purchasing are considered as a source of quality data for input into the Measurement, Analysis and Improvement process.

Clause and Regulation

ISO: ISO 13485:2016: 8.4

ANVISA: RDC ANVISA 665/2022: Art. 120

MHLW/PMDA: MO169: 61

FDA: 21 CFR 820.100]

Additional country-specific requirements

None

Assessing conformity

Collection and analysis of data

The medical device organization is responsible for assuring the supplied product meets specified requirements. In addition to supplier evaluation, the assurance that the supplied product meets specified requirements is accomplished with the implementation of appropriate acceptance activities and monitoring complaints and nonconformities associated with purchased product. The data regarding acceptance activities and nonconformities must be analyzed as appropriate to determine the need for corrective or preventive action.

Links

Measurement, Analysis and Improvement

The medical device organization must determine the appropriate acceptance activities for supplied product, based on the essential design outputs of the device and the risk the device poses if specified requirements are not met. Confirm as necessary that supplied product was evaluated as to the effect on the essential design outputs. Additionally, verify that the appropriate acceptance activities were implemented based on the potential effect the supplied product poses to the essential design outputs.

Organizations are required to determine, collect, and analyze appropriate data to demonstrate the ability of suppliers to provide acceptable product. During the audit of the Measurement, Analysis and Improvement process, confirm that analysis of supplier performance data from evaluation and monitoring supplier process activities has been performed and considered for corrective or preventive action when necessary.

Task 12 – Top management commitment to the purchasing process

Determine, based on the assessment of the overall purchasing, whether management provides the necessary commitment to the purchasing process.

Clause and Regulation

ISO: ISO 13485:2016: 4.1.3, 4.1.5, 5.2

ANVISA: RDC ANVISA 665/2022: Art. 8°, Art. 9°

MHLW/PMDA: MO169: 5-3, 5-5, 11, [Old: 5, 11]

Additional country-specific requirements

None

Links

None

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

Purpose: The requirements in IMDRF/MDSAP WG/N3FINAL:2016 (2nd Ed) for Auditing Organizations that audit medical device manufacturers, and may perform other related functions, include, to the extent possible during on-site audits and in accordance with the applicable regulatory system, aspects of evaluation including:

- product/process related technologies (e.g. injection molding, sterilization); and
- evidence of adequate product technical documentation in relation to relevant regulatory requirements.

It should be noted that:

- IMDRF/MDSAP WG/N3FINAL:2016 (2nd Ed) does not provide additional requirements for product certification (ISO/IEC 17065:2012) or the requirements of product testing (ISO/IEC 17025:2005)

The following is explicitly excluded from the scope of IMDRF/MDSAP WG/N3FINAL:2016 (2nd Ed) due to the lack of regulatory convergence:

- the premarket reviews (e.g. Design Dossier Examinations, Premarket Applications, Shounin Applications, Product Registration/Notifications) typically performed by product specialist(s)
- the final decisions of safety and performance/effectiveness of a medical device made by any Regulatory Authority.

Definitions:

Technical Documentation

Documented evidence normally an output of the quality management system (QMS), which demonstrates compliance of a device to the regulatory requirements for products, and processes.

(Adapted from IMDRF/ MDSAP WG/ N3FINAL:2016 (2nd Ed) – Section 3.5)

Technical Expert

An individual who carries out the following functions at an Audit:
- evaluation of product/process related technologies
- evaluation of Technical Documentation
- evaluation of compliance with Regulations.

IMDRF/ MDSAP WG/ N3FINAL:2016 (Edition 2)

> **Clause 7.1.2** - An Auditing Organization shall have access to the necessary administrative, technical, and scientific personnel with technical knowledge and sufficient and appropriate experience relating to medical devices and the corresponding technologies.

Clause 7.1.5 - An Auditing Organization shall be capable of carrying out all the tasks assigned to it with the highest degree of professional integrity and the requisite technical competence in the specific field, whether those tasks are carried out by the Auditing Organization itself or on its behalf and under its responsibility.

Clause 9.2.4 - Stage 2 audit objectives shall specifically include evaluation of:

- the effectiveness of the Manufacturer's QMS incorporating the applicable regulatory requirements
- product/process related technologies (e.g. injection molding, sterilization)
- adequate product technical documentation in relation to relevant regulatory requirements
- the Manufacturer's ability to comply with these requirements.

Clause 9.3.2 - Surveillance audit objectives during the audit cycle shall specifically include evaluation of the effectiveness of the Manufacturer's QMS incorporating the applicable regulatory requirements and the Manufacturer's ability to comply with these requirements. In addition:

- new or changed product/process related technologies (e.g. injection molding, sterilization)
- new or amended product technical documentation in relation to relevant regulatory requirements.

Clause 9.4.1 - Recertification audit objectives shall specifically include evaluation of:

- the effectiveness of the Manufacturer's QMS incorporating the applicable regulatory requirements
- product/process related technologies (e.g. injection molding, sterilization)
- adequate product technical documentation in relation to relevant regulatory requirements
- the Manufacturer's continued fulfillment of these requirements.

ISO 13485:2016

Clause 4.2.3 – Medical Device File

For each medical device type or medical device family, the medical device organization shall establish and maintain one or more files either containing or referencing documents generated to demonstrate conformity to the requirement of this International Standard and compliance with applicable regulatory requirements.

The content of the file(s) shall include, but is not limited to:

- general description of the medical device, intended use/purpose, and labelling, including any instructions for use
- specifications for product
- specifications or procedures for manufacturing, packaging, storage, handling and distribution
- procedures for measuring and monitoring
- as appropriate, requirements for installation
- as appropriate, procedures for servicing.

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

Clause 7.3.10 - Design and development files

The medical device organization shall maintain a design and development file for each medical device type or medical device family. This file shall include or reference records generated to demonstrate conformity to the requirements for design and development and records for design and development changes.

Auditing Technical Documentation:

The Medical Device File (ISO 13485:2016 Cl 4.2.3) and the Design and Development Files (ISO 13485:2016 Cl 7.3.10) are to contain or reference documents to demonstrate compliance with requirements of the Standard and with applicable regulatory requirements. For compliance with the requirements of N3 (2nd Ed) these records should contain technical documentation that includes, but not limited to:

- Outputs from the design and development process, such as: design outputs, design verification data with acceptance criteria, design validation data with acceptance criteria, a risk management file, human factors analysis, software validation, clinical evaluation report, electrical safety and electromagnetic compatibility, etc.
- Specific design outputs, design verification data with acceptance criteria, design validation data with acceptance criteria for products where a regulatory authority has specific expectations for the type of evidence to demonstrate compliance with regulatory requirements.
- Inputs to the production and service controls process, such as: device production specifications including appropriate drawings, composition, formulation, component specifications, and software specifications.
- Specifications for a production processes including the appropriate equipment specifications, production methods, production procedures, and production environment specifications.
- Quality assurance procedures and specifications including acceptance criteria and the quality assurance equipment to be used.
- Specifications for packaging and labeling, including methods and processes used for validation after transportation and environmental conditioning.
- Procedures and methods for installation, maintenance, and servicing.
- Jurisdiction-specific statements (such as a declaration of conformity, statement on the presence of specific substances, essential principles checklist, etc.).

The information may be a compilation of documented information or, if the documents constituting the technical documentation are maintained separately, may be a summary that includes an explicit reference to each of these documents.

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

Auditors are not expected to fully evaluate the data that substantiates the final decisions of safety and performance/effectiveness of a medical device made by any Regulatory Authority. However, the auditor is expected to apply the MDSAP Audit Approach for the review of Technical Documentation when auditing:

- the Design and Development Process (See Tasks #3-17 in Chapter 5)
- the Production and Service Controls Process (See Task #16 in Chapter 6)
- the Jurisdiction-specific statements identified in the Device Marketing Authorization and Facility Registration Process (See Task #2 in Chapter 2)

The Audit Approach requires the auditor to select design documentation and manufacturing process documentation for review. The selection is to be based on information collected earlier in the audit, and taking into account the risks (risk classification) associated with the device, the novelty of technology used in the device and the associated manufacturing processes or sterilization methods, along with any changes to the device or associated manufacturing processes that have been implemented by the Manufacturer since the last on-site audit, including non-reported changes controlled under the QMS. A minimum of one review of a design and development file and related medical device file should be undertaken per audit to verify that the Manufacturer has established evidence of conformity with regulatory requirements. Additional reviews may be undertaken if time permits or the auditor suspects that the technical documentation previously reviewed is not a representative sample. (See tasks #2 in chapters 5 and 6).

Surveillance audits should also confirm that the Manufacturer has arrangements in place to maintain the currency of the technical documentation for all devices. For example:

- a procedure for reviewing the currency of relevant standards and conducting gap analyses as required
- a requirement to assess design changes and the need for further technical testing
- a plan for post-market clinical trials, where necessary, or periodic literature reviews
- updating risk management documents (e.g. occurrence levels in risk analysis) based on post-market data.

The following table summarizes the tasks that an MDSAP auditor will use to review information that constitutes the Technical Documentation.

Information	**Audit Approach: Process, Task#**
Medical device general description, including variants and accessories	Design and Development, task #5, 7
Evidence of compliance with specified regulatory requirements for products or processes.[5]	Design and Development, task #5, 7

[5] For example, Australia's - Essential Principles, Canada - Safety and Effectiveness Requirements

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

Information	Audit Approach: Process, Task#
Evidence of inclusion of feedback into risk management for monitoring and maintaining the product requirements as well as product realization or improvement processes	
Information that confirms that design and development outputs for the product are traceable to, and satisfy, design input requirements	Design and Development, task #7
Intended use, and indication of use, of the medical device	Design and Development, task #5, 7, 10, 11
Labelling, (i.e. information that accompanies a medical device that is located on the device, its packaging, the instructions for use and in promotional material)	Design and Development, task #1, 7, 8, 16
Confirmation that the product is a medical device	Device Marketing Authorization and Facility Registration, task #1 Design and Development, task #5
Classification	Device Marketing Authorization and Facility Registration, task #1 Design and Development, task #5
Risk management file	Design and Development, task #8
Pre-clinical data (studies in animal models, testing to support compliance with relevant standards, technical performance tests etc.)	Design and Development, task #10
Clinical evidence	Design and Development, task #11
Manufacturing processes	Design and Development, task #7, 16 Production and Service Controls, task #3, 16
Process validation	Design and Development, task #16 Production and Service Controls, task #7, 8, 9
Evidence of compliance with specified regulatory requirements for marketing authorization.	Device Marketing Authorization and Facility Registration, task #1
Declaration of conformity	Device Marketing Authorization and Facility Registration, task #1

Note: this table may not exhaustively cover all information expected under all jurisdictions.

Auditors are expected to verify:

- the existence and the coherence of the information listed in this table
- the applicability of this information to the medical device subject to marketing authorization
- that the methods implemented throughout the Design and Development to generate this information are sound and commensurate to the risk associated with the medical device; and
- that conclusions are substantiated.

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

Although the auditors are not expected to make final device safety and effectiveness decisions based on a review of technical documentation, if an auditor suspects that device safety and effectiveness concerns exist, or that the evidence supporting compliance with safety and effectiveness requirements is lacking, the concerns should be explicitly described in the audit report. If an auditor suspects a public health threat, the Auditing Organisation must submit an early awareness communication notice ("MDSAP 5-day Notice") according to MDSAP AU P0027.001 Post-Audit Activities and Timeline Policy.

The depth and extent of this review should be commensurate with the classification of the medical device, the novelty of the intended use, the novelty of the technology or construction materials, and the complexity of the design and/or technology.

Expectations from participating Regulatory Authorities:

Each participating regulator may have different requirements for the review of technical documentation and for the assessment of the adequacy of that technical documentation at audit.

If inadequacies are identified, nonconformities should be raised in the normal manner, using the most specific and relevant clause of ISO 13485, [see especially ISO 13485:2016 - §4.2.3 and §7.3.10] including those raised against technical documentation under country specific requirements [for example, see ISO 13485:2016 - §7.2.1.c, §7.3.3.b, §7.3.7, §4.1.1]. Refer to MDSAP AU P0037 for further guidance on the selection of appropriate clause and the grading of nonconformities. NCs from the review of technical documentation shall be included in the Nonconformity Grading and Exchange Form (MDSAP AU F0019.2).

Further guidance on the expectations for the evidence of compliance with regulatory requirements is provided in the following sections.

Additional country-specific requirements

Australia – TGA
Auditing Technical Documentation:

The assessment of product requirements for Australian Class I (supplied sterile), Class I (with a measuring function), Class IIa and Class IIb medical devices, and Class 1-3 IVDs, is performed by the TGA on a sampling basis prior to market authorization (aka "Application audit"). Technical documentation review is expected to be performed in the context of audit to increase the pool of sampled devices and strengthen the sampling based approach. Technical documentation review should take into consideration the provisions of IMDRF/MDSAP

Annex 1 – Audit of Product/Process related Technologies and Technical Documentation

WG/N3 – 9.3.1. This documentation shall contain sufficient detail to allow for an evaluation of the data and for the purpose of demonstrating:

- fulfillment of the requirement
- where an appropriate standard exists, fulfilment of the requirements of the relevant Standard that the Manufacturer has chosen as the means for demonstrating compliance with regulatory requirements for products and processes.

In the case of Class III, Active Implantable and Class 4 In Vitro Diagnostic medical devices that have been subject to a Design Examination separately from the QMS audit, the on-site audit should ensure that the technical documentation for these devices is maintained.

The technical documentation should contain, or reference, evidence of compliance with the Essential Principles and the following requirements. An Essential Principles checklist[6], although not mandatory, is often used as an index to identify the applicable Essential Principles, any standard or validated method that has been used to demonstrate compliance, and a reference to the document that contains the evidence of compliance.

The assessment of each set of technical documentation selected for compliance with the Essential Principles, as a minimum, should consist of a review of:

- A detailed description of the product, including the intended use, intended user, risk classification and assigned Global Medical Device Nomenclature (GMDN) code. For IVD medical devices, the description should also include specimen types, a list of kit components, methodology and any instrumentation to be used
- the inclusion of information gathered in feedback processes (e.g. complaints, adverse event reporting or recalls for product correction) as a potential input into risk management for monitoring and maintaining the product requirements as well as the product realization or improvement processes
- an index of the compilation of documents, or if documentation is not collated, a reference to the relevant documentation
- a risk management file (e.g. select a particular risk and confirm that it has been managed in accordance with the requirements of ISO 14971)
- selected report(s) of pre-clinical data and/or bench testing (including studies in animal models, testing to support compliance with relevant standards, technical performance and safety tests for electrical safety,

[6] For reference, manufacturers may choose to complete an Essential Principles Checklist as one way of indexing their evidence of conformity to requirements. The checklist is not mandatory; however, it provides a succinct way of identifying the relevant evidence. A sample template is available at http://www.tga.gov.au and by searching for "Essential Principles Checklist"

mechanical safety, radiation safety etc.) identified by the Manufacturer as evidence of compliance with relevant Essential Principles
- a selected clinical evaluation report to confirm that it is current and was prepared by an appropriately qualified expert (See TG(MD)Regs Sch 3 Part 8)
- any other documentation required for the type of device (e.g.- special requirements for devices incorporating medicinal substances or materials of animal origin);
- the information that accompanies a device (labelling, instructions for use, patient implant cards and leaflets)
- the declaration of conformity, for example, to comply with TG(MD)Reg Sch 3 Part 1 Clause 1.8 (this may be in a draft form for development devices that do not yet have marketing authorization).

Brazil – ANVISA

Brazilian regulations require that product registration / market authorization is entirely performed by ANVISA for all medical device classes.

ANVISA expects that the Auditing Organization follows the Audit Approach for reviewing technical documentation, including the Brazilian specific requirements defined in the document MDSAP AU P0002 – Audit Approach. There are no additional requirements to be reviewed during an MDSAP audit.

Canada - Health Canada

The Medical Devices Directorate, Health Canada, has assigned the responsibility for the review of technical documentation to the Bureau of Evaluation. For Health Canada, the objective of the audits conducted by MDSAP Auditing Organizations is to determine that Manufacturers who intend to license their devices in Canada have implemented a QMS in conformity with the requirements of the international standard ISO 13485 and Part 1 of the Canadian Medical Devices Regulations. Similarly, a holder of a medical device license is to maintain an effective QMS. Health Canada expects Auditing Organizations to confirm during their audits that the Manufacturer maintains evidence of safety and effectiveness and not to make a determination that the devices are safe and effective.

Japan – MHLW/PMDA

The assessment of product requirements is performed prior to market authorization by the regulator or registered certification bodies, hence technical documentation review, as assessment of conformity to the Essential Principles of Safety and Performance of Medical Devices, is not performed in the context of MDSAP audit.

USA – FDA

The US medical device regulations do not require a technical documentation as defined in the present document, although most data composing the technical documentation are direct output of the Design History File (820.30(j)) and the Device Master Record (820.181).

Annex 2 - Audit of Requirements for Sterile Medical Devices

Overview: The control of the sterility of a medical device is the result of a series of controlled processes including (but not limited to):

Design and Development:

a) device cleanliness and sterility requirements
b) compatibility of the device with the sterilization process
c) transport, storage, and presentation of the device at point of use
d) compatibility of the device packaging with the sterilization process
e) ability of the device to be sterilized or re-sterilized
f) shelf-life and device life user requirements
g) rationale for adding the device to a product family covered by a validated sterilization process

Production and Process Controls, as applicable:

a) process validation of the cleaning, sterile barrier packaging, and sterilization processes
b) routine monitoring and measurement of the cleaning, packaging and sterilization processes
c) routine acceptance criteria of the cleaning, packaging and sterilization processes
d) (re-)qualification, (re-)verification, (re-)calibration and maintenance of the cleaning, packaging and sterilization equipment
e) environmental control of production areas (cleanroom design and monitoring)
f) storage of device parts, components, and packaging material
g) storage of finished sterile product and management of shelf life
h) handling process of non-sterile device for re-sterilization
i) lot / batch release of terminally sterilized devices

Purchasing, depending on the purchased product or service:

a) Determination of criteria the supplier must meet to be selected, with regards to the control of the sterility of the device
b) Selection and monitoring of suppliers considering the identified criteria
c) Purchasing information
d) Verification of the purchased product/service (and associated documentation)

Therefore, the audit of the control of the sterility of a medical device requires a holistic approach.

Competencies:
It is up to the Auditing Organization to determine the competencies required to achieve the audit objectives and to assign a competent audit team. However, the AO should identify auditors and/or technical experts having the competencies identified below. The subsequent table identifies the competencies required to audit various aspects of sterilization.

Annex 2 - Audit of Requirements for Sterile Medical Devices

The auditing of activities and processes contributing to the sterility of a medical device may involve the following competencies:

Microbiology:

a) Ability to assess the validation of sterilization processes and methods regardless of the availability of an established standard (or the lack of such a standard)
b) Ability to assess the validation of environmental and microbial contamination controls
c) Ability to assess the validation of packaging activities and sterile barrier systems
d) A person deemed to have this competency would likely be educated as a medical microbiologist.

Packaging and Sterile Barrier Systems:

a) Ability to assess the validation of activities and processes for packaging and sterile barrier systems.

Environmental and Contamination Control:

a) Ability to evaluate the adequacy of environmental and microbial contamination control programs.

Routine Sterilization:

a) Ability to assess the validation of sterilization processes and methods where an existing established standard on the method exists other than aseptic processes
b) Ability to verify the implementation of non-standard sterilization activities and processes previously audited by someone having the microbiology competency
c) Ability to assess the implementation of activities and processes for packaging and sterile barrier systems previously audited by someone having the packaging and sterile barrier systems or microbiology competency
d) Ability to assess the implementation of environmental and microbial control activities previously assessed by someone having the microbiology or environmental and contamination control competency.

An auditor may possess several of these competencies.

Annex 2 - Audit of Requirements for Sterile Medical Devices

The following table summarizes the competencies required to audit the requirements for sterile medical devices:

Topic being evaluated	Microbiology	Packaging and Sterile Barrier Systems	Environmental and contamination control	Routine Sterilization
Sterilization process (re-) validation according to well-established standards (excluding aseptic processes)	✓			✓
Sterilization process (re-) validation according to less common standards, or using less common sterilant, sterilization technologies, validation methods (including aseptic processes)	✓			
Packaging process validation and sterile barrier systems	✓	✓		
Environmental and microbial contamination controls	✓		✓	
Routine implementation of sterilization processes according to previously audited validated processes	✓			✓
Routine implementation of environmental controls and monitoring (including maintenance)	✓		✓	✓
Routine implementation of packaging activities according to previously validated processes	✓	✓		✓

Annex 2 - Audit of Requirements for Sterile Medical Devices

Audit of the Requirements for Sterility and Audit Cycle Considerations:

All ISO 13485 and regulatory requirements for sterile medical devices must be audited at least once during the certification cycle. While Auditing Organizations have flexibility in deciding when these requirements are audited during the certification cycle, they should ensure that the requirements for sterility of a device have been audited before including this device in the scope of certification.

All sterilization methods used by a medical device organization should be covered throughout the certification cycle.

Objectives for the audit of requirements for sterile medical devices should include, but not be limited to, verification that:

- all processes that contribute to a device's sterility are controlled through the medical device organization's QMS and validation has been completed, where applicable (e.g. cleaning, disinfection, aseptic processing, sterile barrier systems, terminal sterilization, storage)
- criteria for re-validation are defined and are followed, (e.g. at defined periodicity, following significant changes and trends)
- processes are implemented and monitored to ensure compliance to their validated parameters
- routine environmental and product cleanliness controls are implemented and monitored
- results are consistent from batch to batch
- batch records(e.g. a device history file) are maintained for each sterilization batch per an approved device master record
- lot release is performed for each batch according to a procedure and by a designated person
- adequate control of suppliers is observed where sterilization is outsourced (process for selection of critical suppliers defined and followed, valid agreements, supplier audits, etc.)

In the absence of significant changes with potential impact on the validated status or new (re)validation activities since the previous audit, the audit should be focused on records review to determine that the validated processes are followed, monitoring is performed, batch records are maintained.

While some aspects may be audited remotely (e.g. review of sterilization process validation documentation), the audit of requirements for sterile medical devices must be conducted on-site.

The outcome of such remote review activities must serve as input to the on-site audit and be incorporated or attached to the MDSAP audit report. The off-site assessment of the controls of the product sterility should not prevent the on-site audit team from following audit trails, including audit trails necessitating the review of documents that had previously been assessed remotely.

The audit of processes for validation of sterilization and sterile barrier systems performed according to well-established standards (e.g. steam sterilization, 25 kGy gamma irradiation, Ethylene Oxide in chambers with

traditional release) can be performed by someone having either the microbiology competency or the routine sterilization competency.

The audit of a validation performed according to less common standards, or using less common sterilant / sterilization technologies / validation methods (e.g. Ethylene oxide sterilization in a bag, ethylene oxide in chambers with parametric release, plasma sterilization, low dose gamma sterilization) should be performed by a person having the microbiology competency. This also applies to the evaluation of aseptic process validation or to the sterilization process validation of the microbiologic safety of devices incorporating substances, cells, tissues of animal or human origin.

Routine implementation of sterilization processes according to previously audited validation studies may be conducted by a person having the routine sterilization competency. This applies to all previously validated and audited sterilization processes including processes conducted according to less common standards, or using less common sterilant/sterilization technologies/validation methods.

If the requirements for sterile medical devices are audited separately by a competent auditor or technical expert, this shall cover all the applicable requirements and the results of this audit shall be part of the MDSAP audit report. This must not prevent the MDSAP audit team from following leads relative to requirements for sterile medical devices. Any nonconformities resulting from the audit of sterile medical devices and sterilization processes shall be graded in accordance with MDSAP policies regarding grading of nonconformities.

Annex 3 - Medical Device Adverse Events and Advisory Notices Reporting Process Quick Reference

The following table is intended to be a quick reference guide for timeframes for submitting reports for individual adverse events and advisory notices. This table is not a substitute for knowledge and understanding regarding criteria required to be reported in the participating MDSAP jurisdictions, or a substitute for the information contained in MDSAP Audit Approach **Chapter 4 - Process: Medical Device Adverse Events and Advisory Notices Reporting**.

Jurisdiction	Individual Adverse Events	Advisory Notices
Australia	Manufacturer to report to the Sponsor or the TGA, as soon as practicable, if an event might have led to death or serious deterioration in health Sponsor must report within 48 hours if an event represents a public health threat Sponsor must report within 10 days if an event led to death or serious deterioration in health Sponsor must report within 30 days if an event might lead to death or serious deterioration in health if it were to recur	Manufacturer to report to the Sponsor or the TGA, as soon as practicable, any technical or medical reason for a malfunction or deterioration that has led to recall
Brazil	Must report within 72 hours in case of death, public health threat or counterfeiting Must report within 10 days in case of serious adverse events not involving death and non-serious adverse events, the re-occurrence of which has the potential to	5 calendar days from the decision to start the field action

Annex 3 - Medical Device Adverse Events and Advisory Notices Reporting Process Quick Reference

Jurisdiction	Individual Adverse Events	Advisory Notices
	cause a serious adverse event to a patient, user, or other person Must report within 30 days in case of malfunction that could lead to a serious adverse event Must report within 10 days in case of death, public health threat or counterfeiting occurred in other countries and associated with health products registered in its name in Brazil	
Canada	For events that occur in Canada: 10 days if the event led to the death or serious deterioration in health 30 days if the event might lead to death or serious deterioration if the event were to recur. For occurences that are captured under the Foreign Risk Notification requirements (61.2-61.3): 72 hours after receiving or becoming aware of a notifiable action	On or before undertaking the recall
Japan	Registered Manufacturing Sites must report any adverse event which meets the criteria specified by **the Ordinance for**	As soon as possible after the action

Annex 3 - Medical Device Adverse Events and Advisory Notices Reporting Process Quick Reference

Jurisdiction	Individual Adverse Events	Advisory Notices
	Enforcement of PMD Act Article 228-20 to the Marketing Authorization Holder as soon as possible. MAHs must report any adverse event which meets the criteria specified by **the Ordinance for Enforcement of PMD Act Article 228-20** to the RA within the timeframe specified by the ordinance.	
United States	5 calendar days if FDA has issued a 5-day notice 30 calendar days reports of death or serious injury. Quarterly summary reporting is allowable for malfunction reports for most product codes.	10 working days of initiating the correction or removal

Annex 4 – Requirements for Written Agreements

There are a number of occasions when the interface between an organization (e.g. a manufacturer represented on the label of a product and responsible for the design, production, packaging, labelling and post-production monitoring activities), and a supplier (an external organization outside of the scope of the organization's QMS), needs to be defined in a written agreement. For example, from ISO 13485:2016;

Clause 3.2 – an authorized representative is a natural or legal person established within a country or jurisdiction who has received a written mandate from the manufacturer to act on their behalf for specified tasks with regard to the latter's obligations under that country or jurisdiction's legislation.

Clause 3.10 – Note 1 to entry: a manufacturer is responsible for ensuring compliance with all applicable regulatory requirements unless this responsibility is specifically imposed on another person by the regulatory authority within that jurisdiction. In many cases written agreements are necessary to establish the arrangements between a manufacturer and authorized representative to ensure the representative can fulfill their legal obligations.

Clause 4.1.5 - requires manufacturers to retain responsibility for conformity to applicable regulatory requirements for outsourced processes. The controls for these processes shall include written quality agreements and be proportionate to the ability of the external party to the meet the requirements identified in Clause 7.4.

Clause 4.2.5 – requires manufacturers to define and implement methods for protecting confidential health information contained in records and for the retention and submission of any record in accordance with regulatory requirements. Arrangements defined in agreements with an Authorized Representative can ensure the confidentiality of information passed to a manufacturer via the representative in the receiving and recording of information for complaint handling and the retention of records held by the Authorized Representative.

Clause 5.2, 5.4.1, 5.5.2, 5.6.2, 7.2.1, 7.3.3, 7.3.7, 7.3.9 – written agreements with Authorized Representatives can be a useful tool for ensuring that a manufacturer and its top management are informed of current regulatory requirements and changes in the jurisdictions to which product is supplied. This information may provide input to some of, and not limited to, the following areas; quality objectives, management review inputs, definition of customer requirements, and design and development controls.

Clause 7.2.3 – requires a manufacturer to communicate with regulatory authorities in accordance with regulatory requirements. In some jurisdictions, the communication channel is through the authorized representative.

Clause 7.4.1, 7.4.2 - requires the manufacturer to address the nonfulfillment of controls for outsourced processes, with the supplier, and in compliance with regulatory requirements. In some jurisdictions, the

authorized representative is to fulfil relevant regulatory requirements with the cooperation of the manufacturer.

Clause 7.5.9.1 - may require an authorized representative to play a part in ensuring the traceability of a product to the extent required by the manufacturer.

Clause 8.2.1 – regulatory requirements may require a manufacturer to incorporate post-production information provided by an authorized representative to be included in a feedback process.

Clause 8.2.2 – a written agreement with an Authorized Representative may be necessary to ensure the timely receiving and recording of information for complaint handling.

Clause 8.2.3 - requires documented procedures for notification to regulatory authorities when complaints meet specified reporting criteria for adverse events or issuance of advisory notices. In some jurisdictions, an in-country authorized representative performs the notification of these events. A written agreement between the manufacturer and the representative is necessary to establish a clear communication channel between the manufacturer and the regulator and to ensure the maintenance of records of reporting.

Clause 8.3.3 - requires procedures for issuing advisory notices in accordance with applicable regulatory requirements. In some jurisdictions, an in-country representative is required to coordinate the approval and issuing of advisory notices with the local regulatory authority, maintain distribution records that would facilitate recall in that jurisdiction and, if necessary, to coordinate a recall under the supervision of the local regulatory authority. A written agreement between the manufacturer and the representative is necessary to ensure that the local representative can fulfil their legal responsibilities and that the responsibilities are clear in the event of a recall.

Additional country-specific requirements

Australia (TGA)

Prior to being granted market authorization, Australian Sponsors (in-country authorized representative) are required to "certify matters" related to the device and its supply, including a commitment to enter into written agreements with an overseas Manufacturer for matters that are specified in Regulations [TG Act - 41FD (e) and (g)]. (Australian "legal" Manufacturers who are responsible for design, production and labelling, whether performed by their organization or on their behalf by another organization, are also, by definition, an Australian Sponsor).

Subsequent conditions for the market authorization include a requirement that the Sponsor continue to supply information related to quality, safety and performance of the device through procedures and a written agreement established with the overseas Manufacturer. This will include information that is only available from

the overseas Manufacturer of the device who is accepting responsibility for the design, production, packaging and labelling etc. of the device (TG Act - s41BG).

Australian conformity assessment procedures also require overseas Manufacturers of medical devices supplied in Australia to make undertakings, to provide records (information, documents and records specified in the Conformity Assessment Procedures) and to notify the TGA or the Sponsor of specified events. These requirements of the Conformity Assessment Procedures, and conditions for marketing authorization, place a legal obligation on the Sponsor to participate in processes that are usually and wholly addressed by the manufacturer's quality management system. For example, some aspects of the ISO13485 requirements for advisory notices (e.g. recalls) are the responsibility of the Sponsor. Hence, the manufacturer must outsource these requirements to the Sponsor, and in doing so renders the Sponsor a supplier.

By entering into written agreements, the Sponsor and Manufacturer demonstrate their commitment to fulfil their obligations and clarify their roles and legal responsibilities within the Australian Regulatory framework for medical devices.

Manufacturers and Sponsors are to identify the regulatory requirements that are relevant to their responsibilities under the legislation (e.g. ISO 13485:2016 Cl 4.1.1). The following table provides some guidance and identifies many of the key requirements that could be identified in a written agreement between an overseas Manufacturer and the Australian Sponsor. The parties to an agreement should incorporate, as appropriate, the arrangements to fulfill these, or any other identified regulatory requirements, and may include any necessary commercial arrangements.

This table is a summary of requirements, intended to raise awareness of the roles and responsibilities that may need clarification in a written agreement. This is guidance and does not substitute for reference to ISO13485:2016 or the relevant legislation. Sponsors and Manufacturers should refer to the *Therapeutic Goods Act, 1989* (*the Act*) and the Therapeutic Goods (Medical Devices) Regulations, 2002 (Regulations) to determine all applicable requirements.

Note that some requirements and conditions apply automatically by the Act and Regulations. The TGA may apply specified additional conditions on the manufacture and supply of a medical device at the time of market authorization, or later. Agreements may need amendment to account for any condition that may subsequently affect the relationship between the Sponsor and Manufacturer.

References to sections of *the Act,* are prefaced with "s" [e.g. s41FD]. References to a regulation of the Regulations are prefaced with "r" [e.g. r5.8]. References to Section, Part or a clause in a Schedule of the Regulations, are prefaced with "S", "P" and "Cl" e.g. [S3 Cl1.8].

Annex 4 – Requirements for Written Agreements

Australian requirements that may require identification in a Written Agreement

Requirement	Ref(s)	Australian Sponsor Role	Manufacturer Role
Application for market authorization	s41FC, s41FD, s41FH, s41FI r5.2	Certify the matters listed in TG Act s41FD including a procedure and written agreement with an overseas manufacturer to provide information from the overseas manufacturer about compliance with the Essential Principles and application of an appropriate Conformity Assessment Procedure, to the TGA, within 20 days of a request.	Provide information to the Sponsor that would allow the Sponsor to certify the matters identified in TG Act s41FD Provide information requested by the TGA in a notice to the Sponsor if the application is selected for an Application Audit. (See also Reg 5.3) If requested by the TGA, assist the Sponsor to provide a reasonable number of samples within the timeframe specified in the notice.
Conditions for market authorization	s41FN, s41FO, s41JA, s41MP2, s41MPA2 s42B s42BAA s42DD s42DJ s42DL(9) r5.6 r5.7, r5.8, r5.9 r5.10 r5.11, r8.1A r8.1	Make arrangements that will permit an authorized person of the TGA to enter premises outside of Australia where a person deals with medical devices that have market authorization, for purposes of inspection, examination, measurement, testing, sampling, image recording etc. and obtaining documentary evidence. (Including the manufacturer's facilities or those of a supplier to the manufacturer) Maintain procedures and agreements to ensure that information from the overseas manufacturer to substantiate compliance with the Essential Principles and application of an appropriate Conformity Assessment Procedure, or relevant changes to previously supplied information, can be	Assist the Sponsor with arrangements to permit the TGA to enter the Manufacturer's premises, or those of a supplier, for inspection activities. If requested by the TGA, assist the Sponsor to provide a reasonable number of samples within the timeframe specified in the notice. Ensure advertising material available for Australia is consistent with the intended purpose of the medical device and the Sponsor's obligation to comply with Australian advertising requirements. Ensure continued provision of information within a timeframe that will permit a Sponsor to meet its regulatory obligations. Ensure problem or complaint information, provided by the

		supplied to the TGA, within 20 days of a request. Provide information to the TGA and the manufacturer that the sponsor is aware of in relation to a device about any malfunction or deterioration, inadequacy, or use, that might lead or might have led, to the death of a patient or a user of the device, or to a serious deterioration in his or her state of health (adverse events or near adverse events) within prescribed timeframes (r5.7); Provide information to the TGA (within prescribed timeframes - r5.7) and the manufacturer that the sponsor is aware of in relation to a device that relates to a technical or medical reason for a malfunction or deterioration that may require an advisory notice or recall of a device that has been distributed;. Comply with the requirement to notify the TGA of information that indicates that a certification document issued to signify: compliance with the essential principles; or the application of relevant conformity assessment procedures has been restricted, suspended, revoked or is no longer in effect. Provide information to the TGA and the manufacturer that the sponsor is aware of in relation	Sponsor, is input for the manufacturer's feedback process. Assist the Sponsor to comply with conditions for records, manufacture, the essential principles etc. that may be imposed at the time of, or after, market authorization Provide the Sponsor with information related to their obligation to notify the TGA about adverse events, recalls/advisory notices, noncompliance with the essential principles or the validity of a certification document related to compliance with the Essential Principles or the application of conformity assessment procedures; including quality management system requirements. Ensure that the Sponsor is aware of the manufacturer's requirements for storage and transport of the device Assist the Sponsor with the provision of data for a report to the TGA as described in Reg 5.11; for Class AIMD, Class III, Class IIb medical devices that are implantable, or a Class 4 IVD. Assist the Sponsor with the provision of data for IVDs described in Reg 5.3(1)(j), for a report described in Reg 5.12. Inform the Sponsor of any poisons that may be present in the device as described in Reg 5.13

		to a device, that a device does not comply with the Essential Principles Provide the Manufacturer of a medical device, information relevant to: the manufacturer's obligations under the conformity assessment procedures; and whether the manufacturer's medical devices comply with the essential principles. Ensure that devices comply with the applicable provisions of the Therapeutic Goods Advertising Code, and other relevant requirements (if any) in legislation and that the advertising material is consistent with the manufacturer's intended purpose. Ensure that an advertisement does not contain a statement, pictorial representation or design suggesting or implying the goods have been recommended or approved by or on behalf of a government or government authority (including a foreign government or foreign government authority), other than in those circumstances described in legislation. Provide information to the manufacturer about events that has led to any complaint or problem in relation to the	Inform the Sponsor of information that indicates that a certificate or other document (other than a TGA issued conformity assessment certificate or other document issued by the TGA) that the Sponsor used to certify matters under s41FD to signify: (i) compliance with the essential principles; or (ii) the application of relevant conformity assessment procedures to a device; has been restricted, suspended, revoked or is no longer in effect. Ensure that manufacturing records are retained, and are available, for a period that is at least the lifetime of the device or for the minimum period defined in Australian conformity assessment procedures; 5 years. Ensure that the responsibility to retain, maintain and make available distribution records, and other records identified in r5.10, is in accordance with r5.10 and 8.1A, using arrangements that have been agreed and verified.

		manufacturer's device, no matter how minor; Comply with the manufacturer's requirements for storage and transport of the device Create and maintain contemporaneous records of complaints, adverse events, recalls and product distribution and retain the records for the periods prescribed in Regulations (r5.10) Comply with additional conditions for records, manufacture, the essential principles, etc., specifically imposed by the TGA at the time of, or subsequent to, market authorization. For a Class AIMD medical device, a Class III medical device, a Class IIb medical device that is an implantable medical device, or a Class 4 IVD medical device, provide a report to the TGA as described in Reg 5.11. For IVDs described in Reg 5.3(1)(j), provide a report as described in Reg 5.12 Ensure that a device is not supplied in Australia if the supply would contravene Part 2 of the current Poisons Standard. Ensure that manufacturing records and distribution records	

		are available for the periods defined in Reg 8.1.	
Public notification and recall of medical devices.	41KB	Follow the guidance in the Uniform Recall Procedure for Therapeutic Goods (URPRG) to take the specified steps, in the specified manner and within such reasonable period as is specified, to recall medical devices of that kind that have been distributed, to publish specified information to inform the public and to notify the TGA of information relating to the persons to whom medical devices have been supplied.	Assist the Australian Sponsor to; meet the requirements outlined in the Uniform Recall Procedure for Therapeutic Goods (URPTG) for the recall of devices, effect a notification to the public of recalls and to inform the TGA of information relating to the persons to whom medical devices have been supplied.
Application of the conformity assessment procedures and requests for information	s41DA, s41JA rP3 Div 3.2, S3P1 Cl1.9, S3P4 Cl4.8, S3P5 Cl5.8	Assist the manufacturer of the device to determine the Class of the device in accordance with the Australian classification rules. Facilitate the provision of the manufacturer's records including, but not limited to; records to demonstrate compliance with the essential principles, conformity assessment procedures and any conditions imposed at the time of, or subsequent to, the granting of marketing authorization that is related to the manufacturer's activities, compliance with advertising requirements, the safety and efficacy of the devices for their intended purpose, the regulatory history of the devices in another country, etc. when such records are requested by the TGA.	Comply with the relevant conformity assessment procedures that are "obligations on the manufacturer". Classify a device. Apply an appropriate CA procedure to: implement a QMS appropriate for the class of the device. Demonstrate compliance with the relevant Essential Principles for use in the Australian market. Allow an authorized officer of the TGA to enter the premises of the manufacturer and whilst on those premises to inspect the premises and medical devices of any kind in accordance with the requirements of the legislation. On request, provide documentation to an authorized person relating to devices of a

		Ensure arrangements are in place to allow the TGA to monitor the operation of, and carry out inspections of, the manufacturer's quality management system. Obtain a Declaration of Conformity from the Manufacturer Where the TGA has performed a Design Examination, ensure that changes to the design are notified to the TGA Ensure that the manufacturer informs the Sponsor of adverse events and recalls that are to be reported to the TGA	kind covered by the TGA issued CA certificate, or to the manufacturer's QMS. Allow the authorized person to copy the documents. Make a Declaration of Conformity and provide to the Australian Sponsor for marketing authorization applications Make the records identified in the conformity assessment procedure applied by the manufacturer, available to TGA either directly or through the Australian Sponsor. Ensure that manufacturing records are retained, and are available, for a period that is at least the lifetime of the device or for the minimum period defined in Australian conformity assessment procedures; 5 years. Inform the relevant Auditing Organization (certification body) of changes to the design or QMS Undertake to inform the Sponsor or the TGA of adverse events or steps taken to recover / recall devices from the market. Ensure reporting to the relevant certification body of a substantial change to the system; or change to the kinds of medical devices to which the system is to be applied.
Conditions on Conformity Assessment	s41EJ	Assist the manufacturer of the device in accordance with the Australian classification rules.	In addition to the roles above for "Application of the conformity assessment procedures "

Certificates issued by the TGA. (If a manufacturer chooses to participate in the MDSAP and is supplying product to Australia, the AO must include the requirements of the Australian jurisdiction within the scope of the audit. If the manufacturer is also required to hold a TGA issued CA Certificate, the conditions of that certificate must also be applied.)		Facilitate the provision of the manufacturer's records requested by the TGA. Ensure arrangements are in place to allow the TGA to monitor the operation of, and carry out inspections of, the manufacturer's quality management system. Obtain a Declaration of Conformity from the Manufacturer. Where the TGA has performed a Design Examination ensure that changes to the design are notified to the TGA Ensure that the manufacturer informs the Sponsor of adverse events and recalls that are to be reported to the TGA	Cooperate with the TGA in a review of whether the requirements of an appropriate CA procedure have been applied including; the application of a QMS and compliance with the essential principles in accordance with the requirements of the legislation. Notify the TGA and the Auditing Organization of any substantial changes to the quality management system, the product range covered by the QMS or changes to the design of products covered by the certificate. Comply with any additional and relevant condition applied to a conformity assessment certificate when issued or subsequently amended.

Clarification on the use of MDSAP in Australia

The TGA formally recognizes MDSAP certificates as a "conformity assessment document" if issued in accordance with MDSAP AU P0026 and references the regulatory requirements of the Australian jurisdiction. The TGA uses these documents as evidence of compliance with the QMS requirements of the Australian conformity assessment procedures. MDSAP certificates are often used when alternative EC Certification is not available.

Note that regardless of any pathway that may have been used, or is used, for marketing authorization in Australia, an MDSAP Auditing Organization must include the requirements of the Australian jurisdiction within the scope of the MDSAP audit if the manufacturer is supplying product to the Australian market

See the document "Use of market authorization evidence from comparable overseas regulators / assessment bodies for medical devices (including IVDs)")

Part 4A of the Therapeutic Goods Act 1989 makes provision for an Australian incorporated organization to be recognized as an Australian Conformity Assessment Bodies Body (CAB) if they satisfy assessment criteria that is

based on the EU's MDR or IVDR Annex VII requirements. The legislation also makes provisions to recognize the product assessments and quality management system regulatory audits performed by Australian CABs.

Australian legislation separately recognizes MDSAP Audit Reports and Certificates as evidence from a comparable overseas regulator. See **Comparable overseas regulators for medical device applications | Therapeutic Goods Administration (TGA)** [s41FDA(c) and **related instruments**].

The assessment processes used to recognize an MDSAP Auditing Organization may be used to support an organization's application to be an Australian Conformity Assessment Body if the applicant is an Australian Corporation.

Brazil – ANVISA

There are no additional expectations for the audit of written agreements during an MDSAP audit.

Canada - Health Canada

There are no additional expectations for the audit of written agreements during an MDSAP audit.

Japan – MHLW/PMDA

There are no additional expectations for the audit of written agreements during an MDSAP audit.

USA – FDA

There are no additional expectations for the audit of written agreements during an MDSAP audit.

Annex 5 – Japan's QMS Ordinance Revision - Tables

The following tables show the correspondence between MHLW MO 169 Chapter 2, as amended in 2020 (aligned with ISO 13485:2003) and amended in 2021 (aligned with ISO 13485:2016). Please see **footnote 3** in the Management process for information as to the MDSAP audit to the 2020 and 2021 versions.

Correspondence between ISO13485:2003 and MHLW MO 169 Chapter 2, as amended in 2020

ISO 13485:2003	**MHLW MO 169, Chapter 2**	**Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020**
Clause 1.2 Application	Section 1 General Rules	
Clause 1.2, paragraph 2 and 3	Article 4	Article 4 specifies the way of application of this chapter to the organization. Article 4.1 specifies that Class 1 medical devices are exempted from the requirements of design and development, Article 30 to Article 36. Article 4.2 and 4.3 specifies the rule of exclusion and non-application of the requirements. These articles are identical to the description of ISO 13485:2003 clause 1.2, paragraph 3.
Clause 4 Quality management system	Section 2 Quality Management System	
Clause 4.1	Article 5	
Clause 4.2.1	Article 6	
Clause 4.2.2	Article 7	
Clause 4.2.3	Article 8	The retention period of obsolete documents required by the ordinance is specified by Article 67 of MHLW MO 169.

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
Clause 4.2.4	Article 9	The record retention period required by the ordinance is specified by Article 68 of MHLW MO 169.
Clause 5 Management responsibility	Section 3 Management responsibility	
Clause 5.1	Article 10	
Clause 5.2	Article 11	
Clause 5.3	Article 12	
Clause 5.4.1	Article 13	
Clause 5.4.2	Article 14	
Clause 5.5.1	Article 15	
Clause 5.5.2	Article 16	
Clause 5.5.3	Article 17	
Clause 5.6.1	Article 18	
Clause 5.6.2	Article 19	
Clause 5.6.3	Article 20	
Clause 6 Resource Management	Section 4 Resource Management	
Clause 6.1	Article 21	
Clause 6.2.1	Article 22	
Clause 6.2.2	Article 23	
Clause 6.3	Article 24	
Clause 6.4	Article 25	

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
Clause 7 Product realization	Section 5 Product realization	
Clause 7.1	Article 26	
Clause 7.2.1	Article 27	
Clause 7.2.2	Article 28	
Clause 7.2.3	Article 29	
Clause 7.3.1	Article 30	
Clause 7.3.2	Article 31	
Clause 7.3.3	Article 32	
Clause 7.3.4	Article 33	
Clause 7.3.5	Article 34	
Clause 7.3.6	Article 35	Clinical evaluations and/or evaluation of results of usage of the medical device are required to be implemented as part of design and development validation, in the case that the medical device is designated by 23-2-5.3 or 23-2-9.4 of PMD Act.
Clause 7.3.7	Article 36	
Clause 7.4.1	Article 37	
Clause 7.4.2	Article 38	
Clause 7.4.3	Article 39	
Clause 7.5.1.1	Article 40	

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
Clause 7.5.1.2.1	Article 41	
Clause 7.5.1.2.2	Article 42	The requirements of Article 42 are only applied to "installation controlled medical devices", which are specified in Article 114-55.1 of Regulation for Enforcement of PMD Act. The installation controlled medical devices are the devices that need assembling for installation and need control for the assembling to prevent occurrence of public health hazard.
Clause 7.5.1.2.3	Article 43	
Clause 7.5.1.3	Article 44	
Clause 7.5.2.1	Article 45	
Clause 7.5.2.2	Article 46	
Clause 7.5.3.1	Article 47	
Clause 7.5.3.2.1	Article 48	
Clause 7.5.3.2.2	Article 49	The requirements of Article 49 are only applied to "designated medical devices" which are specified by the Article 68-5 of PMD Act. The devices are designated by the Minister of Health, Labour and Welfare as those whose location must be known in order to prevent the occurrence or spread of hazards in health and hygiene, such as medical devices which are used by implantation in the human body or other medical devices which might be used outside facilities providing medical treatment. The designated medical devices are included in the active implantable medical devices and

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
		implantable medical devices which are required to be complied with the requirement in Clause 7.5.3.2.2 of ISO 13485:2003. The organization can be considered to comply with the requirement of Article 49 of the ordinance, when they comply with the requirement of Clause 7.5.3.2.2 of ISO 13485:2003. The requirements to maintain records of distribution specified in Clause 7.5.3.2.2 of ISO 13485:2003 are not applied to the organization, when the organization is the person operating the registered manufacturing site.
Clause 7.5.3.3	Article 50	
Clause 7.5.4	Article 51	
Clause 7.5.5	Article 52	
Clause 7.6	Article 53	
Clause 8 Measurement, analysis and improvement	Section 6 Measurement, analysis and improvement	
Clause 8.1	Article 54	
Clause 8.2.1	Article 55	
Clause 8.2.2	Article 56	
Clause 8.2.3	Article 57	

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
Clause 8.2.4.1	Article 58	
Clause 8.2.4.2	Article 59	The requirements of Article 59 are only applied to the designated medical devices (see the note for Article 49 above). The designated medical devices are included in the "active implantable medical devices and implantable medical devices" which are required to comply with the requirement in Clause 8.2.4.2 of ISO 13485:2003. The organization can be considered to comply with the requirement of Article 59 of the ordinance, when they comply with the requirement of Clause 8.2.4.2 of ISO 13485:2003.
Clause 8.3	Article 60	
Clause 8.4	Article 61	
Clause 8.5.1	Article 62	Article 62.6 specifies the requirements of establishment of procedures to notify adverse events for the Marketing Authorization Holder and the person operating the registered manufacturing site. The Marketing Authorization Holder shall establish documented procedures to report adverse events which meet reporting criteria specified by the Article 228-20.2 of Regulation for Enforcement of PMD Act to the Minister of Health, Labour and Welfare. When the organization is the person operating the registered manufacturing site, the organization shall establish documented

Annex 5 – Japan's QMS Ordinance Revision - Tables

ISO 13485:2003	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2020
		procedure to notify the information to the Marketing Authorization Holder.
Clause 8.5.2	Article 63	
Clause 8.5.3	Article 64	

Correspondence between ISO13485:2016 and MHLW MO 169 Chapter 2, as amended in 2021

ISO 13485:2016	MHLW MO 169, Chapter 2	Note for understanding the requirements of MHLW MO 169 Chapter 2, as amended in 2021
Clause 1 Scope	Section 1 General Rules	
Clause 1, paragraph 4-5	Article 4	Article 4.1 specifies that Class 1 medical devices are exempted from the requirements of design and development, Article 30 to Article 36-2. Article 4.2 and 4.3 specifies the rule of exclusion and non-application of the requirements. These articles are identical to the description of ISO 13485:2016 clause 1, paragraph 4 and 5.
Clause 4 Quality management system	Section 2 Quality management system	
Clause 4.1.1	Article 5-1	Roles undertaken by the organization are Marketing Authorization Holder provided by Article 23-2.1 of PMD Act, Registered Manufacturing Site provided by Article 23-2-3.1 and 23-2-4.1 of PMD Act, Seller of pharmaceutical products provided by Article 24.1 of PMD Act, Seller and Leaser of specially-controlled medical devices provided by Article 39.1 of PMD Act,

		Repairer of medical devices provided by Article 40-2.1 of PMD Act, or Seller and Leaser of controlled medical devices provided by Article 39-3.1 of PMD Act.
Clause 4.1.2	Article 5-2	
Clause 4.1.3	Article 5-3	
Clause 4.1.4	Article 5-4	
Clause 4.1.5	Article 5-5	
Clause 4.1.6	Article 5-6	
Clause 4.2.1	Article 6	
Clause 4.2.2	Article 7-1	
Clause 4.2.3	Article 7-2	
Clause 4.2.4	Article 8	The retention period of obsolete documents required by the ordinance is specified by Article 67 of MHLW MO 169.
Clause 4.2.5	Article 9	The record retention period required by the ordinance is specified by Article 68 of MHLW MO 169.
Clause 5 Management responsibility	Section 3 Management responsibility	
Clause 5.1	Article 10	
Clause 5.2	Article 11	
Clause 5.3	Article 12	
Clause 5.4.1	Article 13	
Clause 5.4.2	Article 14	
Clause 5.5.1	Article 15	
Clause 5.5.2	Article 16	

Clause 5.5.3	Article 17	
Clause 5.6.1	Article 18	
Clause 5.6.2	Article 19	The organization is not required to input "reporting to regulatory authorities", the item specified in ISO 13485:2016 5.6.2 c), to management review, when the organization is the person operating the registered manufacturing site.
Clause 5.6.3	Article 20	
Clause 6 Resource Management	Section 4 Resource Management	
Clause 6.1	Article 21	
Clause 6.2, paragraph 1 and 2	Article 22	
Clause 6.2, paragraph 3	Article 23	
Clause 6.3	Article 24	
Clause 6.4.1	Article 25-1	
Clause 6.4.2	Article 25-2	
Clause 7 Product realization	Section 5 Product realization	
Clause 7.1	Article 26	
Clause 7.2.1	Article 27	
Clause 7.2.2	Article 28	
Clause 7.2.3	Article 29	
Clause 7.3.1 and 7.3.2	Article 30	

Clause 7.3.3	Article 31	
Clause 7.3.4	Article 32	
Clause 7.3.5	Article 33	
Clause 7.3.6	Article 34	
Clause 7.3.7	Article 35-1	Clinical evaluations and/or evaluation of performance of the medical devices are required to be implemented as part of design and development validation, in the case that the medical device is designated by 23-2-5.3 or 23-2-9.4 of PMD Act.
Clause 7.3.8	Article 35-2	
Clause 7.3.9	Article 36-1	
Clause 7.3.10	Article 36-2	
Clause 7.4.1	Article 37	
Clause 7.4.2	Article 38	
Clause 7.4.3	Article 39	
Clause 7.5.1	Article 40	
Clause 7.5.2	Article 41	
Clause 7.5.3	Article 42	
Clause 7.5.4	Article 43	
Clause 7.5.5	Article 44	
Clause 7.5.6	Article 45	
Clause 7.5.7	Article 46	
Clause 7.5.8	Article 47	
Clause 7.5.9.1	Article 48	
Clause 7.5.9.2	Article 49	The requirements of Article 49.2 and Article 49.3, which are identical to the requirements of ISO 13485:2016

		7.5.9.2 paragraph 2 and 3, are not applied, when the organization is the person operating the registered manufacturing site.
Clause 7.5.10	Article 51	
Clause 7.5.11	Article 52	
Clause 7.6	Article 53	
Clause 8 Measurement, analysis and improvement	Section 6 Measurement, analysis and improvement	
Clause 8.1	Article 54	
Clause 8.2.1	Article 55-1	
Clause 8.2.2	Article 55-2	This article is identical to the requirement of ISO 13485:2016 8.2.2. However, it should be noted that the organization is required to determine the need to notify the information to the Marketing Authorization Holder instead of the regulatory authorities, when the organization is the person operating the registered manufacturing site.
Clause 8.2.3	Article 55-3	This article is identical to the requirement of ISO 13485:2016 8.2.3. However, it should be noted that the organization is required to notify the information to the Marketing Authorization Holder instead of the regulatory authorities, when the organization is the person operating the registered manufacturing site. Record of the notification shall also be maintained.
Clause 8.2.4	Article 56	
Clause 8.2.5	Article 57	
Clause 8.2.6, paragraph 1-3	Article 58	

Clause 8.2.6, paragraph 4	Article 59	
Clause 8.3.1	Article 60-1	
Clause 8.3.2	Article 60-2	
Clause 8.3.3	Article 60-3	
Clause 8.3.4	Article 60-4	
Clause 8.4	Article 61	
Clause 8.5.1	Article 62	
Clause 8.5.2	Article 63	
Clause 8.5.3	Article 64	

Annex 6 – Acceptable exclusions from an organization's scope of certification

GHTF document N3 clause 8.2.2 requires that "the Auditing Organization shall not exclude any processes, products, or services from the audit scope or the scope of the certificate, unless the regulations administered by the recognizing Regulatory Authority(s) permit the exclusion". This requirement is used to justify that an organization participating in MDSAP must be audited for a scope of certification that includes all the jurisdictions where the medical devices are distributed, and all medical devices being distributed in these jurisdicitions. See item 88 in the **Question and Answers document**. The activities/processes, products or facilities that are eligible for exclusion from an MDSAP Program are outlined in the following table. A device may be excluded from the scope of the MDSAP audit only if it meets the corresponding exclusion criteria from all the jurisdicitions applicable to the audit. A jurisdiction may be excluded only if none of the medical devices are distributed in this jurisdiction, or all medical devices distributed in this jurisdiction can be excluded.

Jurisdiction	Consideration	Comments
Australia	Class I medical devices (non- sterile, no measuring function) are not required to have a certified quality management system.	TG(MD)R Schedule 3 Part 6 establishes obligations / requirements for manufacturers of Class I medical devices (non-sterile, no measuring function) that includes process definition, adverse event and recall reporting. By default, a certified QMS is not required by legislation for Class I medical devices (non-sterile, no measuring function). However, a manufacturer may: - voluntarily choose to apply a more onerous conformity assessment procedure (e.g., Schedule 3 Part 1 or Part 4); OR - request an Auditing Organization to include Class I medical devices (non-sterile, no measuring function) within the scope of an MDSAP ISO13458 certification. In these circumstances, the Auditing Organization should treat the requirements of the relevant Conformity Assessment Procedure (Part 1, 4 or 6) as regulatory requirements when establishing audit criteria.

Annex 6 – Acceptable exclusions from an organization's scope of certification

Brazil	Class I and Class II medical devices are not subject to GMP Certification*. * However, ANVISA Resolution RDC 15/2014 still require that the manufacturer of the finished device have an effective QMS in place.	If all devices in the scope of certification are class I or II, or if the audited facility's contribution to the scope of certification only applies to class I or class II medical devices, the audit at that facility may disregard the requirements of the Brazilian regulation for registration purposes.
Canada	Class I medical devices are not required to have a certified quality management system.	If all devices in the scope of certification are class I or if the audited facility's contribution to the scope of certification only applies to class I medical devices, the audit at that facility may disregard the requirements of the Canadian regulation.
Japan	Class I medical devices are not required to have a certified quality management system.	If all devices in the scope of certification are class I or if the audited facility's contribution to the scope of certification only applies to class I medical devices, the audit at that facility may disregard the requirements of the Japanese regulation.
United States	Some Class 1 medical devices are "GMP-exempt", i.e. not subject to the US quality system regulation.	If all devices in the scope of certification are GMP-exempt or if the audited facility's contribution to the scope of certification only applies to GMP-exempt medical devices, the audit at that facility may disregard the requirements of the US Quality System regulation (21 CFR 820), with the exception of the requirements for maintaining complaint files and recordkeeping. Additionally, requirements still apply for compliance to Medical Device Reporting (21 CFR 803), Medical Devices; Reports of Corrections and Removals (21 CFR 806), and Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices (21 CFR 807).

Summary of Changes from Prior Revisions

Changes from version 006 to 007

Overview

- Added reference to MDSAP AU P0037 - Guidelines on the use of GHTF/SG3/N19:2012 for MDSAP purposes on page 10
- Added reference to new Annex 6 on page 13

Chapter 1 to Chapter 7

- Update Australian regulatory clause references following updates to the *Therapeutic Goods Act 1989* and *Therapeutic Goods (Medical Devices) Regulations 2002*.
- Update Brazilian regulatory clause references
- Update Japanese regulatory clauses references

Device Marketing Authorization and Facility Registration

Task 3

- Clarify FDA premarket notification requirements for changes

Measurement, Analysis and Improvement

Task 12

- Update requirements for Health Canada

Task 15

- Update regulation reference for Brazil

Medical Device Adverse Events and Advisory Notices Reporting

Task 1

- Update requirements for Health Canada

Task 2

- Clarify Australian recall reporting requirements.
- Update regulation references for Brazil
- Update requirements for Health Canada

Summary of Changes from Prior Revisions

Production and Service Controls

Task 9

- Amendment to the Australian country specific requirements and legislative links

Annex 1

- Change GHTF SG3 N19 reference to MDSAP AU P0037.
- Amendment to the Australian country specific requirements to include updated regulatory references.

Annex 4

- Update to Australian regulatory references relating to the maintenance of distribution records.
- Update to the Clarification on the use of MDSAP in Australia section to remove requirements related to Regulation 4.1 (which has been repealed) and to reference TGA guidance on use of comparable overseas evidence and related legislative instruments.

Annex 6

- Explains acceptable exclusions of medical devices or regulations from the scope of certification.

Changes from version 005 to 006

Chapter 1 to Chapter 7

- Added clause number(s) of the new MHLW MO169 in the case that the number(s) is/are different from those for the old ordinance.

Management Process

Task 1

- Added footnote to explain the meaning of the word, "Old", in the sections of Clause and Regulation references for Japanese requirements – page 21

Summary of Changes from Prior Revisions

Purchasing

Task 5

- Deleted a task related to a Japanese country specific requirement, as the requirement is deleted in the new ordinace – page 168

Annex 5

- Added new Annex that has tables showing Japan's new and old QMS ordinance and the relationship between ISO 13485 – page 211

Changes from version 004 to 005

Foreword/Use of this document

- Added statement regarding the combination of the MDSAP Audit Approach and Companion Document, formerly separate documents, into this single document – page 5
- Added statement regarding special access programs – page 7

Audit Sequence

- Clarified that order in which processes are to be audited is fixed, however the sequence of audit tasks within a process may be arranged to allow for an efficient audit; clarified that reasonable exceptions are allowed for following the audit sequence – pages 8-9

Conducting the Audit

- Added clarifying language as to the assessment of the medical device organization's application of risk management principles – page 10

Navigating the Audit Sequence

- Clarified use of clause 4.2.1(e) in conjunction with regulatory requirements – page 10

Terminology

- Added language for "medical device organization", "outsourced" process, product or service, "suppliers", "critical suppliers" – throughout the document as appropriate.

Annexes

- Reference to Annex 1 changed – page 13
- Introduction of two new annexes to summarize country specific requirements for:
    - reporting timeframes for adverse events and advisory notices – page 13

- written agreements – page 13

MDSAP Audit Cycle

- Added statement regarding Stage 1 audits for re-certification audits in certain circumstances– page 17
- Added paragraph regarding sampling during audits – page 18

Surveillance Audits

- Added reference to Appendix 1 of MDSAP AU P0008 – page 16

Management Process

Task 1 – Assessing conformity

- added text under Quality System Procedures and Instructions heading regarding expectations for the term "documented" - page 22;
- added text under Quality Management System Planning heading regarding evidence of quality management system planning – page 23

Task 5 – Added text for Australia country-specific requirement:

- Reference to EP13A for patient implant cards – page 28
- Clarification of the inclusion of Sponsors activities in the medical device organization's internal audit. – page 28

Device Marketing Authorization and Facility Registration Process

Task 1

- Move the matters that relate to Australian requirements for the written agreement to Annex 4 – page 41;
- "Note" to "Assessing conformity"; added text regarding special attention should be paid to instances where devices are being marketed to jurisdictions where marketing authorization has not been granted – page 40;
- corrected expiry dates for Brazil for Registration and Notification – page 42

Task 2

- Clarifying text for Australia country-specific requirements – page 46;
- Corrected expiry dates for Brazil for Registration and Notification – page 46

Task 3

- Added text within the task to emphasize the link between design changes and the need to assess for market authorization – page 48;
- added text to the Australia country-specific requirement regarding notifying TGA of changes in cases where the Manufacturer also holds a TGA Conformity Assessment Certificate – page 48;
- corrected a reference for Japan to PMD Act 23-2-5.12 – page 50

Device Marketing Authorization and Facility Registration

Task 2

- Changed "manufacturer should" to "manufactures must" maintain a list of Australian Sponsors and the products ... – page 46
- Additional reminder that Sponsors are required to have a written agreement with manufacturers – page 46

Measurement, Analysis and Improvement Process

Task 2

- Added statement that information from the organization's analysis of quality data should be used to inform the audit team's decision as to specific products and processes to audit during Design and Development, Production and Service Controls, and Purchasing processes – page 57

Task 7

- Corrected text for country-specific requirements for Australia, added text to the Australia country-specific requirement regarding notifying TGA of changes in cases where the Manufacturer also holds a TGA Conformity Assessment Certificate – page 65

Task 12

- Added criteria for selection of complaints for review – page 71
- Added post-marketing systems as experience to be gained from the post-production experience – page 71;
- added "postmarket surveillance activities" under the "Selecting records" page 75
- added "Risk management" headings to "Assessing conformity" for this task – page 75;
- added text that information from reviewing post-production sources, including complaints and postmarket surveillance reports, should guide the audit team in selecting designs to review and production processes to audit – page 76

Task 14

- Task was rewritten to focus on the audit of the organization's process for evaluating complaints for potential individual adverse event reports – pages 75-76

Task 15

- Task was rewritten to focus on audit of the organization's processes for evaluating quality issues for potential advisory actions – page 77

Medical Device Adverse Events and Advisory Notices Process

Task 1

- Added Note for Canada that requirement to report incidents meeting the requirements of section 59.(1) that occur outside of Canada does not apply unless the Manufacturer has indicated, to a regulatory agency of the country in which the incident occurred, the Manufacturer's intention to take corrective action, or unless the regulatory agency has required the Manufacturer to take corrective action - page **Error! Bookmark not defined.**;
- for United States, added allowance for quarterly summary reporting for malfunction MDRs – page 88

Design and Development Process

Task 5

- Post-production feedback is to be used for maintaining product requirements and improving product realization processes - page 101
- Under "Assessing conformity", "Design inputs" heading, added text relating design inputs to manufacturing processes – page 102

Task 7

- Under "Assessing conformity", "Design outputs" heading, added text that design outputs can include documents such as diagrams, drawings, specifications, and procedures for both products and processes – page 105

Task 13

- Added 8.2.1 as a relevant clause for design changes – page 114
- Added text to the Australia country-specific requirement regarding notifying TGA of changes in cases where the Manufacturer also holds a TGA Conformity Assessment Certificate – page 115

Summary of Changes from Prior Revisions

Production and Service Controls Process

Task 1

- Under "Assessing conformity", "Unique Device Identifier" heading, removed the phase-in dates for device classes – page 123

Purchasing

Task 5

- added text for EP13A for patient implant cards for Australia – pages 168

ANNEXES

Annex 1

- Change of Title to reflect the general content of this section.
- General requirements for Assessing Technical Documentation - Added some clarifying text for the expected output from design control for technical documentation – page 181; and the monitoring of the update of risk management documents – page 182.
- Australian minimum requirement for assessing technical documentation – Added the inclusion of information gathered in feedback processes – page 185; and patient implant cards – page 186

Annex 2

- Clarified requirements for grading nonconformities found during audit of sterilization processes – page 195

Annex 3

- Quick reference guide for reporting timeframes for adverse events and advisory notices – page 192

Annex 4

- Clarification of when Written Agreements may be required to support regulatory requirements and the topics that may need to be included – page 195

Medical Device Single Audit Program

Frequently Asked Questions

Table of Content

A. General Questions about MDSAP

1. What is the Medical Device Single Audit Program?

The Medical Device Single Audit Program (MDSAP) is a program that allows the conduct of a single regulatory audit of a medical device manufacturer's quality management system that satisfies the requirements of multiple regulatory jurisdictions. Audits are conducted by Auditing Organizations authorized by the participating Regulatory Authorities to audit under MDSAP requirements.

The MDSAP is a way that medical device manufacturers can be audited once for compliance with the standard and regulatory requirements of up to five different medical device markets: Australia, Brazil, Canada, Japan and the United States. The program's main mission is to "…jointly leverage regulatory resources to manage an efficient, effective, and sustainable single audit program focused on the oversight of medical device manufacturers."

2. Why was the MDSAP developed?

The MDSAP was developed to:

- The MDSAP was implemented-based on requirements that are defined in the IMDRF MDSAP Model;
- Enable appropriate regulatory oversight of medical device manufacturers' quality management systems while minimizing regulatory burden on industry;
- Promote more efficient and flexible use of regulatory resources through work-sharing and mutual acceptance among regulators while respecting the sovereignty of each authority;
- Promote globally, in the longer term, a greater alignment of regulatory approaches and technical requirements based on international standards and best practices;
- Promote consistency, predictability and transparency of regulatory programs by standardizing;
    - the practices and procedures of participating regulators for the oversight of third party auditing organizations, and
    - the practices and procedures of participating third party auditing organizations; and
    - Leverage, where appropriate, existing requirements and procedures for conformity assessment.

3. Which Regulatory Authorities are part of the MDSAP and what is the plan for expansion of the program?

The MDSAP was developed by representatives of the Australian Therapeutic Goods Administration (TGA), Brazil's Agência Nacional de Vigilância Sanitária (ANVISA), Health Canada, MHLW/PMDA, and the U.S. Food and Drug Administration (FDA). All regulatory authorities participating in the MDSAP are equal partners in the program.

Others Regulatory Authorities may eventually decide to participate in the MDSAP and to become active participants in the Program. For example, the World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme and the European Union (EU) are Official Observer to the MDSAP Regulatory Authority Council (RAC) and Subject Matter Expert (SME) Work Group.

4. What is the difference between a Regulatory Authority being a participant in MDSAP Subject Matter Expert (SME) Working Group (WG) versus being an observer to this working group?

The Regulatory Authority participants provide the resources to support the development, implementation, maintenance and expansion of MDSAP and participate actively in the process of recognizing, monitoring, and re-recognizing Auditing Organizations under the framework of the IMDRF MDSAP. The

participating Regulatory Authorities have committed to use the MDSAP deliverables in order to assess program success. Each Regulatory Authority participant is also represented on the MDSAP Regulatory Authority Council (RAC); the MDSAP's governing board, by two senior level managers.

A Regulatory Authority who is an "observer" may attend MDSAP SME WG meetings, assessments, and other activities, but does not utilize MDSAP program deliverables to replace or supplement its regulatory scheme deliverables or portions of these deliverables. The observers are represented on the MDSAP RAC by one senior level manager.

5. Is the list of medical device manufacturers participating in the MDSAP made publicly available?

No, actually this information is not made publicly available by the Regulatory Authorities.

6. Can industry provide input into MDSAP documents or the program in general?

Yes. There are two venues for the industry to contribute.
Following each MDSAP audit, Medical Device Firms participating in the MDSAP are invited to provide feedback through a survey that is available in MDSAP FDA webpage.

Besides it, the Regulatory Authorities that are participating in the MDSAP have established and are implementing an MDSAP Quality Management System MDSAP Documentation. Feedback on MDSAP can be submitted to any of the participating Regulatory Authorities in written format, electronically, by telephone, or in person. Electronic feedback is preferred and may be submitted to one of the four email addresses listed below. MDSAP participating regulators will address the feedback in accordance with the procedure MDSAP QMS P0011 Complaints and/or Customer Feedback Procedure. Manufacturers are encouraged to provide feedback.

Contact emails:

MDSAP@tga.gov.au
MDSAP.ATENDIMENTO@anvisa.gov.br
QS_MDB_HC@hc-sc.gc.ca
MDSAP@pmda.go.jp
MDSAP@fda.hhs.gov

7. What is the criterion that must be achieved for the MDSAP to be considered successful?

The MDSAP Subject Matter Experts Working Group has developed a plan to gather evidence for a "proof of concept" of the MDSAP. The plan includes eight performance indicators for the measurement of the success of this program. - The criteria are related to audit reports and non-conformities, the audit model, duration of audits, Auditing Organizations and manufacturers. A method for data collection, sampling, method of analysis and targets were defined for each indicator. MDSAP P0007 *Proof of concept for MDSAP Program.*

8. Have there been discussions with WHO regarding the pre-clearance process for IVDs and taking account the results of an MDSAP audit? Will medical devices assessed by the WHO be included in the program at a later stage?

WHO is participating as an observer to the MDSAP. WHO has indicated a willingness to adapt and integrate MDSAP processes as much as possible in their *Prequalification Program*. WHO intends to utilize MDSAP reports where possible if they are available for devices that are subject to their *Prequalification Program*.

9. If an RA decides to change its GMP/QMS or Regulatory requirements, how will the changes be incorporated into MDSAP?

MDSAP Audit Model and the MDSAP Audit Model Companion document can be periodically revised to reflect any changes in regulatory requirements. Accordingly, the impacted MDSAP training will be updated. The IMDRF MDSAP WG N3 document requires "The Auditing Organizations to participate in any regulatory coordination group established for the purpose of keeping the Auditing Organization's personnel current on medical device legislation, guidance documents, standards, and best practice documents adopted in the applicable regulatory systems." (N3 – Clause 6.1.3)

10. How do I find out more specific information on the documents, policies, and procedures used in the MDSAP?

The MDSAP participating Regulatory Authorities and the candidate Auditing Organizations primarily utilize the IMDRF MDSAP WG documents that can be found at: IMDRF Documentation.

In addition, there are many other MDSAP Regulatory Authority Council approved documents in order to implement program, for example: an audit strategy for

auditing medical device manufacturers, requirements for the audit reports, a method for audit time calculation, and the MDSAP Quality Management System procedures. For further information on the MDSAP and associated documents, please refer to the MDSAP Home Page or contact one of the participating Regulatory Authorities at:

MDSAP@tga.gov.au
MDSAP.ATENDIMENTO@anvisa.gov.br
QS_MDB_HC@hc-sc.gc.ca
MDSAP@pmda.go.jp
MDSAP@fda.hhs.gov

B. Questions related to Assessments

11. Which Auditing Organizations can apply to the MDSAP?

During the MDSAP Pilot, only the Auditing Organizations recognised under CMDCAS program were invited to apply to participate in the MDSAP Pilot. From January 1st, 2017 the program was opened for applications from others candidate Auditing Organizations. More information can be found on the announcement available on MDSAP web page.

12. Can Contract Research Organizations participate in MDSAP? What about Certified Quality Auditors?

The MDSAP includes the use of Auditing Organizations, also known as Certification Bodies or Registrars in other schemes. If an Auditing Organization also acts as a Contract Research Organization, the organization's management system must ensure the impartiality of the Auditing Organization.

An independent Certified Quality Auditor may not individually apply for recognition under the MDSAP. Should an auditor become permanently employed or work on a contract basis for an Auditing Organization, and meet the competency and other criteria for auditors as required under MDSAP, e.g. absence of conflict of interest, that auditor may be qualified to perform MDSAP audits as long as the AO is recognized under MDSAP.

13. How will an Auditing Organization pay regulators for the application and training?

Actually there are no application fees or costs associated with the MDSAP Training. Training on the MDSAP Audit Model and the requirements of the participating Regulatory Authorities is available on-line to Auditing Organizations candidate applicants (MDSAP Training Material).

14. How are assessments of Auditing Organizations being conducted by RAs under the MDSAP?

The assessment program is defined in key documents for the planning and conduct of assessments by Regulatory Authority assessment teams; and, the follow-up and monitoring of assessment activities of Auditing Organizations. The sequence of all assessment activities follows a 4-year cycle. The cycle begins with an initial authorization, followed by annual surveillance assessments for three consecutive years. Assessments are performed per document IMDRF MDSAP WG N5, *Regulatory Authority Assessment Method for the Recognition and Monitoring of Medical Device Auditing Organizations* and associated MDSAP documents MDSAP Documentation.

15. Must Auditing Organizations have all documentation in English to be assessed by the Regulatory Authorities?

Auditing Organizations must have at least the documents requested for the application submission and for Stage 1 Assessment in English. During the Stage 2 Assessment, the Auditing Organizations must have personnel with fluency in English to translate documents and records that are not in English. Additionally, records that are specific to the MDSAP program (including but not limited to the documents included in the audit report package) should be in English as well.

16. What is the best way to determine what is expected of the Auditing Organizations with regard to multiple jurisdictions?

Medical device manufacturers will have to be audited according to the scope declared in their application for certification services. Based on the countries where the manufacturer sells (or intends to sell) or has devices registered, the AO will determine the regulatory requirements applicable to that manufacturer.

The AOs will have to refer to the Audit Model MDSAP AU P0002 and Audit Model Companion MDSAP AU G0002.1 to make that determination. The two documents incorporate or reference the regulatory requirements of each of the participating Regulatory Authorities.

17. What oversight do Regulatory Authorities have over the Auditing Organizations?

In accordance with best practices, the MDSAP incorporates a transparent assessment program by Regulatory Authorities who will oversee the compliance of the Auditing Organizations with MDSAP requirements. This program includes a robust plan and schedule for assessing the competence and compliance of MDSAP Auditing Organizations and includes assessments of their head office and critical locations, as well as witnessing the performance of Auditing Organization´s audits ("witnessed" audits), as part of an ongoing four year recognition cycle.

The Regulatory Authorities involved MDSAP will base their recognition and assessment process on the IMDRF MDSAP WG and MDSAP documents in addition to other documents approved by the Regulatory Authority Council. IMDRF Documentation and MDSAP Documentation.

In particular, Regulatory Authorities will evaluate or "assess" an Auditing Organizations' compliance to the requirements of IMDRF MDSAP WG documents N3 and N4.

- IMDRF MDSAP WG N3 *Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition*
- IMDRF MDSAP WG N4 *Competence and Training Requirements for Auditing Organizations*

18. What is a witnessed audit?

A witnessed audit is performed to permit Regulatory Authorities to verify that an Auditing Organization adequately conducts their audits using the MDSAP Audit Model and reports appropriately on the outcomes of audits. It is an essential assessment activity for building and maintaining confidence in the reliability of the third party Auditing Organization. During a witnessed audit, the Auditing Organization's audit team conducts the audit of the medical device manufacturer and the Regulatory Authorities' assessment team observes the AO without interfering in the audit process. The RA Assessment team does not assist or coach the AO auditors, nor does it provide additional information to the AO audit team or collect information on their behalf.

After the Auditing Organization has issued the audit report, the assessment team finalizes and shares their conclusions with the Auditing Organization.

The RA conclusions are not in relation to the compliance of the manufacturer to ISO 13485 and the relevant regulatory requirements. The RA's conclusions only relate

to the ability of the Auditing Organization to audit against the requirements of the MDSAP.

19. Who performs witnessed audits and how are the assessors selected?

The witnessing of an audit being conducted by an Auditing Organization will be performed by qualified MDSAP Regulatory Authority Assessors. These assessors are experienced Regulatory Authority Assessors who will have knowledge of the MDSAP requirements, the requirements of the participating Regulatory Authorities and the device and manufacturing technologies used by the medical device manufacturer that is being audited.

Regulatory Authority Assessors are qualified against the competency requirements as defined in the document IMDRF MDSAP WG N6 FINAL:2013, *Regulatory Authority Assessor Competence and Training Requirements.*

20. Can an Auditing Organization contest an unfavorable recognition decision or a nonconformity and its grading?

If an Auditing Organization disagrees with an unfavorable recognition decision or a nonconformity issued by the Regulatory Authorities, it may formally file for an appeal to the participating Regulatory Authorities. The process is defined in MDSAP AS P0021.002: Appeals Procedure.

21. If a current Notified Body applies for authorization to perform audits under the MDSAP, but does not pass the MDSAP assessment, could they also be de-notified to the EU Directive?

No. European Competent Authorities and Designating Authorities are not participants in the MDSAP. It is therefore unlikely that European Authorities would de-notify a Notified Body based on the outcome of an MDSAP Assessment. Nevertheless, European Authorities are likely to be informed if the reason for refusing the authorization was due to concerns that arose from a concurrent assessment by an Auditing Organization of the relevant European regulations. In such cases, the European Authorities may follow-up with the Auditing Organization and make their own assessment of the situation.

22. Who from the Auditing Organization or the Regulatory Authorities makes the final decision on the compliance of the medical device manufacturer?

The Auditing Organizations are fully responsible for making the decision on compliance to issue MDSAP certification documents under the program.

Independently, each MDSAP participant Regulatory Authority may use the report for different purposes, to support the regulatory decisions in their jurisdiction. If, based on the Auditing Organization's audit report, a Regulatory Authority concludes that the manufacturer is not in compliance with the regulations, the Regulatory Authority may engage in enforcement activities according to their policies, taking into account, if possible, the follow-up activities conducted by the Auditing Organization.

23. How does a regulatory authority inspectorate become an Auditing Organization?

Regulatory Authorities who are seeking recognition under MDSAP need to comply with the same requirements as a commercial Auditing Organization. The other participating Regulatory Authorities will conduct an assessment according to the international standard ISO/IEC 17021-1 and the additional requirements defined in IMDRF MDSAP WG N3 and IMDRF MDSAP WG N4, per the assessment methodology documented in IMDRF MDSAP WG N5.

24. How will MDSAP ensure that every RA has the same evaluation standards for the Auditing Organization?

Auditing Organizations are assessed for compliance with the requirements of IS0/IEC 17021-1 and the additional requirements of N3 and N4. An assessment program and assessment methodology for Auditing Organizations is defined in N5 and guidance for RA Assessors is to be provided in N8. Regulatory Authority assessors execute assessment tasks for each process defined in the documents above and identify objective evidence of definition, implementation and effectiveness of each of the requirements. If nonconformities are identified, a grading system is used to assist in determining the timeline for any corrections or corrective actions and to support a predefined Auditing Organization recognition or Auditing Organization de-recognition process.

Regulatory Authority assessors are qualified against the requirements of IMDRF MDSAP WG N6, *Regulatory Authority Assessor Competence and Training Requirements* to perform the assessment of an Auditing Organization. Regulatory Authority assessors will participate in both face to face and distance training activities. The MDSAP Regulatory Authorities are committed to operating under a joint MDSAP Quality Management System to establish controls over the program and to facilitate continuous improvement. Applicable procedures and forms are publically available at MDSAP Assessment Procedures and Forms.

25. Would an Auditing Organization receive independent recognition by each participating Regulatory Authority?

No. Recognition is a joint exercise and hence recognition of an AO by the MDSAP Regulatory Authority Council (RAC) means recognition by each participating Regulatory Authority. It may be possible that some jurisdictions have to internalize MDSAP Recognition in your national regulatory framework. For example, Anvisa is publishing a Resolution in "*The Brazilian National Gazette*" for each AO that is recognized in the MDSAP. It has the same effective and expiration date of the MDSAP recognition letter.

26. Will Auditing Organizations be informed when there is a complaint against them so that improvements can be made?

Yes. MDSAP QMS P0011 Complaints and/or Customer Feedback Procedure include in its scope complaints related to the Auditing Organizations and to Medical Device Manufacturer participating in MDSAP.

C. Questions related to Audits

27. Which manufacturers are eligible to undergo an MDSAP audit?

As currently planned, any manufacturer of medical devices is eligible to undergo an audit under the MDSAP. However, each regulatory authority may establish exclusion criteria for manufacturers meeting certain conditions if deemed necessary or when limited by legislation. It is important to note that manufacturers that participate in the MDSAP program are responsible for securing and maintaining a contract with an MDSAP recognized AO. AOs operate as fee-for-service organizations. In other words, medical device manufacturers are responsible to paying for MDSAP audits conducted by an AO. The Regulatory Authorities participating in MDSAP are not involved in contractual arrangements / the contract negotiation process between manufacturers and AOs.

28. How can a medical device manufacturer participate in the MDSAP?

All medical device manufacturers interested in participate to MDSAP can contact any of the Auditing Organizations authorized or recognized to perform MDSAP

audits. The list of *Auditing Organization Availability to Conduct MDSAP Audits* is available online.

Medical device manufacturers do not apply to a Regulatory Authority for an audit under MDSAP.

29. Does the MDSAP add requirements for the manufacturer?

No. The MDSAP audit model was developed to cover existing requirements from the Regulatory Authorities participating in the MDSAP. The program does not add any new requirements to existing requirements from ISO 13485 or other country-specific requirements of the participating Regulatory Authorities.

30. What are the potential benefits of a manufacturer participating in the MDSAP?

The MDSAP offers many benefits to medical device manufacturers including the following:

- A single audit is used in lieu of multiple separate audits or inspections by participating regulatory authorities or their representatives. Therefore, for many medical device manufacturers, the MDSAP reduces the overall number of audits or inspections and optimizes the time and resources expended on audit activities.
- Additionally, as a longer term goal, it is expected that the program will enhance confidence in the reliability of third party audits, that more Regulatory Authorities will join the program, and that other Regulatory Authorities will use information made available through the program to limit the need for additional audits.
- Some participating regulatory authorities will use MDSAP audit outcomes as an alternative to their own inspections to process applications for medical device marketing authorization.
- Like in any third party auditing program, the medical device manufacturer is free to choose among all authorized auditing organizations to perform the audits. Routine audits are announced and planned with the manufacturer.
- The MDSAP is expected to improve the predictability of audit outcomes through:
    - enhanced auditing organization recognition criteria,
    - monitoring of auditing organizations by the participating Regulatory Authorities,
    - the use of a standard MDSAP audit model,
    - the grading of any nonconformity using objective criteria to characterize the significance of the finding,

    - the reporting of the audit outcomes using a standard report template.
- Enrolling in the MDSAP may be seen as evidence of a medical device manufacturer's commitment to quality management systems for product quality and regulatory compliance.

31. What are the potential benefits to the manufacturer participating, specific to each jurisdiction?

Australia: The Therapeutic Goods Administration – TGA

Where regulations do not require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will take into account MDSAP- audit reports when considering whether a manufacturer has demonstrated compliance with an Australian Conformity Assessment procedure; or

Where regulations require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will take into account MDSAP audit reports when considering whether to issue or maintain a TGA Conformity Assessment Certificate[1]. Under some circumstances a manufacturer may avoid routine TGA inspections.

Following a successful evaluation of the MDSAP, the following may apply:
Where regulations do not require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will accept MDSAP certificates as evidence of compliance with ISO13485:2003 where the Standard has been used to demonstrate partial compliance with the requirements of an Australian Conformity Assessment Procedure. It is expected that Australian Sponsors may be required to submit to the TGA, additional technical documentation to demonstrate compliance with the requirements of the Essential Principles of Safety and Performance and the manufacturer's chosen Conformity Assessment Procedure.

[1] TGA issued CA certificates are required for; manufacturers of medical devices that incorporate a medicinal substance, or a material of animal origin that has been rendered non-viable, or that contains tissues, cells or substances of microbial or recombinant origin, or that incorporate stable derivatives of human blood or human plasma.

Where regulations require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will continue to take into account MDSAP audit reports when deciding whether to issue or maintain a TGA Conformity Assessment Certificate. Under some circumstances a manufacturer may avoid routine TGA inspections.

Brazil: The Brazilian National Health Surveillance Agency – ANVISA utilizes the outcomes of the program, including the reports, to constitute an important input on ANVISA's pre-market and post-market assessment procedures, providing, when applicable, key information that are expected to support regulatory technical evaluation on these issues.

As defined in RDC 15/2014 and RE 2.347/2015, ANVISA may use MDSAP audits in lieu of a premarket inspection by ANVISA to grant ANVISA's GMP Certificate to manufacturers intending to put medical devices of class III or IV on the Brazilian market. Undergoing an MDSAP audit may accelerate ANVISA´s GMP certification process, which is a pre-requisite to the marketing authorization.

ANVISA can also use MDSAP audits to renew ANVISA's GMP Certificate bi-annually, as an alternative to an ANVISA comprehensive inspection.

Note: ANVISA do not use MDSAP audit reports from manufacturers where the result of ANVISA's previous inspection was considered unsatisfactory and therefore the manufacturer had the certification submission denied. In such cases ANVISA will start using the MDSAP reports only after a new ANVISA inspection with a satisfactory result.

Canada: Health Canada will operate the current Canadian Medical Device Conformity Assessment System (CMDCAS) program and the MDSAP in parallel -. - Health Canada will accept either an MDSAP certificate or a CMDCAS certificate for the purpose of obtaining a new (or maintaining an existing) Class II, III or IV medical device license, pursuant to section 32 of the Regulations.

Additionally, Health Canada's intent is to implement the Medical Device Single Audit Program as the mechanism to assess regulatory compliance for quality management system requirements in Canada.

Japan: When an MDSAP audit report is submitted at the timing of premarket or periodical post-market QMS inspection application, Japan's Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA) will use the report as a trial:

1) To exempt a manufacturing site etc.* from on-site inspection, and/or

2) To allow a Marketing Authorization Holder (MAH) to substitute considerable part of documents required for the inspection with the report.

Note: PMDA may perform on-site inspection or request additional QMS documents, when it is determined necessary after a review of the MDSAP audit report package.

*Exceptions:
a) A Registered Manufacturing Site (RMS) which manufactures medical devices made of human/animal tissues,
b) A RMS which manufactures radioactive IVDs, and
c) An establishment of a MAH.

United States: U.S. Food and Drug Administration's (FDA) Center for Devices and Radiological Health, will accept the MDSAP audit reports as a substitute for FDA routine inspections (biennial by policy). Additional benefits include:

- MDSAP routine audits are announced, scheduled by the Auditing Organization with the manufacturer, with a pre-established duration;
- The FDA will review MDSAP audit reports with a level of scrutiny commensurate to the significance of audit findings, taking into account the review and follow-up performed by the Auditing Organization;
- Firms have one month to provide their full response to critical nonconformities (grade 4 and 5) to the Auditing Organization (as opposed to 15 working days following and FDA inspection);
- Certification documents issued by the Auditing Organization state compliance with applicable US regulations, which may provide a marketing advantage.

Note: Inspections conducted "For Cause" or "Compliance Follow-up" by FDA will not be affected by this program. Moreover, this MDSAP program would **not** apply to any necessary pre-approval or post approval inspections for Premarket Approval (PMA) applications or to decisions under section 513(f)(5) of the Act (21 U.S.C. 360c(f)(5)) concerning the classification of a device.

Firms with activities related to the Electronic Product Radiation Control (EPRC) provisions of the Act will continue to be subject to FDA inspections for the EPRC activities.

World Health Organization (WHO): In the framework of the *Prequalification Program* for diagnostic devices, the WHO may recognize successful MDSAP - audits as acceptable evidence of QMS compliance with international regulations. This may result in either abbreviated or waived WHO inspection depending on the scope of audit.

32. What are the costs associated with MDSAP audits

The cost of conducting an MDSAP audit is dictated by the commercial arrangement between the medical device manufacturer and the authorized MDSAP Auditing Organization.

33. Where can industry find out which jurisdictions an AO is recognized for?

An Auditing Organization authorized or recognized to perform MDSAP audits must have demonstrated competence in each jurisdiction's regulations. Therefore, the recognition is not restricted in terms of a Regulatory Authority's jurisdiction and covers all jurisdictions participating in MDSAP. The letter of recognition to conduct medical device regulatory audits under MDSAP is standardized. .

34. How does the MDSAP ensure that medical devices are being manufactured in accordance with the regulations of multiple jurisdictions?

The MDSAP relies on:

- Annual audits of manufacturers according to an audit model specific to the program. This audit model was developed to review the compliance of a manufacturer's quality management system to the international standard ISO 13485 and additional regulatory requirements applicable to the countries where the devices are sold; and
- Annual assessments of the Auditing Organizations' management system compliance to the international standard ISO/IEC 17021-1 and MDSAP specific requirements as defined in IMDRF MDSAP WG documents.

35. How do Auditing Organizations ensure that duplicate efforts are not performed during an audit of a manufacturer that sells in multiple jurisdictions?

The MDSAP audit process was designed and developed not only to prevent duplication, but also to ensure that the program provides efficient and thorough coverage of the requirements of; Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:-) and any corresponding section(s) of the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Canadian Medical Device Regulations (CMDR, Part 1), the Japanese QMS ordinance (MHLW MO 169), the Quality System Regulation (21CFR 820), and other country-specific requirements.

The MDSAP audit sequence follows a process approach and was designed and developed to allow the audit to be conducted in a logical, focused, and efficient manner.

Additionally, MDSAP AU P0029 Initial Manufacturer Audit and MDSAP Manufacturer Withdrawal Notification Procedure was created to ensure that Auditing Organizations properly notify the MDSAP Team, describing the MDSAP notification process and timeframes that AO must follow when an initial MDSAP audit has been scheduled, rescheduled or transferred. The document also instructs how to properly notify the MDSAP Team when a Medical Device Manufacturer withdraws from MDSAP participation.

Timely notification of MDSAP initial audit schedules by AOs will prevent the duplication of inspection/audit of Medical Device Manufacturers participating in MDSAP. Additionally, adequate notification of situations where a Medical Device Manufacturer no longer elects to participate in MDSAP will ensure that continued regulatory oversight is maintained by all participating RA's.

36. How are regional regulatory differences addressed in the program?

The regulatory requirements of the participating Regulatory Authorities have been incorporated into the MDSAP Audit Model and further discussed in the MDSAP Audit Model Companion Document. An auditing organization will perform audits using this model and record findings in relation to the regulations of the participating Regulatory Authorities.

Each Regulatory Authority independently utilizes the MDSAP audit deliverables (audit reports, certification documents) according to their regulations and policies.

37. How will audits of medical device manufacturers be conducted under the MDSAP?

Authorized Auditing Organizations will perform MDSAP audits according to documents developed by the participating Regulatory Authorities. Some relevant policies and procedures introduced by the program to ensure consistency across Auditing Organizations and/or auditor teams include:

- The sequence of tasks specified in the Audit Model MDSAP AU P0002 will have to be followed; the audit duration will be based on planned audit tasks MDSAP AU P0008 *Audit Time Determination - Procedure*, ensuring consistency across Auditing Organizations. In general, the duration of MDSAP audits will not exceed the accumulated time of audits and inspections

performed currently by each participating Regulatory Authority according to their governing regulatory frameworks.

- An audit report will be issued at the end of each audit, using a standard fillable template specifically designed for medical device regulatory audits.
- Nonconformities identified during an audit will be graded on a scale from 1 (least critical) to 5 (most critical), and will be managed according to criteria defined in the document GHTF/SG3/N19:2012, *Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange*).
- Audited manufacturer will be responsible for timely development and implementation of action plans to address non-conformities identified during audits MDSAP AU P0027 Post Audit Activities and Timeline Policy.
- Auditing Organizations will share the audit outcomes with the participating Regulatory Authorities to support their pre-market or post-market programs. Upon successful certification or recertification audits, Auditing Organizations will issue MDSAP-specific certification documents stating compliance to ISO 13485:- and applicable regulatory requirements. MDSAP AU P0026 Certificate Document Requirements.

38. What is the difference between a Stage 1 and a Stage 2 Audit? (Initial Audit?)

The "Initial" audit also known as an "Initial Certification" audit consists of a Stage 1 and a Stage 2 audit.

- Stage 1 – A first Stage 1 audit consists of a documentation review and the evaluation of the readiness of the manufacturer to undergo a Stage 2 audit.
- Stage 2 – The purpose of a Stage 2 audit is to determine if all applicable QMS requirements of ISO 13485 and all other applicable regulatory requirements from participating regulatory authorities have been effectively implemented.

39. How did the revision of ISO 13485 impact MDSAP?

The audit model was revised to consider the new version of ISO 13485. Both versions (based on ISO 13485:2003 and the one based on ISO13485:2016) are available on the website. During the transition period of the ISO 13485, the AO can use the old or the new version, depending on the manufacturer transition plan.

40. Can an "upgrade audit" be performed to update the MDSAP certificate to ISO 13485 version instead of a full MDSAP re-certification audit?

An "upgrade audit" could be performed as part of a surveillance audit, but this would require the audit to include ALL the new/modified requirements of the revised standard. Since it can become a more comprehensive audit requiring additional

time, a stage 1 or document review may be necessary prior to the onsite audit to maximize audit efficiency.

Please be aware that:

- The manufacturers are required to comply with ISO13485:2016 and the relevant regulatory requirements of the participating RAs within the timeframes set by the ISO whitepaper and Health Canada's announcement for the transition from CMDCAS to MDSAP.
- AO's are required to apply the MDSAP audit model and an MDSAP audit program to determine compliance with these requirements. MDSAP does not introduce additional requirements for manufacturers.
- MDSAP Certificates represent the application of an audit methodology to determine compliance with the requirements of ISO13485:2016 and relevant regulatory requirements for QMS through a single audit for multiple regulators. Hence a certificate cannot reference ISO13485:2016 until the methodology has been applied.
- The prospect of a change to the Standard has been known for many years. To minimize unexpected costs the manufacturer could align their transition to the newer standard with the recertification audit that would naturally occur during the transition period.

41. How is the audit duration determined?

The method and the criteria to be used by the Auditing Organizations to calculate the time necessary to conduct an MDSAP audit of a medical device manufacturer is defined in the procedure MDSAP AU P0008 entitled *Audit Time Determination*.

The MDSAP audit model defines the activities and tasks that are to be performed in an MDSAP Audit Cycle including; the activities and tasks for an Initial (Stage 1 and 2) Audit (a.k.a. Certification Audit), Surveillance, Re-audit (a.k.a. Recertification Audit), and for Special Audits. The appropriate audit tasks defined within the MDSAP Audit Cycle must be used when calculating audit times. When applicable, the appropriateness of the audit duration for subsequent activities should be confirmed during the Stage 1 audit.

There are varying numbers of audit tasks depending on the process being audited. Audit time is calculated based on the number of applicable audit tasks associated with the type of audit to be conducted (as defined in the MDSAP Audit Cycle) and the specific activities of the organization to be audited.

42. At what frequency do MDSAP audits occur?

The medical device manufacturers that will volunteer to participate in the-MDSAP will be audited annually, according to a three-year certification cycle. The Initial

Audit, also referred to as the *"Initial Certification Audit"* is a complete audit of a medical device manufacturer's quality management system (QMS). The initial Audit is followed by partial Surveillance Audits conducted once per year for two consecutive years. The cycle re-commences with a complete Re-audit, also referred to as a "Recertification Audit" in the third (3rd) year.

Special Audits, Audits Conducted by Regulatory Authorities, and Unannounced Audits are potential extraordinary audits that may occur at any time within the audit cycle.

43. Can the scope of an MDSAP audit include combination products?

The implementation of the MDSAP is intended to allow for a single audit to satisfy the regulatory requirements of the participants.

Medical Devices that include; drugs (medicinal substances) or biologics (e.g. materials of animal origin that have been rendered non-viable, or tissues, cells or substances of microbial or recombinant origin, human blood or extracts of human blood or blood products, etc.) (a.k.a. "combination products") may be included in the scope of an MDSAP audit.

The Regulatory Authorities that take into account MDSAP audit reports for combination products expect that the Auditing Organization, when conducting an audit for these products, will:

- undertake, to the extent possible during on-site audits, an assessment of the product / process related technologies in accordance with the requirements of N3 Clauses 9.2.4, 9.3.2 and 9.4.1, and the requirements of the MDSAP audit model for compliance with the country specific requirements;
- assign relevant technical competence to the audit team that is assessing the product / process related technologies and relevant controls for the handling, testing and manufacture of these types of devices; and
- record their findings in accordance with the requirements of MDSAP AU P0019 MDSAP Medical Device Regulatory Audit Reports.

However, due to differences in the way that these products are regulated in the jurisdictions of the participating Regulatory Authorities, MDSAP audit reports and certification documents will not be considered an alternative to the inspection and assessment requirements in some jurisdictions, as described below:

Australia: These products are subject to an off-site examination of the design by the TGA under the Australian Conformity Assessment Procedures. A Design

Examination Certificate will be issued upon the successful completion of the examination.

The TGA is also required to issue a Conformity Assessment Certificate for the Full Quality Assurance procedure applied by the manufacturer for these products. When considering whether to issue or maintain this certificate the TGA may take into account MDSAP audit reports. An effective MDSAP audit report may reduce the frequency of TGA inspections for these devices.

Brazil: According to Brazilian regulations there are no specific requirements for combination products regarding the Quality Management System, and for that, all the requirements already disposed on the MDSAP companion documents promote adequate coverage for the needs established on the Brazilian legislation and regulation for those products. Therefore, combination products that are considered medical devices in Brazil are included in MDSAP –

Canada: The MDSAP Audit model covers the requirements for combination products that are regulated as medical devices.

Japan: There are no Japanese characteristic requirements for combination products which are categorized as devices. Therefore, MDSAP Audit results will be considered as alternatives to confirm the compliance of Quality Management System (QMS) requirements for such products.

United States: The MDSAP audit model only covers the requirements of the US medical device regulations. As additional requirements of the US regulations apply to devices incorporating drugs or biologics, the FDA cannot consider MDSAP - audits of combination product manufacturers as an alternative to FDA inspections. Consequently, such products are still subject to FDA inspections regardless of the participation of the manufacturer in the program. Nevertheless, the FDA may take into account the outcome of an MDSAP - audit covering combination products to optimize the scope of the FDA inspection to be performed.

NOTE: When a combination product manufacturer also manufactures non-combination products, it is expected that during the initial certification audit and at least once during the subsequent certification cycle the audit team includes the technical competence to audit combination products; and, when applicable, the audit plan includes the quality management system processes and activities associated with the combination product. MDSAP audit plans and reports of combination product manufacturers must consider, where applicable:

1) Supplier Controls and acceptance activities (including testing) associated with the starting material that is to be used in the manufacture of the drug or biologic component (in particular Active Pharmaceutical Ingredients);
2) Controls of the manufacturing processes for the drug or biologic

component;
3) Final acceptance and testing activities, including those associated with the drug or biologic component in the finished product; and
4) Stability programs that consider the drug or biologic component in the finished product.

44. Is there a checklist available for industry that compares the ISO 13485 requirements with each participating country's regulations?

The *Audit Model* MDSAP AU P0002 contains specific instructions on the MDSAP audit process. It incorporates an audit sequence and instructions for auditing each specific process. The audit process tasks incorporate references to the applicable ISO 13485:- clause(s) and any corresponding section(s) of the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Canadian Medical Device Regulations (CMDR, Part 1), the Japanese QMS ordinance (MHLW MO 169), and the Quality System Regulation (21CFR 820).

45. Is MDSAP a top down inspection, as with the Quality System Inspection Technique employed by FDA?

The MDSAP Audit Model, which was inspired by the FDA's Quality System Inspection Technique document, is based on a "top-down" auditing approach.

46. Does the audit process include a daily review of areas of concern?

Yes. Auditing Organizations must be in compliance with the requirements of IMDRF MDSAP WG N3, and N4, including the requirements of ISO/IEC 17021-1 and all other related MDSAP documents. ISO/IEC 17021-1, Sub-Clause 9.4.3.1- *Conducting the opening meeting,* requires that "during the audit, the client will be kept informed of the audit progress and any concerns."

47. Are MDSAP audits conducted by single or multiple auditors?

Procedure MDSAP AU P0008 Audit Time Determination specifies how to determine the on-site audit duration in man-days. Auditing Organizations decide how many auditors will compose the audit team. For instance, a 6 man-day audit could be completed in 3 days by a 2-auditors team. Auditing Organisations are also required to take into account the competency of the audit team for the type of audit and the scope of products that are produced under the control of the manufacturer's QMS.

48. Who assigns a particular auditor? The Auditing Organization or Regulatory Authority?

It is the AOs' responsibility to assign auditors for individual audits of medical device manufacturers, taking into account their competence, impartiality and availability.

Unlike other certification programs, a manufacturer may not oppose the choice of the auditor under the MDSAP (IMDRF MDSAP WG N3 *Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition* exception to ISO /IEC 17021-1, section 9.2).

49. If MDSAP becomes mandatory for one or more participating countries will manufacturers be expected to be compliant with regulations in a jurisdiction that it does not market?

The manufacturers are expected to be compliant only with the regulations for the jurisdictions where their products are marketed.

50. Can RA's discredit/void any audits that were conducted by an AO due to inadequate audit method/technique? If so, will manufacturers have to go through re-audits for audits they believed to have passed?

The MDSAP does not include mechanisms for requiring an audit to be re-done. Nevertheless, if an audit report appears to be unreliable, a participating Regulatory Authority may not be able to utilize the report as part of their process to grant a marketing authorization. A misleading audit report may also present a risk to public health and could lead the Regulatory Authorities to conduct its own follow-up inspection. Alternatively, an RA may request that an AO conduct a special audit to follow up on an issue. (IMDRF MDSAP WG N3 – clause 9.6.6.)
Manufacturers may forward a complaint with the participating Regulatory Authorities in relation to an audit performed by an Auditing Organization. The complaint will be processed using the procedure described in MDSAP QMS P0011.

51. If an AO issues a negative final report, does this mean the manufacturer can no longer supply to/sell in all of the regulatory jurisdictions that are participating in the Program?
MDSAP audit reports records the recommendation of the audit team for initial, continuing certification or re-certification of the audited medical device manufacturer. When the AO determines that the audited manufacturer does not meet QMS or other

regulatory requirements, each of the Regulatory Authorities concerned would determine appropriate actions relative to the identified nonconformities. The nonconformities may or may not be associated with regulatory requirements of all participating regulatory authorities.

52. What happens if significant non-conformities are identified by an Auditing Organization and subsequently shared with the Regulatory Authorities?

Non-conformities identified by an Auditing Organization are to be graded in accordance with the document GHTF/SG3/N19:2012 – Quality management system – Medical devices – Nonconformity Grading System for Regulatory Purposes and Information Exchange. Nonconformities are to be recorded and graded by the Auditing Organization using MDSAP AU F0019.2 NC Grading and Exchange Form.

IMDRF MDSAP WG N3 defines that the Auditing Organization shall provide information to the recognizing Regulatory Authority(s) about the audits and decision on conformity to quality management system requirements. The procedure MDSAP AU P0027 Post-Audit Activities and Timeline Policy defined that if the audit identified one or more grade 5 nonconformities, or more than two grade 4 nonconformities, or a public health threat, or any fraudulent activity or counterfeit product, the Auditing Organization shall inform the Regulatory Authorities within 5 working days. For Grade 4 or 5 nonconformities, manufacturers are expected to provide evidence to the Auditing Organization of implementation of the remediation actions addressing any grade 4 or 5 nonconformity within 30 days of the audit end date. Auditing Organizations are subsequently expected to provide the audit package, which includes the NC Grading and Exchange form, to a recognizing Regulatory Authority within 45 days of the end of audit. Post-audit actions timelines for a manufacturer and an Auditing Organization are further described in MDSAP AU P0027 Post-Audit Activities and Timeline Policy.

On receipt of the 5 days' notice the participating Regulatory Authorities will undertake actions that are appropriate for their jurisdictions and notify with the other participating Regulatory Authorities on the actions that should be taken in relation to the manufacturer.

53. How are nonconformities that are identified during an MDSAP audit managed? What is the timeline for a manufacturer to respond to nonconformities?

The document MDSAP AU P0027 Post-Audit Activities and Timeline Policy defines the activities to be completed and timeline that a medical device manufacturer must follow to address the nonconformities identified during an MDSAP audit.

The manufacturer must provide a remediation plan for each nonconformity within 15 calendar days from the date the non-conformity report was issued. The plan must include:

- the outcome of the investigation of the nonconformity and its cause(s),
- the planned correction(s), and
- the planned corrective action(s) to prevent recurrence.

The evidence of implementation of the remediation actions addressing any grade 4 or 5 nonconformity must be provided within 30 calendar days after the audit end date. (Page 1-section 2 Timeline)

54. Who would conduct follow-up visits to close the non-conformities?

An Auditing Organization would normally conduct close-out activities for all non-conformities in accordance with their procedures.

A participating Regulatory Authority may request that an Auditing Organization carry out a Special Audit to further investigate, follow-up or to closeout an audit under the direction of the requesting Regulatory Authority.

A recognizing Regulatory Authority may conduct its own Special Audit at any time it deems necessary and within the purview of its jurisdiction. (IMDRF MDSAP WG N3 – clause 9.6.6.)

55. Do Auditing Organizations collect evidence of nonconformities, or other evidence usually collected during Regulatory Authorities' inspections?

Under the MDSAP, Auditing Organizations are not required to collect any evidence, but the audit report must substantiate any audit finding by reference to audit evidence. Due to this restriction, the US FDA will limit enforcement actions based on MDSAP audit reports to advisory actions only.

This waiver also applies to other evidence usually collected during Regulatory Authorities' inspections, such as evidence of interstate commerce by the FDA.

For example, what does the FD&C Act mean by "Interstate Commerce". *Section 201(b) of the FD&C Act [21 U.S.C. 321(b)] tells what circumstances place a product in interstate commerce:*

(1) Commerce between any State or Territory and any place outside thereof, and
(2) Commerce within the District of Columbia or within any other Territory not organized with a legislative body.

"Interstate commerce" applies to all steps in a product's manufacture, packaging, and distribution. It is very rare that a cosmetic product on the market is not in "interstate commerce" under the law. For example, at least some of your ingredients or packaging most likely originates from out of state, or even out of the country. Likewise, it is foreseeable that your products will leave the state. Although there are certain exemptions [21 CFR 701.9], factors such as these generally cause the requirements of the FD&C Act to apply to your products."

56. During witnessed audits, will Regulatory Authorities prompt AO's in identifying nonconformities? (There is concern that the potential negative influence by RA on an AO)

The RAs will not interfere in the way an AO conducts its audit. The MDSAP is intended to allow competent auditors from MDSAP recognized AOs to conduct a single audit of a medical device manufacturer's quality management system in compliance with the requirements of the RAs participating in the MDSAP program. For this purpose, the RA's will ensure, by periodical assessment, including the witnessing of audits of manufacturers conducted by AOs, that AOs are applying the MDSAP audit model and assigning adequate competence to the task.

57. As a manufacturer, how do I show that I was successfully audited under the MDSAP?

Upon successful completion of an initial audit or re-audit, an Auditing Organization will issue certification documents including a reference to the MDSAP that will state compliance to ISO 13485: and the applicable Medical Device Regulations from each jurisdiction that were used as audit criteria.

58. If a manufacturing site is already under regulatory action with a participating Regulatory Authority, can they participate in the MDSAP?

If a manufacturer is currently subject to regulatory action from one of the participating Regulatory Authorities, then the manufacturer should consult with the RA about their eligibility for an MDSAP audit prior to resolution of the action. There are no exclusion criteria regardless of the past audit/inspection history, and regardless of the type of medical devices manufactured by the organization. Nevertheless, if a manufacturer had a previously unfavorable inspection by a participating Regulatory Authority, this Regulatory Authority may still choose to conduct a follow-up inspection. For example, this is the case with inspections conducted by the U.S. FDA. ANVISA will not use MDSAP audit reports from

manufacturers where the result of ANVISA's previous inspection was considered unsatisfactory and therefore the manufacturer had the certification submission denied. In such cases ANVISA will start using the MDSAP reports only after a new ANVISA inspection with a satisfactory result.

59. What happens to a Manufacturer when the AO recognition is revoked?

The impact of a cessation of recognition or the revocation of the authorization to audit, under the MDSAP may affect a large number of manufacturers. The event should not directly affect any existing marketing authorization. Nevertheless, Regulatory Authorities may need to consider individual or collective transitional arrangements to assure existing or potential public health risks are mitigated.

To stay in the program, a manufacturer would need to contract another Auditing Organization to resume the audit cycle at the point of departure of the de-recognized Auditing Organization.

60. Will industry auditors have access (for a fee) to the AO auditor training? [Will training be available for manufacturers to ensure that its QMS will meet the MDSAP criteria?]

Computer-based on-line training modules have been created describing the MDSAP Audit Model that is to be used by Auditing Organizations to conduct audits of Medical Device manufacturers. This training is a requirement for each Auditing Organization auditor who will be conducting MDSAP audits. Due to limited availability of licenses agreement the training is not being made available to non-Auditing Organization certification bodies or to medical device manufacturers. However some of the MDSAP training modules are available on the MDSAP webpage - CDRH Learn (Postmarket Activities Section/ Inspections – Global Harmonization); scroll down to "Postmarket Activities - *(New module 2/9/17)".*

61. For manufacturers already holding ISO 13485 certification under the CMDCAS program how would they transition to the MDSAP program? Will a full initial audit be required?

In order to minimize the impact on ongoing certifications under CMDCAS, the MDSAP audit cycle may be synchronized with the CMDCAS audit cycle. Medical device manufacturers can participate in the MDSAP Program at their convenience and therefore their first MDSAP audit may be a surveillance audit. To be noted that in this case:

1. The manufacturer would not obtain an MDSAP certificate until a recertification audit is conducted;
2. A regulatory authority may not be able to use a surveillance audit report in their process to issue a marketing authorization.

The medical device manufacturer should therefore make the decision whether to synchronize the MDSAP audit cycle with the CMDCAS audit cycle or not based on their regulatory and business interests.

62. Why aren't MDSAP audit reports used by the FDA as substitutes for inspections for Premarket Approval (PMA) applications?

The FDA explicitly excludes PMA pre-approval and post-approval inspections for Premarket Approval (PMA) due to the lack of regulatory convergence in the following:

1. the premarket device assessment processes performed under the various regulations (e.g. US Premarket Application, Australian Design Dossier or Design Examination, Canadian Device License Application); and,
2. where the responsibilities for final decisions of safety and performance/effectiveness of a medical device are placed (regulatory authority vs. third party organization).

63. Which country specific regulatory requirements are included in the MDSAP audit criteria?

The Medical Device Single Audit Program (MDSAP) audit process was designed and developed to ensure a single audit will provide efficient yet through coverage of the relevant requirements of; Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485-), the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Japanese QMS ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820), and other specific requirements of medical device regulatory authorities participating in the MDSAP program including 21 CFR Part 803 and 21 CFR Part 806.

64. How will the determination be made on whether an audit report supports an FDA advisory action without the supporting evidence?

The determination will be made following existing FDA criteria for situation 1 as described in the applicable Compliance Program, Part V. The evidence will be

described in the narrative descriptions of nonconformities contained in the audit report. The auditor competency (including ability to identify existing nonconformities) is something the regulatory authorities review extensively during Auditing Organization assessment activities. An independent inspection by the FDA would be necessary to support judicial actions.

65. How will Nationally Recognized Testing Laboratory (NRTL) Program audits be accepted?

NRTL tests and MDSAP audit are completely separate programs, evaluating compliance to distinct criteria. NRTL tests are required by the US Occupational Safety and Health Administration.

66. Can Regulatory Authorities not participating in MDSAP have access to audit reports? If so, what amount of information will be made available and at what cost?

Regulatory Authorities not participating in the MDSAP will not have full access to audit reports. Nevertheless, if a Regulatory Authority has a confidentiality agreement with a participating Regulatory Authority, a request may be made to obtain a copy of a particular report.

However, non-participating Regulatory Authorities may request audit reports and certificates from the medical device manufacturer.

67. Do the IMDRF or the Regulatory Authorities participating to the MDSAP plan to influence/revise the International Accreditation Forum (IAF) mandatory document MD9 on the audit of medical device manufacturers to ISO 13485?

No. The document IMDRF MDSAP WG N3 states that “IMDRF Regulatory Authorities have no official status within groups such as the IAF, or any voice in IAF governance or IAF mutual recognition agreements, that would allow the Regulatory Authorities to revise IAF documents to meet the needs of the regulators. It was also determined that the standard most commonly utilized is the ISO (the International Organization for Standardization) and IEC (the International Electro-Technical Commission) standard ISO/IEC 17021-1 entitled, “Conformity assessment – Requirements for bodies providing audit and certification of management systems.” Medical device Regulatory Authorities also have little influence in the standards organization that produces this standard and cannot simply change the standard for medical device regulatory purposes.”

68. Is the CE certification included in the outcome of a successful MDSAP audit?

The MDSAP Audit Model MDSAP AU P0002 does not incorporate the requirements from the European regulations. Nevertheless, the medical device regulatory Audit Report form MDSAP AU F0019. 1 may be used for multipurpose audits and an Auditing Organization may incorporate the European requirements into the MDSAP audit criteria to eliminate duplicate reporting.

69. Can the RAs consider if one report can represent a multi-audit site?

After reconsideration during the 2016 MDSAP Forum, the Regulatory Authorities agreed that a separate report is necessary for each audited site.

70. Do audit tasks have to be repeated during a multi-site audit?

- The implementation of applicable QMS process elements should be audited at each site.
- Content of common procedures does not have to be audited again. However, the implementation of applicable QMS process elements should be audited at all applicable sites.
- The non-implementation of applicable QMS process elements may lead to nonconformities relating to document control (current, approved procedure not available at all sites); or failure to effectively train users of the procedure; or failure to effectively implement the procedure, among others.

71. What additional guidance can RAs provide AOs on the application of the MDSAP audit model to multi-site audits and for suppliers?

- The AO should determine the applicable QMS activities and corresponding audit tasks at each site included in the audit program.
- Content of common procedures does not have to be audited again. However, the implementation of applicable QMS process elements should be audited at all applicable sites.
- The audit team should pay attention to the interaction and coordination of activities between sites.
- MDSAP audit could be extended to a supplier facility if the manufacturer cannot demonstrate effective controls.

72. How should an AO handle companies that have a legal address with no association to the company's daily operations?

- Per IMDRF MDSAP WG N3, the AO shall audit all sites that will be recorded on the certificate.
- AOs can initially visit the site to confirm its activities and relationship to the QMS.
- Describe relationships/activities and site omissions in the audit report.
- Auditors should confirm if changes result in additions of sites to audit program.
- Non-operations/functional sites should not be audited/certified.

73. Should a remote-audited facility be included on the certificate?

According to MDSAP AU P0026, section 7,"The certification document shall record all sites of the manufacturer's quality management system that have been audited on-site. "

74. How should AOs handle "virtual" manufacturers?

Virtual Manufacturers shall be treated as manufacturers and shall be audited accordingly for all activities applicable to the devices designed or manufactured.

75. Manufacturers indicated that the grading system was too complex to understand. Is there any plan to review it?

- The grading system is based off of GHTF/SG3/N19:2012 and there are no plans to change the document at this time.
- RAs will develop a CDRH Learn training module on GHTF/SG3/N19:2012.

76. Can RA provide additional guidance on how to distribute the audit activities among the audit team, using the audit model?

- Audits require effective pre-audit planning.
- While one auditor is reviewing a primary process of the audit model (e.g., Management), another auditor can cover a supporting process. (e.g., Facility Registration)
- Auditors covering the same process can cover different audit tasks.
- Maintaining audit team communication is essential.

- Additional guidance is discussed in the Articulate Online Module; “Introduction to MDSAP” slides 37 and 38.

77. How should an AO apply the audit model when sites are not responsible for all QMS activities?

- AO should determine the applicable QMS activities and corresponding audit tasks at each site included in the audit program. This can be done in Stage 1 of the audit.
- The audit time calculation procedure, MDSAP AU P0008, and associated spreadsheets, MDSAP AU F0008.1 (Audit Model 2013) and MDSAP AU F0008.2 (Audit Model 2017) can assist in identifying/planning audit tasks.

78. When should an AO employ a Technical Expert during an MDSAP audit?

ISO/IEC 17021-1 states: “The criteria for the selection of technical experts are determined on a case-by-case basis by the needs of the audit team and the scope of the audit.”

79. Can audit tasks be accomplished during pre-on-site audit activities?

Yes. RAs encourage AOs to use pre-audit planning, communications and other activities as a mechanism to complete or assist in the completion of audit tasks when appropriate.

80. Under what circumstances the AO audit may be considered not sufficient and RAs may perceive that an RA inspection is still required?

A RA inspection may be required if:

- An MDSAP audit report failed to provide evidence required to support market authorization decisions.
- An audit reveals public health safety concerns or fraudulent activity.
- Combination product device manufacturers may still require RA audits/inspections. See question #44 of the MDSAP Q&A document for additional guidance on combination products.
- Some situations when the manufacturer is currently subject to regulatory action (see question #57)

81. When should multi-site audit reports be submitted?

Audit reports must be submitted following the audit of each site, as stated in MDSAP AU P0027, Post-Audit Activities and Timeline Policy.

82. How should AOs handle sharing of audit reports with RAs that are not participating in MDSAP?

This should be worked out between the AO and its clients and spelled out in contracts when necessary.

83. Have the RAs defined the term "Public Health Threat"?

Public Health Threat is synonymous to the GHTF/SG2/N54R8:2006 term, Serious Public Health Threat – *Any event type, which results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action*.

84. How should AO auditors structure nonconformity statements?

Nonconformities should be written in accordance with GHTF/SG3/N19:2012, section 4.1; and section 5.0 Appendix A.

85. Why have the RAs imposed an initial response period of fifteen (15) calendar days?

RAs operate under time constraints that require an awareness of audit outcomes within a specified number of days. In order to make informed decisions about audit outcomes, the RAs must assess the manufacturer's response.

86. For a consistent interpretation, could the RAs define the term "implementation" in MDSAP AU P0027 and AS F0015.1?

- NCs cited by AOs after an MDSAP audit of a manufacturer: In the context of a manufacturer replying to nonconformities identified during an MDSAP audit, the term "implement" relates to the implementation of the actions specified in the manufacturer's correction and corrective action plan.
- Please refer to MDSAP AU P0027, sections 2 and 3.
- NCs cited by RAs following and assessment of an AO: In the context of an auditing organization replying to nonconformities identified during an RA assessment, the term "implementation" relates to the implementation, and

confirmation of the effectiveness of corrections and corrective actions, subsequent to the review and acceptance by the RAs of the AO's correction and corrective action plan.
- Please refer to MDSAP AS F0015.1 AO Nonconformity Process Flowchart.

87. What does the MDSAP certificate represent?

- The MDSAP certificate is an attestation by the AO that the facilities listed in the certificate have been audited against the listed criteria for the listed scope and found to conform to those requirements, including the regulatory requirements for the specified jurisdictions of the RAs.
- It does not represent a marketing authorization nor does it oblige participating Regulatory Authorities to issue any such marketing authorization or endorsement of the manufacturer or its devices.

88. Can suppliers be MDSAP certified?

Yes, if the supplier meets the participation criteria for any participating Regulatory Authority.

89. Can the RAs provide additional guidance on what should be recorded if the minimum N4 requirements cannot be fulfilled by an initial start-up AO?

- The RAs recognize that not all AOs will have the initial client participation to fulfill prerequisite annual experience requirements.
- AOs should document the circumstances and justify why requirements were not met in accordance with the principles for pre-requisite experience described in N4 Clause 6.2.
- RAs will consider each justification on a case-by-case basis.

90. Can MDSAP Survey results be periodically posted?

Yes. We plan to post them at six month intervals. However, if there is limited survey participation, the updates may not occur at this frequency.

91. Can the RAs clarify the requirements for the transfer of certification for participating manufacturers?

Transfer guidelines are currently being discussed by the RAs.

92. Can the RAs develop a single dispute resolution to minimize inconsistency if a manufacturer uses multiple AOs?

MDSAP P0031 – Documenting Differing Professional Opinion and Dispute Resolution Policy sets out a single mechanism for resolving disputes within the MDSAP program.

93. How long will RAs allow an MDSAP certificate to reference a jurisdiction where no product is distributed?

- MDSAP AOs can issue certificates referencing jurisdictions where the manufacturer does not yet have market authorization.
- Recognizing that market entry can take time, such certifications can be extended for a full three years.
- If at the end of three years, the manufacturer has not obtained or applied for market authorization, the requirements for the affected jurisdiction should be removed from the certificate until such time as the manufacturer can demonstrate implementation and effectiveness.

94. What is the process requesting a D-U-N-S number?

To meet the requirements described in the MDSAP AU P0029 Initial Manufacturer Audit and MDSAP Manufacturer Withdrawal Notification Procedure, medical device manufacturers will have to submit a D-U-N-S number(s) which may take time to obtain. For this reason, we encourage any facility, site, or organization that does not have their D-U-N-S number readily available to begin as soon as possible the process of obtaining that information.

A D-U-N-S number is required to uniquely identify each physical location of the business's facility or site (e.g., branches, divisions, and headquarters). A D-U-N-S number is a unique nine-digit sequence provided by Dun & Bradstreet. The D-U-N-S number is specific for each site. Each distinct physical location of an entity (e.g., branch, division, and headquarter) would be assigned a different D-U-N-S number.

The site-specific D-U-N-S number is a widely recognized business identification tool and serves as a useful resource for MDSAP in identifying and verifying certain business information submitted by a user.

If no D-U-N-S number has been assigned, a business entity may obtain one at no cost directly from Dun & Bradstreet. A new number may be obtained, or an existing number verified, by phone or online.

Note: It takes Dun & Bradstreet approximately 30 business days to process a new D-U-N-S number and communicate it via email. A business entity may receive a D-U-N-S number in approximately 10 business days for an expedited service fee. Please note that a business entity may not request or apply for a new D-U-N-S number on behalf of another business entity due to the verification procedures used by Dun & Bradstreet.

More information is available at the Dun & Bradstreet web page. See also the step-by-step instructions for obtaining a D-U-N-S number for businesses based either in the United States or abroad.

95. Can the manufacturer exclude a jurisdiction from the scope of an MDSAP audit?

A manufacturer may exclude the requirements of a jurisdiction where the organization does not intend to supply medical devices. In other words, audit criteria under the MDSAP include at a minimum ISO 13485 and the medical device regulations that are applicable in any of the participating regulatory authority's jurisdiction where the organization supplies medical devices.

96. What constitutes a counterfeit medical device or a fraudulent activity requiring to inform the Regulatory Authorities?

For all practical purpose:

- A counterfeit medical device is a medical device that is represented as, and likely to be mistaken for, an authentic medical device with a valid marketing authorization, or whose identity, nature and/or source are fraudulently misrepresented, or that is otherwise intended to defraud.
- A fraudulent activity is an intentional, reckless, dishonest and recurrent, or systematic, activity resulting, for example, in the production of a counterfeit product, or in the creation of fake records, false representations, or the alteration of genuine records to imply compliance. The unintentional failure to comply with requirements, despite due diligence, does not qualify as fraudulent activity.