MDSAP Chapter 2: Device Marketing Authorization and Facility Registration - Sue Finneran

Scope of MDSAP

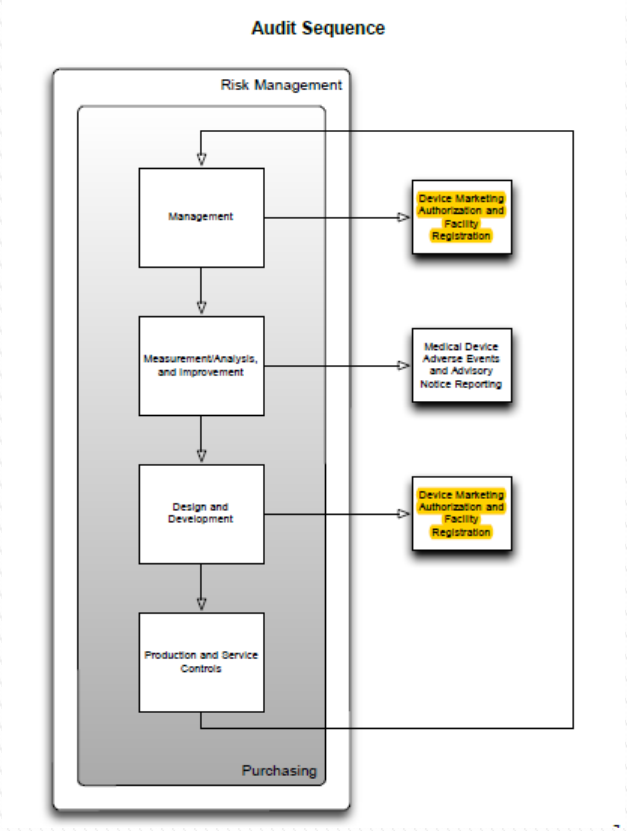
Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016)

- Quality System Regulation (21 CFR Part 820)
- SOR98/282 Canadian Medical Device Regulations
- Australian Therapeutic Goods (Medical Devices) Regulations (TG(MD)R Sch3)
- Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013)
- Japanese QMS Ordinance (MHLW MO 169)

Scope of MDSAP

The MDSAP audit process has two additional supporting processes:

- (1) Device Marketing Authorization and Facility Registration and
- (2)Medical Device Adverse Events and Advisory Notices Reporting



Supporting Processes

Audit Sequence

Device Marketing Authorization and Facility Registration

Can be audited as a linkage to the Management Process or the Design and Development Process.

Will provide objective evidence that the organization has:

1. Complied with the requirements to register facilities
2. Submitted Device listing information to authorities as applicable.
3. Obtained marketing authorization is the appropriate jurisdictions.
4. Has a process for assessing changes to marketing authorization or QMS as required

Chapter 2: Device Marketing Authorization and Facility Registration

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

2. Confirm the organization has receive the appropriate marketing clearance or approval in the regulatory jurisdictions where the organization markets their devices.

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

Regional differences

Auditor will want to know… based on geography?

- Who is the labeled manufacturer?
- Who is the importer?
- Who is the marketing authorization holder?
- Who is the sponsor?

In some regions Market Authorization is the responsibility of the Sponsor or Market Authorization Holder…

QMS Documents

- Supplier Evaluation
- Written Agreements/ Assignment of Responsibilities
- SOP to cover Regulatory Requirements
- Assessment of Changes
- Documented Impact to Marketing Authorization

US FDA – Establishment Registration

- Owner / operator must register establishment and submit listing information to FDA for all devices in commercial distribution
- Each establishment must also register (a place of business under one management at one general physical location)
- Annual establishment registration and listing
- Classification and links to product marketing applications

FDA- Establishment Registration

1. Initiates or develops specifications for a device that is manufactured by another party
2. Manufactures device for commercial distribution (for itself or another party)
3. Repackages or relabels device
4. Acts as an initial importer (listing can be done by manufacturer)
5. Manufactures components or accessories which are intended for health related purposes and are packaged and labeled for commercial distribution
6. Completes Sterilization
7. Acts as complaint file establishment

US FDA- Marketing application

Device Submission Types

- Class I exempt
- Class II premarket notification 510k
- Class III PMA

- Documentation should be on file to explain why changes do not require new submission

- Suggest detailed justification using guidance documents

Changes that may require submission

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

- New indications
- Labeling changes
- Facility change
- Change in sterilization
- Change in packaging
- Changes in performance / design spec
- Extension of exp date

510(k)

PMA

FDA Guidance

- Deciding When to Submit a 510(k) for a Software Change to an Existing Device - Guidance for Industry and Food and Drug Administration Staff
- Deciding When to Submit a 510(k) for a Change to an Existing Device - Guidance for Industry and Food and Drug Administration Staff
- Modification to Devices Subject to the Premarket Approval (PMA):the PMA Supplement Decision

Canada- Marketing Authorization

- *Manufacturer means a person who sells a device under their own name who is responsible for designing manufacturing, assembling processes, labeling, packaging, refurbishing… whether those tasks are performed by that person or on their behalf.*
- Company must apply for an establishment license
- Class II, III, IV must have a medical device license
- Must include a copy of the Quality management system certificate
- Class I only establishment license is required

Canada Device Modifications

(a) in the case of a Class III or IV medical device, a significant change;
(b) a change that would affect the class of the device;
(c) a change in the name of the manufacturer;
(d) a change in the name of the device;
(e) a change in the identifier of the device, 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;

Canada- Device Modifications

- **Guidance for the Interpretation of Significant Change of a Medical Device-2011**
- As per section 43 of the regulation, Annual statement of changes is due November 1st each year.
- Company must inform within 30 days of discontinuation
- Must submit new/ updated QMS cert within 30 days
- https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/forms.html

Australia Registration

Manufacturer of a medical device is the person responsible for design, production, packaging, labeling of the device before it is supplied under the person's name ; regardless if they carry out these operations.

Sponsor: Australian company (importer) will register products in ARTG(Australian Register of Therapeutic Goods.

Manufacturer must complete the following:

- Classify according to Australian classification rule
- Identify conformity assessment process
- Prepare Declaration of conformity
- Completion of a third party QMS assessment (13485)

Australia

AND…

Provide or have a written agreement to supply upon request:

- Evidence of conformity with essential principles and declaration
- Provide information to assist in annual reporting of high risk devices
- Provide feedback including complaints, reportable adverse events, advisory notices, and recalls.
- Permit TGA to inspect the manufacturer including pictures and video

Procedures should specify that the product is not exported unless Sponsor has been issued with a Certificate of Inclusion in the ARTG (Australian Register of Therapeutic Goods)

Australia- Device Application/ Changes

- Marketing Authorization is granted to Sponsor after inclusion in ARTG
- Manufacturer should notify their assessment body of
  - Substantial Changes to the QMS
  - Change to the type of Medical Devices to be applied
  - Class III / AIMD, a proposed change to design or intended performance
- Australian regulatory guidelines for medical devices

https://www.tga.gov.au/sites/default/files/devices-argmd-p2.pdf

Brazil

- **Manufacturer** means any person who designs, manufactures, assembles or processed finished devices including only sterilization and packaging
- GMP certification is a prerequisite for medical device registration- site inspection precedes registration request. (not required for class I/II)
- Importer will request device marketing authorization in the case of companies in US.
- Notification required class I, II/ Registration required III, IV
- Registration must be renewed every 5 years, notifications have no expiry date.
- Importer is considered to be the legal representative in Brazil is holds license to import store and distribute devices. Brazil Registration Holder

Brazil- Marketing Authorization

Significant Changes must be submitted for approval

- Features of safety and effectiveness, including measures to communication information
- Identification of device or its manufacturer/ site
- Indication for use, type of patient, environment
- Device classification
- Technical specifications of the device, including composition and other operational physical features
- Manufacturing method

Brazil- Device modifications

- Features of safety and effectiveness, including measures to communication information
- Identification of device or its manufacturer/ site
- Indication for use, type of patient, environment
- Device classification
- Technical specifications of the device, including composition and other operational physical features
- Manufacturing method
- Sterilization method
- New / additional manufacturer
- Material change
- Indications for use
- Operating conditions of use
- Sterile barrier packaging
- New software version
- Inclusion of new accessories
- Commercial name

General categories	Example

Japan- Marketing Authorization

- Marketing Authorization Holder mean person who resides in Japan and is granted a license for marketing..
- Class II, III, IV Market authorization application
- Class I notification for marketing.
- MAH submits application for marketing approval Submitted to PMDA
- MAH also submits “Application for QMS audit” An audit to and Registered Certification Body (RCB) if no valid QMS certificate.

Japan- Establishment Listing

Medical Device manufacturing site which conducts one of the designated process should be registered with PMDA

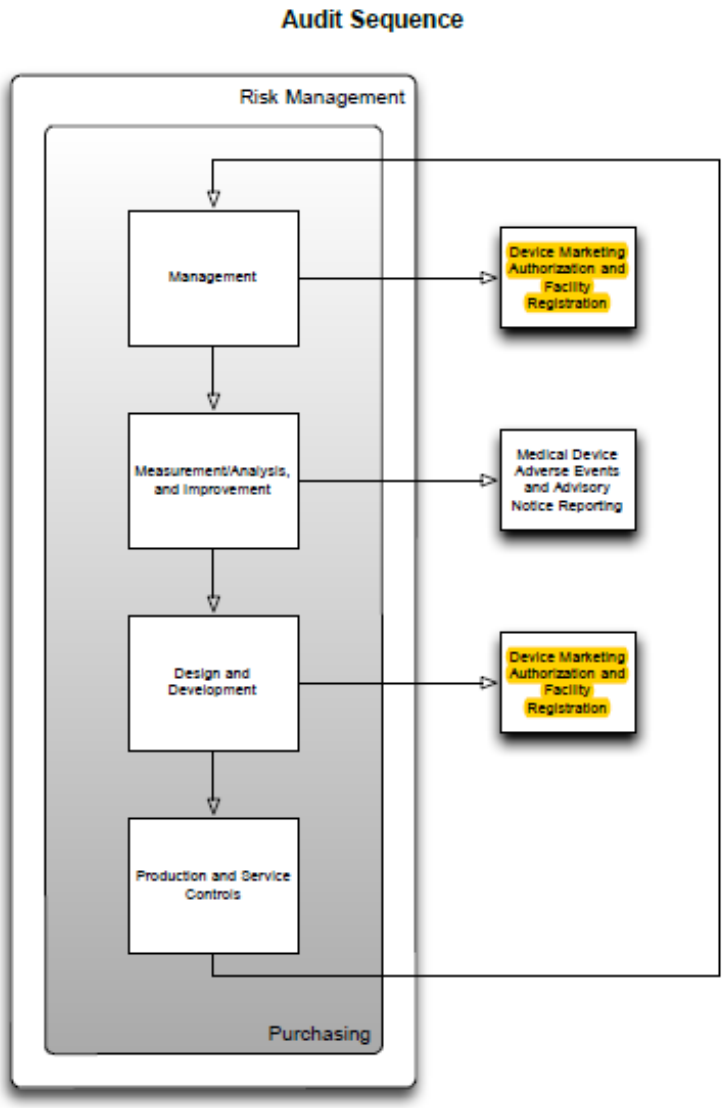
- Main designing
- Main Assembly
- Sterilization
- Domestic Storage before final release

Japan- device modifications

A change to a medical device may require a new application or a change notification. Changes that should be considered include:

- 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;

Links to other processes



Management

1.*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*

Review of documented procedures for marketing authorization, establishment registration, and regulatory assessment of changes.

Review of objective evidence that changes have been properly assessed and notifications have been completed: change to QMS Scope etc.

Management

4. *Review the manufacturer'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.*

Review of organization charts, job description, assignment of responsibilities, competency to complete regulatory filings and assessments.

Management

8. *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*

***Australia (TGA)**:*

If an Australian Sponsor undertakes an activity that is outsourced by the manufacturer, or required, to be under the control of the manufacturer, verify that the roles and responsibilities of the Australian Sponsor are documented in the manufacturer's quality management system and that the Sponsor is qualified and controlled as a supplier. For example, but not limited to; a labeling activity to ensure that the name and address of the Australian Sponsor accompanies the device [TG(MD)R Reg 10.2], the installation of a device, or the servicing of a device.

Canada (HC):

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

Management

10. Confirm that the 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.

- **Controls to ensure appropriate market authorization –** segregation by part number, location, sales order, etc**.**

Measurement Analysis and Improvement

7. *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.*

Australia (TGA):

Confirm that when a manufacturer plans to make a substantial change 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), the manufacturer notifies the auditing organization who will determine if an assessment of the change is required before implementation [TG(MD)R Sch3 P1 1.5(2)].

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].***TGA/ Canada page 31***

Design and Development

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

Australia (TGA):

When a manufacturer applies TG(MD)R Regs Division 3.2 and selects the Full Quality Assurance conformity assessment procedures [TG(MR)R Schedule 3, Part1], 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 16/2013: 4.1.7, 4.2].

Design and Development

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

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, which are equivalent to the requirement of design and development in ISO13485 [MHLW MO169:4.1].

Design and Development

5.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.

Australia (TGA):

Verify that the manufacturer has identified the relevant Essential Principles that apply to the medical device

[TG(MD)R Sch1 Essential Principles].

United States (FDA):

For the selected device(s), verify that the organization has the appropriate marketing clearance [510(k)] or pre-market approval (PMA) if distributing the devices in the United States [21 CFR 807].

Design and Development

13. Verify that design and development changes were controlled, verified (or where appropriate validated), and approved prior to implementation.

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)].

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].

Design and Development

13. Verify that design and development changes were controlled, verified (or where appropriate validated), and approved 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 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- 2-5.17, 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 organization obtained a new 510(k) or supplement to the pre-market approval if required [21 CFR 807].

Purchasing

5. Verify that suppliers are selected based on their ability to supply product or services in accordance with the manufacturer's specified requirements.

Australia (TGA):

If the manufacturer outsources to the Australian Sponsor; a quality management system requirement, an obligation on the manufacturer from the Australian regulations, or where the manufacturer appoints the Sponsor to act on their behalf for dealings with the TGA, verify that the manufacturer treats the Sponsor as a supplier and has adequate supplier controls included in a written agreement [TG Act 41FN] for those activities. For example, 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)], adverse event reporting, as the first point for handling customer complaints, or as an intermediary in recalls of products [TG(MD) Regs Schedule 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) Regs Schedule 3 - Part 1:1.5, 1.9], or other matters that may be required to allow the Sponsor to fulfill market authorisation conditions [TG Act Part 4-5 Div 2].

Canada (HC):

Verify that any regulatory correspondent used by the manufacturer is treated as a supplier and is adequately qualified.

Purchasing

5. Verify that suppliers are selected based on their ability to supply product or services in accordance with the manufacturer's specified requirements.

Japan (MHLW):

(For Marketing Authorization Holder)

If the Marketing Authorization Holder (MAH) has outsourced any process that affects product conformity with requirements, to a Registered Manufacturing Site(RMS), then verify the MAH has performed the necessary verification that the RMS has an appropriate quality management system. If the site of a supplier is a Registered Manufacturing Site, then verify the MAH has performed the necessary verification that the supplier has an appropriate quality management system [MHLW MO169: 65].

(For Registered Manufacturing Site)

If the RMS has outsourced any process that affects product conformity with requirements, to another RMS, then verify the outsourcing RMS has performed the necessary verification that the outsourced RMS has an appropriate quality management system. If the site of a supplier is a RMS, then verify the purchase controlling RMS has performed the necessary verification that the supplier has an appropriate quality management system [MHLW MO169: 65].

Thank you for your Attention

Questions

Comments???