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Review Article

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Audit requirements and expectations, The good and better about MDSAP Regulations

Vidya Sagar*, Deepak Patel, Piyush Patel, Anil Kumar, Avni Rana, Bhavin Trivedi, Vipul Bavisa

Aegis Lifesciences Pvt. Ltd, Ahmedabad, Gujarat, India – 382213

Abstract

The most sure-fire way to pass MDSAP audit with flying colours is to have an effective Quality Management System (QMS). Having a good QMS will make sure work is correctly documented, kept up to date, and easy to present to an auditor. For regulators too, it means a reduced burden. There is pooling of regulatory resources. The audits are conducted by Auditing Organizations designated by the regulatory bodies. The MDSAP program is expected to improve audit predictability because a standardized audit model has been introduced. Every audit follows the same set of steps. For the first time, a grading system is introduced for noncompliance. This approach helps reduce subjectivity. MDSAP has a very rigid auditing process to ensure the proper market authorizations have been obtained and facility registrations have occurred but not represent Marketing Authorization. Recently proposed greater alignment of FDA Quality System Regulation (QSR) with ISO 13485, would bring US QMS requirements for medical device manufacturers closer in line with quality system requirements in markets such as the European Union, Japan and Australia, potentially streamlining medical device registration and compliance processes across the US and other markets.

Keywords: Auditing, Authorization, MDSAP, IMDRF, Medical Device, QMS, Regulations, Quality Management System (QMS)

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*Corresponding author

1. Introduction

1. MDSAP - IMDRF

The International Medical Device Regulators Forum (IMDRF) External Link Disclaimer recognizes that a global approach to auditing and monitoring the manufacturing of medical devices could improve their safety and oversight on an international scale. At its inaugural meeting in Singapore in 2012, the IMDRF identified a work group to develop specific documents for advancing a Medical Device Single Audit Program (MDSAP).

The Medical Device Single Audit Program allows an MDSAP recognized Auditing Organization to conduct a single regulatory audit of a medical device manufacturer that satisfies the relevant requirements of the regulatory authorities participating in the program. (1)

International partners that are participating in the MDSAP include:

1.1 MDSAP Members (2-4)

a. Therapeutic Goods Administration of Australia
b. Brazil's Agência Nacional de Vigilância Sanitária
c. Health Canada
d. Japan's Ministry of Health, Labour and Welfare, and the Japanese Pharmaceuticals and Medical Devices Agency
e. U.S. Food and Drug Administration

1.2 MDSAP Official Observers:

a. European Union (EU)
b. United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA)
c. The World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme

1.3 MDSAP Affiliate Members: (New)

a. Argentina's National Administration of Drugs, Foods and Medical Devices (ANMAT)

b. Republic of Korea's Ministry of Food and Drug Safety

c. Singapore's Health Sciences Authority (HSA)

From 01 January 2014 to 31 December 2016, FDA, alongside its international partners, participated in a Medical Device Single Audit Program Pilot. On 29 June 2017, a report was generated summarizing the outcomes of prospective "proof-of-concept" criteria established to confirm the viability of the Medical Device Single Audit Program. The outcomes documented in the Final MDSAP Pilot Report are based on data generated during the three (3) year pilot. (5)

Based on its evaluation of the MDSAP Final Pilot Report, the MDSAP Regulatory Authority Council (the international MDSAP governing body) determined that the MDSAP Pilot had satisfactorily demonstrated the viability of the Medical Device Single Audit Program.

2. MDSAP Work

MDSAP uses recognized third-party auditors – auditing organizations (AOs) – to conduct a single quality management system audit that satisfies the requirements of multiple regulatory authorities. The MDSAP Pilot covered the requirements of ISO 13485:2003 plus Good Manufacturing Practice (GMP) requirements for each applicable regulatory authority. For example, for the US, the GMP requirements of 21 CFR 820 were addressed; for Brazil, the GMP requirements of RDC ANVISA 16/2013 were applied. Manufacturers only needed to comply with the regulations from the jurisdictions where they sell their products. The MDSAP program is mandatory for medical device licence in Canada. In other countries, it is still a voluntary program.

Participation in the MDSAP Pilot was voluntary, and device manufacturers chose which regulatory authorities would receive the MDSAP audit report, from just one to all five countries. In addition, manufacturers chose their own AOs, and they paid for the AO's services. MDSAP has added ISO 13485:2016 requirements to the audit model, and it will continue as a voluntary program – with the exception of Canada, where starting in 2019 manufacturers selling in Canada will be required to have a valid MDSAP certificate. (6)

3. MDSAP Certificate Represent

The MDSAP certificate indicates that a manufacturer complies with the regulatory requirements for the markets defined in the certificate. The certificate does not represent marketing authorization, nor does it require any regulatory authority to issue a marketing authorization or endorsement to the device manufacturer.

4. Potential Benefits of MDSAP for Medical Device Organizations

i. Device manufacturers that choose to participate in MDSAP may expect:

ii. Fewer regulatory audits

iii. More predictable audits and outcomes through:

a. Using a standard MDSAP audit model

b. Grading of nonconformities using objective criteria to characterize the significance of the finding(s)

c. Reporting of audit outcomes using a standard report template

d. Monitoring of the AOs by the participating regulatory authorities

iv More efficient marketing authorization applications in countries where a quality management system audit is a prerequisite

Global access to safe, high-quality devices requires continued work toward harmonizing requirements and audit approaches across the globe. Manufacturer participation, however, is the key to MDSAP's success, and it is too early to tell how many manufacturers will join.

Then take our Internal Auditing to MDSAP class. Designed for experienced auditors, participants learn how to apply MDSAP's process-based audit approach and align your current internal audit program to the MDSAP requirements. You will also take a detailed look at country-specific requirements for the five MDSAP participant markets.

5. Medical Device Single Audit Program Certification is a Rolling Three-Year Process (1)

The MDSAP certification cycle is a series of three audits conducted over a three-year period.

Your first certification audit will be a comprehensive look at your QMS conducted in accordance with ISO/IEC 17021-1:2015. There are two initial stages: Stage 1 and Stage 2.

The Auditing Organization (AO) will first conduct a Stage 1 audit focused on evaluating your QMS documentation. Basically, the auditors want to see if you are prepared for the rigorous Stage 2 audit, during which they will assess your actual compliance with ISO 13485 plus the specific nuances of the US, Japanese, Canadian, Australian, and Brazilian QMS requirements. Your Stage 2 audit may occur the next day after your Stage 1 audit, or weeks later. Be prepared for it to happen immediately.

In Years 1 and 2 following your initial certification audit, the AO will conduct surveillance audits focusing on any changes to your products or QMS processes during the previous year. After three years, the AO will return to conduct a recertification audit. The surveillance audits differ from your initial certification audit because they will focus on evaluating your ability to continue meeting QMS requirements under the MDSAP. After that, the cycle continues – two annual surveillance audits followed by a recertification audit.

The US Food and Drug Administration has published a highly anticipated proposed rule to harmonize its medical device quality management system (QMS) regulation, 21 CFR Part 820, to the ISO 13485 QMS standard. (7)

Recently, FDA's proposed rule "would harmonize quality management system requirements for FDA-regulated devices with requirements used by many other regulatory authorities around the world,". Greater alignment of FDA Quality System Regulation (QSR) with ISO 13485, first proposed by the regulator in May 2018, would bring US QMS requirements for medical device manufacturers closer in line with quality system requirements in markets such as the European Union, Japan and Australia, potentially streamlining medical device registration and compliance processes across the US and other markets. (6-13)

6. Preparing for a Medical Device Single Audit Program Audit

If you have already scheduled your MDSAP audit with your Auditing Organization, here are some tips on how to prepare.

I. MDSAP Actors (14)

a) **Regulatory authorities (RAs):** They are responsible for designating the Auditing Organizations (certification bodies like BSI, TUV etc.). There are several criteria that these organizations must fulfill to be designated. The regulatory bodies continue to monitor the program and have the final say. The audit reports are sent to them.

b) **Auditing Organization (AO):** They are selected only if they satisfy the criteria involved. They plan, conduct, and report the audit to the regulatory authorities. The audits are conducted as a three-year cycle: The initial audit comprises of Stage 1 (documentation and preparedness audit) and then a Stage 2 (implementation) audit in the first year is followed by 2 surveillance audits and a re-certification audit in the third year.

c) **Manufacturers:** They engage with the auditing organizations just like the QMS audits, and they schedule the audits. If there are non-conformances, they need to provide the corrective action plan and evidence.

II. MDSAP Audit Process

The MDSAP audit follows a specific sequence and approach so that the audits are conducted in a logical, focused, and efficient manner by the auditors. There are four primary processes and two supporting processes. Purchasing is considered an enabling process. (14, 15)

a. Primary processes:

(1) Management

(2) Measurement, Analysis and Improvement

(3) Design and Development

(4) Production and Service Controls

(5) Purchasing

b. Supporting Processes:

(6) Device Marketing Authorization and Facility Registration, and

(7) Medical Device Adverse Events and Advisory Notices Reporting.

The last two processes fulfill the regulatory requirements of the jurisdictions.

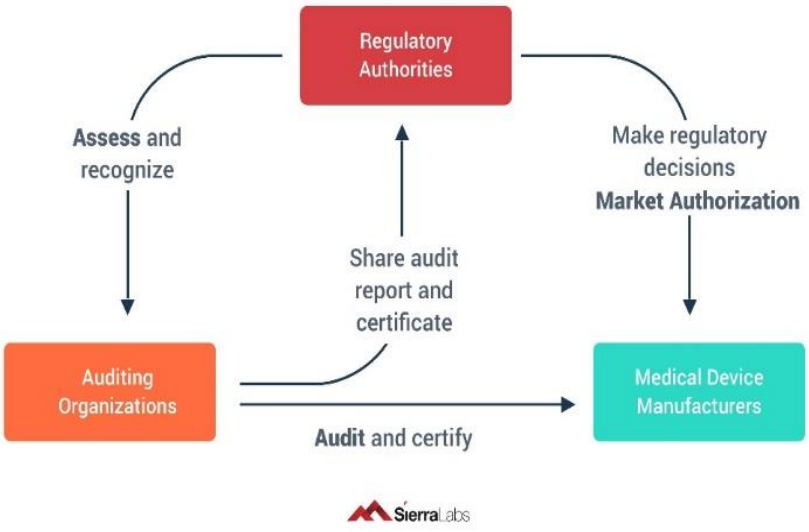

Figure 1: MDSAP audits schematic design (Courtesy Sierra Labs) (15)

MDSAP audit will cover 7 main areas (15):

- Management

- Measurement, Analysis, and Improvement
- Design and Development
- Production and Service Controls
- Purchasing
- Device Marketing Authorization and Facility Registration
- Medical Device Events and Advisory Notices Reporting

With 4 main focal points:

- Risk activities
- Outsourced processes
- Design and process validations
- Change management and associated risks

I. Create your own report card.

Examine your past nonconformities from your Notified Body and internal audits, and grade them using the MDSAP nonconformities grading system. This will give you an internal report card that can be useful in elevating the importance of the initiative to management if resources are scarce.

II. Open a CAPA for gaps and be sure to make progress.

Even if an AO finds a non-conformance during the audit, having a CAPA in progress minimizes the sting as long as the appropriate containment is effective.

III. Be prepared to address regulatory issues.

MDSAP audits have a broader scope that pulls regulatory into the fray. You will be asked questions related to your registration processes, adverse event notification system, how regulatory strategy impacts product design, and more. Expect a heavy emphasis on risk! Make sure you have someone from Regulatory on your audit team.

F1: An MDSAP Certification Audit Is Rigorous

Remember, this is not a typical FDA inspection or ISO 13485 audit with a few extra RA/QA questions related to Canada, Brazil, etc. Many companies have endured initial MDSAP certification audits ranging between one and two weeks long. And you'll be delighted to know that if your AO is also your European Notified Body, you may be able to schedule your EN ISO 13485:2016 audit the following week. You'll likely have two auditors attend your MDSAP certification audit. They will probably split up, which means you may need to have two escorts, two sets of Subject Matter Experts (SMEs), and maybe even two conference rooms available. If you work for a small company and you don't have duplicates of anything, just make sure you have everything quickly accessible.

Don't be surprised if an observer from FDA, Health Canada, or Brazil ANVISA also shows up. As part of the recognition process for AOs, regulators will observe three audits plus one each following year to maintain the AO's recognition. It's important to understand that the observer is there to assess the AO, not audit you! During the audit, make sure you address the auditors and not the observer.

F2: MDSAP Audits Are on a Strict Time Schedule So You Need to Be Organized!

The audit is timed, with very specific durations for each process. This means you have to produce documentation very quickly. Consider pre-printing documents or create a dedicated MDSAP folder with electronic versions that can be quickly accessed. Don't hunt for documents on your company intranet while displaying your search attempts and other "interesting documents" for all to see on the conference room screen – a task made infinitely harder when someone is looking over your shoulder. We recommend having only one "back room" where you store documents for easy access and so you can compare notes on where each auditor is going.

Make sure you study the published MDSAP Audit Model to figure out where the auditor will go next. Remember is a guide (it's not a secret!) and by studying it you can anticipate which links might be followed and what questions may come next.

F3: Be Mindful of the "Process Approach" and Shiny Object Syndrome

MDSAP audits follow a process approach. This means an AO auditor may follow linkages and threads, whereas an internal auditor will usually look at one functional area at a time. For example, if an AO auditor is examining Receiving and Inspection, he/she may ask about process inputs such as where the testing methods and specifications originate. The answer is likely Design, so the auditor may chase the "shiny object" and visit the R&D department next. If you took that approach during an internal audit, the R&D manager would say, "Hey, our audit isn't supposed to happen until September. I'm busy. Why are you here now?"

Following the process approach during internal audits can be disruptive and annoying to co-workers, but cooperation is not a choice during an AO certification audit and your co-workers need to understand this. With that reality in mind, you can still have an annual audit program with a schedule, but keep really good notes so you can pick up threads left dangling from the last audit.

Typically, in internal audits we see nonconformities that might be related to multiple areas or processes. You might choose to write up two nonconformities or, rather than "double-dipping" and writing a nonconformity for each area, you might write one nonconformity and link the two issues. Each organization will have to determine their process, keeping in mind that the number of nonconformities from an internal audit might trigger an escalation to management. So, if your process changes and you decide to write more nonconformity, make sure management and the rest of the organization understand and recalibrate for the new escalation triggers.

F4: Maintaining Your Medical Device Single Audit Program Certification

Some large medical device companies have an auditing department at the enterprise level. These auditors travel around and audit many sites over a year. They can mimic the MDSAP schedule and be at one site for a week, and then not return for a year. Smaller companies really have to organize and plan so they can cover all the processes that will to be addressed during the actual MDSAP audit. The key is to plan and document the rationale for your approach.

F4: Proving Your Competency

Preparing for the initial certification audit may stress many RA/QA managers, but maintaining compliance is the primary concern of Auditing Organizations. This is becoming a bigger issue, because many Auditing Organizations are asking companies to demonstrate that their internal auditors are qualified to maintain MDSAP compliance. Even if you have done dozens of internal ISO 13485 or FDA QSR audits, proving proficiency in MDSAP can be difficult. You cannot simply say you read the MDSAP Audit Model or each participating country's regulations.

7. Conclusion

With a single audit, the manufacturer can now approach ISO 13485: 2016 requirements along with the regulatory compliance of the five participating jurisdictions which are built into the QMS requirements. There are no additional requirements and the need for multiple audits is eliminated. For regulators MDSAP reduces burden. There is pooling of regulatory resources. The audits are conducted by Auditing Organizations designated by the regulatory bodies. The MDSAP program is expected to improve audit predictability because a standardized audit model has been introduced. Every audit follows the same set of steps. For the first time, a grading system is introduced for noncompliance. This approach helps reduce subjectivity, meaning there are no surprises.

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Conflict of Interest

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