Medical Device Single Audit Program (MDSAP) - Introduction

March 2017
Agenda

What is MDSAP?
How does MDSAP work?
How does MDSAP fit with other certifications?
What is MDSAP
Medical Device Single Audit Program (MDSAP)

- Result of one of the 6 Working Groups created by the International Medical Device Regulatory Forum (IMDRF)
- Global approach to auditing and monitoring the manufacturing of medical devices to ensure safe medical devices
- Objective: to jointly leverage regulatory resources to manage an efficient, effective, and sustainable single audit program focused on the oversight of medical device manufacturers.
International Medical Device Regulatory Forum (IMDRF)

• IMDRF born February 2011 as a forum to discuss future directions in medical device regulatory harmonization.

• Voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF)

• Accelerate international medical device regulatory harmonization and convergence.
International Medical Device Regulatory Forum (IMDRF)

• IMDRF Management Committee (MC) regulators:
  • Australia, Brazil, Canada, China, the European Union, Japan, Russia, and the United States of America

• Observers:  • WHO - World Health Organization
  • APEC LSIF (Asia Pacific Economic Cooperation Life Science Innovation Forum)

• Affiliate Organizations:  • Asian Harmonization Working Party
  • Pan American Health Organization

• Working Groups:
  • Standards; MDSAP; Submissions; UDI; NCAR; Software
MDSAP Objectives

• Develop, manage, and oversee a single audit program that will allow a single regulatory audit to satisfy the needs of multiple regulatory jurisdictions

• To promote greater alignment of regulatory approaches and technical requirements

• To promote consistency, predictability, and transparency of regulatory programs
MDSAP Benefits

• Single Audit by Auditing Organization (AO) would:
  • minimize medical device manufacturing disruptions due to multiple regulatory audits
  • leverage regulatory resources
  • provide global benefit both on short term goals and longer term goals by IMDRF regulators – harmonization
  • benefit patient health and patient access
MDSAP Pilot

• Pilot started in January 2014 (for 3 years, to Dec 2016)
• Certification Bodies from participating member states can apply to become AO’s
  • Initially CMDCAS (Canada) recognized registrars
• Office audits and witnessed audits required
  • Conducted by Regulatory Authorities (RAs)
• September 2014 AO’s started conducting audits
• Operational program started January 2017
How will Regulatory Authorities utilize MDSAP and the resulting audit report/certificate?

United States:

- FDA will accept the MDSAP audit reports as a substitute for FDA routine inspections.
- Inspections conducted “For Cause” or “Compliance Follow-up” by FDA will not be affected by this program.
- MDSAP would not apply to any necessary pre-approval or post approval inspections for Premarket Approval (PMA) applications.
United States (continued):

• The FDA will review MDSAP Pilot 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 AO.

• Firms have one month to provide their full response to critical nonconformities (grade 4 and 5) to the AO (as opposed to 15 working days following a FDA inspection)

• FDA recognizes MDSAP audit reports as a substitute for FDA Establishment Inspection Reports (EIRs)
Canada:

• 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 CMDR, until January 2019.

• From January 2019, Health Canada will only accept MDSAP certificates.

• As of 1 January 2019, manufacturers must have submitted an MDSAP certificate in order to avoid suspension of license.
Brazil:

• The Brazilian National Health Surveillance Agency – ANVISA will utilize the outcomes of the program, including the reports, to constitute an important input on ANVISA’s pre-market and postmarket assessment procedures, providing, when applicable, key information that are expected to support regulatory technical evaluation on these issues.
Brazil (continued):

• 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.
Australia:

- The Therapeutics Goods Administration - TGA will use an MDSAP audit report as part of the evidence that is assessed for compliance with medical device market authorization requirements unless the medical device is otherwise excluded or exempt from these requirements or if current policies restrict the use of MDSAP audit reports.
Japan:

• Japan’s Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA)

• For manufacturers intending to put medical devices of class II, III or IV on the Japanese market, an MDSAP audit report can be utilized for a desk review instead of a premarket inspection performed by PMDA or registered certification bodies in Japan.

• An MDSAP audit report can also be utilized in this manner for periodical post market inspections.

• Trial period June 2016 to March 2018 (exceptions such as animal/human tissue, radioactive IVDs).
How MDSAP Works
How Does MDSAP Work?

Regulatory Authorities
- Assessments
- Reports

Auditing Organizations
- Audits
  - NCs/CAPs

Manufacturers
  - NCs/CAPs
MDSAP Operations – Ensuring Consistency

• Standardized Audit and Assessment Models
  • Auditing of a Manufacturer by an MDSAP Recognized AOs
  • Assessment of MDSAP AOs by participating RAs
• IMDRF (MDSAP Regulatory Authority Council)
  • Initial Recognition, Surveillance, and Re-Recognition Criteria for MDSAP Recognized Auditing Organizations
  • Standardized Recognized AO Auditor Competency and Competency Maintenance Requirements
  • Standardized Regulatory Authority Assessor Competency and Competency Maintenance Requirements
MDSAP Information – Official Sources

- Pilot Program Announcement (brief description) - [link](#)
- Program Announcement (including benefits) - [link](#)
- MDSAP FAQs - [link](#)
- Eligible Auditing Organizations – [link](#)
- MDSAP Audit Procedures & Forms – [link](#)
- Website = www.fda.gov/MedicalDevices/InternationalPrograms/MDSAPPilot/
Medical Device Single Audit Program (MDSAP) Pilot

The International Medical Device Regulators Forum (IMDRF) 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).

Beginning in January 2014, FDA will be participating in a MDSAP Pilot alongside other international partners. FDA will accept the MDSAP audit reports as a substitute for routine Agency inspections.

The MDSAP Pilot is intended to allow MDSAP recognized Auditing Organizations to conduct a single audit of a medical device manufacturer that will satisfy the relevant requirements of the medical device regulatory authorities participating in the pilot program.

International partners that are participating in the MDSAP Pilot include:

- Therapeutic Goods Administration of Australia
- Brazil’s Agência Nacional de Vigilância Sanitária
- Health Canada
- Japan’s Ministry of Health, Labour and Welfare, and the Japanese Pharmaceuticals and Medical Devices Agency
- The World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme and the European Union (EU)
Audit Cycle

• Three Year Audit Cycle
  • Initial Audit (Stage One & Stage Two)
  • Surveillance Audits (Years 1 and 2)
  • Re-audit (Recertification Audit)
    • Note that not all Regulatory Authorities require “certificate”

• Other Possible Audits
  • Special Audits
  • Audits by Regulatory Authorities
  • Unannounced Audits
MDSAP Audit Procedures

• Audit Procedures & Forms available, e.g., relevant documents
  • Audit Model   AU P0002.003 & .004 (81 pages)
  • Companion Document   AU G0002.1.003 & .004 (122 pages)
  • Audit Time Determination Procedure   P0008.004
  • Nonconformity Grading   GHTF/SG3/N19:2012
  • Post-Audit Activities and Timeline Policy   MDSAP AU P0027.004
  • Others on “MDSAP Documents” page
MDSAP Audit Model

- Follows the process approach, top down
- Four Primary processes
  - Management
  - Measurement, Analysis and Improvement
  - Design and Development
  - Production and Service Controls
- Three Supporting Processes
  - Purchasing
  - Device Marketing Authorization and Facility Registration
  - Medical Device Adverse Events and Advisory Notices Reporting
Requirements

• ISO 13485 :2003 or :2016

• Country-specific requirements (where applicable)
  • If shipping product to an MDSAP jurisdiction, country-specific requirements WILL apply (cannot opt out)
  • TGR Sch 3, RDC 16, MO 169, CFR 21 Part 820
  • Clearly identified in the Audit Model & Companion Document
MDSAP Nonconformity Grading

• Definition of nonconformity unchanged (non fulfillment of requirement)
MDSAP Nonconformity Grading

- Nonconformity identification
- Step 1 – Initial Grading – Impact & Occurrence
- Step 2 – Escalation rules
- Final nonconformity grading
MDSAP Nonconformity Initial Grading - Impact

• Indirect QMS Impact
  • Indirect influence on safety and performance of medical device
  • ISO 13485:2003 clauses 4.1 through 6.3
  • Considered “enablers” for QMS processes to operate

• Direct QMS Impact
  • Direct influence on safety and performance of medical device
  • ISO 13485:2003 clauses 6.4 through 8.5
  • Considered to have direct influence on design, and manufacturing controls
MDSAP Nonconformity Initial Grading - Occurrence

• First
  • Nonconformity in a particular sub-clause (X.X.X)
  • First time = not observed in two previous QMS audits

• Repeat
  • Nonconformity in the same sub-clause (X.X.X)
  • Identified within either of two previous QMS audits
MDSAP Nonconformity Escalation Rules

- Escalation
  - Absence of documented process or procedure
  - Release of a nonconforming medical device
  - Escalation by 1 level on the Matrix (next page)
### MDSAP Nonconformity Grading - Final

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<td>First Occurrence Escalation Criteria</td>
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Maximum grade is a 5.
## MDSAP NC Grading & Exchange Form

### Related Regulatory Requirement

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<th>Task-related clauses</th>
<th>Clause</th>
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<td>Australia TG (MD) R &amp; TG Act</td>
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<tr>
<td>Brazil RDC ANVISA</td>
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<td>Canada MDR</td>
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<tr>
<td>Japan MHLW MO169 &amp; PMD Act</td>
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<td>USA 21 CFR</td>
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### NC Grading Attributes

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<th>Lack of</th>
<th>Grade</th>
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</table>

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<th>Corrective Action</th>
<th>Closed?</th>
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</table>
Post Audit Activities and Timelines

(Ref. MDSAP Document AU P0027)

• $D_0 = \text{Audit end date}$

• $D_0 + 15 \text{ Calendar Days} - \text{Manufacturer to provide remediation plan}$
  • Outcome of investigation of all NCs and cause(s)
  • Planned correction and Planned corrective action

• $D_0 + 30 \text{ Calendar Days} - \text{Manufacturer to provide evidence of implementation of remediation actions addressing any Grade 4 or 5 NCs}$
  • Outcome of investigation of NC and its cause(s)
  • Planned correction and Planned corrective action
Post Audit Activities and Timelines

(Ref. MDSAP Document AU P0027)

- $D_0 + 5$ Working Days - AO to inform Regulatory Authorities
  - 1 or more Grade 5 NCs or 3 or more Grade 4 NCs
  - Any public health threat, fraudulent activity, counterfeit product

- $D_0 + 45$ Calendar Days - AO to provide complete audit report package for any audits meeting above 5-day notice criteria

- $D_0 + 90$ Calendar Days - AO to provide complete audit report package for any audits not meeting above 5-day notice criteria
Post Audit Activities and Timelines

• Unannounced Audits
  • Upon request of Regulatory Authority
  • Triggered by 1 or more Grade 5 NCs or 3 or more Grade 4 NCs
  • Typically 6 to 9 months post-audit
  • By two auditors, not less than one day
  • Could take place at critical supplier
Access to Reports

• All Regulatory Authorities that are part of MDSAP gets the reports
• MDSAP Database expected to be implemented once formal program commences – controlled access
How MDSAP fits with other certifications and Timelines
For Manufacturers Currently Holding ISO 13485, ISO 13485 CMDCAS, CE MDD/IVD/AIMD Certificates

- Check with current Certification / Notified Body whether authorized AO
- Investigate best plan for timing of MDSAP audit considering:
  - Current ISO audit cycle/expiry and CMDCAS termination date
  - Transition plans to ISO 13485:2016, considering deadlines
  - Consider business plans (new markets?)
- Note that new marketing authorizations from a Regulatory Authority will require a full audit (rather than a surveillance audit)
- MDSAP audit includes ISO 13485
- Investigate with CB/NB whether the audit can include CE requirements
## Timelines - QMS

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Drivers for Manufacturers

- Single audit saves time, resources, money
- Speed to market (reduce ANVISA wait)
- Routine audits are planned & scheduled with AO
- Improved predictability – one audit rather than multiple
- Canada requirement – January 2019
Enrollment continues to grow

MDSAP Participating Manufacturer Sites - Calendar Year

- Number of Firms Added
- Cumulative Total

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<tr>
<th>Quarter</th>
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<tr>
<td>Q4</td>
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BSI Status

• BSI assessed early 2014 (first)
• Commenced audits fall 2014 (first)
• Completed assessments and witness audits (first)
• Continuing audits through present time (100+)
• Continued & increasing interest from manufacturers
# Update – AO’s  (as of 1 March 2017)

<table>
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<tr>
<th>Auditing Organization</th>
<th>Application Received</th>
<th>Authorized to Conduct Audits</th>
<th>Recognition</th>
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Focus – Key Points for Manufacturers
Key Points – for Manufacturers

• **Canada** – Health Canada QMS section:


Key Points – for Manufacturers

MDSAP Transition Reminder

In accordance with Health Canada’s announced MDSAP transition plan, CMDCAS certificates will no longer be accepted after December 31st 2018. Manufacturers will be required to submit valid MDSAP certificates by no later than January 1st, 2019 in order to maintain their medical device licences. To facilitate a smooth transition, Health Canada is encouraging manufacturers to begin the transition process in a timely manner to ensure compliance with the regulatory requirements at the end of the transition period. More information on the MDSAP transition plan and the regulatory requirements can be found in a Health Canada notice.

- Other MDSAP related information in “Activities – International”
Key Points – for Manufacturers

- **Q4 from FAQ document excerpt:**
  
  **Q4: I sell devices only in Canada. Do I still need the MDSAP certificate?**
  
  **A:** Yes. All manufacturers must transition from CMDCAS to MDSAP certificates to meet the quality management system requirements of the [Medical Devices Regulations](#). For manufacturers who only sell in Canada, the regulatory requirements of the other MDSAP participants (United States, Brazil, Australia, and Japan) will not be audited. Distributors and retailers are not subject to the quality management system requirements.

- **Cannot opt out IF shipping to any of 5 jurisdictions**
  - refer to excerpt from Description/Announcement document:

  Can the manufacturer exclude a jurisdiction from the scope of an MDSAP pilot 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 Pilot include at a minimum ISO 13485:2003 and the medical device regulations that are applicable in any of the participating regulatory authority’s jurisdiction where the organization supplies medical devices.
Key Points – for Manufacturers

• Cannot opt out IF shipping to any of 5 jurisdictions
  • refer to excerpt from FAQ document Question 100:

100. Can the manufacturer exclude a jurisdiction from the scope of an MDSAP pilot 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 Pilot include at a minimum ISO 13485:2003 and the medical device regulations that are applicable in any of the participating regulatory authority’s jurisdiction where the organization supplies medical devices.
Key Points – for Manufacturers

• Manufacturers’ Feedback
  • Audits followed a set sequence of activities which allowed for planning for employee participation
  • An increased focus on risk helped to drive risk-based thinking deeper into their organization
  • Strong focus on product and process quality and risks associated with change implementation
  • Cost benefit for a single audit for multiple jurisdictions
  • Need to get other jurisdictions to embrace the program to enhance benefit
  • Less business disruption
  • Consistent audit process