MDSAP: FDA Insights and Perspectives

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What is MDSAP?
What is MDSAP?

The Medical Device Single Audit Program (MDSAP) is a regulatory audit program that was jointly developed by four jurisdictions.

It allows a medical device manufacturer to have a single quality management system audit to satisfy the requirements of all participating regulatory authorities.
What is MDSAP?

The four initial participating regulatory authorities (RAs):

- Therapeutic Goods Administration (TGA)
- Agência Nacional de Vigilância Sanitária (ANVISA)
- Health Canada (HC)
- Food and Drug Administration (FDA)
Formal Statement of Cooperation Regarding the Development of a Medical Device Single Audit Program

Australia
Therapeutics Goods Administration (TGA)

Brazil
Agência Nacional de Vigilância Sanitária (ANVISA)

Canada
Health Canada/Santé Canada

United States of America
Food and Drug Administration (FDA)
Formal Statement of Cooperation Regarding the Development of a Medical Device Single Audit Program

The goal of the MDSAP is to provide for more effective, efficient and less burdensome regulatory oversight of the quality management systems of medical device manufacturers.

The implementation of the MDSAP is intended to allow for a single audit to satisfy the regulatory requirements of the Participants.

Source: Statement of Cooperation
The objectives of the MDSAP are to:

Operate a single audit program that provides confidence in program outcomes;

Enable the 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 Participants, while respecting the sovereignty of each country;

Source: Statement of Cooperation
The objectives of the MDSAP are to (continued):

Promote, over the longer term, greater global alignment of regulatory approaches and technical requirements based on international standards and best practices;

Promote consistency, predictability and transparency of regulatory programs by standardizing oversight practices and procedures of Participants over third-party auditing organizations, and the practices and procedures of participating third-party auditing organizations; and

Leverage, where appropriate, existing conformity assessment structures.

Source: Statement of Cooperation
Also Participating

• Japan

• Official observers:
  – World Health Organization
  – Medicines and Healthcare Products Regulatory Agency (MHRA)
  – Health Products Regulatory Authority (HPRA)
What is MDSAP?

As currently implemented, MDSAP allows any medical device manufacturer to contract with an MDSAP recognized Auditing Organization (AO) to have a single regulatory quality management system audit that meets the requirements of all participating Regulatory Authorities.

Each country defines how MDSAP outcomes are used within its jurisdiction in accordance with its legislation and regulatory framework.
Why was MDSAP developed?
MDSAP Development

The MDSAP objectives are:

• To operate a single audit program that provides confidence in program outcomes

• To enable the appropriate regulatory oversight of medical device manufacturers’ quality management systems while minimizing regulatory burden on industry
MDSAP Development

The MDSAP objectives are (continued):

• To promote more efficient and flexible use of regulatory resources through work-sharing and mutual acceptance among regulators while respecting the independence of each authority.

• To promote, in the longer term, greater alignment of regulatory approaches and technical requirements globally based on international standards and best practices.
What is the MDSAP audit model?
MDSAP Audit Model

• The MDSAP audit model has a total of seven processes, arranged in a set sequence, and built on a foundation of risk management.
MDSAP Audit Model

• The MDSAP audit sequence follows a process approach and has four primary processes:
  (1) Management
  (2) Measurement, Analysis and Improvement
  (3) Design and Development
  (4) Production and Service Controls

And a supporting process:
(5) Purchasing
MDSAP Audit Model

• These five processes are built on a foundation of requirements for risk management and comprise the requirements of a quality management system for medical device manufacturers according to:
  – Brazilian Good Manufacturing Practices (RDC ANVISA)
  – Japan Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Reagents (MHLW Ministerial Ordinance No. 169)
  – FDA Quality System Regulation (21 CFR Part 820)
The MDSAP audit process has two additional supporting processes:

1. Medical Device Adverse Events and Advisory Notice Reporting
2. Device Marketing Authorization and Facility Registration.

These processes are necessary to fulfill specific requirements of the participating MDSAP regulatory authorities.
What is the MDSAP audit sequence?
MDSAP audit sequence

- The MDSAP audit model was designed for the audit of the MDSAP processes in the following sequence:
MDSAP Pilot Audit Process

- Designed and developed to ensure a single audit will provide efficient yet thorough coverage of the requirements of medical devices – quality management systems
  - ISO 13485:2003
  - Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013)
  - Quality System Regulation (21 CFR Part 820)
MDSAP Pilot Audit Process

• AND other specific requirements of medical device regulatory authorities participating in the pilot MDSAP program, such as:
  – Registration
  – Licensing
  – Adverse event reporting
How will Regulatory Authorities utilize the Single Audit Program and resulting audit report/certificate?

- **Australia:** 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.
How will Regulatory Authorities utilize the Single Audit Program and resulting audit report/certificate?

- **Brazil:** ANVISA will utilize 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 is expected to support regulatory technical evaluation on these issues.
How will Regulatory Authorities utilize the Single Audit Program and resulting audit report/certificate?

- **Health Canada**: HC will use an MDSAP audit as part of their Canadian Medical Device Conformity Assessment System (CMDCAS) certification program. Upon the successful completion of the pilot, Health Canada’s intent is to implement the Medical Device Single Audit Program as the mechanism to achieve regulatory compliance for quality management system requirements in Canada.
How will Regulatory Authorities utilize the Single Audit Program and resulting audit report/certificate?

- **Japan**: Japan’s Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA) will utilize these audit reports in both premarket and periodical post market audit under regulations in Japan. Undergoing the MDSAP Pilot audits is expected to reduce some burden on Japanese regulatory processes.
How will Regulatory Authorities utilize the Single Audit Program and 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. Moreover, the MDSAP would not apply to any necessary pre-approval or post-approval inspections in support of Premarket Approval (PMA) applications.
Harmonization in the Audit

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<tr>
<th>MDSAP</th>
<th>FDA Medical Device Inspections</th>
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<td>MDSAP Audit Model</td>
<td>Quality System Inspection Technique</td>
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<tr>
<td>ISO 13485:2003 (will soon be revised to ISO 13485:2016)</td>
<td>21 CFR 820</td>
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<td>Nonconformities written on MDSAP nonconformity forms</td>
<td>FDA-483 in eNSpect</td>
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<td>Audit report in MDSAP audit report template</td>
<td>Establishment inspection report (EIR) in eNSpect</td>
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Benefits for the Regulatory Authorities

• Promotes efficient and flexible use of regulatory resources through work-sharing and mutual acceptance among regulators while respecting the independence of each participating regulatory authority.

• Promotes greater alignment of regulatory approaches and technical requirements globally based on international standards and best practices.

• Moves to create an international coalition of countries dedicated to pooling technology, resources, and services to improve the safety and oversight of medical devices in a more efficient manner that is also less burdensome for industry.
Benefits for Manufacturers

• May be acceptable alternative to inspection required for marketing authorization in some countries
• Reduced burden on manufacturer resources (by reducing the number of regulatory inspections/audits from as many as four a year to one a year)
• Common audit criteria capturing the requirements of all participating regulatory authorities to be used by recognized auditing organizations
• Predictability in outcome, based on the use of a standardized non-conformity grading system
How can medical device manufacturers participate?

- After a successful assessment, the MDSAP Auditing Organization applicants will be allowed to perform MDSAP audits for medical device manufacturers that will be utilized by the Regulatory Authorities as previously discussed.
ISO 13485:2016
ISO 13485

• Regulators worldwide have integrated ISO 13485 into their regulatory systems, including those in the EU, Canada, Australia and Japan.

• The standard is sometimes adapted to meet local requirements, for example, EN ISO 13485:2012 in the EU adds a forward and several annexes to the standard specific to the region.

• ISO 13485 is also used for the Medical Device Single Audit Program (MDSAP)
New Revision

• Released in late February 2016

• The new revision places a greater emphasis on QMS throughout the supply chain and product lifecycle, as well as device usability and postmarket surveillance requirements.

• Over the next three years, ISO 13485:2003 and ISO 13485:2016 will coexist, allowing manufacturers, accreditation/certification bodies and regulators time to transition to the new standard.
Major Changes

• Some of the biggest changes between the 2003 and 2016 version include:
  – Incorporation of risk-based approaches beyond product realization. Risk is considered in the context of the safety and performance of the medical device and in meeting regulatory requirements;
  – Increased linkage with regulatory requirements, particularly for regulatory documentation;
  – Application to organizations throughout the lifecycle and supply chain for medical devices;
  – Harmonization of the requirements for software validation for different software applications (QMS software, process control software, software for monitoring and measurement) in different clauses of the standard;
Major Changes

- Some of the biggest changes between the 2003 and 2016 version include: (continued)
  - Emphasis on appropriate infrastructure, particularly for production of sterile medical devices, and addition of requirements for validation of sterile barrier properties;
  - Additional requirements in design and development on consideration of usability, use of standards, verification and validation planning, design transfer and design records;
  - Emphasis on complaint handling and reporting to regulatory authorities in accordance with regulatory requirements, and consideration of post-market surveillance
  - Planning and documenting corrective action and preventive action, and implementing corrective action without undue delay
Examples of Harmonization Between ISO 13485:2016 and 21 CFR 820

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<tr>
<td>4.1.6 Procedures for validation of application of software in the QMS</td>
<td>7.5.2.1 Validation of software used for production and service provisions</td>
<td>Requires procedures for validation of software used in QMS</td>
<td>Requirement for validation of automated processes used as part of production or the QMS [21 CFR 820.70(i)]</td>
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<tr>
<td>4.2.3 Medical device file</td>
<td>4.2.1 QMS must include…a file for each model of medical device which contains product specifications and QMS requirements</td>
<td>Requirement now includes labelling and packaging specifications in addition to product and manufacturing specifications</td>
<td>Requirement for labeling and packaging specifications in addition to product and manufacturing specifications [21 CFR 820.181]</td>
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Examples of Harmonization Between ISO 13485:2016 and 21 CFR 820

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<td>5.6 Management Review</td>
<td>No explicit requirement for management review procedures</td>
<td>Requirement for a documented procedure</td>
<td>Requirement for implemented procedure [21 CFR 820.20(c)]</td>
</tr>
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<td>6.3 Infrastructure</td>
<td>No explicit requirement for adequate space to prevent product mix-ups</td>
<td>Documented requirements to prevent product mix-ups and ensure orderly handling</td>
<td>Requires building have suitable design and sufficient space to ensure orderly handling of product and prevent mix-ups [21 CFR 820.70(f)]</td>
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Examples of Harmonization Between ISO 13485:2016 and 21 CFR 820

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<td>7.4.2 Purchasing information</td>
<td>No requirement regarding notification to the manufacturer of changes in purchased product</td>
<td>Requirement for a written agreement to ensure manufactures are notified in changes to purchased product</td>
<td>Requirement for a agreement to ensure manufactures are notified in changes to purchased product or services [21 CFR 820.50(b)]</td>
</tr>
<tr>
<td>7.5.8 Identification</td>
<td>7.5.3 No explicit requirement for unique device identifier</td>
<td>Updated to include unique device identifier if required by regulatory authorities</td>
<td>Updated to include unique device identifier to device history record information [21 CFR 820.184(f)]</td>
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### Examples of Harmonization Between ISO 13485:2016 and 21 CFR 820

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<td>8.2.2 Complaint handling</td>
<td>8.2.1, 8.5.1 No specific requirements regarding information needed for complaint handling</td>
<td>Requirements for procedures to include certain information for complaint handling</td>
<td>Requirements for procedures to include certain information for complaint handling [21 CFR 820.198]</td>
</tr>
<tr>
<td>8.4 Analysis of data</td>
<td>No requirement to establish appropriate statistical techniques</td>
<td>Updated to include determination of appropriate statistical techniques to analyze data</td>
<td>Requirement to analyze data and processes using appropriate statistical techniques [21 CFR 820.100(a)]</td>
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How does the new ISO 13485 affect MDSAP?

• Same transition period planned

• Better alignment to certain requirements in 21 CFR 820 and RDC ANVISA 16/2013
  – Some FDA and Brazilian requirements are better covered in the new standard and many country-specific requirements in the Audit Model may eventually be eliminated
How do I find out more specifics on the documents, policies, and procedures that will be utilized in the MDSAP pilot?

- http://www.fda.gov/MedicalDevices/InternationalPrograms/default.htm
Thank-you!