THE MDSAP: EASING THE AUDIT PATH FOR QUALITY MANAGEMENT SYSTEMS

Initiated in 2012 by the International Medical Devices Regulators Forum (IMDRF), the Medical Device Single Audit Program (MDSAP) offers medical device manufacturers a mechanism to significantly streamline the process of pre- and post-market audits required by regulatory authorities in jurisdictions around the world. Under the MDSAP, a single audit performed by an authorized Auditing Organization (AO) is deemed sufficient to assess compliance with the quality management system requirements of regulatory agencies in multiple major medical device markets, including the U.S., Canada, Japan, Brazil and Australia. This single audit approach reduces the need for duplicate quality management audits, helping device manufacturers to better manage costs and ease market access.

This UL white paper provides an overview of the MDSAP and discusses how the single audit approach can benefit medical device manufacturers. Beginning with a brief history of the formation of the MDSAP, the paper then describes the audit process prescribed under the program and reviews the results of the recently completed three-year pilot MDSAP audit initiative involving more than 150 device manufacturing locations around the world. The white paper concludes with information about the anticipated roll-out of the MDSAP in 2017, as well as recommendations on how device manufacturers can take advantage of the MDSAP.

The Origins of the MDSAP

Although growing global interest in advanced medical technologies offers significant market potential for medical device manufacturers, the process of obtaining regulatory approval remains a challenging process. This is especially true when it comes to pre- and post-market audits of a device manufacturer's quality management system (QMS). Even in cases where auditing requirements are substantially similar, independent regulatory authorities in key jurisdictions often decline to accept audit reports that address requirements of other regulators or regions. The absence of a mutual recognition scheme for QMS audits results in a significant added expense for device manufacturers selling in multiple economic areas, as well as longer lead times for market acceptance.

Enter the International Medical Device Regulators Forum (IMDRF), a voluntary consortium of national regulators from major markets around the world. Established in 2011, the IMDRF is building on the work of the former Global Harmonization Task Force on Medical Devices (GHTF) to "accelerate international medical device regulatory harmonization and convergence." In its relatively brief history, the IMDRF has successfully completed initial work on three major programs ("work items"), and is currently addressing seven additional issues that may well impact the future regulatory approval of medical devices.

The IMDRF management committee membership includes representatives from the national regulatory authorities in eight major medical device markets: the U.S., the European Union (EU), China, Japan, Brazil, Canada, Australia and Russia. Official Observers to the IMDRF include the United Nation's World Health Organization (WHO) and the Life Sciences Innovation Forum of the Asia-Pacific Economic Cooperation (APEC). Two additional entities, the Asian Harmonization Working Party (AHWP) and the Pan American Health Organization (PAHO), are IMDRF Affiliate Organizations. This extensive network of participants from around the world helps to provide important visibility and support for IMDRF efforts.

The MDSAP Pilot Program

Like other initiatives undertaken by the IMDRF since its inception, the medical device single audit program (MDSAP) began with the formation of a working group in 2012, charged with developing a common set of requirements for those auditing entities responsible for conducting regulatory audits of manufacturers' quality systems. As part of that effort, the working group launched an initial three-year pilot study in January 2014 to evaluate how a proposed single audit program structure would work under real-world conditions.

Regulatory participants in the MDSAP pilot study included the U.S. Food and Drug Administration (FDA), Health Canada, Australia's Therapeutic Goods Administration (TGA), Brazil's National Health Surveillance Agency (ANVISA) and Japan's Pharmaceuticals and Medical Devices Agency (PMDA).[1] Under the terms of the pilot study, participating regulatory authorities agreed to accept QMS audit reports prepared by authorized Auditing Organizations (AOs) and based on audits conducted in accordance with the requirements of ISO 13485, *Medical devices - Quality management systems - Requirements for regulatory purposes*. Additional MDSAP audit requirements included several specific provisions applicable in the countries participating in the pilot study.

For the pilot study, the IMDRF working group established eight separate criteria for evaluating whether the proposed MDSAP structure would achieve the performance goals and objectives necessary for a successful single audit program. These so-called proof of concept criteria (PoCC) stipulated the following benchmarks:

1. Whether the format and content of audit and nonconformity results comply with the prescribed requirements;

2. Whether the evidence provided in audit and nonconformity reports for common QMS requirements support the findings and nonconformity grades;

3. Whether the audit and nonconformity reports would substantiate regulatory decisions;

4. Whether the audit model and task sequence appropriately assesses QMS and regulatory requirements;

5. Whether the assessment model and task sequence appropriately assesses compliance with MDSAP requirements;

6. Whether time provided in the audit duration model is suitable for evaluating and recording evidence of conformity/nonconformity with the requirements;

7. Whether a sufficient number of candidate AOs are recognized; and

8. Whether a sufficient number of manufacturers participate in MDSAP.

Although the final results of the MDSAP pilot study have not yet been compiled, the IMDRF provided an interim report on the progress of the program at its September 2016 meeting in Brazil. According to a report presented by the Chair of the MSDAP working group, approximately 85 separate audits have been conducted under the scope of the MSDAP pilot study through August 2016. In addition, a total of 126 individual manufacturing sites worldwide are listed as pilot study participants. Finally, there are 13 AOs located worldwide that are either currently authorized to conduct MDSAP audits or that are expected to complete the authorization process by the end of the pilot study or shortly thereafter.[2]

Anticipated Adoption of the MDSAP

The IMDRF is currently moving forward with plans to transition from the pilot study to the full implementation of the MDSAP as of January 2017. At the same time, several key regulatory authorities have taken steps to formally adopt MDSAP protocols as part of their processes for the review and approval of medical devices.

The U.S. FDA has already indicated that it will recognize MDSAP audit reports in lieu of its own currently-required audit reports. In a September 2016 letter to medical device manufacturers, the FDA noted that the standardized MDSAP audit report template "was developed to assure the reporting requirements of all participating regulatory authorities (including the U.S. FDA) are effectively documented." Therefore, the letter continues, "the (FDA) recognizes MDSAP audit reports as a substitute for FDA Establishment Inspection Reports (EIRs)." [3]

Perhaps the most significant development regarding the acceptance of MDSAP audit reports involves Health Canada, which has announced its intentions to replace the current Canadian Medical Devices Conformity Assessment System (CMDCAS) with the IMDRF's MDSAP as of January 1, 2017. Ultimately, this change will result in the MDSAP becoming the only mechanism by which manufacturers can demonstrate their compliance with Canada's QMS requirements under that country's medical device regulations. The application of the MDSAP requirement would apply even to those manufacturers who intend to sell or distribute their medical devices solely and exclusively in Canada.

During a two-year transition period, Health Canada is expected to accept certificates verifying QMS audits that have been issued in accordance with either the CMDCAS or the MDSAP protocol. However, as of January 1, 2019, the MDSAP route will be the only approach accepted by Health Canada for verifying QMS audits, and existing QMS audit certificates issues under the CMDCAS system will need to be replaced with an MDSAP certificate.[4]

The decision by Health Canada to accept only MDSAP audit reports has potentially significant implications for medical device manufacturers and their efforts to achieve compliance with audit requirements in jurisdictions around the world. The International Trade Administration of the U.S. Department of Commerce values Canada's market for medical devices at approximately $8 billion (USD), making it the ninth largest medical device market in the world. Therefore, most device manufacturers will be required to consider MDSAP audit requirements as part of their overall compliance strategy if they wish to gain access to this important market.

The value of the Canadian market for medical devices is especially important for U.S.-based medical device manufacturers. The U.S. is the single biggest exporting country of medical devices to Canada, representing about 45 percent of all Canadian medical device imports, with an estimated value of $3 billion.[5] Since the U.S. FDA also accepts audits based on the MDSAP protocol as evidence of compliance with its QMS audit requirements, U.S. device manufacturers can be expected to quickly adopt the MDSAP protocol to reduce the overall burden of audit compliance and to ease the regulatory review and acceptance path.

Finally, MDSAP audit reports can be included as part of medical device approval requests submitted to other countries whose regulators participate in the IMDRF. As noted earlier, IMDRF participants represent some of the world's largest markets for medical devices, including the EU, Brazil, Japan, Australia and China. This broad acceptance of MSDAP QMS audit reports in major medical device markets will potentially lead to even more widespread acceptance of MDSAP audits among non-IMDRF participants.

MDSAP Auditing Specifics and Considerations

As noted earlier in this paper, the MDSAP audit has been designed to meet the requirements of ISO 13485. The audit specifically addresses five primary processes, including: 1) management; 2) measurement, analysis and improvement; 3) design and development; 4) production and service controls; and 5) purchasing. In addition, the MDSAP audit process includes two additional supporting processes intended to address specific requirements of participating MDSAP regulatory authorities. These processes are: 1) device marketing authorization and facility registration; and 2) medical device adverse events and advisory notices reporting.

Similar to other management system audit programs, the MDSAP audit program is based on a three-year audit cycle that includes the following auditing activities:

- *Initial certification audit* - The initial certification audit is a complete audit of a manufacturer's QMS, and consists of two separate stages conducted in accordance with the requirements of ISO/IEC 17021, Conformity assessment - Requirements for bodies provide audit and certification of management systems. Audit activities in Stage 1 are chiefly intended to evaluate available QMS documentation and the extent of a manufacturer's preparedness to undergo Stage 2 audit activities. Stage 2 audit activities evaluate the actual compliance of the QMS with the requirements of ISO 13485, as well as other requirements of MDSAP-participating regulatory authorities.

- *Surveillance audits* - In each of the two years following the initial MDSAP certification audit, a surveillance audit is conducted to assess ongoing compliance with MDSAP QMS requirements. Annual surveillance audits do not include the Stage 1 review activities that are part of an initial certification audit, and do not need to address all MDSAP requirements that are part of Stage 2 activities. However, surveillance audits are expected to assess any changes in the manufacturer's products or QMS processes since the initial certification audit.

- *Recertification audit* - Conducted in the third year following the initial certification audit, the recertification audit is intended to evaluate a manufacturer's QMS for its continued suitability and effectiveness in meeting QMS requirements under the MDSAP. Through more selective and focused sampling, recertification audits typically take less time than initial certification audits.

In addition to the audit activities conducted under the scope of the three-year audit cycle, device manufacturers may also be subject to special audits or audits conducted by regulatory authorities, as well as unannounced audits.

In the near term, one factor that may complicate planning and preparation by device manufacturers for an audit under MDSAP is the introduction of the 2016 version of ISO 13485. Published in March 2016, the latest revision to the standard incorporates several significant changes from the 2003 edition.[6] The International Organization for Standardization (ISO) will withdraw ISO 13485:2003 as of March 1, 2019, and medical device manufacturers currently certified to ISO 13485:2003 have until then to modify their current QMS to comply with the requirements of the revised standard.

Further, regulatory authorities participating in the MDSAP may adopt different timetables for transitioning their regulations to the latest ISO 13485 revision. Health Canada, for example, has aligned its timetable for acceptance of ISO 13485:2016 to coincide with that of the ISO[7] but regulators in other jurisdictions may adopt a more aggressive timetable that would require an earlier switchover to the requirements of the newly revised standard.

Auditing Organization Selection and Accreditation

Under the MDSAP, only AOs that have been reviewed and authorized by the IMDRF are eligible to conduct audits for compliance with the program's requirements. When the MDSAP pilot study was initiated in 2014, 13 different auditing organizations were identified as eligible for initial AO authorization, based on their accreditation under Canada's CMDCAS. Candidate AOs were then subject to a thorough evaluation in accordance with requirements established by the IMDRF's MDSAP working group.[8]

Over the ensuing three years, all 13 eligible auditing organizations have either received AO authorization from the IMDRF or have passed initial IMDRF application review and assessment for AO authorization. With the full implementation of the MDSAP in January 2017, the IMDRF is expected to open the AO authorization process to auditing organizations other than those accredited by Health Canada. This step is likely to significantly increase the number of available AOs during 2017, providing the MDSAP with additional capacity to audit medical device manufacturers and thereby increasing overall participation in the MDSAP.

The MDSAP Benefits for Device Manufacturers

For the medical device industry, the IMDRF MDSAP is expected to transform the approach used to conduct pre- and post-market QMS audits and significantly reduce the audit compliance challenges facing device manufacturers. Specific benefits of the MDSAP include:

- *Harmonization of auditing requirements* - MDSAP pre- and post-market auditing requirements are based on ISO 13485, the internationally-accepted

standard for QMS, and have been harmonized to address specific concerns of national regulatory agencies participating in the IMDRF.

- *Broader acceptance of audit reports* - MDSAP audit reports will be accepted by IMDRF-participant regulators in lieu of current report requirements. And acceptance of MDSAP audit reports by regulators in many of the world's major medical device markets will likely foster acceptance by non-IMDRF regulators as well.

- *Reduced overall auditing time and expense* - The broad application of one set of audit requirements means that manufacturers will spend less time and expense preparing for and meeting the QMS audit requirements of individual jurisdictions, expediting the approval process and allowing for the reallocation of critical resources.

- *Reduced time responding to findings* - Further, since MDSAP audit requirements are harmonized, any findings of non-compliance are more likely to be consistent from audit to audit, and more quickly and easily addressed by device manufacturers.

- *Wider choice of 3rd party audit organizations* - Medical device manufacturers will have access to a wider selection of AOs who are authorized to conduct QMS audits under the MDSAP program. Competition among AOs should lead to an increase in the overall quality and value of audit services.

- *More transparent and consistent oversight by regulators* - Finally, a single, harmonized set of pre- and post-market QMS audit requirements will help to ensure more regular and consistent oversight by regulatory authorities. Coordination between regulators will also help to facilitate the evaluation of facilities based outside of individual jurisdictions.

Ultimately, these and other benefits of the MDSAP will reduce the complexity of a critical aspect of the medical device approval process, thereby removing many current barriers to market entry and allowing device manufacturers to bring new and innovative medical devices to global markets more quickly and efficiently.

Summary and Conclusion

Developed by the international regulatory community, the IMDRF's MDSAP represents an important development for medical device manufacturers. With its full-scale implementation now in progress, the MDSAP offers a harmonized set of pre- and post-market QMS audit requirements that will significantly ease the compliance process for medical device manufacturers and help them achieve access to major medical device markets around the world. The MDSAP model also offers a potential pathway for the harmonization of other medical device requirements, and the promise of more wide-spread access to advanced technologies that can improve the health and well-being of people around the world.

UL is an authorized AO under the IMDRF's MDSAP, and can provide medical device manufacturers with QMS pre- and post-market auditing services in all MDSAP jurisdictions. For additional information about the UL's MDSAP services, contact Medical.Inquiry@ul.com, or go to www.ul.com/medical.

References:

[1] Japan's Pharmaceuticals and Medical Devices Agency (PMDA) agreed to a trial acceptance of audit reports produced under the MDSAP pilot study during the period from June 15, 2016 through December 31, 2015. Web. 4 November 2016. http://www.pmda.go.jp/english/review-services/gmp-qms-gctp/0004.html.

[2] "Medical Device Single Audit Program (MDSAP) Pilot Update," Presentation by Fabio P. Quintino at IMDRF Meeting, September 2016. Web. 4 November 2016. http://www.imdrf.org/docs/imdrf/final/meetings/imdrf-meet-160913-brazil-mdsap-pilot-update.pdf.

[3] Letter from the Center for Devices and Radiological Health, U.S. Food and Drug Administration, September 29, 2016. Web. 4 November 2016. http://www.fda.gov/downloads/MedicalDevices/InternationalPrograms/MDSAPPilot/UCM523315.pdf.

[4] For additional information about Health Canada's transition to the MDSAP, see "Notice: Transition Plan for the Medical Device Single Audit Program (MDSAP)," issued by Health Canada, December 4, 2015. Web. 4 November 2016. http://www.hc-sc.gc.ca/dhp-mps/md-im/activit/int/mdsap-trans-notice-avis-eng.php.

[5] "2016 Top Market Report, Medical Devices: Country Case Study, Canada," International Trade Administration, U.S. Department of Commerce, June 2016. Web. 4 November 2016. http://trade.gov/topmarkets/pdf/Medical_Devices_Canada.pdf.

[6] For additional information about the changes in ISO 13485:2016, see "Common Questions About ISO 13485:2016," posting on UL's website, April 8, 2016. Web. 4 November 2016. http://medicalsolutions.ul.com/common-questions-about-iso-13485-2016/?gclid=CL3IjMnnlNACFQoGhgodFSsMEA.

[7] See "Notice: Transition to the Revised Version of ISO 13485 and its impact on the Compliance of the Quality Management System Requirements of the Canadian Medical Device Regulations," issued by Health Canada, August 3, 2016. Web. 4 November 2016. http://www.hc-sc.gc.ca/dhp-mps/md-im/qualsys/iso13485-trans-notice-avis-eng.php.

[8] See "Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition," International Medical Device Regulators Forum, IMDRF MDSDAP Working Group, 24 March 2016. Web. 4 November 2016. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-160324-requirements-auditing-orar.pdf.