Medical Device Single Audit Program

Frequently Asked Questions

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A. General Questions about MDSAP

1. What is the Medical Device Single Audit Program Pilot?

The Medical Device Single Audit Program Pilot or "MDSAP Pilot" is a program that will allow the conduct of a single regulatory audit of a medical device manufacturer's quality management system that will satisfy the requirements of multiple regulatory jurisdictions. Audits will be conducted by Auditing Organizations authorized by the participating Regulatory Authorities to audit under MDSAP.

The MDSAP is a way that medical device manufacturers can be audited once for compliance with the standard and regulatory requirements of up to five different medical device markets: Australia, Brazil, Canada, Japan and the United States. The program's main mission is 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 Regulators Forum Medical Devices Single Audit Program, International Coalition Pilot Program Sheet, January 2014 – IMDRF Home Page].

The MDSAP Pilot is planned to run from January 2014 until Dec. 2016.

2. Why is the MDSAP Pilot being developed?

The MDSAP Pilot was developed to:

- Pilot the implementation of the requirements that are defined in the IMDRF MDSAP Model;
- Enable 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 regulators while respecting the sovereignty of each authority;
- Promote globally, in the longer term, a greater alignment of regulatory approaches and technical requirements based on international standards and best practices;
- Promote consistency, predictability and transparency of regulatory programs by standardizing;
    - the practices and procedures of participating regulators for the oversight of third party auditing organizations, and
    - the practices and procedures of participating third party auditing organizations; and
    - Leverage, where appropriate, existing requirements and procedures for conformity assessment.

3. Which Regulatory Authorities are part of the MDSAP Pilot and what is the plan for expansion of the program?

The MDSAP Pilot is being developed by representatives of the Australian Therapeutic Goods Administration (TGA), Brazil's Agência Nacional de Vigilância Sanitária (ANVISA), Health Canada, MHLW/PMDA, and the U.S. Food and Drug Administration (FDA). All regulatory authorities participating in the MDSAP Pilot are equal partners in the program.

Regulatory Authorities may eventually decide to participate in the MDSAP and to become active participants in the Pilot Program. For example, the World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme and the European Union (EU) are Official Observer to the MDSAP Regulatory Authority Council (RAC) and Subject Matter Expert (SME) Work Group.

4. When is it anticipated that the MDSAP will go live?

The MDSAP Pilot, that is designed to confirm the proof-of-concept, was launched on January 1st, 2014 and will run through to the end of calendar year 2016. Full implementation of the MDSAP is anticipated sometime in 2017.

5. What is the difference between a Regulatory Authority being a participant in MDSAP Subject Matter Expert (SME) Working Group (WG) versus being an observer to this working group?

The Regulatory Authority participants provide the resources to support the development, implementation, maintenance and expansion of MDSAP and participate actively in the process of recognizing, monitoring, and re-recognizing Auditing Organizations under the framework of the IMDRF MDSAP. The participating Regulatory Authorities have committed to use the MDSAP deliverables during the Pilot in order to assess program success. Each Regulatory Authority participant is also represented on the MDSAP Regulatory Authority Council (RAC); the MDSAP's governing board, by two senior level managers.

A Regulatory Authority who is an "observer" may attend MDSAP SME WG meetings, assessments, and other activities, but does not utilize MDSAP program deliverables to replace or supplement its regulatory scheme deliverables or portions of these deliverables. The observers are represented on the MDSAP RAC by one senior level manager.

6. Is the list of medical device manufacturers participating in the MDSAP Pilot made publicly available?

During the Pilot, the information on who is participating will not be made publicly available by the Regulatory Authorities. However, the participating Regulatory Authorities plan to develop an Internet Portal on which the information may become available.

7. Will industry be able to provide input into MDSAP documents or the program in general?

Yes. There are two venues for the industry to contribute. IMDRF MDSAP documents either under development, or undergoing a revision, are made available on the IMDRF's web site for consultation. (IMDRF Consultations) The Regulatory Authorities that are participating in the MDSAP Pilot have established, documented and are implementing an MDSAP Quality Management System MDSAP Documentation. Feedback on MDSAP can be submitted to any of the participating Regulatory Authorities in written format, electronically, by telephone, or in person. Electronic feedback is preferred and may be submitted to one of the four email addresses listed below. MDSAP participating regulators will address the feedback in accordance with the procedure MDSAP QMS P0011 Complaints and/or Customer Feedback Procedure

Manufacturers are encouraged to provide feedback.
Contact emails:

MDSAP@tga.gov.au
MDSAP.ATENDIMENTO@anvisa.gov.br
QS_MDB_HC@hc-sc.gc.ca
MDSAP@pmda.go.jp
MDSAP@fda.hhs.gov

8. **What is the criterion that must be achieved for the MDSAP Pilot to be considered successful?**

   The MDSAP Subject Matter Experts Working Group has developed a plan to gather evidence for a "proof of concept" of the MDSAP Pilot. The plan includes eight performance indicators for the measurement of the success of the Pilot. The criteria are related to audit reports and non-conformities, the audit model, duration of audits, Auditing Organizations and manufacturers. A method for data collection, sampling, method of analysis and targets were defined for each indicator. MDSAP P0007 *Proof of concept for MDSAP Pilot.*

9. **Have there been discussions with WHO regarding the pre-clearance process for IVDs and taking account the results of an MDSAP audit? Will medical devices assessed by the WHO be included in the program at a later stage?**

   WHO is participating as a member of the IMDRF MDSAP Working Group and as an observer to the MDSAP. WHO has indicated a willingness to adapt and integrate MDSAP processes as much as possible in their *Prequalification Program*. WHO intends to utilize MDSAP reports where possible if they are available for devices that are subject to their *Prequalification Program*.

10. **If an RA decides to change its GMP/QMS or Regulatory requirements, how will the changes be incorporated into MDSAP?**

    The MDSAP Subject Matter Experts would revise the MDSAP Audit Model and the MDSAP Audit Model Companion document to reflect any changes in regulatory requirements. Accordingly, the impacted MDSAP training would be updated. The IMDRF MDSAP WG N3 document requires "The Auditing Organizations to participate in any regulatory coordination group established for the purpose of keeping the Auditing Organization's personnel current on medical device legislation, guidance documents, standards, and best practice documents adopted in the applicable regulatory systems." (N3 – Clause 6.1.3)

11. **How will the revision of ISO 13485 impact MDSAP?**

    When ISO 13485:2003 is superseded by a new version, the impact on the MDSAP Pilot will be analyzed and any affected documents, the Audit Model, in particular - will be revised as necessary.

12. **How do I find out more specific information on the documents, policies, and procedures that will be used in the MDSAP Pilot?**

    The MDSAP Pilot participating Regulatory Authorities and the candidate Auditing Organizations will primarily utilize the IMDRF MDSAP WG documents that can be found at: IMDRF Documentation

In addition, there are many other MDSAP Regulatory Authority Council reviewed and approved documents that are to be used for implementing the Pilot and include: an audit strategy for auditing medical device manufacturers, requirements for the audit reports, a method for audit time calculation, and the MDSAP Pilot Quality Management System procedures. For further information on the Pilot and associated documents, please refer to the MDSAP Home Page or contact one of the participating Regulatory Authorities at:

MDSAP@tga.gov.au
MDSAP.ATENDIMENTO@anvisa.gov.br
QS_MDB_HC@hc-sc.gc.ca
MDSAP@pmda.go.jp
MDSAP@fda.hhs.gov

B. Questions related to Assessments

13. Which Auditing Organizations can apply to the MDSAP Pilot?

During the MDSAP Pilot, all Auditing Organizations currently recognised under CMDCAS program are invited to apply for authorization to participate in the MDSAP Pilot by submitting an MDSAP application. These Auditing Organizations (recognized Registrars) undergo an application review, stage 1 assessment, stage 2 on-site assessment, and, if applicable, on-site assessment at their critical locations, and successfully resolve any identified deficiency will be authorized to perform any MDSAP Pilot Audits. The participating Regulatory Authorities will decide whether to officially recognize Auditing Organizations upon completion of the MDSAP Pilot. Additional auditing organizations may apply for recognition under MDSAP following the successful conclusion of the pilot.

The reason for this initial restriction is that the participating Regulatory Authorities already have some involvement with the CMDCAS Registrars through various agreements and programs. Australia's TGA Inspectorate has a Memorandum of Understanding with Health Canada on the reciprocal recognition of quality management system (QMS) certificates for medical device manufacturers utilizing the CMDCAS Program. The U.S. FDA has worked closely with Health Canada over the last 10 years on the use of third party auditing organizations in a regulatory program, including within the CMDCAS program. In addition, those third parties that were recognized under FDA's Third Party Inspection program and also accredited under the CMDCAS program, had for several years performed pilot Multi-Purpose Audits (pMAP) under a separate initiative.

ANVISA, TGA, and the U.S. FDA have also observed several assessments of CMDCAS Registrars as well as observed witnessed audits that have been performed by those Registrars. Therefore, the Regulatory Authorities involved in this Pilot already have several years of confidence building with the CMDCAS Registrars. Many of the CMDCAS Registrars are also designated as Notified Bodies under the European regulatory scheme.

The list of Registrars Recognized by Health Canada can be found at: CMDCAS recognized registrars.

14. Can Contract Research Organizations participate in MDSAP Pilot? What about Certified Quality Auditors?

The MDSAP includes the use of Auditing Organizations, also known as Certification Bodies or Registrars in other schemes. During the Pilot, only CMDCAS recognized registrars may apply for recognition.

If an Auditing Organization also acts as a Contract Research Organization, the organization's management system must ensure the impartiality of the Auditing Organization.

An independent Certified Quality Auditor may not individually apply for recognition under the MDSAP Pilot. Should an auditor become permanently employed or work on a contract basis for an Auditing Organization, and meet the competency and other criteria for auditors as required under MDSAP, e.g. absence of conflict of interest, that auditor may be qualified to perform MDSAP audits as long as the AO is recognized under MDSAP.

15. Who will be entitled to perform audits of medical device manufacturers under the MDSAP Pilot?

During the MDSAP Pilot, candidate Auditing Organizations who successfully complete an application review process, the stage 1 and stage 2 assessment processes, the assessment of any critical location and the resolution of any identified nonconformity, will be authorized to perform audits under the Pilot program. The initial audit of a medical device manufacturer conducted by an authorized MDSAP AO will be witnessed by representatives of at least two of the four participating regulatory authorities. The governing documents for assessing candidate Auditing Organizations can be found on the MDSAP Pilot webpages.

The recognition of Auditing Organizations who satisfactorily fulfil program requirements will be promulgated after the completion of the MDSAP Pilot.

16. How will an Auditing Organization pay regulators for the application and training?

During the MDSAP Pilot (2014-2016) there are no application fees. Also, there are no costs associated with the MDSAP Training. Training on the MDSAP Audit Model and the requirements of the participating Regulatory Authorities is available on-line to registered candidate applicants MDSAP Training Material. Instructions on how to apply for an account are also provided.

17. How are assessments of auditing organizations being conducted by RAs under the MDSAP Pilot?

The assessment program is defined in key documents for the planning and conduct of assessments by Regulatory Authority assessment teams; and, the follow-up and monitoring of assessment activities of Auditing Organizations. The sequence of all assessment activities follows a 4-year cycle. The cycle begins with an initial authorization, followed by annual surveillance assessments for three consecutive years.

Assessments are performed per document IMDRF MDSAP WG N5 FINAL:2013, *Regulatory Authority Assessment Method for the Recognition and Monitoring of Medical Device Auditing Organizations* and associated MDSAP documents MDSAP Documentation.

18. Must Auditing Organizations have all documentation in English to be assessed by the Regulatory Authorities?

Auditing Organizations must have at least the documents requested for the application submission and for Stage 1 Assessment in English. During the Stage 2 Assessment, the Auditing Organizations must have personnel with fluency in English to translate documents and records that are not in English.

Additionally, records that are specific to the MDSAP program (including but not limited to the documents included in the audit report package) should be in English as well.

19. What is the best way to determine what is expected of the Auditing Organizations with regard to multiple jurisdictions?

Medical device manufacturers will have to be audited according to the scope declared in their application for certification services. Based on the countries where the manufacturer sells (or intends to sell) or has devices registered, the AO will determine the regulatory requirements applicable to that manufacturer.

The AOs will have to refer to the Audit Model MDSAP AU P0002 and Audit Model Companion MDSAP AU G0002.1 to make that determination. The two documents incorporate or reference the regulatory requirements of each of the participating Regulatory Authorities.

20. What oversight do Regulatory Authorities have over the Auditing Organizations?

The audits of medical device manufacturers will be performed by MDSAP Auditing Organizations that will be assessed and monitored by Regulatory Authorities. In accordance with best practices, the MDSAP Pilot incorporates a transparent assessment program by Regulatory Authorities who will oversee the compliance of the Auditing Organizations with MDSAP requirements. This program includes a robust plan and schedule for assessing the competence and compliance of MDSAP Auditing Organizations and includes assessments of their head office and critical locations, as well as witnessing the performance of AO audits ("witnessed" audits), as part of an ongoing four year recognition cycle.

The Regulatory Authorities involved in the Pilot will base their recognition and assessment process on the IMDRF MDSAP WG and Pilot MDSAP documents in addition to other documents drafted and approved by the Regulatory Authority Council. IMDRF Documentation and MDSAP Documentation.

In particular, Regulatory Authorities will evaluate or "assess" an Auditing Organizations' compliance to the requirements of IMDRF MDSAP WG documents N3 and N4.

- IMDRF MDSAP WG N3 FINAL:2013 *Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition*
- IMDRF MDSAP WG N4 FINAL:2013 Competence and Training Requirements for Auditing Organizations

21. What is a witnessed audit?

A witnessed audit allows Regulatory Authorities to verify that an Auditing Organization adequately conducts their audits using the MDSAP Audit Model, and reports appropriately on the outcomes of audits. It is an essential assessment activity for building and maintaining confidence in the reliability of the third party Auditing Organization.

During a witnessed audit, the Auditing Organization's audit team conducts the audit of the medical device manufacturer and the Regulatory Authorities' assessment team observes the AO without interfering in the audit process. The RA Assessment team does not assist or coach the AO auditors, nor does it provide additional information to the AO audit team or collect information on their behalf.

After the Auditing Organization has issued the audit report, the assessment team finalizes and shares their conclusions with the Auditing Organization.

The RA conclusions are not in relation to the compliance of the manufacturer to ISO 13485 and the relevant regulatory requirements. The RA's conclusions only relate to the ability of the Auditing Organization to audit against the requirements of the MDSAP Pilot.

22. Who performs witnessed audits and how are the assessors selected?

The witnessing of an audit being conducted by an Auditing Organization will be performed by qualified MDSAP Regulatory Authority Assessors. These assessors are experienced Regulatory Authority Assessors who will have knowledge of the MDSAP requirements, the requirements of the participating Regulatory Authorities and the device and manufacturing technologies used by the medical device manufacturer that is being audited.

Regulatory Authority Assessors are to be qualified against the competency requirements as defined in the document IMDRF MDSAP WG N6 FINAL:2013, *Regulatory Authority Assessor Competence and Training Requirements.*

23. Can an Auditing Organization contest a nonconformity or its grading?

If an Auditing Organization disagrees with a nonconformity issued by the Regulatory Authorities or its grading, it may formally file for an appeal to the participating Regulatory Authorities. The process is defined in IMDRF MDSAP WG N11 FINAL:2014).

24. If a current Notified Body applies for authorization to perform audits under the MDSAP Pilot but does not pass the MDSAP assessment, could they also be de-notified to the EU Directive?

No. European Competent Authorities and Designating Authorities are not participants in the MDSAP Pilot. It is therefore unlikely that European Authorities would de-notify a Notified Body based on the outcome of an MDSAP Pilot Assessment. Nevertheless, European Authorities are likely to be informed if the reason for refusing the authorization was due to concerns that arose from a concurrent assessment by an Auditing Organization of the relevant European regulations. In such cases, the European Authorities may follow-up with the Auditing Organization and make their own assessment of the situation.

25. Who from the Auditing Organization or the Regulatory Authorities makes the final decision on the compliance of the medical device manufacturer?

The Auditing Organizations are fully responsible for making the decision on compliance to issue MDSAP certification documents under the program.

Independently, each MDSAP participant Regulatory Authority may use the report for different purposes, to support the regulatory decisions in their jurisdiction. If, based

on the Auditing Organization's audit report, a Regulatory Authority concludes that the manufacturer is not in compliance with the regulations, the Regulatory Authority may engage in enforcement activities according to their policies, taking into account, if possible, the follow-up activities conducted by the Auditing Organization.

26. How does a regulatory authority inspectorate become an Auditing Organization?

Regulatory Authorities who are seeking recognition under MDSAP need to comply with the same requirements as a commercial Auditing Organization. The other participating Regulatory Authorities will conduct an assessment according to the international standard ISO/IEC 17021-1 and the additional requirements defined in IMDRF MDSAP WG N3 FINAL:2013, and IMDRF MDSAP WG N4 FINAL:2013 per the assessment methodology documented in IMDRF MDSAP WG N5 FINAL:2013.

27. How will MDSAP ensure that every RA has the same evaluation standards for the Auditing Organization?

Auditing Organizations are assessed for compliance with the requirements of IS0/IEC 17021-1 and the additional requirements of N3 and N4. An assessment program and assessment methodology for Auditing Organizations is defined in N5 and guidance for RA Assessors is to be provided in N8. Regulatory Authority assessors execute assessment tasks for each process defined in the documents above and
identify objective evidence of definition, implementation and effectiveness of each of the requirements. If nonconformities are identified, a grading system is used to assist in determining the timeline for any corrections or corrective actions and to support a predefined Auditing Organization recognition or Auditing Organization de-recognition process.

Regulatory Authority assessors are qualified against the requirements of IMDRF MDSAP WG N6 FINAL:2013, *Regulatory Authority Assessor Competence and Training Requirements* to perform the assessment of an Auditing Organization. Regulatory Authority assessors will participate in both face to face and distance training activities. The MDSAP Regulatory Authorities are committed to operating under a joint MDSAP Quality Management System to establish controls over the program and to facilitate continuous improvement. Applicable procedures and forms are publically available at MDSAP Assessment Procedures and Forms.

28. Would an Auditing Organization receive independent recognition by each participating Regulatory Authority?

No. Recognition is a joint exercise and hence recognition of an AO by the MDSAP Regulatory Authority Council (RAC) means recognition by each participating Regulatory Authority.

29. Will Auditing Organizations be informed when there is a complaint against them so that improvements can be made?

Yes. MDSAP QMS P0011 Complaints and/or Customer Feedback Procedure defines a complaint to include "alleged deficiencies or expression of dissatisfaction related to the MDSAP Auditing Organizations and manufacturers"

The procedure requires the MDSAP Lead Project Manager to collaborate "with project managers and other stakeholders on the evaluation of the complaint or feedback and the determination of what (if any) process or product changes are needed."

C. Questions related to Audits

30. Which manufacturers are eligible to undergo an MDSAP Pilot audit?

As currently planned, any manufacturer of medical devices will be eligible to undergo an audit under the MDSAP Pilot. However, each regulatory authority may establish exclusion criteria for manufacturers meeting certain conditions if deemed necessary or when limited by legislation. It is important to note that manufacturers that participate in the MDSAP program will be responsible for securing and maintaining a contract with an MDSAP recognized AO. AOs operate as fee-for-service organizations. In other words, medical device manufacturers will pay for MDSAP audits conducted by an AO. The Regulatory Authorities participating in MDSAP are not involved in contractual arrangements / the contract negotiation process between manufacturers and AOs.

31. How can a medical device manufacturer participate in the Pilot MDSAP?

All medical device manufacturers that must comply with the regulations of any of the four Regulatory Authorities participating in the MDSAP Pilot are encouraged to participate in the Pilot.

Regardless of the manufacturing organization's size, scope of activity, type or number of products, or number of years of compliance, the MDSAP assessment process is the same. A medical device manufacturer may contact directly a Health Canada recognized registrar (CMDCAS recognized registrar) of their choice to enquire whether they have applied for MDSAP recognition and whether they are authorized to undertake audits under the MDSAP Pilot.

Medical device manufacturers do not apply to a Regulatory Authority for an audit under MDSAP.

32. Does the MDSAP Pilot add requirements for the manufacturer?

No. The MDSAP Pilot audit model was developed to cover existing requirements from the Regulatory Authorities participating in the MDSAP Pilot. The program does not add any new requirements to existing requirements from ISO 13485:2003 or other country-specific requirements of the participating Regulatory Authorities.

33. What are the potential benefits of a manufacturer participating in the MDSAP Pilot?

The MDSAP Pilot offers many benefits to medical device manufacturers including the following:

- A single audit is used in lieu of multiple separate audits or inspections by participating regulatory authorities or their representatives. Therefore, for many medical device manufacturers, the MDSAP Pilot reduces the overall number of audits or inspections and optimizes the time and resources expended on audit activities.
- Additionally, as a longer term goal, it is expected that the program will enhance confidence in the reliability of third party audits, that more Regulatory Authorities will join the program, and that other Regulatory Authorities will use information made available through the program to limit the need for additional audits.
- Some participating regulatory authorities will use MDSAP Pilot audit outcomes as an alternative to their own inspections to process applications for medical device marketing authorization.
- Like in any third party auditing program, the medical device manufacturer is free to choose among all authorized auditing organizations to perform the audits. Routine audits are announced and planned with the manufacturer.
- The MDSAP Pilot is expected to improve the predictability of audit outcomes through:
    - enhanced auditing organization recognition criteria,
    - monitoring of auditing organizations by the participating Regulatory Authorities,
    - the use of a standard MDSAP audit model,
    - the grading of any nonconformity using objective criteria to characterize the significance of the finding,
    - the reporting of the audit outcomes using a standard report template.
- Enrolling in the MDSAP Pilot may be seen as evidence of a medical device manufacturer’s commitment to quality management systems for product quality and regulatory compliance.

34. What are the potential benefits to the manufacturer participating, specific to each jurisdiction?

Australia: The Therapeutic Goods Administration – TGA

Where regulations do not require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will take into account MDSAP Pilot audit reports when considering whether a manufacturer has demonstrated compliance with an Australian Conformity Assessment procedure; or

Where regulations require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will take into account MDSAP Pilot audit reports when considering whether to issue or maintain a TGA Conformity Assessment Certificate[1]. Under some circumstances a manufacturer may avoid routine TGA inspections.

Following a successful evaluation of the MDSAP Pilot, the following may apply:
Where regulations do not require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will accept MDSAP certificates as evidence of compliance with ISO13485:2003 where the Standard has been used to demonstrate partial compliance with the requirements of an Australian Conformity Assessment Procedure. It is expected that Australian Sponsors may be required to submit to the TGA, additional technical documentation to demonstrate compliance with the requirements of the Essential Principles of Safety and Performance and the manufacturer's chosen Conformity Assessment Procedure.

Where regulations require a manufacturer or product to hold a TGA Conformity Assessment Certificate;

- The TGA will continue to take into account MDSAP audit reports when deciding whether to issue or maintain a TGA Conformity Assessment Certificate. Under some circumstances a manufacturer may avoid routine TGA inspections.

[1] TGA issued CA certificates are required for; manufacturers of medical devices that incorporate a medicinal substance, or a material of animal origin that has been rendered non-viable, or that contains tissues, cells or substances of microbial or recombinant origin, or that incorporate stable derivatives of human blood or human plasma.

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 post-market assessment procedures, providing, when applicable, key information that are expected to support regulatory technical evaluation on these issues.
Due to recent regulatory changes (RDC 15:2014 and RE 2.347:2015), ANVISA may use MDSAP Pilot 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 Pilot audit may accelerate ANVISA´s GMP certification process, which is a pre-requisite to the marketing authorization.

ANVISA can also use MDSAP Pilot audits to renew ANVISA's GMP Certificate bi-annually, as an alternative to an ANVISA comprehensive inspection.

Note: ANVISA will not use MDSAP audit reports from manufacturers where the result of ANVISA's previous inspection was considered unsatisfactory and therefore the manufacturer had the certification submission denied. In such cases ANVISA will start using the MDSAP reports only after a new ANVISA inspection with a satisfactory result.

Canada: Health Canada will operate the current Canadian Medical Device Conformity Assessment System (CMDCAS) program and the MDSAP in parallel during the three year pilot. During the Pilot, 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 Regulations.

Upon the successful conclusion of the MDSAP Pilot, Health Canada's intent is to implement the Medical Device Single Audit Program as the mechanism to assess regulatory compliance for quality management system requirements in Canada.

Japan: Japan's Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA) are evaluating the following possibilities:

- For manufacturers intending to put medical devices of class II, III or IV on the Japanese market, an MDSAP Pilot audit report might be utilized in a premarket inspection performed by PMDA or registered certification bodies in Japan. Undergoing an MDSAP Pilot audit may accelerate the Marketing Authorization with fewer burdens. An MDSAP Pilot audit report might be utilized in periodical post market inspection performed by PMDA or registered certification bodies in Japan. Undergoing an MDSAP Pilot audit may reduce some burden even for a post market phase.

United States: U.S. Food and Drug Administration's Center for Devices and Radiological Health – FDA – will accept the MDSAP Pilot audit reports as a substitute for FDA routine inspections (biennial by policy). Additional benefits include:

- MDSAP Pilot routine audits are announced, scheduled by the Auditing Organization with the manufacturer, with a pre-established duration;
- 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 Auditing Organization;
- Firms have one month to provide their full response to critical nonconformities (grade 4 and 5) to the Auditing Organization (as opposed to 15 working days following and FDA inspection);
- Certification documents issued by the Auditing Organization state compliance with applicable US regulations, which may provide a marketing advantage.

Note: Inspections conducted "For Cause" or "Compliance Follow-up" by FDA will not be affected by this program. Moreover, this MDSAP program would not apply to any necessary pre-approval or post approval inspections for Premarket Approval (PMA) applications or to decisions under section 513(f)(5) of the Act (21 U.S.C. 360c(f)(5)) concerning the classification of a device.

World Health Organization (WHO): In the framework of the *Prequalification Program* for diagnostic devices, the WHO may recognize successful MDSAP Pilot audits as acceptable evidence of QMS compliance with international regulations. This may result in either abbreviated or waived WHO inspection depending on the scope of audit.

35. What are the costs associated with MDSAP audits?

The cost of conducting an MDSAP Pilot audit is dictated by the commercial arrangement between the medical device manufacturer and the authorized MDSAP Auditing Organization.

36. Where can industry find out who is a recognized AO and which jurisdictions they are recognized for?

During the MDSAP Pilot, participating Regulatory Authorities will not recognize Auditing Organizations, but will "authorize" those AOs that meet the recognition criteria. This authorization will allow AOs to perform audits under the MDSAP Pilot. A list of Auditing Organizations who are formally recognized to perform audits under the MDSAP Pilot will not be published until after the end of the MDSAP Pilot. Therefore, a medical device manufacturer needs to enquire directly with candidate Auditing Organizations on whether they are authorized.

An Auditing Organization authorized to perform MDSAP audits during the pilot must have demonstrated competence in each jurisdiction's regulations. Therefore the authorization is not restricted in terms of a Regulatory Authority's jurisdiction. A standardized letter of authorization will be issued for AOs authorized to perform audits under the Medical Device Single Audit Program (MDSAP) Pilot.

37. How does the MDSAP Pilot ensure that medical devices are being manufactured in accordance with the regulations of multiple jurisdictions?

The MDSAP Pilot relies on:

- Annual audits of manufacturers according to an audit model specific to the program. This audit model was developed to review the compliance of a manufacturer's quality management system to the international standard ISO 13485:2003 and additional regulatory requirements applicable to the countries where the devices are sold; and
- Annual assessments of the Auditing Organizations' management system compliance to the international standard ISO/IEC 17021-1and MDSAP specific requirements as defined in IMDRF MDSAP WG documents.

38. How do Auditing Organizations ensure that duplicate efforts are not performed during an audit of a manufacturer that sells in multiple jurisdictions?

The Medical Device Single Audit Program (MDSAP) audit process was designed and developed not only to prevent duplication, but also to ensure that the program provides efficient and thorough coverage of the requirements of; Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2003) and any corresponding section(s) of the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Canadian Medical Device Regulations (CMDR, Part 1), the Japanese QMS ordinance (MHLW MO 169), the Quality System Regulation (21CFR 820), and other country-specific requirements.

The MDSAP audit sequence follows a process approach and was designed and developed to allow the audit to be conducted in a logical, focused, and efficient manner.

Additionally, MDSAP AU P0029 Initial Manufacturer Audit and MDSAP Manufacturer Withdrawal Notification Procedure was created to ensure that Auditing Organizations properly notify the MDSAP Team, describing the MDSAP notification process and timeframes that AO must follow when an initial MDSAP audit has been scheduled, rescheduled or transferred. The document also instructs how to properly notify the MDSAP Team when a Medical Device Manufacturer withdraws from MDSAP participation.

Timely notification of MDSAP initial audit schedules by AOs will prevent the duplication of inspection/audit of Medical Device Manufacturers participating in MDSAP. Additionally, adequate notification of situations where a Medical Device Manufacturer no longer elects to participate in MDSAP will ensure that continued regulatory oversight is maintained by all participating RA's.

39. How are regional regulatory differences addressed in the program?

The regulatory requirements of the participating Regulatory Authorities have been incorporated into the MDSAP Audit Model and further discussed in the MDSAP Audit Model Companion Document. An auditing organization will perform audits using this model and record findings in relation to the regulations of the participating Regulatory Authorities.

Each Regulatory Authority independently utilizes the MDSAP Pilot audit deliverables (audit reports, certification documents) according to their regulations and policies.

40. How will audits of medical device manufacturers be conducted under the MDSAP Pilot?

Authorized Auditing Organizations will perform MDSAP audits during the pilot according to documents developed by the participating Regulatory Authorities for the implementation of the Pilot. Some relevant policies and procedures introduced by the program to ensure consistency across Auditing Organizations and/or auditor teams include:

- The sequence of tasks specified in the Audit Model MDSAP AU P0002 will have to be followed, the audit duration will be based on planned audit tasks MDSAP AU P0008 Audit Time Calculation Procedure, ensuring consistency across Auditing Organizations. In general, the duration of MDSAP audits will not exceed the accumulated time of audits and inspections performed currently by each participating Regulatory Authority according to their governing regulatory frameworks.
- An audit report will be issued at the end of each audit, using a standard fillable template specifically designed for medical device regulatory audits.
- Nonconformities identified during an audit will be graded on a scale from 1 (least critical) to 5 (most critical), and will be managed according to criteria defined in the document GHTF/SG3/N19:2012, *Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange*).
- Audited manufacturer will be responsible for timely development and implementation of action plans to address non-conformities identified during audits MDSAP AU P0027 Post Audit Activities and Timeline Policy.
- Auditing Organizations will share the audit outcomes with the participating Regulatory Authorities to support their pre-market or post-market programs.

Upon successful certification or recertification audits, Auditing Organizations will issue MDSAP-specific certification documents stating compliance to ISO 13485:2003 and applicable regulatory requirements. MDSAP AU P0026 Certificate Document Requirements.

41. What is the difference between a Stage 1 and a Stage 2 Audit? (Initial Audit?)

The "Initial" audit also known as an "Initial Certification" audit consists of a Stage 1 and a Stage 2 audit.

- Stage 1 – A first Stage 1 audit consists of a documentation review and the evaluation of the readiness of the manufacturer to undergo a Stage 2 audit.
- Stage 2 – The purpose of a Stage 2 audit is to determine if all applicable QMS requirements of ISO 13485:2003 and all other applicable regulatory requirements from participating regulatory authorities have been effectively implemented.

42. How is the audit duration determined?

For the purpose of the MDSAP Pilot, the method to be used by authorized Auditing Organizations to calculate the time necessary to conduct an audit of a medical device manufacturer is defined in the procedure MDSAP AU P0008 entitled *Audit Time Calculations*. The procedure is available at MDSAP Documentation.

Audit Time Calculations also specifies criteria that shall be used by recognized Auditing Organizations to calculate audit time necessary to conduct an MDSAP Audit.

The MDSAP audit model defines the activities and tasks that are to be performed in an MDSAP Audit Cycle including; the activities and tasks for an Initial (Stage 1 and 2) Audit (a.k.a. Certification Audit), Surveillance, Re-audit (a.k.a. Recertification Audit), and for Special Audits. The appropriate audit tasks defined within the MDSAP Audit Cycle must be used when calculating audit times. When applicable, the appropriateness of the audit duration for subsequent activities should be confirmed during the Stage 1 audit.

There are varying numbers of audit tasks depending on the process being audited. Audit time is calculated based on the number of applicable audit tasks associated with the type of audit to be conducted (as defined in the MDSAP Audit Cycle) and the specific activities of the organization to be audited.

43. At what frequency do MDSAP audits occur?

The medical device manufacturers that will volunteer to participate in the pilot will be audited annually, according to a three-year certification cycle. The Initial Audit, also referred to as the *"Initial Certification Audit"* is a complete audit of a medical device

manufacturer's quality management system (QMS). The initial Audit is followed by partial Surveillance Audits conducted once per year for two consecutive years. The cycle re-commences with a complete Re-audit, also referred to as a "Recertification Audit" in the third (3rd) year.

Special Audits, Audits Conducted by Regulatory Authorities, and Unannounced Audits are potential extraordinary audits that may occur at any time within the audit cycle.

44. Can the scope of an MDSAP Pilot audit include combination products?

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

Medical Devices that include; drugs (medicinal substances) or biologics (e.g. materials of animal origin that have been rendered non-viable, or tissues, cells or substances of microbial or recombinant origin, human blood or extracts of human blood or blood products, etc.) (a.k.a. "combination products") may be included in the scope of an MDSAP Pilot audit.

The Regulatory Authorities that take into account MDSAP audit reports for combination products expect that the Auditing Organization, when conducting an audit for these products, will:

- undertake, to the extent possible during on-site audits, an assessment of the product / process related technologies in accordance with the requirements of N3 Clauses 9.2.4, 9.3.2 and 9.4.1, and the requirements of the MDSAP audit model for compliance with the country specific requirements;
- assign relevant technical competence to the audit team that is assessing the product / process related technologies and relevant controls for the handling, testing and manufacture of these types of devices; and
- record their findings in accordance with the requirements of MDSAP AU P0019 MDSAP Medical Device Regulatory Audit Reports.

However, due to differences in the way that these products are regulated in the jurisdictions of the participating Regulatory Authorities, MDSAP audit reports and certification documents will not be considered an alternative to the inspection and assessment requirements in some jurisdictions, as described below:

Australia: These products are subject to an off-site examination of the design by the TGA under the Australian Conformity Assessment Procedures. A Design Examination Certificate will be issued upon the successful completion of the examination.

The TGA is also required to issue a Conformity Assessment Certificate for the Full Quality Assurance procedure applied by the manufacturer for these products. When considering whether to issue or maintain this certificate the TGA may take into account MDSAP audit reports. An effective MDSAP audit report may reduce the frequency of TGA inspections for these devices.

Brazil: According to Brazilian regulations there are no specific requirements for combination products regarding the Quality Management System, and for that, all the requirements already disposed on the MDSAP companion documents promote adequate coverage for the needs established on the Brazilian legislation and regulation for those products. Therefore combination products that are considered medical devices in Brazil are included in MDSAP Pilot Program.

Canada: The MDSAP Audit model covers the requirements for combination products that are regulated as medical devices.

Japan: There are no Japanese characteristic requirements for combination products which are categorized as devices. Therefore MDSAP Audit results will be considered as alternatives to confirm the compliance of Quality Management System (QMS) requirements for such products.

United States: The MDSAP audit model only covers the requirements of the US medical device regulations. As additional requirements of the US regulations apply to devices incorporating drugs or biologics, the FDA cannot consider MDSAP Pilot audits of combination product manufacturers as an alternative to FDA inspections. Consequently such products are still subject to FDA inspections regardless of the participation of the manufacturer in the program. Nevertheless, the FDA may take into account the outcome of an MDSAP Pilot audit covering combination products to optimize the scope of the FDA inspection to be performed.

NOTE: When a combination product manufacturer also manufactures non-combination products, it is expected that during the initial certification audit and at least once during the subsequent certification cycle the audit team includes the technical competence to audit combination products; and, when applicable, the audit plan includes the quality management system processes and activities associated with the combination product. MDSAP audit plans and reports of combination product manufacturers must consider, where applicable:

1) Supplier Controls and acceptance activities (including testing) associated with the starting material that is to be used in the manufacture of the drug or biologic component (in particular Active Pharmaceutical Ingredients);
2) Controls of the manufacturing processes for the drug or biologic component;
3) Final acceptance and testing activities, including those associated with the drug or biologic component in the finished product; and
4) Stability programs that consider the drug or biologic component in the finished product.

45. Will there be a checklist available for industry that would compare the ISO 13485 requirements with each participating country's regulations?

The *Audit Model* MDSAP AU P0002 contains specific instructions on the MDSAP audit process. It incorporates an audit sequence and instructions for auditing each specific process. The audit process tasks incorporate references to the applicable ISO 13485:2003 clause(s) and any corresponding section(s) of the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Canadian Medical Device Regulations (CMDR, Part 1), the Japanese QMS ordinance (MHLW MO 169), and the Quality System Regulation (21CFR 820).

46. Will MDSAP be a top down inspection, as with the Quality System Inspection Technique employed by FDA?

The MDSAP Audit Model, which was inspired by the FDA's Quality System Inspection Technique document, is based on a "top-down" auditing approach.

47. Will the audit process include a daily review of areas of concern?

Yes. Auditing Organizations must be in compliance in accordance with the requirements of IMDRF MDSAP WG N3, and N4, including the requirements of ISO/IEC 17021-1 and all other related MDSAP documents, but will conduct the audit according to the Audit Model. Additionally, ISO/IEC 17021-1, Sub-Clause 9.4.3.1- *Conducting the opening meeting,* requires that "during the audit, the client will be kept informed of the audit progress and any concerns."

48. Will MDSAP Pilot audits be conducted by single or multiple auditors?

Procedure MDSAP AU P0008 Audit Time Calculations, specifies how to determine the on-site audit duration in man-days. Auditing Organizations decide how many auditors will compose the audit team. For instance, a 6 man-day audit could be completed in 3 days by a 2-auditors team. Auditing Organisations are also required to take into account the competency of the audit team for the type of audit and the scope of products that are produced under the control of the manufacturer's QMS.

49. Who assigns a particular auditor? The Auditing Organization or Regulatory Authority?

It is the AOs' responsibility to assign auditors for individual audits of medical device manufacturers, taking into account their competence, impartiality and availability.

Unlike other certification programs, a manufacturer may not oppose the choice of the auditor under the MDSAP Pilot (IMDRF MDSAP WG N3 FINAL:2013, *Requirements*

for Medical Device Auditing Organizations for Regulatory Authority Recognition exception to ISO /IEC 17021-1, section 9.1).

50. If MDSAP becomes mandatory for one or more participating countries will manufacturers be expected to be compliant with regulations in a jurisdiction that it does not market?

The manufacturers are expected to be compliant only with the regulations for the jurisdictions where their products are marketed.

51. Can RA's discredit/void any audits that were conducted by an AO due to inadequate audit method/technique? If so, will manufacturers have to go through re-audits for audits they believed to have passed?

The MDSAP Pilot does not include mechanisms for requiring an audit to be re-done. Nevertheless, if an audit report appears to be unreliable, a participating Regulatory Authority may not be able to utilize the report as part of their process to grant a marketing authorization. A misleading audit report may also present a risk to public health and could lead the Regulatory Authorities to conduct its own follow-up inspection. Alternatively, an RA may request that an AO conduct a special audit to follow up on an issue. (IMDRF MDSAP WG N3 – clause 9.5)
Manufacturers may forward a complaint with the participating Regulatory Authorities in relation to an audit performed by an Auditing Organization. The complaint will be processed using the procedure described in MDSAP QMS P0011

52. The initial pilot audits are based on the quality system regulations of the four initial regulators. If other regulators recognize the program will their requirements be incorporated?

Yes. If other Regulators choose to participate, Subject Matter Experts from the participating Regulatory Authorities will update the MDSAP AU P0002 Audit Model and MDSAP AU G0002.1 Companion Document with the relevant regulatory requirements of the new MDSAP recognizing Regulatory Authority.

53. If an AO issues a negative final report, does this mean I can no longer supply to/sell in all of the regulatory jurisdictions that are participating in the Pilot?

MDSAP audit reports will record the recommendation of the audit team for initial, continuing certification or re-certification of the audited medical device manufacturer. When the AO determines that the audited manufacturer does not meet QMS or other regulatory requirements, each of the Regulatory Authorities concerned would determine appropriate actions relative to the identified nonconformities. The nonconformities may or may not be associated with regulatory requirements of all participating regulatory authorities.

54. What happens if significant non-conformities are identified by an Auditing Organization and subsequently shared with the Regulatory Authorities?

Non-conformities identified by an Auditing Organization are to be graded in accordance with the document GHTF/SG3/N19:2012 – Quality management system – Medical devices – Nonconformity Grading System for Regulatory Purposes and Information Exchange. Nonconformities are to be recorded and graded by the Auditing Organization using MDSAP AU F0019.2 NC Grading and Exchange Form.

IMDRF MDSAP WG N3 FINAL: 2013 defines that the Auditing Organization shall provide information to the recognizing Regulatory Authority(s) about the audits and decision on conformity to quality management system requirements. The procedure MDSAP AU P0027 Post-Audit Activities and Timeline Policy if the audit identified one or more grade 5 nonconformities, or more than two grade 4 nonconformities, or a public health threat, or any fraudulent activity or counterfeit product, the Auditing Organization to inform the Regulatory Authorities within 5 working days. For Grade 4 or 5 nonconformities, manufacturers are expected to provide evidence to the Auditing Organization of implementation of the remediation actions addressing any grade 4 or 5 nonconformity within 30 days of the audit end date. Auditing Organizations are subsequently expected to provide the audit package, which includes the NC Grading and Exchange form, to a recognizing Regulatory Authority within 45 days of the end of audit. Post-audit actions timelines for a manufacturer and an Auditing Organization are further described in MDSAP AU P0027 Post-Audit Activities and Timeline Policy.

On receipt of the 5 days' notice the participating Regulatory Authorities will undertake actions that are appropriate for their jurisdictions and notify with the other participating Regulatory Authorities on the actions that should be taken in relation to the manufacturer.

55. How are nonconformities that are identified during an MDSAP audit managed? What is the timeline for a manufacturer to respond to nonconformities?

The document *Post-Audit Activities and Timeline Policy* MDSAP AU P0027 defines the activities to be completed and timeline that a medical device manufacturer must follow to address the nonconformities identified during an MDSAP audit.

The manufacturer must provide a remediation plan for each nonconformity within 15 calendar days from the date the non-conformity report was issued. The plan must include:

- the outcome of the investigation of the nonconformity and its cause(s),
- the planned correction(s), and
- the planned corrective action(s) to prevent recurrence.

The evidence of implementation of the remediation actions addressing any grade 4 or 5 nonconformity must be provided within 30 calendar days after the audit end date. (Page 1-section 2 Timeline)

56. Who would conduct follow-up visits to close the non-conformities?

An Auditing Organization would normally conduct close-out activities for all non-conformities in accordance with their procedures.

A participating Regulatory Authority may request that an Auditing Organization carry out a Special Audit to further investigate, follow-up or to closeout an audit under the direction of the requesting Regulatory Authority. (IMDRF MDSAP WG N3 FINAL:2013 - Clause - 9.5.1)

A recognizing Regulatory Authority may conduct its own Special Audit at any time it deems necessary and within the purview of its jurisdiction. (IMDRF MDSAP WG N3 FINAL:2013 - Clause - 9.5)

57. Do Auditing Organizations collect evidence of nonconformities, or other evidence usually collected during Regulatory Authorities' inspections?

Under the MDSAP Pilot, Auditing Organizations are not required to collect any evidence but the audit report must substantiate any audit finding by reference to audit evidence. Due to this restriction, the US FDA will limit enforcement actions based on MDSAP Pilot audit reports to advisory actions only.

This waiver also applies to other evidence usually collected during Regulatory Authorities' inspections, such as evidence of interstate commerce by the FDA.

For example, what does the FD&C Act mean by "Interstate Commerce". *Section 201(b) of the FD&C Act [21 U.S.C. 321(b)] tells what circumstances place a product in interstate commerce:*

(1) Commerce between any State or Territory and any place outside thereof, and
(2) Commerce within the District of Columbia or within any other Territory not organized with a legislative body.

"Interstate commerce" applies to all steps in a product's manufacture, packaging, and distribution. It is very rare that a cosmetic product on the market is not in "interstate commerce" under the law. For example, at least some of your ingredients or packaging most likely originates from out of state, or even out of the country. Likewise, it is foreseeable that your products will leave the state. Although there are certain exemptions [21 CFR 701.9], factors such as these generally cause the requirements of the FD&C Act to apply to your products."

58. During witnessed audits, will Regulatory Authorities prompt AO's in identifying nonconformities? (There is concern that the potential negative influence by RA on an AO)

The RAs will not interfere in the way an Auditing Organization (AO) conducts audits. The Medical Device Single Audit Program (MDSAP) is intended to allow competent auditors from MDSAP recognized AOs to conduct a single audit of a medical device manufacturer's quality management system in compliance with the requirements of the medical device regulatory authorities (RA) participating in the MDSAP program. For this purpose, the RA's will ensure, by periodical assessment, including the witnessing of audits of manufacturers conducted by AOs, that AOs are applying the MDSAP audit model and assigning adequate competence to the task.

59. As a manufacturer, how do I show that I was successfully audited under the MDSAP Pilot?

Upon successful completion of an initial audit or re-audit, an Auditing Organization will issue certification documents including a reference to the MDSAP, that will state compliance to ISO 13485:2003 and the applicable Medical Device Regulations from each jurisdiction that were used as audit criteria.

60. If a manufacturing site is already under regulatory action with a participating Regulatory Authority, can they participate in the MDSAP Pilot?

If a manufacturer is currently subject to regulatory action from one of the participating Regulatory Authorities then the manufacturer should consult with the RA about their eligibility for an MDSAP audit prior to resolution of the action. There are no exclusion criteria regardless of the past audit/inspection history, and regardless of the type of medical devices manufactured by the organization. Nevertheless, if a manufacturer had a previously unfavorable inspection by a participating Regulatory Authority, this Regulatory Authority may still choose to conduct a follow-up inspection. For example, this is the case with inspections conducted by the U.S. FDA.

61. What happens to a Manufacturer when the AO recognition is revoked?

The impact of a cessation of recognition, or the revocation of the authorization to audit, under the MDSAP Pilot may affect a large number of manufacturers. During the MDSAP Pilot, the participation in the program is strictly voluntary. The event should not directly affect any existing marketing authorization. Nevertheless, Regulatory Authorities may need to consider individual or collective transitional arrangements to assure existing or potential public health risks are mitigated.

To stay in the program, a manufacturer would need to contract another Auditing Organization to resume the audit cycle at the point of departure of the de-recognized Auditing Organization.

62. When will industry auditors have access (for a fee) to the AO auditor training? [Will training be available for manufacturers to ensure that its QMS will meet the MDSAP criteria?]

Computer-based on-line training modules have been created describing the MDSAP Audit Model that is to be used by Auditing Organizations to conduct audits of Medical Device manufacturers. This training is a requirement for each Auditing Organization auditor who will be conducting MDSAP Pilot audits. The training is not being made available to non-Auditing Organization certification bodies or to medical device manufacturers. Future availability is under consideration.

63. For manufacturers already holding ISO 13485 certification under the CMDCAS program how would they transition to the MDSAP program? Will a full initial audit be required?

During the MDSAP Pilot, in order to minimize the impact on ongoing certifications under CMDCAS, the MDSAP audit cycle may be synchronized with the CMDCAS audit cycle. Medical device manufacturers can participate in the MDSAP Pilot at their convenience and therefore their first MDSAP audit may be a surveillance audit. To be noted that in this case:

1. The manufacturer would not obtain an MDSAP certificate until a recertification audit is conducted;
2. A regulatory authority may not be able to use a surveillance audit report in their process to issue a marketing authorization.

The medical device manufacturer should therefore make the decision whether to synchronize the MDSAP audit cycle with the CMDCAS audit cycle or not based on their regulatory and business interests.

64. Why aren't MDSAP Pilot audit reports used by the FDA as substitutes for inspections for Premarket Approval (PMA) applications?

The FDA explicitly excludes PMA pre-approval and post-approval inspections for Premarket Approval (PMA) due to the lack of regulatory convergence in the following:

1. the premarket device assessment processes performed under the various regulations (e.g. US Premarket Application, Australian Design Dossier or Design Examination, Canadian Device License Application); and,
2. where the responsibilities for final decisions of safety and performance/effectiveness of a medical device are placed (regulatory authority vs. third party organization).

65. Which country specific regulatory requirements are included in the MDSAP Pilot audit criteria?

The Medical Device Single Audit Program (MDSAP) audit process was designed and developed to ensure a single audit will provide efficient yet through coverage of the relevant requirements of; Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2003), the Australian Therapeutic Goods (Medical Devices) Regulations (SR 236, 2002), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the Japanese QMS ordinance (MHLW MO 169), the Quality System Regulation (21 CFR Part 820), and other specific requirements of medical device regulatory authorities participating in the MDSAP program including 21 CFR Part 803 and 21 CFR Part 806.

66. How will the determination be made on whether an audit report supports an FDA advisory action without the supporting evidence?

The determination will be made following existing FDA criteria for situation 1 as described in the applicable Compliance Program, Part V. The evidence will be described in the narrative descriptions of nonconformities contained in the audit report. The auditor competency (including ability to identify existing nonconformities) is something the regulatory authorities review extensively during Auditing Organization assessment activities. An independent inspection by the FDA would be necessary to support judicial actions.

67. If the FDA has access to the MDSAP portal database, are audit reports, including evidence collected and retained, subject to US FOI?

The report package itself is not subject to FOI but any record generated by the FDA, for example the review memo, is subject to FOI.

68. How will Nationally Recognized Testing Laboratory (NRTL) Program audits be accepted?

NRTL tests and MDSAP audit are completely separate programs, evaluating compliance to distinct criteria. NRTL tests are required by the US Occupational Safety and Health Administration.

69. Can Regulatory Authorities not participating in MDSAP Pilot have access to audit reports? If so, what amount of information will be made available and at what cost?

Regulatory Authorities not participating in the MDSAP Pilot will not have full access to audit reports. Nevertheless, if a Regulatory Authority has a confidentiality agreement with a participating Regulatory Authority, a request may be made to obtain a copy of a particular report.

However, non-participating Regulatory Authorities may request audit reports and certificates from the medical device manufacturer.

70. Do the IMDRF or the Regulatory Authorities participating to the MDSAP Pilot plan to influence/revise the International Accreditation Forum (IAF) mandatory document MD9 on the audit of medical device manufacturers to ISO 13485?

No. The document IMDRF MDSAP WG N3 FINAL:2013 states that "IMDRF Regulatory Authorities have no official status within groups such as the IAF, or any voice in IAF governance or IAF mutual recognition agreements, that would allow the Regulatory Authorities to revise IAF documents to meet the needs of the regulators. It was also determined that the standard most commonly utilized is the ISO (the International Organization for Standardization) and IEC (the International Electro-technical Commission) standard ISO/IEC 17021-1 entitled, "Conformity assessment – Requirements for bodies providing audit and certification of management systems." Medical device Regulatory Authorities also have little influence in the standards organization that produces this standard and cannot simply change the standard for medical device regulatory purposes."

71. Is the CE certification included in the outcome of a successful MDSAP Pilot audit?

The MDSAP Audit Model MDSAP AU P0002 does not incorporate the requirements from the European regulations. Nevertheless, the medical device regulatory Audit Report form MDSAP AU F0019. 1 may be used for multipurpose audits and an Auditing Organization may incorporate the European requirements into the MDSAP audit criteria to eliminate duplicate reporting.

72. When will Auditing Organizations be able to include Japan's requirements in MDSAP audits?

On 13 October 2015, the materials necessary for Auditing Organizations to begin auditing against Japanese requirements were posted on the MDSAP webpage. MDSAP Auditing Organizations are now able to establish and obtain competencies; and revise processes in order to include Japan's requirements in MDSAP audits.

Once an AO completes the necessary training (and other competency and process requirements as deemed necessary), the AO may include Japanese requirements in MDSAP audits. Please contact your CMDCAS registrar to determine its availability to conduct MDSAP audits to include Japan's requirements.

73. Can the RAs consider if one report can represent a multi-audit site?

After reconsideration during the forum, the Regulatory Authorities agreed that a separate report will be necessary for each audited site.

74. Do audit tasks have to be repeated during a multi-site audit?

- The implementation of applicable QMS process elements should be audited at each site.
- Content of common procedures does not have to be audited again. However, the implementation of applicable QMS process elements should be audited at all applicable sites.
- The non-implementation of applicable QMS process elements may lead to nonconformities relating to document control (current, approved procedure not available at all sites); or failure to effectively train users of the procedure; or failure to effectively implement the procedure, among others.

75. What additional guidance can RAs provide AOs on the application of the MDSAP audit model to multi-site audits and for suppliers?

- The AO should determine the applicable QMS activities and corresponding audit tasks at each site included in the audit program.
- Content of common procedures does not have to be audited again. However, the implementation of applicable QMS process elements should be audited at all applicable sites.
- The audit team should pay attention to the interaction and coordination of activities between sites.
- MDSAP audit could be extended to a supplier facility if the manufacturer cannot demonstrate effective controls.

76. How should an AO handle companies that have a legal address with no association to the company's daily operations?

- Per N3, the AO shall audit all sites that will be recorded on the certificate.
- AOs can initially visit the site to confirm its activities and relationship to the QMS.
- Describe relationships/activities and site omissions in the audit report.
- Auditors should confirm if changes result in additions of sites to audit program.
- Non-operations/functional sites should not be audited/certified.

77. Should a remote-audited facility be included on the certificate?

According to MDSAP AU P0026, section 7, "The certification document shall record all sites of the manufacturer's quality management system that have been audited on-site. "

78. How should AOs handle "virtual" manufacturers?

Virtual Manufacturers shall be treated as manufacturers and shall be audited accordingly for all activities applicable to the devices designed or manufactured.

79. Manufacturers indicated that the grading system was too complex to understand

- The grading system is based off of N19 and there are no plans to change the document at this time.
- RAs will develop a CDRH Learn training module on N19 .

80. Can RAs provide additional guidance on applying the audit model using an audit team?

- Audits require effective pre-audit planning.
- While one auditor is reviewing a primary process of the audit model (e.g., Management), another auditor can cover a supporting process. (e.g., Facility Registration)
- Auditors covering the same process can cover different audit tasks.
- Maintaining audit team communication is essential.
- Additional guidance is discussed in the Articulate Online Module, “Introduction to MDSAP,” slides 37 and 38.

81. How should an AO apply the audit model when sites are not responsible for all QMS activities?

- AO should determine the applicable QMS activities and corresponding audit tasks at each site included in the audit program. This can be done in Stage 1 of the audit.
- The audit time calculation procedure, MDSAP AU P0008, and associated spreadsheet, MDSAP AU F008, can assist in identifying/planning audit tasks.

82. When should an AO employ a Technical Expert during an MDSAP audit?

ISO/IEC 17021-1 states, “The criteria for the selection of technical experts are determined on a case-by-case basis by the needs of the audit team and the scope of the audit.”

83. Can audit tasks be accomplished during pre-on-site audit activities?

Yes. RAs encourage AOs to use pre-audit planning, communications and other activities as a mechanism to complete or assist in the completion of audit tasks when appropriate.

84. Under what circumstances do the RAs perceive that an RA audit may still be required?

Additional RA audits may be required if:

- An MDSAP audit report failed to provide evidence required to support market authorization decisions.
- An audit reveals public health safety concerns or fraudulent activity.
- Combination product device manufacturers may still require RA audits/inspections. See question 44 of the MDSAP Q&A document for additional guidance on combination products.

85. Can RAs provide an explanation on how they will react following an audit?

Please refer to questions #34 and 44 in the “Medical Device Single Audit Program Frequently Asked Questions” document: http://www.fda.gov/downloads/MedicalDevices/InternationalPrograms/MDSAPPilot/UCM430563.pdf

86. When should multi-site audit reports be submitted?

Audit reports must be submitted following the audit of each site, as stated in MDSAP AU P0027, Post-Audit Activities and Timeline Policy.

87. How should AOs handle sharing of audit reports with RAs that are not participating in MDSAP?

This should be worked out between the AO and its clients and spelled out in contracts when necessary.

88. Have the RAs defined the term “Public Health Threat”?

- Public Health Threat is synonymous to the GHTF/SG2/N54R8:2006 term, Serious Public Health Threat – *Any event type, which results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action*.

89. How should AO auditors structure nonconformity statements?

- Nonconformities should be written in accordance with GHTF/SG3/N19:2012, section 4.1; and section 5.0 Appendix A.

90. Why have the RAs imposed an initial response period of fifteen (15) calendar days?

RAs operate under time constraints that require an awareness of audit outcomes within a specified number of days. In order to make informed decisions about audit outcomes, the RAs must assess the manufacturer’s response.

91. For a consistent interpretation, could the RAs define the term "implementation" in MDSAP AU P0027 and AS P0015?

- NCs cited by AOs after an MDSAP audit of a manufacturer: In the context of a manufacturer replying to nonconformities identified during an MDSAP audit, the term “implement” relates to the implementation of the actions specified in the manufacturer’s correction and corrective action plan.
- Please refer to MDSAP AU P0027, sections 2 and 3.

92. “Implementation”

- NCs cited by RAs following and assessment of an AO: In the context of an auditing organization replying to nonconformities identified during an RA assessment, the term “implementation” relates to the implementation, and confirmation of the effectiveness of corrections and corrective actions, subsequent to the review and acceptance by the RAs of the AO’s correction and corrective action plan.
- Please refer to MDSAP AS P0015 AO Nonconformity Process Flowchart.

93. What does the MDSAP certificate represent?

- The MDSAP certificate is an attestation by the AO that the facilities listed in the certificate have been audited against the listed criteria for the listed scope and found to conform to those requirements, including the regulatory requirements for the specified jurisdictions of the RAs.
- It does not represent a marketing authorization nor does it oblige participating Regulatory Authorities to issue any such marketing authorization or endorsement of the manufacturer or its devices.

94. Can suppliers be MDSAP certified?

Yes, if the supplier meets the participation criteria for any participating Regulatory Authority.

95. Can the RAs provide additional guidance on what should be recorded if the minimum N4 requirements cannot be fulfilled by an initial start-up AO?

- The RAs recognize that not all AOs will have the initial client participation to fulfill prerequisite annual experience requirements.
- AOs should document the circumstances and justify why requirements were not met in accordance with the principles for pre-requisite experience described in N4 Clause 6.2.
- RAs will consider each justification on a case-by-case basis.

96. Can MDSAP Survey results be periodically posted?

Yes. We plan to post them at six month intervals. However, if there is limited survey participation, the updates may not occur at this frequency.

97. Can the RAs clarify the requirements for the transfer of certification for participating manufacturers?

Transfer guidelines are currently being discussed by the RAs.

98. Can the RAs develop a single dispute resolution to minimize inconsistency if a manufacturer uses multiple AOs?

MDASP procedure P0031.001 MDSAP Documenting Differing Professional Opinion and Dispute Resolution Policy sets out a single mechanism for resolving disputes within the MDSAP program.

99. How long will RAs allow an MDSAP certificate to reference a jurisdiction where no product is distributed? One three year certification cycle? Other?

- MDSAP AOs can issue certificates referencing jurisdictions where the manufacturer does not yet have market authorization.
- Recognizing that market entry can take time, such certifications can be extended for a full three years.
- If at the end of three years, the manufacturer has not obtained or applied for market authorization, the requirements for the affected jurisdiction should be removed from the certificate until such time as the manufacturer can demonstrate implementation and effectiveness.

100. What is the process requesting a D-U-N-S number?

To meet the requirements described in the MDSAP AU P0029 Initial Manufacturer Audit and MDSAP Manufacturer Withdrawal Notification Procedure, medical device manufacturers will have to submit a D-U-N-S number(s) which may take time to obtain. For this reason, we encourage any facility, site, or organization that does not have their D-U-N-S number readily available to begin as soon as possible the process of obtaining that information.

A D-U-N-S number is required to uniquely identify each physical location of the business's facility or site (e.g., branches, divisions, and headquarters). A D-U-N-S number is a unique nine-digit sequence provided by Dun & Bradstreet. The D-U-N-S number is specific for each site. Each distinct physical location of an entity (e.g., branch, division, and headquarter) would be assigned a different D-U-N-S number.

The site-specific D-U-N-S number is a widely recognized business identification tool and serves as a useful resource for MDSAP in identifying and verifying certain business information submitted by a user.

If no D-U-N-S number has been assigned, a business entity may obtain one at no cost directly from Dun & Bradstreet. A new number may be obtained, or an existing number verified, by phone or online.

Note: It takes Dun & Bradstreet approximately 30 business days to process a new D-U-N-S number and communicate it via email. A business entity may receive a D-U-N-S number in approximately 10 business days for an expedited service fee. Please note that a business entity may not request or apply for a new D-U-N-S number on behalf of another business entity due to the verification procedures used by Dun & Bradstreet.

More information is available at the Dun & Bradstreet web page. See also the step-by-step instructions for obtaining a D-U-N-S number for businesses based either in the United States or abroad.