Regulatory Impact on Medical Device Quality Management Systems

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Presentation Slides

- This slide deck is the presentation performed on 2015-09-10.
    - A more detailed slide deck will be posted with expanded information in a number of the slides, and additional references and resources added within the next few weeks.
    - Please check back on the ASQ Baltimore website for the expanded version
    - Alternatively, email efinegan@asqbaltimore.org to get a notice when the slide deck is posted.

Regulatory Environment

- Complicated network of regulations, laws, standards, guidances that impact the manufacture and sale of medical devices
- International regulatory changes have a significant impact on the ability for a company to get its product to market

Why should Quality care?

- Quality and Regulatory have been linked with product, service and process development for some time
  - ISO 13485:1996 – Medical Device Quality system.
  - ISO / TS 16949:1999 (QS9000:1994) – Automotive supply chain.
  - AS 9100 (AS 9000:1998) – Aerospace Basic Quality System Standard.
  - ISO 14000 (BS 7750:1992) – Environmental
  - ISO 22000 – Food safety management

Why should Quality care?

- Within the Medical Device regulatory world, regulatory requirements have been an input into product design, but also the quality management system
  - FDA regulations 21 CFR 820, “GMP”.
  - For years, the FDA GMP requirements were the “standard” around the world.
  - ISO 13485:1996 changed this, attempting global harmonization which fell a little short

Why should Quality care?

- Because Regulatory is moving in to our turf . . .
- Because Regulatory is making our jobs harder. . .
- Because Regulatory decision-makers know that implementing a correct Quality system framework is the best way to put safe and effective medical devices out in the market . . .
- Because Regulatory decision-makers realize that a globally harmonized quality system is the best way to meet that goal . . .

QMS Impacts

- **Supply chain**
- **Audit burden**
- **MDSAP program**
- QMS Certification Choices
- Post-market surveillance
- Qualified person
- General business impacts (resources, costs, etc)

Supply Chain Impact

- Although currently driven by Europe, major regulatory bodies are now scrutinizing the supply chain much more than before
    - Poly Implant Prothéses Scandal
- Contract Management
    - ISO 9001:1994 had “Contract review”, and future versions of the standard moved that under customer requirements.

Supply Chain Impact

- Unannounced Audits
    - Europe is directly looking into suppliers
    - FDA and Health Canada are looking into indirect enforcement
- New standards / regulations
    - ISO 13485:201x is now expanding its scope to suppliers of medical device manufacturers.

Supply Chain Impact

- Risk-based
  - The entire review of supplier management will need to be risk-based.
  - Move within quality community to review/document decisions across all aspects of the QMS
    - "risk-based" thinking / "risk-based" approach
    - documentation increase of risk based decisions

Supply Chain Impact

- Practical Implications
  - Supplier management is expected to increase
  - “Approved supplier list” will not be adequate
  - Risk based management of crucial suppliers / critical suppliers and suppliers of critical components will be required
  - Documentation of supplier reviews will become necessary, particularly for Notified Bodies
  - Balance of what suppliers are determined to be critical versus non-critical

Audit Burden

- Regulatory requirements impact manufacturers
  - Announced audits.
    - Scheduled and under control of the manufacturer
    - For example, internal audits, registration/surveillance audits and supplier audits
  - Unannounced audits.
    - Variety of unannounced audits are now required to be performed for medical device manufacturers

Announced Audits

- Internal audits
  - Already exist within current QMS framework
  - New requirements (regulatory, technical file, MDD)
- Registration/Surveillance audits
  - ISO 9001 / ISO 13485 audits.
    - will include be impacted by MDD, CMDCAS/MDSAP

Announced Audits

- Organization-Supplier audits
  - Already exist within current QMS framework
  - Your suppliers will be impacted by new requirements
- Customer-Supplier audits
  - Already exist within current QMS framework
  - Customers will be impacted by new requirements and your organization may be audited based on risk/requirements

Unannounced Audits

- Types of Unannounced Audits:
  - FDA Inspections
  - EU Notified Body Audits
  - MDSAP Audits
  - EU Importer/Distributor Audits (proposed)
  - NTRL Product Audits

Unannounced Audits

- FDA Inspections
  - FDA inspects medical device manufacturers.
    - No statutory authority to audit suppliers, only if they already produce medical devices
  - Currently, 5 day notice.
  - MDSAP program – impact.

Unannounced Audits

- EU Notified Body Audits
  - New style of “unannounced” audits
    - Unannounced, “10-minute rule”
    - Minimum once every three years, risk-based
    - Multiple auditors, cost borne by manufacturer
  - Reasons why
    - European Growth, no updates in 20 years
    - Poly Implant Prothéses Scandal

Unannounced Audits

- EU Notified Body Audits
  - Notified Bodies audit technical files for products placed on markets
  - Notified bodies will audit manufacturers and suppliers
    - At least 2 audit-days (depending on the device)
    - Two auditors will be used per unannounced audit, instead of a single auditor
  - Notified bodies reserve the right to audit through the supply chain (risk based)

Unannounced Audits

- EU Notified Body Audits
  - Manufacturers - Practical Impact
    - Unannounced audits will need to be accepted, rejection will mean loss of ISO 13485
    - Constant information on production schedules to Notified Bodies is required, depending on your business
    - Production line will need to be “running” to provide access to auditors without notice
    - Audits will include technical file and physical review

Unannounced Audits

- EU Notified Body Audits
  - Manufacturers - Practical Impact
    - Personnel will need to be available without notice to accompany auditors
    - Internal auditors will need to add EU-focused audits to ensure that any unannounced audits will be successful
    - Post-market surveillance and Vigilance records will be more important in the future, and may be copied during the audits to be added to the regional databases

Unannounced Audits

- EU Notified Body Audits
  - Suppliers - Practical Impact
    - Audits will be unannounced for suppliers
    - Suppliers will be audited against their quality management systems, even if they do not have one.
    - If suppliers do not allow the audit to proceed, immediate suspension of ISO 13485 certificates
    - Expectation that contractual requirements will be in place

Unannounced Audits

- EU Notified Body Audits
  - Suppliers - Practical Impact
    - Suppliers will need to be actively managed, rather than passively
    - Contracts with suppliers will need to make them aware that they may be audited.
    - Contracts with supplier good idea to give them a “heads up” about what is upcoming.

Unannounced Audits

- EU Notified Body Audits
  - Suppliers - Practical Impact
    - Notified Bodies will consider contract management with suppliers part of supplier management (i.e., no contracts implies that Notified Bodies cannot audit suppliers, a violation of MDD requirements)
    - Current proposal requires companies to include supplier's suppliers.

Unannounced Audits

- EU Notified Body Audits
  - Suppliers - Practical Impact
    - Companies need to be clear on definition of critical suppliers and how they are designated and reported to the Notified Bodies
    - Any changes to the status of critical / non-critical supplier will need to be justified to the Notified Bodies
    - If suppliers reject audits and ISO 13485 certificate is rejected, it is unknown this will impact MDSAP
    - Manufacturer will not be notified that the audit is occurring. Supplier will probably inform.

Unannounced Audits

- EU Notified Body Audits
  - Suppliers - Practical Impact
    - Relationships with our individual suppliers will become more important
    - Ease of simply changing suppliers needs to be managed with the regulatory impact to be taken into account
    - Business risk – an unhappy supplier can jeopardize our ISO 13485 certification .

Unannounced Audits

- NTRL Audits
  - Safety and EMC testing – product audits.
- EU Importer / Distributor audits
  - EU is changing the current Medical Device Directive (MDD)
  - Importers will be held responsible for product received from manufacturers
  - Distributors will be responsible for compliance of products received from importers/distributors
  - Expected to take effect in 2017

MDSAP – What is it?

- MDSAP = Medical Device Single Audit Program
  - MDSAP is intended to allow recognized Auditing Organizations to conduct a single audit of a medical device manufacturer that will satisfy the relevant requirements of the medical device regulatory authorities
  - Based on ISO 13485:2003
  - Pilot program begun January 2014, ongoing

MDSAP – Countries involved

- Initially 4 countries are signatories to the Pilot program
  - Australia
  - Brazil
  - Canada
  - United States
- Additionally, other countries/agencies are observers
  - Japan
  - Europe, China, Russia
  - World Health Organization (WHO)

MDSAP – Countries involved

- Practical Impact – Regulatory standpoint
  - For any item being audited, the most stringent countries' requirements will apply
  - Results from any audit will be sent to any MDSAP country where manufacturer has products
  - Idea of a single audit covering every country will be a benefit (fewer audits, cost savings).

MDSAP – Audits

- Practical Impact – Auditing standpoint
  - Limited number of auditing organizations
  - Limited number of auditors
  - Auditor requirements are very stringent
  - Problem with all MDSAP Auditing Agencies moving forward
  - Estimations by regulators are that audits will be 35% to 100% longer than CMDCAS audits

MDSAP – Audits

- Practical Impact – Auditing standpoint
  - Audits will be QSIT-style (process based) audits, falling under the CAPA+1 for surveillance and the entire system during registration, with particular focus on:
    - Management
    - Measurement/Analysis/Improvement
    - Design and Development
    - Production and Service Controls
    - Purchasing / Supplier Management
    - Authorizations / Registration / Adverse Event / Advisory Reports

MDSAP – Audits

- Practical Impact – Auditing standpoint
  - All audits shall be expected to be much more in-depth than current ISO 9001 / ISO 13485 audits
  - Non-conformities will be graded in 5 levels. Most serious non-conformities will be closed out via an unannounced MDSAP audit
  - All regulatory bodies will receive audit results, good or bad. One bad audit will flag all relevant regulatory bodies.
  - Management Reviews, internal audit results and supplier audit results will be eligible to be provided to the FDA (not currently)

MDSAP – Audits

- Practical Impact – Auditing standpoint
    - MDSAP materials provide useful training materials for organizations (even non-medical)

MDSAP – FDA View

- FDA is performing both QSIT and MDSAP audits
  - Unknown when FDA will switch completely from QSIT to MDSAP
  - May require Congressional involvement.
- FDA is allowing MDSAP audits to substitute for “routine audits”
  - Does not benefit smaller companies who may not being routinely audited
  - Additionally, benefit lasts for a year and MDSAP audits are required to be performed annually

MDSAP – Canadian View

- Canada is currently performing the CMDCAS program
  - CMDCAS is ISO 13485 with a number of specific requirements introduced by Health Canada
  - Limited number of auditing companies to perform CMDCAS audits

MDSAP – Canadian View

- CMDCAS ➔ MDSAP
  - Although a pilot program, MDSAP will be replacing CMDCAS in January 2017
  - This forces the switch from a voluntary program to a mandatory program for any country selling into Canada and the U.S.
  - Fewer auditors will be available for the MDSAP program

QMS Certifications

- ISO 9001 and ISO 13485
  - Although once well harmonized, they have been drifting apart.
  - ISO 13485 has not followed the new ISO High level format.
  - If the company wishes to maintain both ISO 9001 and ISO 13485 standards, there will be more work involved moving forward.

Post market surveillance/vigilance

- Regulatory requirements worldwide for post-market vigilance, surveillance, adverse event review, product service issues are increasing
    - Increases to existing complaint / non-conformance management program.
    - Management review of results are becoming expected (regulation / ISO 13485).
    - Risk management moving from a regulatory / design expectation to a general quality aspect of the product.

Qualified Person (EU)

- Definition
  - "manufacturers must have available within their organization at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of medical devices."
  - Expertise shown via:
    - A diploma, certificate or other evidence of formal qualification awarded on completion of a university degree or of an equivalent course of study, in law, natural sciences, medicine, pharmacy, engineering or another relevant discipline;
    - Three years of professional experience in regulatory affairs or in **quality management systems** relating to medical devices.

Qualified Person (EU)

- Resource impact
  - Although a “regulatory” requirement, for companies who outsource regulatory requirements, quality personnel may be called on to perform QP duties.
  - May already exist within the projects.
- Responsibilities
  - Conformity of the devices is appropriately assessed.
  - Review of corrective actions, vigilance, incidents
  - Necessary filings to regulatory bodies

Practical Impacts

- Increased Costs for Manufacturers
  - Financial.
    - Work required to meet new requirements
    - Cost of new certifications
    - Flow-down costs (goods from suppliers)
    - (MDSAP) Audit costs will increase, shift to manufacturer
  - Resources.
    - Audits will increasingly rely on SME/Regulatory personnel to meet needs
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Practical Impacts

- Stricter requirements impacting the regulators
  - Notified Bodies, shortage of auditors.
  - Longer times for audits mean impact on schedules
  - Notified Bodies are leaving the medical device field due to increased requirements
  - Manufacturers will need to manage certification program
  - “Special” Notified Bodies will be created for higher-risk devices, stretching resources

Practical Impacts

- Increased costs of medical devices
  - Financial.
  - Supply impact.
- Audit exposure
  - Audits for certification are normally used not only for market requirements, but for improvement
  - Audit result exposure can have a larger impact on manufacturers (good or bad)

Practical Impacts

- Difficulty in gaining entrance into markets
    - Greater time-to-market, upfront resources.
    - Greater “paperwork” burden.

Practical Impacts

- Peripheral impacts of upcoming regulatory issues
  - Cyber-security
  - Protected Health Information
  - Unique Device Identifiers
  - Additive Manufacturing (3D printing)
  - Mobile health devices
  - Medical device follow-on from Pharmaceutical

Questions ?

Thank you