What is New in Medical Device Quality Management Systems

Introduction to new and revised Medical Device regulations and standards

- What we will cover
  - Identify what has/is changing for medical device standards and regulations
  - Discuss the implementation time line for these
  - Discuss how each of these changes could effect you QMS

World Wide Changes

- ISO 13485:2016
  - Medical devices — Quality management systems — Requirements for regulatory purposes
- Medical Device Single Audit Program (MDSAP)
  - Canada, Australia, Japan, Brazil
  - US Food & Drug Administration (FDA)
- New European Medical Device Regulations
  - Will replace MDD, AIMDD, IVD
- EN ISO 14971:2012
  - Medical devices - Application of risk management to medical devices

ISO 13485:2016

- Still required for CE mark
- Must be certified to the 2016 version by end of Feb. 2019
  - Plan your certification audit now!
  - Do a GAP analysis
  - Begin implementation of changes

ISO 13485:2016

- Changes/Implications
  - Risk Management required throughout all QMS processes
  - Some reorganization of subsections
    - See slides at the end if you want to know what these are
  - Explicitly states it can be used by suppliers and others
  - Emphasis on Regulatory requirements
    - Especially Europe, but also other countries where you sell devices
  - Added details covering a lot of what was previously "Expected"
    - e.g. GHTF and other guidance documents
  - Now incorporates most FDA requirements
    - Validation of QMS software
    - More details on Complaint handling
    - Design Controls

ISO 13485:2016

- Definition: Documented means establish, implement and maintain
- Definition: Product means the output of a process
  - This includes services, software and physical devices
- Must document the roles of the organization
  - Manufacturer, distributor, etc.
- Requires a medical device file
  - Known in the FDA as Device master Record

ISO 13485:2016

- Requires written supplier agreements with all suppliers of Outsourced Processed
- Requirement on the protection of confidential health information
- Explicitly requires some added procedures
  - Management Review
  - Determining employee competence, training & awareness
  - Work environment
  - Product identification and identification of product status

ISO 13485:2016

- Information systems are now considered part of infrastructure
  - This includes any outsourcing or suppliers of IT products and services must be considered suppliers
- Some new requirements for sterile products
- Requires both supplier monitoring and re-evaluations
- New product cleanliness requirement
- Added requirement for Unique Device Identifier (UDI)
- Separate sub-sections for Servicing and installation
- Requires analysis of service records
- Requirement to identify test equipment used to preform measurement activities

ISO 13485:2016

- Separate requirement for nonconformities discovered before and after product is delivered to customers
- More details on analysis of data and use of statistical techniques
- Requirement to verify that a corrective actions and preventive actions do not have an adverse effect

ISO 13485:2016

- For more details get a copy of the standard
  - Also there are many papers on the internet and many courses offered to help you prepare for this
  - I have a list of the sections at the end of this presentation
  - I also have a printout of the list of changes from the 2003 version that you can look at
- If you require ISO 13485 certification and do not yet have a certification audit for this – Do it NOW!

MDSAP

- Medical Device Single Audit Program
  - The Medical Device Single Audit Program (MDSAP) is intended to allow competent auditors from MDSAP recognized Auditing Organizations (AOs) to conduct a single audit of a medical device manufacturer's quality management system that will satisfy the requirements of the medical device regulatory authorities participating in the MDSAP program.
- Participating Countries
  - United States (Food & Drug Administration, FDA
  - Canada (Health Canada)
  - Australia (Therapeutic Goods Administration)
  - Brazil (Agência Nacional de Vigilância Sanitária)
  - Japan (Ministry of Health & drug and device agency)

MDSAP

- Canada requires certification by Jan. 2019
  - Must be done by MDSAP certified auditor
  - Will be a subset of European Notified Bodies
- Main FDA information page
  - https://www.fda.gov/medicaldevices/internationalprograms/mdsappilot/default.htm
  - Gives and overview and link to other information
  - MDSAP is not required by the FDA

MDSAP

- This is a structured auditing program
  - Covering all of your QMS
  - For all the quality and regulatory requirements of the participating countries
  - You will be audited only on the requirements of the participating countries where you sell products
- Nonconformities are graded on a scale
  - Risk based
  - To pass and audit
    - You can have a limited number of the highest grades
    - You can have more of the lower grades

MDSAP

- Good news
  - You only have to comply with the regulations of the participating countries where you sell products
  - These must all be covered in you Quality Manual
    - May require that you create a compliance procedure for each countries' regulatory requirements
    - e.g. may need a procedure that covers FDA Establishment Registration and Listing
    - e.g. Canadian compliance for licensing and mandatory reporting

MDSAP

- Bad News
  - You have to comply with all the regulations of the participating countries where you sell products
  - Even if that country does not or does not yet require MDSAP
- For Example
  - if you are required to have MDSAP because you sell products in Canada
  - Your audit report will also go to all the other participating countries where you sell products
    - So the FDA will see your MDSAP audit report!
      - This could eliminate a routine cGMP audit
      - This could also trigger an FDA audit!
    - And if you sell product there so will Brazil, Australia, and Japan

MDSAP

- Requirements are those of the participating countries
  - FDA Quality System Regulation
  - ISO 13485
  - Other regulatory and quality requirements
- There are some documents that can help you better understand the MDSAP approach
  - Audit Model
  - Companion Document
  - Assessment Checklist

See next slide for where to find these

MDSAP - References

- FDA Main page to document links
  - www.fda.gov/medicaldevices/internationalprograms/mdsappilot/ucm377578.htm
- MDSAP AU P0002.004 Audit Model
  - https://www.fda.gov/downloads/medicaldevices/internationalprograms/mdsappilot/ucm390382.pdf.
- MDSAP G0002.1004 Companion Document_rev 2017-04-13
  - www.fda.gov/downloads/medicaldevices/internationalprograms/mdsappilot/ucm390383.pdf
- MDSAP_QMS_F0008.2.003_Internal_Assessment_Checklist_ 2017_03_01
  - www.fda.gov/downloads/medicaldevices/internationalprograms/mdsappilot/ucm379462.pdf

New European Regulations

- Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
- Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU

New European Regulations

- Regulations, not Directives
  - All EU states are required to follow
  - Does not require adoption by a member state
  - The regulations are much longer and more detailed
- MDR 2017/745 (MDR)
  - An unfortunate acronym
    - Do no confused with the FDA Medical Device Reporting (MDR) Regulation
    - 123 articles, 92 pages, plus 83 pages of Annexes
- IVDR 2017/746 (IVDR)
    - 113 articles, 83 pages, plus 74 pages of Annexes

I will primarily discuss the MDR, but issues are similar for IVDR

European MDR - Highlights

- Medical Device (MD) and Active Implantable MD are combined into the MDR
- Definition of medical devices is extended
  - Some accessories and other devices not previously covered are not considered devices
- EN ISO 13485:2016, which was released in March 2016, also becomes mandatory in early 2019
- Notified Bodies (NBs) are more heavily regulated
  - NBs would be placed under a strict regimen of supervision
  - The qualification requirements for auditing and reviewing NB staff are steeply increased
  - **This means fewer NBs will be available for audits and product assessments**

European MDR - Highlights

- “Risk” is now defined as in the ISO EN 14971:2012
- Mandatory Unique Device Identification (UDI)
- Authorized Representative duties and responsibilities are spelled out in detail
- Economic Operators (EOs) – new group covered
  - Defined as Distributors and Importers
  - Very different form Authorized Reps
  - duties and responsibilities are spelled out in detail
  - In the definition of economic operator also the assembler of procedure packs and the person sterilizing procedure packs and systems are mentioned

European MDR - Highlights

- Post Market Surveillance is explicitly intended for gathering and analyzing information with the aim of deciding about preventive and corrective actions
- Manufacturers are required to report a serious incident (or Field Safety Corrective Action (FSCA)) to the relevant Competent Authorities by using EUDAMED database
  - Timeframes given based on severity
- The introduction of strict rules for clinical investigations and alignment to the Clinical Trials Regulation
  - For implantable Class III devices, clinical investigations will be expected since NBs will generally no longer accept the equivalence approach, although some exceptions can be made.

European MDR - Highlights

- EU Member States have the possibility to levy fees to cover costs associated with this Regulation
- Reprocessing of single-use devices is only allowed under specific conditions
- Some new devices and non-medical devices are regulated
  - Devices for cleaning, disinfection or sterilization of devices
  - Devices that deliver drugs, that were not previously considered medical devices
    - E.g. a product that is implanted to control fertility by slow release of hormones
  - Substances that are carcinogenic or that have other potential high-risk effects on the human body

European MDR

- Guidance documents are important
  - Global Harmonization Task Force (GHTF)
  - International Medical Device Regulators Forum (IMDRF).
  - Both found on IMDRF website
    - http://www.imdrf.org/documents/documents.asp
  - MEDDEV documents
    - http://ec.europa.eu/growth/sectors/medical-devices/guidance_en

European MDR – Transition

- The Regulation entered into force on 26 May 2017.
- It applies from 26 May 2020.
  - EC Certificates issued under the current system may remain valid until they expire.
  - NBs may issue certificates to the MDD or AIMDD up until 26 May 2020
    - these certificates are valid for five years to allow for a smoother transition
    - the latest become void no later than 25 May 2024
- Devices legally placed on the market compliant to the MDD or AIMDD and prior to 26 May 2020 can be sold until five years after that date i.e. until 26 May 2025.
- NBs accredited before 26 May 2020 can start issuing certificates under the MDR once accredited

European IVDR – Transition

- The Regulation entered into force on 25 May 2017.
- It applies from 26 May 2022.
  - EC Certificates issued under the IVD Directive remain valid until they expire if before 26 May 2024.
  - IVDR Certificates are required by 26 May 2024
- NBs may issue certificates to the IVD Directive until 26 May 2022, but expire no later than 26 May 2024
- NBs accredited before 26 May 2022 can start issuing certificates under the IVDR once accredited

European MDR & IVDR- References

- EU Medical Device Regulations
  - http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=OJ:L:2017:117:FULL&from=EN
  - Gives links MDR & IVDR to pdf & text versions in many languages
- Understanding Europe's New Medical Device Regulation - MDR 2017/745
  - https://www.emergobyul.com/resources/articles/whitepaper-understanding-europes-medical-devices-regulation
- Understanding Europe's New IVDR 2017/746
  - https://www.emergobyul.com/resources/articles/white-paper-eu-ivdr
- EU Guidance Documents (MEDEVS & Others)
  - http://ec.europa.eu/growth/sectors/medical-devices/guidance_en

EN ISO 14971:2012

- Medical devices - Application of risk management to medical devices
  - Required for CE mark to sell devices in Europe
- The **requirements** of BS EN ISO 14971:2012 are *identical* to those of ISO 14971:2007
  - Medical devices – Application of risk management to medical devices
- Addition of 3 ***Informative*** Annexes is the only difference
- Only for European version EN ISO 14971:2007

EN ISO 14971:2012

- Annex ZA (Informative)
  - Relationship between EN ISO14971 and Requirements of EU Directive 93/42/EEC on Medical Devices (MDD)
- Annex ZB (Informative)
  - Relationship between EN ISO14971 and Requirements of EU Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD)
- Annex ZC (Informative)
  - Relationship between EN ISO14971 and Requirements of EU Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMDD)

EN ISO 14971:2012 – Differences (MDD)

- All risks must be reduced as much as possible
  - Must consider all risks
    - ISO14971 - you may discard negligible risks
  - Regardless of any "acceptability" assessment
    - ISO14971 - Implies manufacturer may set a threshold for risk acceptability level
    - ISO14971 - Only unacceptable risks are considered in overall Risk/Benefit analysis
  - Regardless of cost
    - ISO14971 - Introduces "**as low as reasonably practicable" (ALARP),** This implies a cost consideration

EN ISO 14971:2012 – Differences (MDD)

- All risks be balanced, together with all other risks, against the benefit of the device
  - Risk/Benefit analysis always be done
    - ISO14971 - When residual risk is not acceptable then Risk / Benefit analysis may be used to determine acceptability of residual risk
  - May do Risk/Benefit analysis for each individual risk
  - Must also do Risk/Benefit of all residual risks combined
  - Undesirable side-effects must have an acceptable risk when measured against intended performance

EN ISO 14971:2012 – Differences (MDD)

- Risk Control Options
  - Consider state-of-the art and consecutively apply all options in this order
    - Safety by design
    - Protective measures
    - Information to the use
    - **Reduce risk by design whenever it is possible**
    - Implies must apply all the control options possible
    - Can't stop at an acceptable level of risk
    - Unless additional controls do not further reduce the risk
  - ISO14971 - Use one or more of the control options in order as above, but only requires one be done if risk is then acceptable

EN ISO 14971:2012 – Differences (MDD)

- Information for Users
  - Users must be informed of residual risks
    - This implies information to users does not further reduce risk
  - Therefore must not use “information for users” to reduce risk
  - ISO 14971 - Information for Users is a control measure
    - Therefore can reduce risk

Thank You

- Questions?

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FYI

ISO13485:2016 Sections

On the next few slides

ISO 13485:2016

- 4 Quality Management System
  - 4.1. General requirements
  - 4.2. Document requirements
    - 4.2.1. General
    - 4.2.2. Quality manual
    - 4.2.3. Medical device file
    - 4.2.4. Control of documents
    - 4.2.5. Control of records

ISO 13485:2016

- 5 Management responsibility
  - 5.1. Management commitment
  - 5.2. Customer focus
  - 5.3. Quality policy
  - 5.4. Planning
    - 5.4.1. Quality objectives
    - 5.4.2. Quality management system planning
  - 5.5. Responsibility, authority and communication
    - 5.5.1. Responsibility and authority
    - 5.5.2. Management representative
    - 5.5.3. Internal communication
  - 5.6. Management review

ISO 13485:2016

- 6 Resource management
  - 6.1. Provision of resources
  - 6.2. Human resources
  - 6.3. Infrastructure
  - 6.4. Work environment and contamination control
    - 6.4.1 Work environment
    - 6.4.2 Contamination Control

ISO 13485:2016

- 7 Product realization
  - 7.1. Planning of product realization
  - 7.2. Customer-related processes
    - 7.2.1 Determination of requirements related to product
    - 7.2.2 Review of requirements related to product
    - 7.2.3 Communication
  - 7.3. Design and development
  - 7.4. Purchasing
  - 7.5. Production and service provision
  - 7.6. Control of monitoring and measuring equipment

ISO 13485:2016

- 7.3. Design and development
  - 7.3.1 General
  - 7.3.2 Design and development planning
  - 7.3.3 Design and development inputs
  - 7.3.4 Design and development outputs
  - 7.3.5 Design and development review
  - 7.3.6 Design and development verification
  - 7.3.7 Design and development validation
  - 7.3.8 Design and development transfer
  - 7.3.9 Control of design and development changes
  - 7.3.10 Design and development files

ISO 13485:2016

- 7.4. Purchasing
  - 7.4.1 Purchasing process
  - 7.4.2 Purchasing information

ISO 13485:2016

- 7.5. Production and service provision
  - 7.5.1 Control of production and service provision
  - 7.5.2 Cleanliness of product
  - 7.5.3 Installation activities
  - 7.5.4 Servicing activities
  - 7.5.5 Particular requirements for sterile
  - 7.5.6 Validation of processes for production
  - 7.5.7 Particular requirements for validation sterile barrier systems
  - 7.5.8 Identification
  - 7.5.9 Traceability
  - 7.5.10 Customer property
  - 7.5.11 Preservation of product

ISO 13485:2016

- 8 Measurement, analysis and improvement
  - 8.1. General
  - 8.2. Monitoring and measurement
    - 8.2.1. Feedback
    - 8.2.2. Complaint handling
    - 8.2.3. Reporting to regulatory authorities
    - 8.2.4. Internal audit
    - 8.2.5. Monitoring and measurement of processes
    - 8.2.6. Monitoring and measurement of product

ISO 13485:2016

- 8.3. Control of nonconforming product
  - 8.3.1 General
  - 8.3.2 Actions in response to nonconforming product detected before delivery
  - 8.3.3 Actions in response to nonconforming product detected after delivery
  - 8.3.4 Rework
- 8.4. Analysis of data
- 8.5. Improvement
  - 8.5.1. General
  - 8.5.2. Corrective action
  - 8.5.3. Preventive action