Association of British Healthcare Industries

MDR – Members Webinar

Quality Management Systems

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Presentation Structure

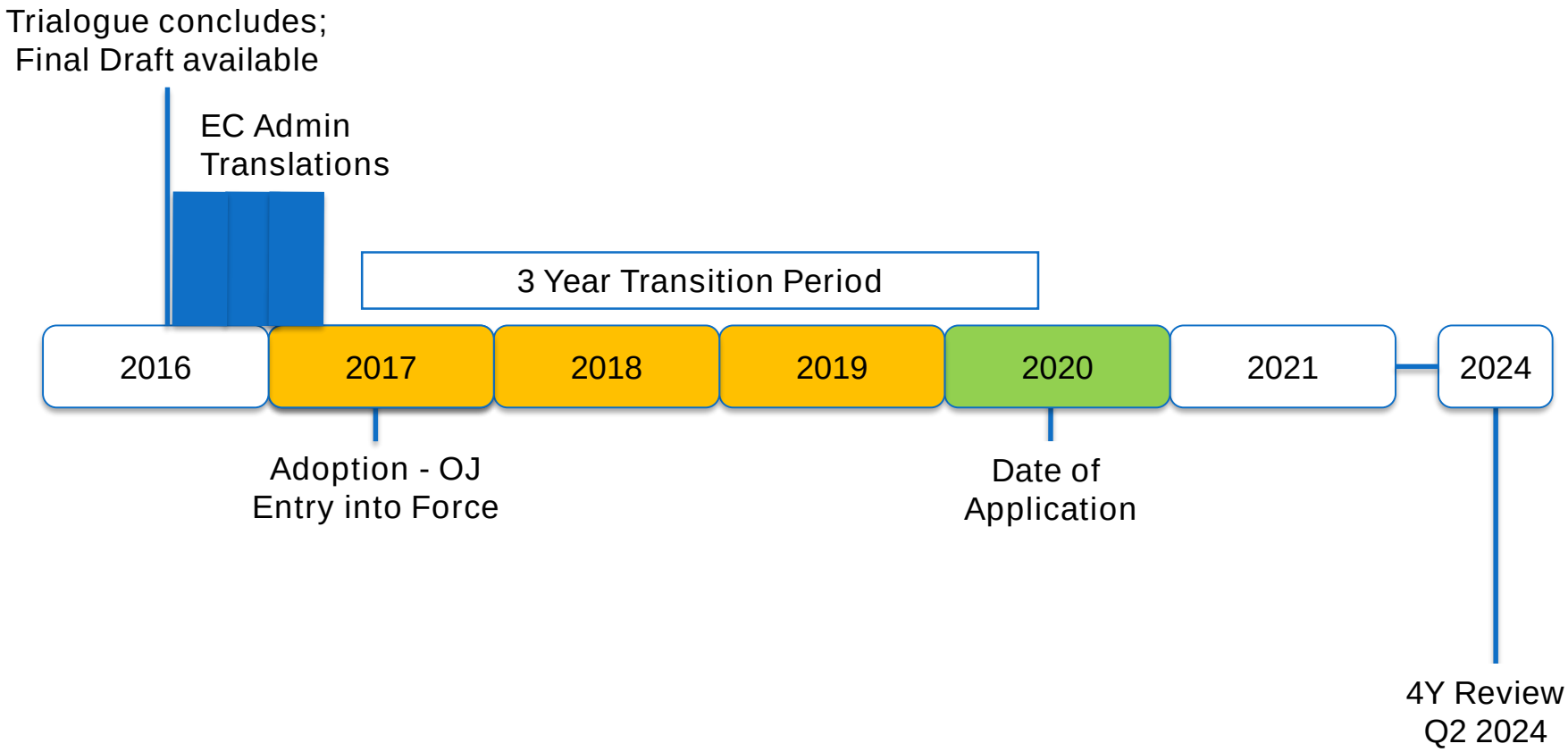
1. Background & Timings of Changes: MDR and ISO 13485
2. MDD vs. MDR – Document Comparison
3. MDR: Quality Management Systems (QMS) Requirements
4. Economic Operators
5. ISO 13485:2016 – Key Focal Points
6. ISO 13485:2016 – Detailed analysis of changes (Clauses 1 – 8)
7. ISO 13485:2016 – Annexes
8. Implications & Next Steps

Background

- ISO 13485:2003 – Quality Management Systems – requirements for regulatory purposes
  - Under revision since April 2012
  - Finally released March 1st 2016 as ISO 13485:2016

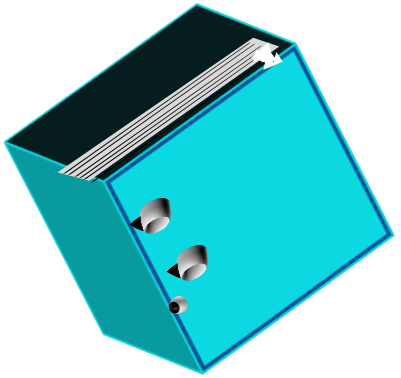
- Medical Device Directive (93/42/EEC) - MDD
  - As amended (M5) 2007/47/EC
  - Under revision in EU since 2012 (first draft MDR published)
  - Draft released as Medical Device Regulation (MDR) – June 2016
  - Final draft issued on 22nd February 2017

MDR Timings


Trialogue concludes;
Final Draft available
EC Admin
Translations
3 Year Transition Period
2016
2017
2018
2019
2020
2021
2024
Adoption - OJ
Entry into Force
Date of
Application
4Y Review
Q2 2024

MDD *vs*. MDR Document Comparison

Content	MDD	MDR 2016	MDR 2017
Recitals	20	71+	101
Articles	23	97	123
Pages	60	c. 360	566
Annexes	12	16	17
Document Status	Directive	Regulation	Regulation
Delegated Acts	n/a	12 citations	tbc
Implementing Acts	n/a	29 citations	tbc



There is a useful correlation table in Annex XVII at the end of the MDR, which links the articles in the new regulations (MDR) with the equivalent articles in the current MDD

QMS Requirement: MDD -> MDR

- **93/42/EEC requires**
  - "quality assurance" as per Article 11 (Conformity assessment procedures)
  - "quality system" citations in Annexes II, V and VI
  - ISO 13485:2003 is the harmonised standard used for conformity assessment

- **MDR expands QMS requirements significantly**
  - Recital 32: "*all manufacturers should have a quality management system* "
  - Chapter II, Article 8.1 addresses compliance with harmonised standards for "***economic operators*** ……. *including those related to the quality management system, risk management, the post-market surveillance plan system, clinical investigations, clinical evaluation or post-market clinical follow-up.* "
  - Chapter II, Article 10.9 outlines the detailed requirements for the quality management system (QMS) for manufacturers

MDR QMS Requirements

Chapter II, Article 10.9 *General obligations of the manufacturer* requires that "***The quality management system shall*** *address at least the following aspects*" :

- a strategy for regulatory compliance, including compliance with conformity assessment procedures and management of modifications to the devices covered by the system;
- identification of applicable general safety and performance requirements and exploration of options to address these;
- responsibility of the management;
- resource management, including selection and control of suppliers and sub-contractors;
- risk management as set out Section 3 of Annex 1;
- clinical evaluation, according to Article 61 and Annex XIV, including post-market clinical follow-up;
- product realisation, including planning, design, development, production and service provision;
- Verification of the UDI assignments made in accordance with Article 27(3) to all relevant devices ensuring consistency of information provided according to Article 29;
- setting-up, implementation and maintenance of a post-market surveillance system in accordance with Article 83;
- handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;
- processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;
- management of corrective and preventive actions and verification of their effectiveness;
- processes for monitoring and measurement of output, data analysis and product improvement.

Economic Operators

- Defined in MDR Chapter I Article 2.35 as "a **manufacturer**, an **authorised representative**, an **importer*,** a **distributor** *or the person referred to in Article 22(1) and 22(3)** <<*Systems and procedure packs*>> "

- Chapter II => new MDR sections – …***Obligations of Economic Operators*** … (Articles 10 -14)

- Articles 10 -14 outline the various **Economic Operator** Roles & Responsibilities in some detail

* New *vs*. 93/42/EC (MDD)

Economic Operators

Manufacturer

- means the natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under his name or trademark

Authorised Representative

- means any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer (Recital 35 & Article 11)located outside the European Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under this Regulation

Importer

- means any natural or legal person established within the Union that places a device from a third country on the Union market

Distributor

- means any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market, up until the point of putting into service

Economic Operators R&R Matrix

	Manufacturer	Authorised Rep	Importer	Distributor
Reference	Article 10	Articles 11 & 12	Article 13	Article 14
EUDAMED Registration	Before placing the device on the market (Article 31) NCA provides SRN #	Before placing the device on the market verify Mfgr SRN # (Article 31)	In order to place a device on the market, verify Mfgr & EUAR SRN #'s (Article 31).	
EU DoC & CE Marking	Article 19 Article 20	Verify EU DoC	Verify CE Marking & EU DoC	Verify CE Marking & EU DoC (sampling allowed)
Technical Documentation	Draws up Tech Doc as per Annexes II & III. Keeps available for NCA for 10y after after last placing on market (15y for implantables).	Verify - Tech Docn has been drawn up. Keeps permanently available for CA, including for 10y after after last placing on market. Provides NCA evidence of device conformity in an official EU language.	Verifies that Manufacturer is identified & EUAR is designated. Identify themeselves on device OR packaging OR accompanying document. Ensures compliance with labelling.	
Non conforming devices			Not to place on the market. Inform Mfgr / EUAR / NCA.	Not to place on the market. Inform Mfgr / EUAR / NCA.
Non conforming devices placed on the market	Take corrective action to bring in conformity OR recall. Inform all other Economic Operators	EUAR jointly and severally liable with manufacturer	Take corrective action to bring in conformity OR recall. Inform Inform Mfgr / EUAR and NCA (serious risk)	Ensure corrective action is taken Inform Mfgr / EUAR / Importer / NCA (serious risk)
UDI Labelling	Register Manufacturer & Devices in UDI database (Articles 27-29)	Verify Manufacturer compliance vs. Article 27-29	Verify that Manufacturerer is registered in UDI database, & that device has been labelled with UDI by Manufacturer	Verify that device is accompanied by IFU (Article 10.11), & is labelled with UDI (sampling allowed)
Complaints PMS	PMS Plan (risk-based) complaints, post-market clinical f/u, incident reporting, FSCA's	Inform Manufacturer of complaints. Intermediate: NCA - Manufacturer for sample requests. Co-operate with NCA's on CAPA actions.	Keep a register of complaints, NC products, recalls. Inform other Economic Operators	Keep a register of complaints, NC products, recalls. Inform other Economic Operators.
Persons responsible for regulatory compliance (PRRC)	Required	Needs to have at least one permanently and continuously at their disposal (Article 15.6).		

Person Responsible for Regulatory Compliance

The "Person Responsible for Regulatory Compliance" is a new concept - Article 15

"Manufacturers shall have available within their organisation at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of medical devices"

PRRC Qualifications

1y x of professional experience in regulatory affairs or in quality management systems relating to medical devices (graduate)

OR

4y x of professional experience in regulatory affairs or in quality management systems relating to medical devices

Person Responsible for Regulatory Compliance

The person *responsible for regulatory compliance* shall at least be responsible for ensuring the following:

(a) that the conformity of the devices is appropriately *checked in accordance with the quality management system under which these devices are manufactured* before a device is released;

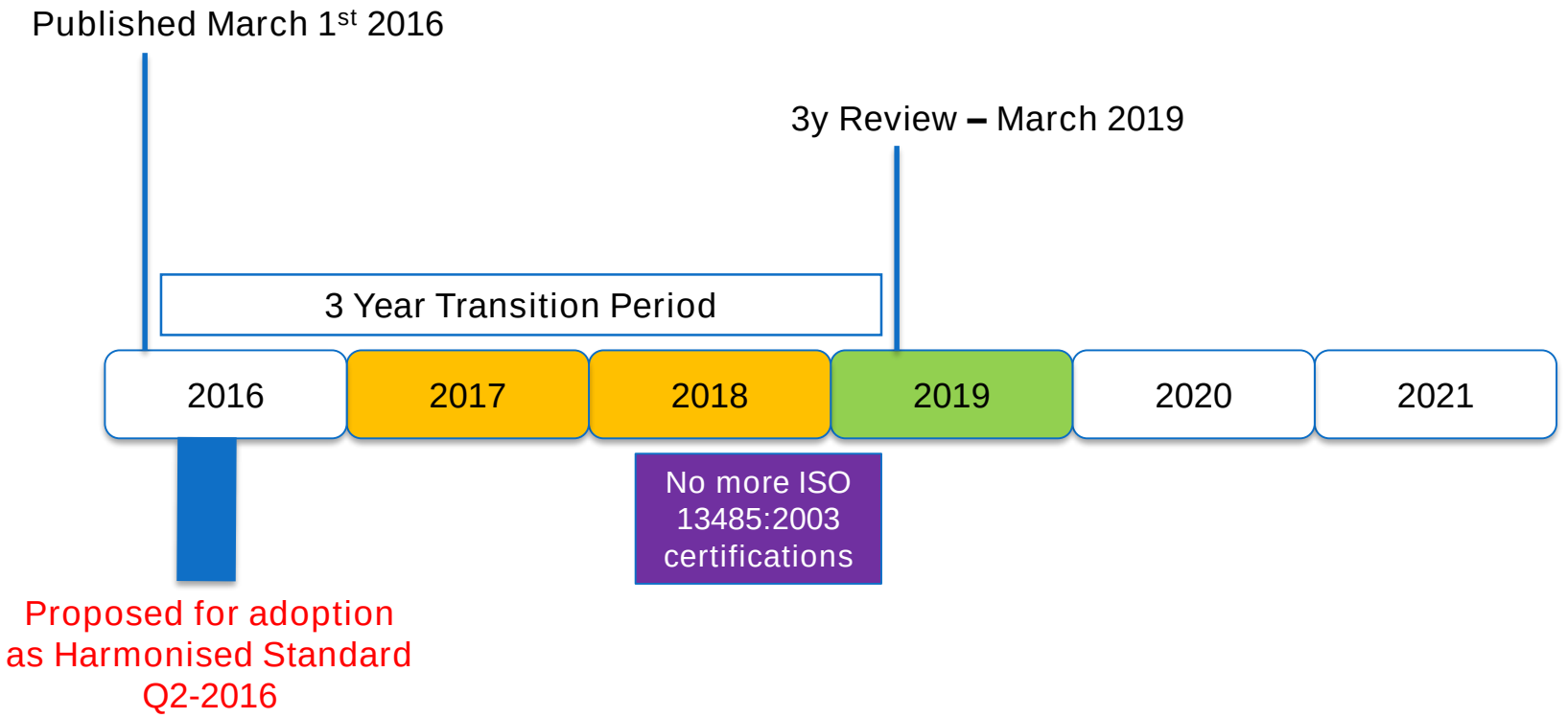
(b) that the technical documentation and the declaration of conformity are drawn up and kept up-to-date;

(c) that the post-market surveillance obligations in accordance with Article 10.10 are complied with;

(d) that the reporting obligations in accordance with Articles 87 to 91 are fulfilled *[PMS – Vigilance – Market Surveillance]*;

(e) in the case of investigational devices, that the statement referred to in Section 4.1 of Chapter II of Annex XV – clinical Investigations is issued.

ISO 13485 Timings



ISO 13485:2016 – Key Focal Points

What's new *vs*. ISO 13485:2003* ?

1. **Scope** – was for device manufacturers – now expanded to include "*suppliers* & *external parties who provide quality management system-related services*"
2. **Risk Management** – was mentioned just twice in 2003 edition – now part of Purchasing / Design / Development / Manufacturing / Feedback etc. (16 references)
3. **Design & Development** – organisations must now document all planning & review stages throughout design process, including input / output traceability, plus resourcing & competency
4. **Purchasing** – was merely "*evaluate suppliers*" – now -> organisations "*shall establish criteria for the evaluation & selection of supp*liers"; also new risk-based purchased product verification
5. **Software Validation** – now required within QMS, for production & services usage and for monitoring & measurement requirements
6. **Complaint Handling** – was vague in 2003 edition (*Feedback, Improvement* etc.) – now explicit in new sub-clause *8.2.2 Complaint Handling*
7. **Regulatory Requirements** – appears x 9 times in 2003 – found x 37 times in 2016 edition (within normative clauses 4 – 8). 2016 standard now requires that all key stakeholders demonstrate regulatory compliance

*Annex A of 2016 standard includes comparison of content 2003 vs. 2016. Note: nothing has been removed from 2003 version

Clause 1: Scope

	ISO 13485:2003	ISO 13485:2016
Objectives	Facilitate harmonization	Facilitate global alignment
Structure	Sections 1 – 8	Sections 1 – 8 (no changes)
Scope & Role	" … where an organization needs to demonstrate its ability to provide Medical devices and related services …"	" .. where organizations can be involved in one or more stages of the life-cycle including the design and development, production, storage and distribution, installation, or servicing of a medical device and the design and development or provision of associated activities (e.g. technical support). This International Standard can also be used by suppliers or external parties that provide product including quality management system-related services to such *organizations."*

Full life-cycle

Clause 1: Scope

The ISO 13485:2016 standard can be used by organizations that, for example:

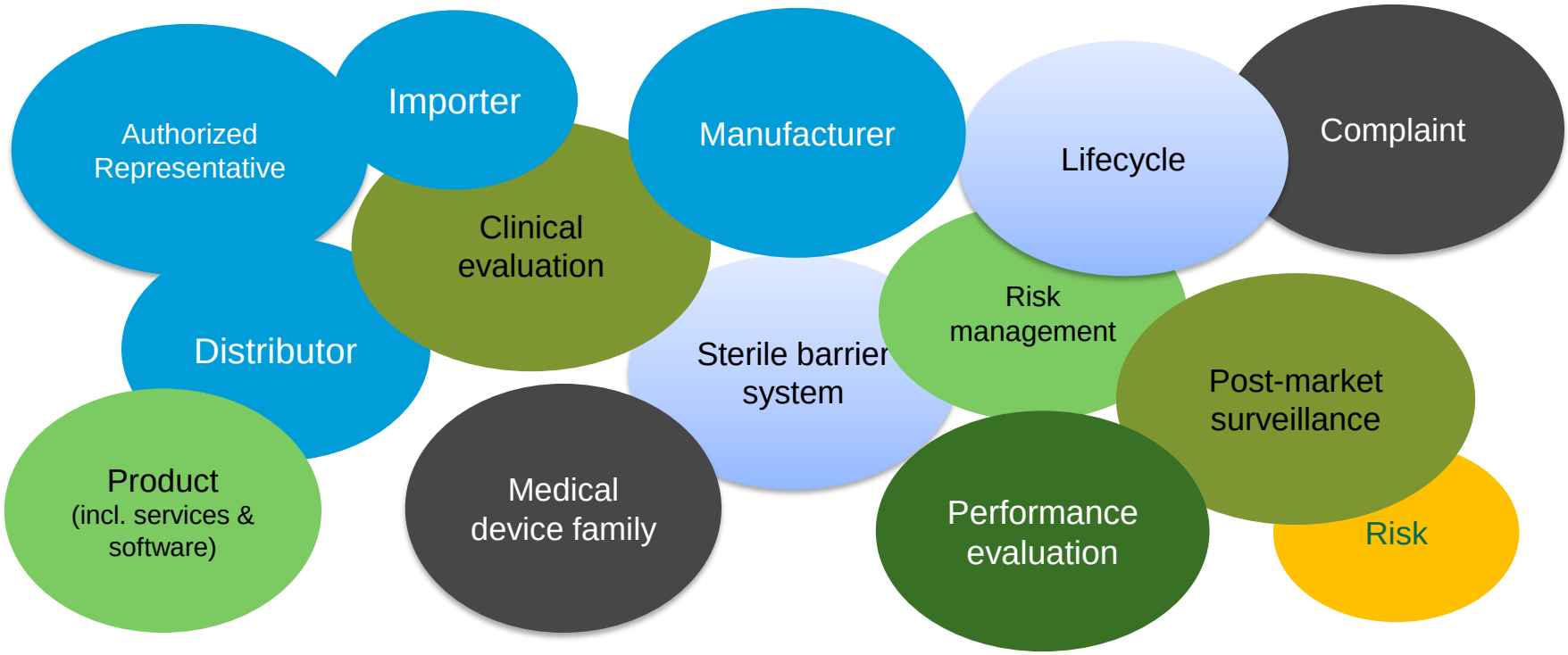
- undertake part of the medical device lifecycle, e.g. design & development / repair & maintenance;
- are part of the supply chain for a medical device e.g. raw material / component / subassembly / mfg.;
- provide services as part of the supply chain e.g. contract mfg. / sterilization / logistics / calibration;
- are economic operators in the supply chain such as importer / distributor /authorized representative.

Additionally, changes in the scope clarify that:

- the requirements of standard are applicable irrespective of the size of the organization;
- certain requirements do not apply based on the role undertaken by the organization; and
- the QMS processes apply to the organization rather than the medical device.

Clause 2: Normative References

Clause 3: Definitions



- **Note definitions for "economic operators" – essentially the same as in MDR**
- **Sources of new definitions are cited in text**

Clause 4: Quality management system

4.1 General requirements – major changes

- Applicable regulatory requirements – x7 references to include these within QMS, including roles (e.g. economic operators, specifications, suppliers, contract manufacturers) plus maintenance of QMS itself (4.1.3).
- Risk-based QMS (4.1.2b) – apply risk management principles to the QMS, and not merely at “Product realisation”; perform process mapping (4.1.2c).
- QMS change management (4.1.4) - evaluate for effect both on the QMS and on the medical devices covered by QMS, and manage in accordance with the requirements of the standard and applicable regulatory requirements.
- Outsourcing (4.1.5) - expanded - organizations retain responsibility for compliance to this standard for outsources activities, and these are to be controlled under the requirements for purchasing (7.4), proportionate to the associated risks, and that these controls include written quality agreements.
- Computer software used in the QMS (4.1.6) – as well as existing product software, software used in the quality management system (e.g. doc control, CAPA applications) must be validated prior to use and after change.

Clause 4: Quality management system

4.2 Documentation requirements – major changes

- Clarification that documents of external origin necessary for the planning or operation of the QMS need to be controlled.
- Explicit statement that document controls be designed to prevent loss or deterioration of documents and that record management addresses integrity and security of records.
- Explicit requirement for changes made to records to be identifiable.
- Protection of confidential health information: a new requirement (4.2.5) has been added … in accordance with regulatory requirements; previously addressed as part of a note as an example of customer property (ISO 13485:2003 7.5.4).
- New requirement for the medical device file with detail on its content (4.2.3 a-f).

Clause 5: Management responsibility

5. General requirements

- Increased emphasis on regulatory requirements

5.4.1 Quality Objectives

- Must now address applicable regulatory requirements as well as product requirements

5.5.1 Responsibility and authority

- Top management shall document the interrelation of all personnel who manage, perform and verify work affecting quality, and shall ensure the independence and authority necessary to perform these tasks.

5.5.2 Management representative

- Focus on processes needed for quality management system to be documented
- Replacement of "customer requirements" with QMS requirements in 5.5.2 c

5.6 Management review

- 5.6.1 Procedures required, plus *documented planned intervals*
- 5.6.2 Inputs: new inputs (complaints, reporting to regulatory authorities, etc.)
- 5.6.3 Outputs: improvement needed to maintain the suitability, adequacy, and effectiveness of the QMS and its processes, plus new section (5.6.3 c) on what changes may be needed to respond to applicable new or revised regulatory requirements

Clause 6: Resource management

6.2 Human resources

- Document processes for competence, training and awareness
- Focus on achieving & maintaining the necessary competency (6.2 b)
- Effectiveness …methodology (for actions taken to achieve / maintain competence) linked to risk of work for which training is provided

6.3 Infrastructure

- Document requirements to prevent product mix up & ensure orderly handling
- New requirement: document maintenance activities (incl. PM intervals) of equipment - applies to (i) production, (ii) control of work environment, and (iii) monitoring and measurement

6.4.1 Work environment

- Document requirements for the work environment
- Reference to cleanroom standards (ISO 14644 & ISO 14698)

6.4.2 Contamination control (new section)

- Document requirements arrangements *for the control of contaminated or potentially contaminated product in order to prevent contamination of the work environment, personnel, or product*
- Sterile medical devices: requirements for *contamination control for particles and microorganisms* to be documented and that the required cleanliness of product is maintained during assembly or packaging

Clause 7: Product realisation

7.1 Planning of product realisation

- New, explicit references in the planning process: planning for infrastructure and work environment needs, handling, storage, distribution and traceability activities (UDI)

7.2 Customer related processes

- New, explicit requirement for the organization to identify user training needs to ensure safe use of the medical device (7.2.1), followed subsequently (7.2.2) by a new requirement that any training so identified is either available or planned to be available when the product is placed on the market.
- New, explicit requirement that regulatory requirements for the product are met (7.2.2),
- New requirement for communication with regulatory authorities (7.2.3: regulators = customers).

7.3 Design and development (documented procedures required)

- Planning must address the transfer from design and development into production (7.3.8), as well as ensuring traceability of design inputs to design outputs (7.3.2) and the availability of resources, including personnel competence, needed for the design and development project
- Inputs need to include explicit usability requirements (7.3.3), and address regulatory requirements and standards (IEC 62366). These need to be addressed in design & development outputs (7.3.4) and subject to review, verification & validation (7.3.5-6-7))
- More detail is required on the nature of the product used in validation so that it is representative and that the rationale for the choice of product used is recorded (7.3.7)
- Design and development changes (7.3.9) - requirements for documented procedures for changes and linkage of the review of the change with the risk management process;
- Explicit reference to design and development records in a file of the history of the d & d activities (7.3.10)

Clause 7: Product realisation

7.4 Purchasing

- 2003: "*evaluate suppliers*" vs 2016 "*establish criteria for the evaluation and selection of suppliers*" based on (7.4.1):
  - *the supplier's ability to provide product that meets the organization's requirements;*
  - *the performance of the supplier;*
  - *the effect of the purchased product on the quality of the medical device;*
  - <criteria being> *proportionate to the risk associated with the medical device*.

- *The organization shall plan the monitoring and re-evaluation of suppliers. … The results of the monitoring shall provide an input into the supplier re-evaluation process* (7.4.1)

- *Product specifications & written supplier agreements* (for change notification) added to Purchasing Information (7.4.2)

- Verification of purchased product – now risk-based; *change impact assessment* requirement added (7.4.3)

Clause 7: Product realisation

7.5 Production and service provision

- List of *potential production controls* has been extensively revised and reformatted; a new requirement on *qualification of infrastructure* has been added (7.5.1).
- Section on "*Cleanliness of product*" is augmented by inclusion of "*product that cannot be cleaned prior to sterilization or its use, and its cleanliness is of significance in use (7.5.2c)*"
- Use of 3rd party for *device installation* => supplier relationship => purchasing controls (7.5.3)
- *Servicing records* are identified as …. a potential source of complaint (regulatory) & process improvement information (7.5.4)
- *Validation* – statistical sampling techniques & rationale (7.5.6.d) & change approvals added, plus change validation of computer software (7.5.6)
- "*Processes for sterilization and sterile barrier systems shall be validated ….prior to implementation and following product or process changes*" - <<major cause of recalls>> (7.5.7)
- "*…the organization shall document a system to assign unique device identification to the medical device" (7.5.8)*
- "*Preservation of product* "- requirements expanded to use of *packaging* and *shipping* methods. When special conditions are required during storage / transport => they must be controlled, monitored and recorded (7.5.11).

7.6 Control of monitoring and measuring equipment

Alignment of requirements on *validation of software* used in monitoring and measuring with the parallel clauses for software used in the QMS (4.1.6) and in production and service provision (7.5.6)

Clause 8: Measurement, analysis and improvement

8.2.1 Feedback

- Methodology now linked to risk management (previously just linked to CAPA)

8.2.2 Complaint Handling

- New section – term did not exist in 2003 version
- Explicit requirements: *documentation*, *timeliness*, *regulatory compliance* & *reporting* (8.2.3)

8.2.6 Monitoring and measurement of product

- New requirement - the identity of test equipment (for conformity to acceptance criteria) shall be identified as appropriate

8.3 Control of nonconforming product

- Extra details added in respect of *controls (pre- and post-delivery) & concessions*. Clause restructured
- New requirement to document procedures & records for advisory notices

8.4 Analysis of data

- More comprehensive scope for data sources (audits, service reports)

8.5.2 and 8.5.3 Corrective and preventive action

- Verifying that CAPA actions are (i) *taken without undue delay* (8.5.2), and (ii) *do not have an adverse effect on the ability to meet regulatory requirements, and (iii)* are subject to *planning and documenting*

ISO 13485:2016 Annexes

Annex A	Comparison of content between ISO 13485:2003 and ISO 13485:2016 – comments on changes (useful)
Annex B	Correspondence between ISO 13485:2016 and ISO 9001:2015 – top level clause mapping
European Annexes - ZA (AIMD), ZB (MDD) and ZC (IVD)	Identifies relationship between the European Standard (EN ISO 13485:2016) and Conformity Assessment Requirements of the respective EU Medical Device Directives via each conformity assessment route for each directive. Note: future Annex Z's will be required to map to MDR

Implications & Next Steps - MDR

MDR

- Text is essentially final – no further content changes expected
- Increase in regulatory scope / infrastructure / usage of QMS
- Significant impact on companies // aligned with ISO13485:2016
- Gap analysis needed => implementation planning required

Timings

- Expected Entry into Force: May / June 2017
- Date of Application: May / June 2020
- Watch out for Delegating / Implementing Acts being published

Implications & Next Steps – ISO13485:2016

ISO 13485:2016

- Widely used QMS standard - aligned to MDSAP (MDSAP AU P0002-004 Audit Model)
- Much better alignment to 21.CFR.820 (FDA's QSR)
- Stronger emphasis on risk analysis & management
- Gap analysis needed => implementation planning

Timings

- After early 2018, only 2016 standard certifications allowed => START NOW
- Consider resource demands from (re)certifications
- Distributors / Importers / AR's – evaluate what QMS needs are
- Consult with your notified body ASAP

Thank You

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ABHI 2017 Events Diary

Event	Date	Venue
Seminar: Making Value-Based Procurement a Reality	23 March, 09.00 – 14.00h	FieldFisher, London
Seminar: Human Rights & the Role of Corporations	30 March, 11.30 – 14.00h	Norton Rose Fulbright, London
ABHI Briefing for Members and Potential Members	09 May, 09.00 – 13.30h	ABHI, London
Malcolm Carlisle Memorial Lecture	01 June, 17.30 – 20.30h	CMS Cameron McKenna, London
Seminar: AAR & Industrial Strategy	21 June, 09.00 – 14.00h	TBA, London
Seminar: Health and Care System Update	14 September, 09.00 – 14.00h	Simmons & Simmons, London
ABHI Briefing for Members and Potential Members	04 October, 09.00 – 13.30h	ABHI, London
Conference: ABHI Annual Regulatory Conference	05 October, 09.00 – 17.00h	Norton Rose Fulbright, London

For information about any of these events, please contact:
ukevents@abhi.org.uk