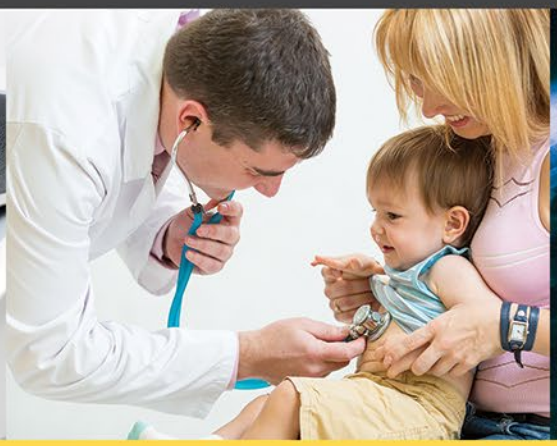
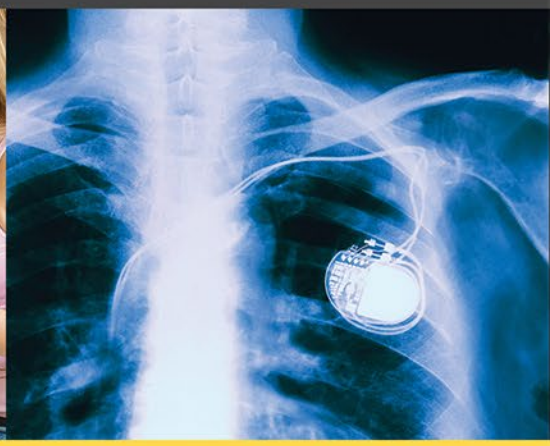
ISO 13485:2016 and How It Impacts Medical Device Companies

An examination of key changes, transition timelines, and implementation strategies

Author
Richard Vincins, CBA, CQA, RAC (US/EU)
EMERGO
Vice President, Quality Assurance Consulting
richard@emergogroup.com

April 2016

EMERGO

ISO 13485 Introduction and Background

After more than 10 years, the updated Quality Management standard with the revision of ISO 13485 for the medical device industry is here. The origins of ISO 13485 standard were closely related to the ISO 9001 standard that provides organizations guidance, context, and requirements for implementing a quality management system. In 1994, the most prominent edition of ISO 9001 was published in three versions: ISO 9001, ISO 9002, and ISO 9003.

Shortly after in 1996, the ISO 13485 and ISO 13488 standards specific to medical devices were published. The difference between the two medical device industry standards were fundamentally the inclusion of design controls in the ISO 13485 standard where ISO 13488 did not include design control requirements. A few years later the ISO 9001 standard was revised with a process approach that the ISO 13485 standard shortly followed thereafter (reference Figure 1). This provided us with the ISO 13485:2003 that the medical device industry has been using for regulatory certification purposes.

The Evolution of ISO for Medical Devices

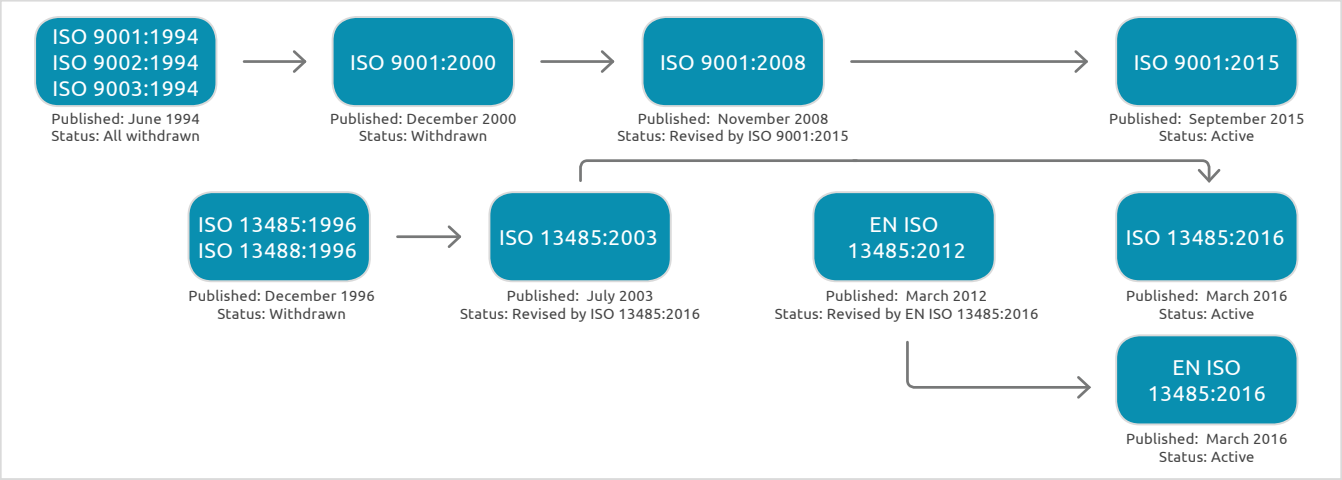


Figure 1 - ©Emergo

The 2003 version of the ISO 13485 standard has content that is quite similar to ISO 9001 with the addition of requirements specific to medical devices such as work environment, sterile devices, and advisory notices. With the introduction of the 2003 version, the prominence of certification increased significantly because many country requirements mirrored the ISO 13485 standard. There is now a new challenge because the ISO 9001:2015 standard was recently released[1] that departs significantly from the structure of ISO 13485; this will be discussed later on.

There are a few changes to the standard that are significant and others that are aimed more at clarification on wording that will be discussed throughout this white paper. The ISO 13485 standard was published 1 March 2016, which has maintained an overall structure that is the same as the previous 2003 version with some slight numbering changes. In most cases, the changes to the standard are closing the gaps between regulatory requirements today and what was expected over the last 10 years.

A significant driver of the revision of the standard was to create a truly global harmonized platform for quality systems and emphasizing risk management throughout a quality system. Beyond necessary changes that were apparent for the standard, the normal review process for the ISO standard was voted on by Technical Committee 210 (TC 210) to revise the standard, leading us to a newly published standard in early 2016.

Timeline for Publication of the New Standard

When the ISO 13485 initial Draft International Standard (DIS) was published back in July 2014, there were expectations that the standard would be published in the first part of 2015. However, the ISO/DIS 13485 received a negative vote with a significant number of comments that were reviewed later in 2014.

Many of the comments received and reasons for the negative vote pertained to the incorporation of detailed regulatory requirements that posed issues for global harmonized use of the standard. This obligated the TC 210 group to issue a second Draft International Standard (DIS2) published February 2015 that received an approval vote a few months later. This allowed the ISO/FDIS 13485 to proceed being published on 29 October 2015 for a two month voting period.

The finalized ISO 13485 standard was published 1 March 2016 as shown by the timeline in Figure 2. Guidance from TC 210 have stated that there will be a three-year transition period with only new certifications being issued in the last year of the transition period. The EN ISO 13485 standard was updated at the same time to revise the Annex Zs to correspond with new numbering stucture in relation to the Directives.

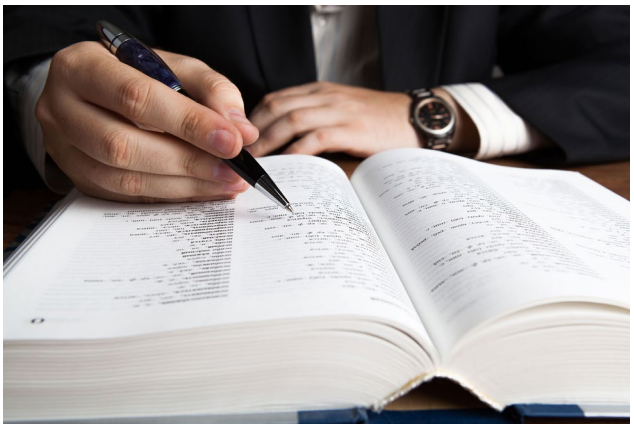
The main idea providing information via this white paper is to help companies prepare for the changes and assure that they will be able to meet the three-year transition period without undue delays or potential of their current certificate being suspended or cancelled.

Anticipated Timeline for Finalized ISO 13485	
Date	**DIS Versions**
July 2014	DIS version published that received a negative vote
December 2014	Voting and significant comment period to generate DIS2
February 2015	DIS2 published with changes from the DIS version
October 2015	FDIS published for final voting period of standard
March 2016	Final ISO 13485:2016 standard published
March 2019	End of transition period for updating certificates to new version

***Figure 2** - ©Emergo*

Now onto the discussion of the changes that have been made to the ISO 13485 standard. This will be followed by a discussion about global harmonization of the standard, relationship with the EN ISO version, and relationship to ISO 9001. We will then finish with some tips and helpful advice that a medical device manufacturer can do to prepare and plan for the transition with the revised standard. Sections 1 and 2 of the standard discuss scope and normative references so we will be starting with Section 3.

Section 3 – Definitions



There are a number of new definitions that were introduced in the new standard. The addition of these terms is meant to align with definitions that have been provided in other regulations or other guidance documents for consistency; references to definitions include ISO 9000 and GHTF documents. Definitions related to manufacturer, importer, and distributor have been clarified as there have always been many questions raised about who is the actual legal manufacturer of a medical device.

However, the standard does state that these definitions should be regarded as generic because definitions provided in specific regulations should take precedence. Manufacturers should be more aware of these definitions to determine the impact on their quality system requirements, including specific context of the new ISO 13485 standard.

Section 4 – Quality Management System

Aspects of the quality system have been strengthened and clarified in this section, which includes many requirements for documentation controls. As mentioned previously, the essence of the quality management system requirements have been updated and clarified to the current expectations to close the gaps with other regulatory requirements. A summary of the changes are as follows:

- The organization needs to document the role and responsibility they are taking under the regulatory requirements, e.g. manufacturer, authorized representative, importer, or distributor. Clarification of roles and responsibilities of each organization within the delivery chain is made with the revision; the organization must clearly delineate their role in order to assure the actual legal manufacturer is identified.
- Outsourced processes need to be clearly identified, including the sequence and interaction of those processes. Organizations must determine the processes needed taking into account the roles taken by each party, including the company itself.
- It is understood that the legal manufacturer cannot "absolve" itself of the responsibilities for quality system requirements that they must retain responsibility of conformity; written agreements may be required between the parties. If any processes are outsourced, these must have the proper controls applied proportional to the risk involved and the activities that are outsourced.
- Validation of the applicable computer software in the quality system needs to be assessed and performed. This includes electronic Quality Management Systems (eQMS), complaint management systems, corrective action systems, or Enterprise Resource Planning (ERP) systems that may require validation.
- There is now more synergy with the FDA's Device Master Record (DMR) that has been in place for many years. The standard clarifies the establishment and maintenance of a file, called the Medical Device File, that references intended use, specifications, manufacturing, labeling, packaging, monitoring, traceability, installation, and/or servicing.
- The standard clarifies the record retention period for quality records and obsolete documents; these need to be maintained at least the lifetime of the medical device as defined by the organization.
- As the electronic management of documents has significantly changed since 2003, the standard clarifies controls that are required for identification, storage, security, and integrity of records. Many organizations are keeping their quality data in some type of electronic format whether it is a simple Excel log sheet or eQMS system.

Section 5 – Management Responsibility

A stronger emphasis has been placed on top management or management with executive responsibility because it is always understood that quality, safety, and performance requirements for a medical device start from the top of an organization. As this has continued to be a weak area for many organizations with management disengaged from the quality management system, this area has been clarified and strengthened.

Even though the wording has not been necessarily changed, there is a stronger emphasis on the Management Representative being responsible for the promotion and awareness of regulatory and customer requirements throughout the organization.

Specifically some of the modifications in this section can be seen as the following:

Modification Types	
Section	**Details**
Section 5.1	Only change has been the removal of the 'Note' that statutory requirements are limited to the safety and performance of the medical device.
Section 5.2	Removed the reference to Section 7.2.1 and 8.2.1 to understand that Customer Focus should be applied through all facets of the quality management system.
Section 5.3	Only changed one of the bullet points about the Quality Policy being 'applicable' instead of 'appropriate' to the organization.
Section 5.4	• Clarified that Quality Objectives shall also meet regulatory requirements as well as requirements for the product as many organizations miss the need to include regulatory requirements. • Quality objectives are established at all relevant functions and levels of the organization to ensure that all employees are engaged and aware of the objectives and planning of the quality system.
Section 5.5	• Clarified that the Management Representative is responsible for the effectiveness of the quality management system and ensuring the promotion of the awareness of applicable regulatory requirements throughout the organization.
Section 5.6	• Specified that Management Reviews needs to be performed at planned intervals. The idea is that an organization should have rationale for when management review meetings are held as once a year may not be appropriate, and that the organization needs to document when these meetings occur. • Clarified that management review input of customer feedback is overall feedback, not related to only customer complaints but may be other sources of customer or product information. • Included the requirement that changes of the quality system need to be assessed in response to applicable new or revised regulatory requirements.

Section 6 – Resource Management

Throughout the resource management section there have not necessarily been new requirements added as much as clarification and expectation of the requirements. One of the strongest emphases is on the competence of employees to perform their job functions related not only to manufacturing but also design, purchasing, post-production monitoring, and all functions of the organization.

The requirements for infrastructure and work environment have not drastically changed from what is expected by organizations today. However, there is stronger emphasis on systems in the facility that need to be periodically inspected, and special arrangements need to be clearly defined. A summary of the changes are as follows:

- Even though competence is not new terminology for the standard, it has been clarified that training must be provided to maintain the necessary competence of the employees. This is also not specific to manufacturing personnel. All personnel within the organization need to ensure they have necessary training to maintain their qualification, experience, and competency for the tasks for which they are responsible.

- The effectiveness check of the methodology for work activities is noted that this is proportional to the risk associated with the work for completed training. This should be defined in a training matrix or job description that detail tasks individuals are responsible for because an individual performing verification testing may pose a higher or a different risk than an individual performing maintenance of soldering equipment.

- Over the years there have been many instances where the maintenance of equipment is not properly completed, so the standard now clarifies and strengthens the requirement for equipment maintenance. This includes the documentation of requirements for maintenance for equipment used in production, control of work environment, and testing.

- Work environment has been significantly changed to ensure that requirements for product conformity are clearly defined and evaluated on a routine basis. The standard has been clarified to state that this is not only limited to manufacturing activities, but also to any condition for components, sub-assemblies, and finished goods through handling, storage, and distribution.

- The standard added a 'Note' that specifically references ISO 14644 and ISO 14698 series to evaluate work environment in terms of not just physical factors. These include environmental and other factors, such as microbiology, noise, temperature, humidity, lighting, or weather (external factors to the facility) that must all be considered through the life cycle of the medical device.

- A new section 6.4.2 concerning contamination control must be planned by the organization to prevent contamination of work environment, personnel, or product. Finally, the particular requirements for sterile medical devices have been moved from Section 7 to Section 6 to ensure that contamination issues are addressed within the work environment.

Section 7 – Product Realization

Being the largest section of the standard there were quite a few modifications made in Section 7 with some added requirements in addition to clarification of the current wording. New sections were added in Section 7.3 Design Control that are now more consistent with the FDA QSR regulations[2]. Overall, the section numbering has been "raised" to not have indented levels of numbering that may introduce confusion, e.g. the requirements for Identification has been renumbered from 7.5.3.1 to 7.5.8.

Much of the remainder of the sections were updated for clarification of wording and the inclusion of sterile device packaging (sterile barrier systems) that must be validated for use. Specifically, some of the modifications in this section can be seen as the following:

Modification Types	
Section	**Details**
Section 7.1	• Rewording the section on risk management being applied throughout the product realization process. There is a significantly increased emphasis on risk assessment being applied throughout the quality management system and not only being done for the product. • Including the requirement that not only verification and validation are to be implemented, but also monitoring, measuring, inspection, handling, storage, and traceability that are specific to the product criteria for acceptance needs to be considered.
Section 7.2	• There have been references added that applicable user training needed for the performance and safe use of the device needs to be applied. This has a strong reference to the need for usability engineering or usability testing performed for safe use of the finished device. • Clarifies that any regulatory requirements that must be met as part of the customer order must be fulfilled, this has been inferred to any specific country requirements such as registration. • Removed the 'Note' about Internet sales as there are common acceptance activities that occur for a customer order through the Internet. • Section 7.2.3 was specifically added for communication with customers and regulatory authorities in relation to product information, inquiries, customer feedback, and advisory notices. Additional requirements that communication with regulatory authorities need to be performed in accordance with applicable regulatory requirements, e.g. adverse event reporting or market withdrawals
Section 7.3	• Design and development planning was strengthened and clarified for what is to be included in the planning activities. This section was clarified to support how design and development planning shall be conducted by organizations. • Design inputs were clarified with a stronger emphasis on regulatory requirements and outputs of risk management. There was a 'Note' added for the reference to usability regarding the standard IEC 62366. • A 'Note' was added that a person independent of the design stage under review should participate to meet applicable regulatory requirements. This is to align more with FDA QSR and other regulatory requirements to have an independent reviewer. • Design verification and validation were clarified to confirm that design requirements and user requirements are met at each stage of the design activities. (*Continues*)

Modification Types	
Section	**Details**
Section 7.3 (*Continued*)	• A new section 7.3.8 Design and Development Transfer was added to ensure that the manufacturing is suitably applied based on final production specifications and production capability. This additional section aligns with FDA QSR for design transfer. • Design changes were clarified to indicate how these should be identified and records maintained as changes to development occur prior to and after production transfer. • A new section 7.3.10 Design and Development Files was added to maintain a design and development file for each medical device type or medical device family. This additional section aligns with the FDA QSR for design history file.
Section 7.4	• The supplier management process has been expanded to specify requirements for supplier approval, monitoring of suppliers, and supplier records. As more and more organizations are outsourcing their activities, there is a much stronger emphasis on supplier management. • Purchasing information has been reworded and clarified to ensure that purchasing requirements are being met, including specifications, product acceptance, personnel, and quality system requirements. An alignment has been made with the FDA QSR that a written agreement must be established stating that changes in the purchased product must be notified prior to the implementation of any changes. • Strengthened the wording associated with verification of purchased products that this must be appropriate based on the supplier evaluation and proportionate to the risks associated with the purchased part/component.
Section 7.5	• Many of the sections in production and service provisions have been reworded for clarification on the intent of how the requirements are to be applied. These sections have been reorganized to flow better and emphasize areas that have been lacking at organizations as observed over the previous years. • The levels of the numbering outline have been raised to help streamline the standard with more clarification on the requirements; the outline numbering only goes down three levels now instead of five in the previous version. • There was a clarification added in the servicing section stating that analysis of servicing records needs to be performed to determine if the event is considered a customer complaint. • As noted previously, there was information added about sterile barrier systems of sterile devices stating that these are part of the entire system. The organization needs to consider any special conditions for not just the finished device, but all constituent parts that are included in a sterile medical device.
Section 7.6	• The information contained in the section for calibration of monitoring and measuring devices has been clarified and streamlined to be consistent with current expectations. • This section has been linked to Section 6.3 for infrastructure for the handling, maintenance, storage, and necessary review of equipment at a facility. Even though it may seem that some requirements were removed, these are still there and expected to be performed.

Section 8 – Measurement, Analysis and Improvement

The final section of the ISO 13485 standard has not significantly changed as many of these processes have been consistently performed over many years, and the changes are to better align with other regulatory requirements. There is also a much stronger emphasis that post-production information needs to serve as an input in the risk management process for identification of new hazards and confirming current hazard assessment. There is clarification that a determination needs to be made for any nonconformance, whether detected before or after delivery, as to what further actions may need to be taken, e.g. investigation, evaluation, concession, or corrective action. A summary of the changes are as follows:

- There has been a clarification that the feedback process it not necessarily just customer complaints as has been more commonly understood over the last few years. The feedback process needs to be clearly defined to gather data from production as well as post-production activities to ensure the full picture of the product safety and performance is evaluated.
- A new requirement has been added that information gathered in the feedback process shall serve as input in the risk management process as well as the product realization process to assure that monitoring for the product is being completed.
- A new section, 8.2.2 Complaint Handling and 8.2.3 Reporting to Regulatory Authorities, was added (and moved from Section 8.5.1) to align more with the FDA QSR and other regulatory requirements for receiving complaints, investigation, and elevation to corrective action.
- New requirements have been added to clarify that if a complaint is not investigated the justification shall be documented. In addition, any corrections or corrective action resulting from the complaint process shall be properly documented.
- Monitoring and measurement of processes has been a challenge for organizations to comply with during implementation of a quality system. The sections have been updated to clarify that these activities are performed at applicable stages of product realization and appropriate for the organization.
- Nonconforming product was clarified and expanded for handling nonconforming product before and after delivery to ensure that these instances are each handled appropriately.
- A new section, 8.3.4 Rework, was included to ensure that rework activities are performed according to document procedures or instructions. Any rework that is performed needs to ensure that these are tested in the same manner as the original product to assure the specifications, requirements, and applicable regulatory requirements are met.

One of the main purposes of the new ISO 13485 revision is to provide an international standard that can be truly harmonized across multiple regions and regulatory requirements. This has already been seen by the revised standard through a much closer alignment with the US FDA QSR with the incorporation of specific sections to the standard.

Other regulatory agencies are also aligning their requirements with ISO 13485, as an example, Japan has recently changed their regulatory requirements to completely follow the ISO 13485 standard, as seen in Figure 3. There is also strong intent to create a global auditing process through the Medical Device Single Audit Program (MDSAP)[3] that, rather than having three or four audits throughout the year, these could all be combined into one audit. The International Medical Device Regulators Forum (IMDRF)[4] has been administering and guiding the MDSAP with the US, Brazil, Canada, Japan, Europe, Australia, and China currently involved at some level either through observation or fully adopting the MDSAP program.

With the release of the new ISO 13485 the goal of being able to perform one audit for multiple countries may be more realized. However, it should be cautioned that there might still be country-specific deviations that need to be considered, evaluated, and implemented in an organization's quality system.

Chapter 2 (Basic Requirements Regarding Manufacturing Control and Quality Control of Medical Devices) is identical to Clauses 4 to 8 of ISO 13485:2003

***Figure 3** - Source: Translated excerpt from Ministerial Ordinanace No. 169*

Relationship with EN ISO 13485

With the ISO 13485:2003 standard there was an associated EN ISO 13485:2012 standard that had Annex 'Z's that provide alignment to the Directives for Europe (reference a brief example from the revised standard in Figure 4). This has not changed dramatically with the introduction of the ISO 13485:2016 standard. The EN ISO 13485 standard was published shortly after that incorporates similar Annexes as currently published – the EN version was updated to match the numbering section of the revised standard.

There is realignment of the Annex 'Z's with the new standard because of new sections and clarifications of wording that have been minimal. The biggest unknown at this time is what the EN ISO 13485 standard would look like when the new European Medical Device Regulation and In Vitro Diagnostic Medical Device Regulation are published in 2016 or 2017.

Relationship of Medical Device Directive 93/42/EEC with EN ISO 13485		
Paragraph of 93/42/EEC	**Section of EN ISO 13485**	**Coverage**
Paragraph 3.1 Second Sentence Second Indent	Not Applicable	Not covered
Paragraph 3.1 Second Sentence Third Indent	Not Applicable	Not covered
Paragraph 3.1 Second Sentence Fourth Indent	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.6, 4.2.1, …	Covered. The documentation required in this European Standard covers the quality system documentation …
Paragraph 3.1 Second Sentence Fifth Indent	4.1, 5.1, 5.4, 5.5, and 5.6	Covered
Paragraph 3.1 Second Sentence Sixth Indent	4.1, 5.1, 5.4, 5.5, and 5.6	Covered

Figure 4 - *Source: Excerpt of Table ZB.1 – Relationship of Medical Device Directive 93/42/EEC with EN ISO 13485*

Relationship with ISO 9001

The biggest challenge moving forward is going to be for medical device manufacturers to maintain both ISO 9001 and ISO 13485 certifications. As briefly mentioned, the ISO 9001 standard is severely deviating from the structure of ISO 13485 as the new ISO 9001 standard will be following the High Level Structure (referred to as Annex SL[5]).

All is not lost though, because the new ISO 13485 standard includes Annex B that compares the content of the two standards with cross-reference tables. This is still going to be challenging in terms of updating and maintaining a quality management system that conforms to both standards as the structure is now completely different.

In addition, there is content from ISO 9001:2015 that has been removed, like Management Representative and Preventive Action, that will be interesting to configure in a quality management system that applies both ISO 9001 and ISO 13485. The biggest challenge is going to be how the quality system will be audited considering that the ISO 9001 standard is new to everyone, while the ISO 13485 standard structure is going to remain fairly the same.

Emergo understands that some medical device companies that do not specifically require the ISO 9001 certification will be dropping their certification in lieu of maintaining only medical device-specific quality management systems. This is certainly going to be a challenge for medical device suppliers that have achieved ISO 13485 certification for their medical device customers and maintain ISO 9001 certification for all of their other customers.

Now that the revised ISO 13485:2016 standard has been published we have a better understanding of content for changes, modification, updates, and requirements moving forward. Like everything in life, time is of the essence and it seems there is never enough time to get things done, our resources are continually stretched, so planning in advance prior to making any significant changes to the quality system is key.

There is a short summary below that provides key activities that medical device manufacturers should be working on today and throughout the transition period. Make sure that your organization has the proper resources and ability to move to the new standard, updating procedures, and training personnel for the new requirements. Definitely perform a gap analysis or multiple gap analyses internally or utilizing external parties like consulting firms to understand where your organization is today and where you need to be in the next two to three years. Develop, document, and establish a quality plan that will take the organization from Point A to Point B for specifically meeting ISO 13485:2016 requirements. Provide the appropriate training to all applicable personnel and continually communicate on the changes that are being made to the quality system to meet revisions of the requirements.

Finally, once the transition work has been completed, perform a thorough internal audit or obtain an external independent assessment by a third party prior to your re-certification audit to the revised ISO 13485 standard.

Planning

- Obtain a copy of the FDIS to start pre-publication planning
- Identify resources that are needed including personnel for updating the QMS
- Understand the timing of current certification and transition requirements
- Discuss timing and needs with Registrar/Notified Body well in advance
- Generate a quality plan that details the activities needed to be completed
- Train personnel to the new standard and communicate the quality plan
- Perform necessary gap analysis of the quality system
- Assure internal audits are incorporating the changes required
- Prepare for the re-certification audit by Registrar/Notified Body

To Learn More...

Summary

The next few years are going to be interesting and busy for many of us. Now that the new ISO 13485 standard has been published, not only will medical device manufacturers be busy, but Registrars and Notified Bodies will need to achieve new accreditation, and regulatory agencies will need to assess their current regulatory requirements; as such, all of these impacts will be felt across the entire medical device industry.

Many of the changes, clarifications, and re-organization in the standard are not necessarily new information – these could be considered to be closing the gap between what is currently expected to be done and expected requirements over the last 10 years. While there are new requirements added to the standard, these should not be any surprise to a medical device manufacturer. The best advice is to ensure that an organization has support from their top management and understands the changes that are going to be needed. Also make sure that a quality plan or transition plan is developed that defines the resources, activities, and timelines needed to achieve those goals.

A well-structured approach to transitioning for compliance with the revised standard will remove many difficulties and ensure that your organization is ready for re-certification to the revised ISO 13485 standard when that time comes.

About the Author

Richard Vincins, CBA, CQA, RAC (US/EU): Richard Vincins is Vice President, Quality Assurance Consulting at Emergo. With over 25 years of experience in the medical device industry, Richard's areas of expertise include ISO 13485, US FDA QSR, and many other country quality system implementations including Canada, Japan, Brazil. Additional areas of expertise include US FDA 510(k) registration, European CE Marking, multiple country product registrations, risk management, and clinical investigations. Richard's main focus and responsibilities are advising compliance of medical device and IVD companies to the ever expanding regulatory requirements.

To Learn More...

References:

1 http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=62085

2 http://www.ecfr.gov/cgi-bin/text-idx?SID=eb6c05113884041ba6fe5b13f7341da0&mc=true&node=pt21.8.820&rgn=div5

3 http://www.imdrf.org/workitems/wi-mdsap.asp

4 http://www.imdrf.org

5 http://www.iso.org/iso/news.htm?refid=Ref1621