THE NEW ISO 13485 STANDARD

Impact on medical device quality systems.

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ISO 13485 introduction and background

After more than 10 years, we are getting an updated Quality Management standard with revision of ISO 13485 for the medical device industry. The origins of the 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 that, in 1996, the ISO 13485 and ISO 13488 standards specific to medical devices were published. The difference between the two medical device industry standards was 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 the current ISO 13485:2003 that the medical device industry has been using for regulatory certification purposes.

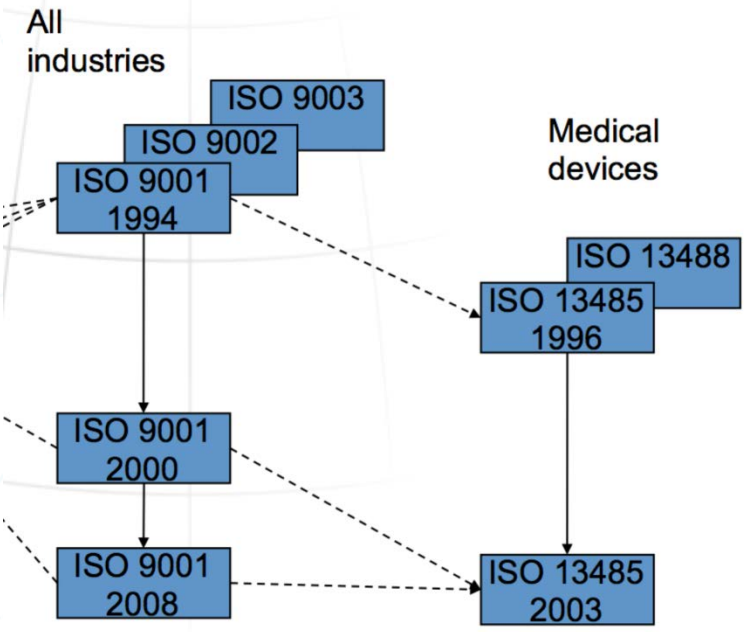


Figure 1

Source: 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 working environment, sterility, 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 is currently in the Final Draft International Standard (or FDIS) stage[2] that has maintained an overall structure that is the same as the previous 2003 version. 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 is 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 the next few months.

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.

We are anticipating that the finalized ISO 13485 standard will be published March 2016 as shown by the overall timeline in Figure 2. Guidance from TC 210 have indicated that there will be a three-year transition period with only new certifications being issued in the last year of the transition period. In addition, it is expected that the EN ISO 13485 standard will be updated shortly after in the May/June timeframe, but we will talk more about this later.

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.

[1] http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=62085
[2] http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=59752

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 to be published
March 2019	• End of transition period for updating certificates to new version

Figure 2

Source: Emergo

Now onto the discussion of the changes that are being 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 start preparing and planning for the transition with the new standard.

Definitions

There are a number of new definitions shown in the sidebar list that are being 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. 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.

ISO 13485:2016 Definitions

- Manufacturer
- Authorized Representative
- Distributor
- Importer
- Clinical Evaluation
- Performance Evaluation
- Post Market Surveillance

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.

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, distributor, or specification developer. 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. This also includes the requirement to apply a risk-based approach to the processes that are implemented throughout the quality system.
- The legal manufacturer cannot "absolve" itself of the responsibilities for quality system requirements. 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 that references intended use, labeling, packaging, manufacturing, 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 until the end of life of the medical device.
- As the electronic management of documents has significantly changed since 2003, the standard clarifies 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.

Management responsibility

A stronger emphasis has been placed on executive 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 being 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.

There has also been a distinction made that an individual 'might be' nominated for monitoring experience from post-production activities; this has been changed to more strongly clarify the nomination of a person for this role and responsibility. Specifically some of the modifications in this section can be seen as the following:

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. • Added a 'Note' in Section 5.4.2 about how quality planning is intended to meet the need of accomplishing the organization's quality objectives.
Section 5.5	• Clarified and strengthened the wording in the 'Note' that applicable regulatory requirements might require the nomination of a specific person responsible for post-market production activities. Most medical device manufacturers are currently aware this is an important part of post market surveillance that is required by almost every country with regulatory requirements. • 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 the interval for Management Reviews needs to be documented and that the rationale for the interval shall be recorded. The idea is that an organization having management review once a year may not be appropriate, and that the organization needs to document the rationale for the interval period. • Clarified that management review input of customer feedback is just not related to 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.

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 the training necessary 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 proportional to the risk associated with the work for completed training. This should be defined in a training matrix or job description that details tasks the individuals are responsible for because an individual performing verification testing may pose significantly higher 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 series and the need 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.

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.

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 the Section 7.3 Design Control section that are now more consistent with the FDA QSR regulations[3]. There were also new sections added in supplier management to clarify qualification and monitoring of suppliers for an organization.

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

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

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. • There has been a 'Note' added referencing specifically IEC/ISO 62304 for software life cycle processes that are not only applicable to the product, but within the entire quality system.
Section 7.2	• There has been a section 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. • It was clarified through a 'Note' that post-delivery activities also include warranty provisions, maintenance services, recycling, or final disposal of the device. These requirements were added to be consistent with many regulatory requirements for maintenance and disposal of finished medical devices. • Clarifies that any regulatory requirements that must be met as part of the customer order must be fulfilled, such as importation, registration, and post-market activities. • Removed the 'Note' about Internet sales as there are common acceptance activities that occur for a customer order through the Internet. • Section 7.2.3.2 was specifically added for communication with regulatory authorities in accordance with planned arrangements. This means that any changes to the regulatory status of the product, changes to the quality system, or post-production activities must have a mechanism for notification of the applicable regulatory agencies.
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 utilizing the standard ISO/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. • 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 Records was added to maintain a design and development file for each medical device 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 specifically add sections on 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. • 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 activities. • 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.

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 internal or external, 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, 8.2.1.2 Complaint Handling and 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 correction 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. A ‘Note’ was added that the organization needs to consider the extent of monitoring or measuring that is appropriate for their product realization.

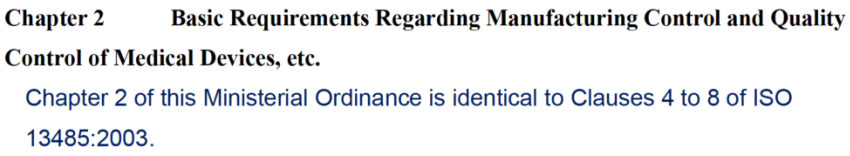
- Nonconforming product was clarified and expanded for handling nonconforming product before and after delivery to ensure that these instances are each handled appropriately.
- A new section, 8.3.4 Rework, was included to ensure that rework activities are performed according to document procedures or 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.

A globally harmonized standard

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. There is also strong intent to create a global auditing process through the Medical Device Single Audit Program (MDSAP)[4] 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)[5] has been administering and guiding the MDSAP with the US, Brazil, Canada, Japan, Europe, Australia, and China currently involved.

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, etc.

Chapter 2 of this Ministerial Ordinance is identical to Clauses 4 to 8 of ISO 13485:2003.

Fig 3

Japan's Ministerial Ordinance is following the ISO 13485 standard.

Relationship with EN ISO 13485

Currently with the ISO 13485:2003 standard we have an associated EN ISO 13485:2012 standard that has Annex 'Z's that provide alignment to the Directives for Europe (reference a brief example in Figure 4). This is not expected to change dramatically with the introduction of the ISO 13485:2016 standard. It is anticipated that in roughly May or June 2016 that a new EN ISO 13485 standard would

[4] http://www.imdrf.org/workitems/wi-mdsap.asp
[5] http://www.imdrf.org

be published that incorporates similar Annexes as currently published – though this is just conjecture that is presumed by the author as the Directives themselves are not changing.

There may be some realignment of the Annex 'Z's with the new standard because of new sections and clarifications of wording that are anticipated to be 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.

Because these European regulations are not finalized, it is not clear at this time what the content of the Annex 'Z's would constitute. The only thing that can be hoped for at this juncture is that ISO 13485 can be applied as a global harmonized standard with the European requirements.

Paragraph of 93/42/EEC	Section of EN ISO 13485	Addressed
Paragraph 3.1 Second Sentence Second Indent	N/A	Not addressed
Paragraph 3.1 Second Sentence Third Indent	N/A	Not addressed
Paragraph 3.1 Second Sentence Fourth Indent	4.1 and 4.2	The document required by 4.2 is not covered entirely as detailed in Annex II
Paragraph 3.1 Second Sentence Fifth Indent	4.1, 5.1, 5.4, 5.5, and 5.6	Addressed
Paragraph 3.1 Second Sentence Sixth Indent	4.1, 5.1, 5.4, 5.5, and 5.6	Addressed

Table ZB.1 – Relationship of Medical Device Directive 93/42/EEC with EN ISO 13485 (Fig. 4)

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[6]).

All is not lost though, because the new ISO 13485 standard will include Annex B that compares the content tables of the two standards. 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

[6] http://www.iso.org/iso/news.htm?refid=Ref1621

system that applied 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 has already understood 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.

Planning for the revision to ISO 13485

Now that the Final Draft International Standard (FDIS) has been published we have a better understanding of content for the final published version of ISO 13485. Like everything in life, time is of the essence and there is never enough time to get things done, so planning in advance is key.

There is a short summary in the sidebar 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

Summary

The next few years are going to be interesting and busy for many of us. When the new ISO 13485 standard is published, not only will medical device manufacturers be busy, but Registrars and

Notified Bodies will need to achieve new accreditation, 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 executive 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, 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.

To learn more:

Emergo helps medical device companies with regulatory compliance and market access worldwide. To learn more, visit www.emergogroup.com/services