

Quality Systems and CE Marking — the Transition to EN ISO 13485:2003

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An effective quality management system is a key element for achieving the CE mark. This article explains the relationship among various quality system standards and their revisions, the current status of transition to ISO 13485:2003, and some future trends. Words in *italics* are defined in a glossary at the end of the article.

ISO 13485:2003 and the Quality System Regulation

As companies gain experience implementing ISO 13485:2003, they may find that, although the stated requirements are quite similar, the ISO 13485 perspective is a little different from that of the FDA's Quality System Regulation. The FDA's primary goal is to ensure that devices are safe and effective. While this may be an unstated goal of ISO 13485, the ISO standard focuses on anticipating and meeting customer needs to a greater extent than does the Quality System Regulation.

For example, the ISO standard includes "customer focus" as part of Management Responsibility. The organization is required to determine not only requirements specified by the customer, but also requirements not stated by the customer but necessary for specified or intended use.

The ISO standard also devotes a section to "Feedback," requiring the organization to monitor information relating to whether it has met customer requirements. This feedback system is intended to be more proactive than simply handling complaints as required by the FDA. ISO/TR 14969:2004 explains that many sources exist for obtaining customer-related feedback pertaining to the quality of medical devices and associated services. Examples of customer-related information include not just

customer complaints, but also customer and user surveys, contract information, peer-reviewed journals, and other sources.

Quality Systems and the CE Mark

Manufacturers wishing to sell medical devices in the European Union (EU) must affix the CE mark to their products. The CE mark is the manufacturer's claim that the product meets the *essential requirements* of the applicable European medical device *directive*: Active Implantable Medical Devices Directive (90/385/EEC), Medical Devices Directive (93/42/EEC), or In-Vitro Diagnostic Medical Devices Directive (98/79/CE).

Recent milestones in ISO 13485:2003

- The standard has been harmonized as EN ISO 13485:2003
- EN ISO 13485:2000 and EN ISO 13488:2000 will be withdrawn in 2006 and replaced by EN ISO 13485:2003
- The earlier standards EN 46001, EN 46002 and EN 46003 have been withdrawn and declared superseded by ISO 13485:2003
- The guidance document for using ISO 13485:2003 has been updated and issued as ISO/TR 14969:2004, "Medical devices—Quality Management Systems—Guidance on the application of ISO 13485:2003."
- Standard EN 1441 has been withdrawn and declared superseded by EN ISO 14971:2000

Each of the three device directives requires that the manufacturer have an established quality system. Although the directives vary in their details, they all require manufacturers of high-risk devices to implement a full quality system

to control design, production, and inspection. For low-risk devices, the manufacturer may choose to submit product for testing and thereby employ a more limited quality system. To avoid submitting product for testing, however, the manufacturer of low-risk devices may also choose to implement a full quality system.

Contrary to what many people believe, the directives do not require that the quality system comply with any particular standard. Indeed, a company may use a unique quality system of its own design, provided that the system is appropriately documented and can be shown to ensure that the resulting devices meet the requirements of the directive.

Most device companies in the past have chosen to implement a system that complies with the *harmonized standards* of either ISO 13485/13488 or the ISO 9000/EN 46000 series¹ despite the availability of other options. Compliance with a harmonized standard affords a presumption of conformity with the applicable essential requirements. All *notified bodies* are familiar with the harmonized standards, and will rather easily understand a quality system that is based on those standards. By contrast, you may have to do a lot of explaining to convince your notified body that you meet the requirements for CE marking if you implement a different type of quality system.

Standards, Standards, Standards

The ISO 9000 series provides for a basic quality system. The provisions are rather general so that they can be applied across a wide range of industries. The

1. The terms "ISO 9000 series" and "EN 46000 series" are used in this article to mean ISO 9001/9002/9003 and EN 46001/46002/46003, respectively.

Message from GMP Labeling

We hope this newsletter includes information that you can use. Our goal is to periodically publish articles, written by quality professionals, that are timely and informative to the companies in our marketplace. Of course, along the way, we also hope to reinforce our image as a valuable resource to our customers.

Businesses regulated by the FDA and/or are ISO 9000 registered will find GMP Labeling products helpful in maintaining compliance. More than 5000 facilities in the U.S., Canada and Europe use GMP Labeling products on a daily basis.

European Commission believed that the medical device industry needed more prescriptive requirements than those in the ISO 9000 series. The European standard-setting bodies then developed a set of three harmonized standards (the EN 46000 series) that referenced the ISO 9000 series, but added quality system requirements specific to the medical device industry. The EN 46000 revisions were:

EN 46001: 1996 (used with ISO 9001:1994), EN 46002: 1996 (used with ISO 9002:1994), and EN 46003:1999 (used with ISO 9003:1994). Similarly, the International Organization for Standardization (ISO) also recognized the need to modify the ISO 9000 series for application to the medical device industry. They developed two more standards: ISO 13485:1996 for use in conjunction with ISO 9001:1994, and ISO 13488:1996 for use in conjunction with ISO 9002:1994. The EU later harmonized these standards as EN ISO 13485:2000 and EN ISO 13488:2000. Device companies could then comply with either the EN 46000 series or EN ISO 13485/13488 in order to apply the CE mark. The EN 46000 series has now been superseded by EN ISO 13485:2003.

The ISO 9000 standards have been adopted by many countries as national standards. Because these standards are so widely recognized, many medical device companies in the past chose to certify their quality system to ISO 9000/EN 46000 for the purpose of CE marking. However, this is no longer an option since the latest revision of the ISO 9000 series.

Impact of the ISO 9000 Series Revision

The December 2000 revision of the ISO 9000 series incorporated several changes. The format was changed to consolidate what had been three separate

standards (ISO 9001:1994, ISO 9002:1994, and ISO 9003:1994) into one standard—ISO 9001:2000. Companies are permitted to exclude requirements related to product realization if they are not applicable to their business.

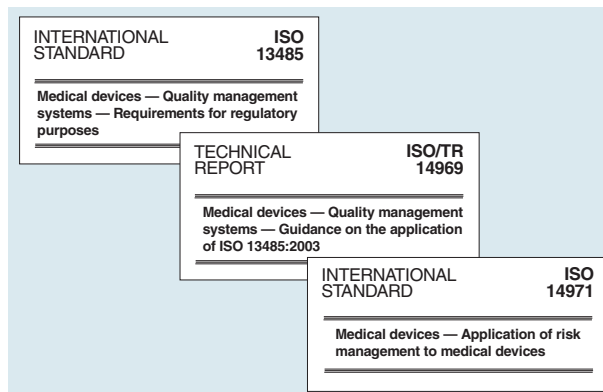
Another significant change was replacing the earlier 20-element approach to quality assurance with a more integrated, process-based approach to quality management. Associated with this change was a reduction in the number of required written procedures. Other major changes included a new focus on enhancing customer satisfaction and an emphasis on continual improvement. With the latest revision, ISO 9001 changed from a relatively prescriptive standard slanted toward manufacturing operations, to a more general, “total quality management” standard that was easier to apply to service-related business, the educational sector, and other non-manufacturing concerns.

For example, while continual improvement may be an admirable business model, it does not fit the “either you meet it or you don’t” nature of regulations and could allow regulators to continually raise the bar for compliance. The new focus on customer satisfaction was another concern. Not only was it difficult to define in a precise manner, it also had the potential for imparting legal significance to nonsafety/nonefficacy issues such as pricing or on-time delivery. And of course, the regulatory agencies were opposed to the elimination of the many previously required written procedures.

For these reasons, regulatory authorities in the European Union and elsewhere felt they could not adopt ISO 9001:2000. Meanwhile, the ISO organization was planning to revise 13485/13488, because the original edition specifically referenced the 1994 version of ISO 9001/2. The GHTF urged the ISO organization to revise 13485/13488 with a view toward achieving a standard that could be used by regulatory authorities throughout the world.

The revised standard ISO 13485:2003 was published July 15, 2003. The revision consolidated 13488 into 13485. Companies are permitted to exclude requirements for product realization if these are not applicable to the nature of their devices. The revised standard mandates more documentation than ISO 9001:2000 and contains requirements specific for medical devices. ISO 13485:2003 excludes those troublesome provisions of ISO 9001:2000 that are not appropriate as regulatory requirements.

For example, ISO 13485:2003 focuses on meeting customer requirements instead of enhancing customer satisfaction, and replaces the requirement for continual improvement with the require-



Important documents for ISO 13485 compliance

Many of these changes troubled the regulatory bodies in the *Global Harmonization Task Force (GHTF)*, who were trying to move toward harmonizing world-wide GMP regulations with ISO 9001 requirements. Both regulators and the device industry were concerned that the new requirements in ISO 9001 went beyond what was needed to control the safety and effectiveness of devices.

ment for maintaining the effectiveness of the quality management system. ISO 13485:2003 incorporates much of the wording of ISO 9001:2000 verbatim rather than referencing that standard. With ISO 13485:2003, medical device companies now have a stand-alone standard for demonstrating compliance of their quality management systems to regulatory requirements.

ISO 13485:2003 incorporates a process-approach for quality management. This is reflected by a change in the title of the standard. The 1996 versions were called “Quality Systems—Medical devices—Particular requirements for the application of ISO 9001 [or ISO 9002].” The 2003 version was renamed “Medical devices—Quality management systems—Requirements for regulatory purposes.” ISO 13485:2003 has now been harmonized as EN ISO 13485:2003.

Although certification to ISO 9001:2000 will not suffice for CE marking, some device companies may want to obtain certification to that standard as well, as a way to incorporate customer satisfaction and continual improvement into their company practices.

Schedule for Transition

The transition period from the ISO 9000:1994 series to ISO 9001:2000 ended December 15, 2003. ISO 9001/2/3:1994 are no longer in effect. The EN 46000 series was fully withdrawn March 1, 2004.

Companies that were certified to the EN 46000 series could either: 1) obtain certification to the similar standard EN ISO 13485/88:2000, and then transition to ISO 13485:2003; or 2) obtain certification directly to ISO 13485:2003.

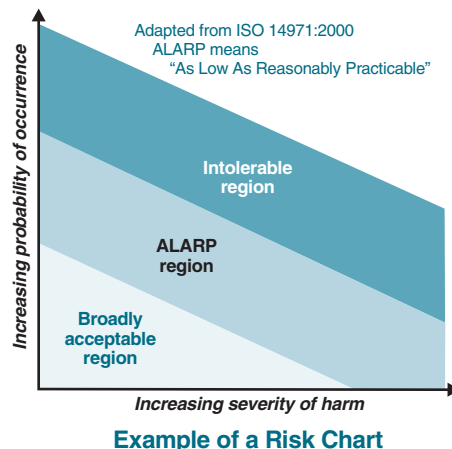
For Canada, the transition period from ISO 13485/88:1996 to ISO 13485:2003 ends March 15, 2006, after which the 1996 versions will be withdrawn. For the European Union, the transition period ends July 31, 2006². Companies that are currently certified to EN ISO 13485/88:2000 should already be working to obtain certification to ISO 13485:2003 during the transition period. Companies that plan to start applying the CE mark in the future should obtain certification directly to ISO 13485:2003.

2. Some non-European countries that require certification to ISO 13485/88 have a different deadline for transition to ISO 13485:2003.

The first step toward compliance is to conduct a gap analysis of your existing quality system against the requirements of ISO 13485:2003. The standard has two annexes that can help. Annex A is a chart showing the correspondence between ISO 13485:2003 and ISO 13485:1996. Annex B is a chart explaining the differences between ISO 13485:2003 and ISO 9001:2000. Guidance for implementing ISO 13485:2003 is now available in ISO Technical Report 14969:2004, which has been updated for the new standard.

The Big Challenge

Risk management is an area that is receiving increasing emphasis. The 1996 version of ISO 13485 simply required the organization to evaluate the need for risk analysis throughout the design process. The 2003 version requires the organization to establish documented requirements for risk management, not just risk analysis. Also, requirements for risk management must now be established, not just during the design process, but throughout product realization.



A major hurdle for many companies is understanding and executing risk management. ISO 13485:2003 refers to ISO 14971, “Medical devices—Application of Risk Management to Medical Devices,” for guidance related to risk management. This standard, which has been harmonized as EN ISO 14971:2000, replaced the earlier standard EN 1441:1997 as of April 1, 2004.

EN 1441 addressed the more narrow topic of risk assessment. ISO 14971 has a wider focus that includes managing risk throughout the life cycle of the product. In addition to risk assessment, ISO 14971 also requires risk evaluation and

control, and collection of post-production information.

Organizations are frequently adopting ISO 14971 as part of their quality system. Applying risk management from early design through post-production may be a new concept for companies that have never conducted risk assessment, or that have only used risk analysis techniques as a tool during design development. In addition, ISO 14971 requires that an evaluation of overall residual risk be done after completing risk assessment and control of individual hazards, and this final evaluation may entail performing a risk-benefit analysis as well.

Unfortunately, there is little guidance available as yet on how to conduct either the overall residual risk evaluation or the risk-benefit analysis. “Risk management is clearly the #1 challenge for companies implementing ISO 13485:2003,” says John Pulley, lead auditor for Intertek, a Notified Body for the Medical Device Directives.

The GHTF has issued a proposed draft guidance, “Risk Management as an Integral Part of the Quality Management System.” The guideline discusses integrating risk management into management responsibilities, each step of design control, traceability, purchasing and acceptance activities, production and process controls, servicing, corrective and preventive action, and statistical techniques. The GHTF guidance is meant to complement ISO 14971, and is not intended to be used for assessing compliance with regulatory requirements.

The FDA does not plan to revise the Quality System Regulation to match the format of ISO 13485:2003. However, the agency sees no conflicting requirements between the two documents. U.S. companies can integrate the requirements of both into one quality system. The FDA also is increasing its focus on risk management, and has recognized ISO 14971 as a consensus standard. This means that a declaration of conformity to ISO 14971 may be used to satisfy the risk management needs for a Special 510(k).

Conclusion

ISO 13485:2003 is a truly international standard for medical device quality systems. The European Union and countries such as Canada and

ISO 13485/13488:1996 are now actively transitioning to EN ISO 13485:2003 or to their national versions of the standard.

Some countries that never adopted ISO 13485/13488 as a national standard will accept certification to ISO 13485:2003 as evidence that the organization has an acceptable quality system.

Under Japan's revised Pharmaceutical Affairs Law, which went into effect April 1, 2005, device manufacturers and exporters must obtain certification to ISO 13485:2003 as part of the product licensing process.

Certification to ISO 13485:2003 has become a necessary first step towards entering much of the global marketplace.

About the author

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Glossary

Competent Authority: the body appointed by each national government within the EU to enforce compliance with the directives in that country.

Directives: European Union legislation published in the *Official Journal of the European Communities*.

Essential Requirements: those requirements in each directive that must be addressed and documented before the CE mark can be applied to a medical device.

European Commission: the administrative branch of the European Union (EU). The Commission proposes and implements policies approved by the member states of the EU.

Global Harmonization Task Force (GHTF): a voluntary group of representatives from national medical device reg-

ulatory authorities and industry. The GHTF encourages convergence in regulatory practices for medical devices. The founding members are Australia, Canada, the European Union, Japan, and the United States.

Harmonized Standards: standards that 1) have been mandated by the European Commission; 2) have been developed by the European standard-setting bodies; 3) address essential requirements of the directives; and 4) have been published in the *Official Journal of the European Communities*. Harmonized standards carry the prefix "EN."

Notified Body: an entity approved by the competent authority to assess manufacturers' compliance with the directives.

The original version of this article appeared in the April 2004 issue of FDC Control, a publication of the Food, Drug and Cosmetic Division of the American Society for Quality, and its contents are reprinted here by permission.

The article, as it is presented here, has been updated by the author to reflect changes with regard to ISO 13485 as of June 2005.

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