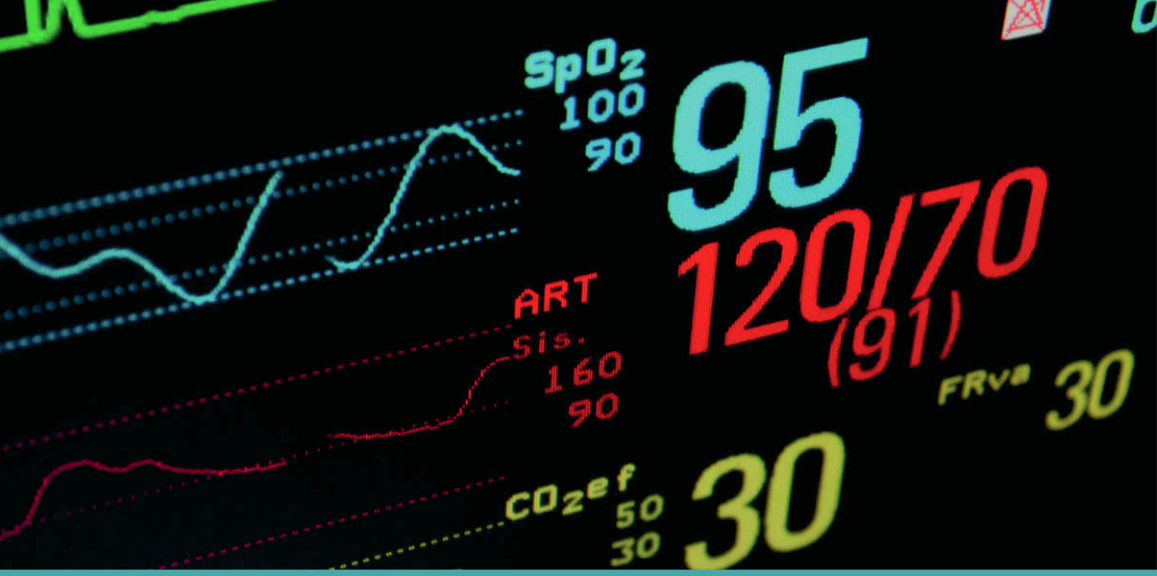

5.5 Quality Management

INTRODUCTION

An engineer looks over the shoulder of a cardiologist and sees something that never should have happened – a broken nitinol stent now embedded in a patient's artery. Shortly thereafter, several other doctors from hospitals across the country start reporting the same finding, although many others indicate that they have experienced no problems at all. After studying all the films, it is confirmed: despite the fact that all cycle testing before commercial launch was successful, some of the stents are now breaking in the field. In an effort to understand why some are breaking and others are not, the engineer thoroughly reviews the causes of failure. By checking the detailed records maintained at the company as part of its quality management system, he determines that only stents from certain lots seem to be involved in the failures, and within these lots, records to support device traceability reveal that the failure is associated only with devices using a particular nitinol. In fact, the failures can be isolated to a specific material source. Stents from this ingot are then recalled and, after communicating the issue and its resolution to the proper authorities, the company is able to overcome this challenge, eliminating the failures and returning to the market to achieve great success.

OBJECTIVES

- Appreciate the critical role that quality systems play in facilitating the transition from an idea to a scalable, reliable product.
- Understand the key components of quality systems and why early implementation of certain subsystems is of strategic importance to managing a business.
- Understand the FDA's quality-related regulatory requirements and how they may differ from what is required in other countries.

Scenarios like the one above highlight the fact that a disciplined and rigorous approach to development and production is essential when bringing any innovation to market. If the innovator's end goal is to create a new medical device that can be manufactured according to precise specifications and used safely and reliably in medical care, then rigorous quality processes are central to making this happen. Not only are such processes critical for achieving regulatory clearance for a new technology, but they allow the innovator and team to transition from producing one device at a time to reliably manufacturing batches of products whose performance can be tested and validated. Moreover, patient lives may be put at risk if the quality process guiding development and subsequent production fails to ensure the creation of a product that performs as intended and meets all specified safety requirements.

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QUALITY MANAGEMENT FUNDAMENTALS

In the early stages of the biodesign innovation process, there is typically not a "real" medical technology company – that is, an innovator might be working alone or with a small group of engineers to solve problems and produce enough **prototypes** for preliminary testing. But, at some point as testing begins, this informal approach to development must incorporate defined operating procedures to ensure that the product can achieve regulatory clearance. Further, the team must transition into an entity with precise systems capable of producing devices predictably and reliably, delivering them to the end **user** in a timely fashion, and monitoring their performance in the clinical environment.

While essential, this transition is fraught with risks. If the systems put into place are inadequate in any way, they can potentially undermine the success of the venture. Even from an early stage, rigorous processes are needed to govern all of the activities that must be scaled up as a company prepares for commercialization, including those related to initial product development, manufacturing, packaging, labeling, storage, distribution, installation, and service of medical devices. The systems used to manage and monitor these processes are collectively referred to as "quality management systems" (**QMS**) or more simply quality systems.

Quality management in product development and manufacturing

The term "quality" broadly refers to the activities undertaken by the company to ensure that certain regulatory requirements are met and that products delivered to the customer (primarily patients and physicians) are safe and reliable. Relevant regulations require that detailed specifications are developed for the devices, that the devices are tested and manufactured according to these specifications, and that the devices perform according to these specifications once distributed and/or installed. Their performance must also be monitored so that problems can be reported to the regulatory bodies as they are identified and corrected.

Quality systems can be a source of competitive advantage for a company if they lead to rapid product development cycles, superior quality as measured by extremely low defect rates, and low production costs. Additionally, strong quality systems contribute to the perceived **value** of a product (and, conversely, prevent the value of a product from being undermined by in-market failures). Finally, since quality systems are required by regulatory bodies, such as the US Food and Drug Administration (**FDA**) and other governmental authorities around the world, they are closely considered a part of any regulatory submission. The FDA, for one, demands that "companies establish and follow quality systems to help ensure that their medical devices consistently meet applicable requirements and specifications."[1] The agency has precise regulations, called Quality System Regulations (**QSR**) – called out in the Code of Federal Regulations Title 21 Part 820 (also referred to as simply **21 CFR 820**) – that specify the exact requirements that a company's quality system will need to meet before a product can be cleared or approved for the market. Despite the close ties of quality systems and regulatory processes, it is important to note that quality is much more than just a requirement or checkmark in a regulatory approval or clearance process. When considered more holistically, quality management can be thought of as one specific approach to **risk management** in a medical technology company in that it involves the systematic application of policies, procedures, and practices to the tasks of identifying, analyzing, controlling, and monitoring risk.[2]

Traditionally, quality management has carried the stigma of being a "policing" function within many organizations. For instance, quality measures have been perceived as imposing extra work steps and stringent requirements that necessitate a lot of effort for little measurable return. Busy employees sometimes question why the company needs formal quality processes, especially in young start-ups that may not yet have products in the market. However, recent cases demonstrate that the cost of not having an effective quality system in place can be devastating, no matter what stage of development the company has reached.

For example, consider the case of Boston Scientific. In 2000 and 2004, FDA quality inspectors found hundreds of quality control lapses in six of the company's US-based manufacturing facilities. As a result, the agency issued

three warning letters to Boston Scientific. When subsequent inspections in three additional plants revealed quality control and regulatory issues, the FDA issued a broad "corporate warning letter," indicating that the company's corrective actions to address prior violations were inadequate. Such a move by the FDA, which was considered a broad critique of the company's entire quality control systems, is unusual.[3] Disclosure of the letter led to an almost immediate 5 percent drop in Boston Scientific's share price.[4]

Examples of the quality problems uncovered at the company varied from facility to facility, but all related to the procedures, processes, and timeliness of Boston Scientific's corporate quality management system. At one plant, employees were unaware that company headquarters had recalled a needle used to treat tumors in cancer patients. In another location, managers missed deadlines for notifying the FDA of reports linking Boston Scientific devices to serious injuries (federal regulations require notification within 30 days).[5] While the corporate warning was in effect, the FDA informed Boston Scientific that it would not approve any new devices that could be affected by the quality problems. At the time the warning was issued, this had potentially damaging consequences for the company since it was preparing to submit its new drug-eluting stent for FDA approval.

After receiving the FDA's warning, Boston Scientific launched one of the most systematic and extensive quality system enhancement programs in medical device history. The company dedicated two years, millions of dollars, and hundreds of employees to implementing changes in its manufacturing, distribution, and monitoring systems.[6] For example, one action the company took was to consolidate 23 separate processes for tracking complaints into a single system.[7] Based on the company's remediation efforts, the FDA lifted a number of the restrictions it imposed in the warning letter as the company worked with the agency to resolve the remaining issues.[8]

Even in small start-ups, the cost of not having effective quality systems can be high. These costs are known as failure costs, which represent the expenses incurred by a company as a result of having products or services that do not conform to requirements or satisfy customer **needs**. They are divided into internal and external failure categories by the American Society of Quality (**ASQ**).[9] Internal failure costs occur prior to delivery or shipment of the product (or the furnishing of a service) to the customer. This includes scrap, rework, reinspection, retesting, material review, and downgrading. External failure costs occur after a product or service has been delivered to the customer. These costs include processing customer complaints, customer returns, warranty claims, product **recalls**, and even the risk of being shut down by the FDA or another regulatory body. "Soft" costs must also be taken into account, particularly as a company is seeking to establish itself in the marketplace. These include the negative effect of poor quality on a company's reputation, its ability to attract investors, and its ability to attract and retain valuable employees.

Organizations that proactively address quality early in the design and development of a product have the potential to save significant time, money, and other resources in the long run while reducing the likelihood of devastating product safety issues and/or recalls. Innovators and young start-ups often feel overwhelmed by the amount of work required to implement a quality system, but it is important to note that not all elements of a complete system need to be put into effect right away. Initially, innovators can focus only on those elements that are relevant to their stage of growth. Then, as the start-up expands, so too can the quality system. This staged approach ensures that a solid foundation and good quality practices are established, while not overburdening an early-stage company.

Components of quality management

The concept of quality management is best understood by breaking it down into two components (see Figure 5.5.1). Quality assurance (**QA**) refers to processes that attempt to ensure – in advance – that products will meet desired specifications and perform according to specifications when delivered to the end user. As defined, QA is a broad concept that covers all company-wide activities, including design, development, production, packaging, labeling, documentation, and service, as well as support activities such as employee training and procedures. Quality control (**QC**) refers to activities

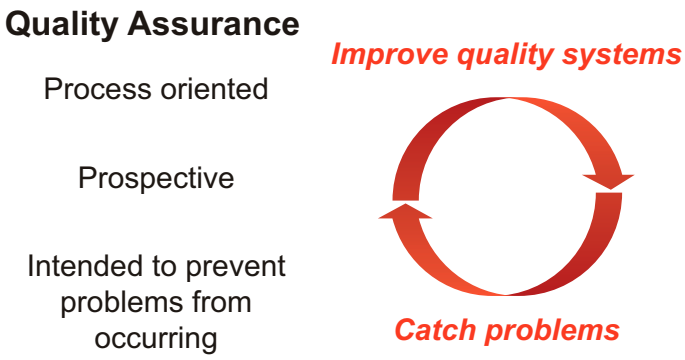

FIGURE 5.5.1
The concepts of QA and QC are distinct, but closely interrelated.

performed after these processes have been executed (e.g., once a product has been produced but before it is released to the customer) to confirm that the specifications have, in fact, been met. Unit testing, with the intent of finding defects, is one way that QC is executed.[10] QC applies to all stages of production from incoming materials, in-process materials/subassembly testing, and finished goods testing.

The primary difference is that QA is *process* oriented and QC is *product* oriented. QA makes sure a company does the right things, the right way, whereas QC makes sure that the results of what the company has done perform as expected. Stated another way, QA is a prospective process and QC is a retrospective process in product development. However, the two are interrelated: QC is a component of a QA system used to identify problems that can then lead to changes in QA practices to prevent the same problems from resurfacing.

Quality management systems

A QMS is the vehicle through which both QA and QC activities are implemented. A QMS includes policies, processes, and procedures for the planning and execution of all quality-related activities within an organization. It also delineates clear responsibilities, starting with the senior executive level, and helps drive performance improvement through the measurement and careful management of core business processes. Importantly, quality activities were historically the responsibility of an isolated functional team; however, senior executives across functions are now considered accountable for quality activities.

A typical QMS that would satisfy the basic requirements of most regulatory bodies involves as many as seven components, which are interrelated in specific ways. The aspects of the QMS shown in Figure 5.5.2 reflect the requirements of FDA's quality system regulation but the underlying principles are also generally applicable to other countries with well-developed regulatory systems.

At the highest level, **management controls** provide processes and guidelines for administering the complete system and are essential from the outset. **Design controls** refer to specific processes used to manage design specifications and their modifications. Implementing and spending time on design controls relatively early in the innovation process is important as these processes are the cornerstone of any good quality system. Production and process controls (**P&PC**) ensure that production processes have minimum deviations from their desired performance targets and result in a safe product. Corrective and preventive actions (**CAPA**) refer to the systems used to prevent and correct failures. According to FDA's inspection techniques, these four subsystems make up the heart of a company's quality system. The three remaining components – **material controls**; **records, documents, and change controls**; and **facilities and equipment controls** – complement the primary subsystems. Of these, records, documents, and change controls are usually the most important to implement early in the innovation process as they are central to providing a solid framework for initial product development.

Importantly, quality practitioners in the field often point out that there is not a single successful quality system model. The best way to evaluate whether a

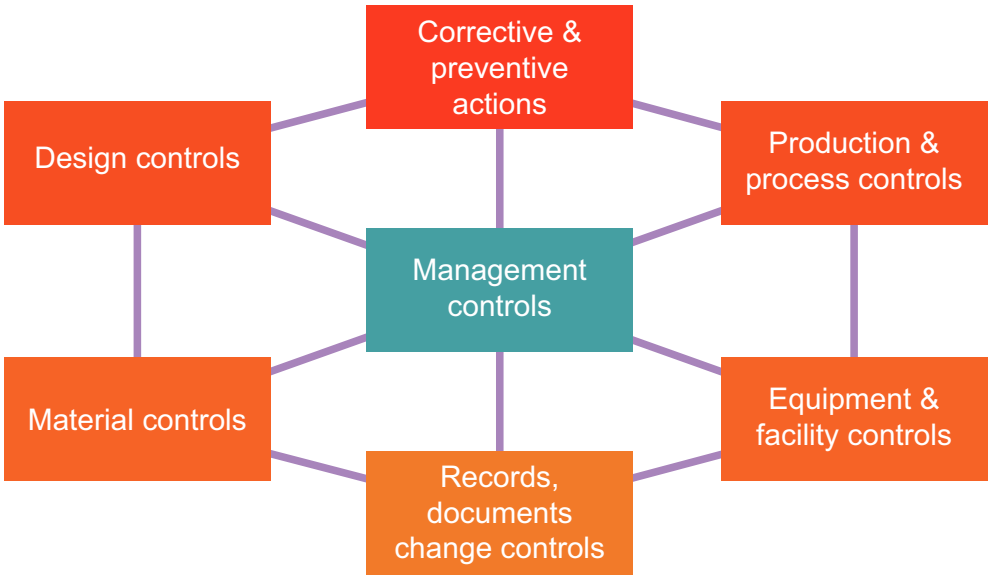

FIGURE 5.5.2
The components of a quality management system (based on FDA's quality system regulation).

company's quality system is adequate is to verify that it achieves certain core objectives:

- It results in the documentation of all product and system requirements.
- Employees are well-trained and follow the documented requirements.
- Records are generated to prove that the requirements are consistently followed.
- It establishes proactive systems to deal with the identification and resolution of problems and improvement opportunities.

Innovators should also understand that quality-related regulations by the FDA and other authorities are written as directional guidelines and must be interpreted appropriately for each company's products and business model. As such, there is no correct sequence in which to implement the various subsystems though, in general, management, design, and records, document, and change controls are often needed as a practical matter before other elements of a QMS. Subsystems such as P&PC and CAPA can usually be more thoroughly implemented a bit later. However, given that these two subsystems are considered core elements of a quality system by the FDA and are assessed as such during audits, putting some basic pieces of these subsystems in place may be useful. How a company interprets and documents its approach then becomes the standard against which the FDA will audit it for compliance (i.e., the company is audited against its own quality policies and internal documentation).

The seven subsystems of a typical QMS are explained at a high level in the sections that follow. A listing of more detailed references can be found in the Getting Started section.

Management controls

The purpose of the management control subsystem is to ensure that a company's management team provides adequate resources to support effective device design, manufacturing, distribution, installation, and servicing activities. It also establishes mechanisms for ensuring that the quality system is functioning properly, and for allowing management to monitor the quality system and make necessary adjustments on an ongoing basis. According to the FDA, the rationale for this subsystem is that a quality system that has been implemented effectively and is monitored to identify and address problems is more likely to produce devices that function as intended.[11] The key components of the management control subsystem include:[12]

1. Clearly defined, documented, and implemented quality policies and plans.
2. Well-defined quality objectives.
3. An executive in charge of quality management.

4. An organizational structure that includes provisions for resources dedicated to quality management that enable the organization to fulfill stated quality objectives and requirements.
5. Systems for management reviews to monitor the suitability and effectiveness of the quality system and take corrective action where necessary to bring the system into a state of effectiveness.
6. Audit processes to verify that deficient matters are being addressed.

Design controls

From an engineering perspective, design controls are absolutely essential to any quality system and are likely to be the first aspect of a quality system that an early start-up needs to address. The key objectives of design controls are to demonstrate that the design itself is reproducible and traceable and is proven to be both safe and effective. The basis for design controls is initiated in 4.5 Concept Exploration and Testing, as detailed **user requirements** are collected. However, the process for organizing and documenting this information is formalized with the implementation of a design control process.

Design control requirements are implemented to help ensure that every device performs as intended when produced for commercial distribution. To conform with these requirements, device engineers must establish and maintain design plans and procedures that describe design and development activities, define responsibility for implementation, and identify/describe the interfaces with different groups or activities that provide (or result in) input to the design and development process.[13] These plans must be reviewed, updated, and approved as the design and development of a device evolves. These activities are not prescriptive, but provide a method for management to exercise appropriate control over early design work, as well as to assign responsibilities that are consistent with the scope of the design effort.

Risk management is an important part of design controls.[14] Within risk management, hazards refer to potential sources of harm; harm includes physical injury or damage to the health of people, or damage to the property or the environment; and risks represent the probability that harm will occur, as well as the potential severity of that harm.[15] To assist innovators in formally identifying and addressing risks, QSR advocates for the integration of risk assessment and management activities throughout the design process. With this approach, unacceptable risks can be recognized and mitigated earlier, when changes are less expensive and easier to implement. Again, management has responsibility for applying its experience, insight, and judgment to successfully address this guidance.[16]

Two other important concepts that are central to design controls are **design verification** and **design validation**. Sometimes, these elements are termed "V & V." Design verification confirms that the product meets the specifications laid out by the product development team, while design validation confirms that the design specifications meet customer requirements. Any design specification will need to be validated before it is implemented in a production system and verified before the product is delivered to the customer. A simplistic example that highlights this difference involves a company that has decided to produce a cement lifejacket. Following design input and output, the company can verify that its cement lifejacket meets the **product specification** (i.e., it is made of cement). However, when the company seeks to validate the design against user needs, it encounters problems, since the cement lifejacket clearly will not float (therefore, it will not satisfy user requirements or the lifejacket's intended use).

In the US, premarket approval (**PMA**) and **510(k)** submissions for **Class III** devices typically must include a complete description of the design controls that the company implements. Without this information, the FDA cannot complete its premarket quality inspection (more information about quality inspection is provided later in this chapter). Table 5.5.1 presents guidelines from the FDA that outline the main activities, including those related to risk assessment and management, that must be accomplished to achieve an effective design control system.[17]

Production and process controls

The P&PC subsystem is focused on ascertaining that companies develop processes to ensure that manufactured devices meet their specifications. It also focuses

Table 5.5.1 Understanding and implementing design controls can be valuable even before the innovator has a full-fledged quality system in place.

Activity	Description
Identify design requirements for the device	• Establish and maintain procedures to ensure that the design inputs (or requirements) relating to a device are appropriate and address the intended use of the device, including the needs of the user and/or patient. • The procedures should include a mechanism for addressing incomplete, ambiguous, or conflicting requirements. • Design input is the starting point for product design, providing a basis for performing subsequent design tasks and validating the design. Therefore, development of a solid foundation of requirements is the single most important design control activity. If the majority of design time is spent upfront, doing things correctly, later stages of design can be expedited. • Design input requirements must be comprehensive and include functional (what the device does), performance (speed, strength, response time, accuracy, reliability, etc.), and interface (compatibility user, patient, and other external needs) requirements. Almost every device will have requirements of all three types. • Perform risk analysis to identify all possible sources of failures for different components of the device, acceptable failure rates, consequences of these failures, and corrective actions. The more severe the consequences of a failure, the lower the acceptable failure rates and the more robust the **correction** actions and back-up systems should be.
Develop the design output or specifications for the device	• Establish and maintain procedures for defining and documenting design output (i.e., the physical manifestation of the design planning and input) in terms that allow an adequate evaluation of conformance to design input requirements. Input requirements generally result in what is called a product specification (a document that details the technical and clinical needs the device should meet to satisfy the design intention). • Design output procedures should contain or make reference to acceptance criteria (in the product specification) to ensure that those design outputs that are essential for the proper functioning of the device are identified.
Verify that the design output meets the design input	• Establish and maintain procedures for verifying that the design output meets the design input requirements (i.e., does the device adhere to the design specification?).
Hold design reviews throughout the design process to identify significant problems with the design or the design process	• Establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development. • Multiple reviews of design verifications are not uncommon for complex devices that undergo successive design iterations, and will occur at each

Table 5.5.1 (*cont.*)

Activity	Description
	stage of the design process. Reviews must be conducted by cross-functional teams, thoroughly documented, and approved (signed off) by responsible personnel up through the senior management level.
Validate that the design meets defined user needs and intended uses	• Establish and maintain procedures for validating that devices conform to defined user needs and intended uses. This should include the testing of production units under actual or simulated use conditions.[18] • Design validation should also be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. • Design validation should include software validation and risk analysis, where appropriate.
Transfer the device design to production specifications	• Establish and maintain procedures to ensure that the device design is correctly translated into production specifications.
Control changes to the design during the design process and changes in the design of products on the market	• Establish and maintain procedures for the identification, documentation, validation or (where appropriate) verification, review, and approval of design changes before their implementation. • This is commonly addressed under a document control or change control system. Especially during the design process, the design teams often manage change and then move the design into the document control systems as part of transferring the design to manufacturing for production.
Document design control activities in the **design history file** (DHF)	• The DHF should be set up to contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and all design control requirements. • The DHF must be made available to the FDA (or other certified inspectors) for review. The FDA will evaluate the adequacy of manufacturers' compliance with design control requirements in preapproval inspections for class III devices and also during routine quality systems inspections for all classes of devices subject to design control. • A product cannot be legally marketed in the US without a **DHF**.

on validating (or fully verifying the results of) those processes and activities to monitor and control them.[19] It is important to note that validation in this context does not refer to design validation and verification as was discussed under design controls. Rather, in this case, it refers to process validation and verification, in which the focus is on the processes themselves and the operation and use of equipment involved in the enabling these processes. Validation of sterilization processes used to ensure that a product is indeed sterile when delivered to a user provides a good example of process validation. As part of this activity, the sterilization equipment, the

sequence of steps followed, and the environment would all be tested in order to establish a threshold for performance and an acceptable operating range in order to meet the specification of consistently delivering sterile products. As a company's R&D efforts move it toward a device that is ready for production, it must consider these types of controls, though implementing some basic elements of this control subsystem may be helpful in preparation for any FDA audits.

In developing P&PC systems it is important to understand when deviations from device specifications could occur as a result of the manufacturing process or environment and to pay special attention to processes with high risk of potential deviations. Management should be on the lookout for potential P&PC problems when a process is new or unfamiliar to the company, is used to produce higher-risk devices, or is used for manufacturing multiple devices. P&PC problems may also be indicated when a problem with a particular process is identified through the CAPA subsystem, when a process has a high risk of causing device failures, employs a variety of different technologies and profile classes, or has never been examined or inspected.[20]

Once processes with a higher than average risk for P&PC problems are flagged based on the presence of one of more of these indicators, methods can be developed and implemented for controlling and monitoring them to minimize production deviations.

Corrective and preventive actions

The purpose of the CAPA subsystem is to establish processes for collecting and analyzing information related to product and quality problems. Referring back to the QA/QC distinction, QC results are a core part of CAPA, but CAPA also incorporates the process used to act upon the QC results. QA is more of a broad, umbrella concept that reflects the combination of all components of the QMS and how they work together to provide the infrastructure for prospectively delivering a high-quality product.

CAPA is made up of processes such as non-conforming raw materials reporting, production process deviations, and customer complaints. Systems are put into place not only to ensure that deviations, complaints, and other problems are reported and documented, but that appropriate actions are taken to correct and prevent the recurrence of problems and that these actions are verified. Communicating CAPA activities to responsible parties, providing relevant information for management review, and documenting these activities is essential to dealing effectively with product and quality problems, preventing their recurrence, and minimizing device failures.[21] As a result, this subsystem is one of the most critical components of the quality system and is viewed as such by the FDA. However, as product and quality problems often arise a little further downstream in the product development cycle, it is usually sufficient for innovators early in the innovation process to be aware when a CAPA subsystem and its attendant processes need to be fully implemented and focus initially on establishing good management, design, and document controls, after which a general framework for this subsystem can be put into place.

Key activities that should be undertaken in this area include defining, documenting, and implementing robust CAPA processes that ensure the visibility of quality-related problems all the way to the top of the organization. The CAPA subsystem is closely related to medical device reporting (**MDR**). MDR is the mechanism through which the FDA receives information about significant adverse events from manufacturers so they can be corrected quickly. For this reason, CAPA and MDR processes must be tightly integrated (see online Appendix 5.5.1 for more information about MDR).

Equipment and facility controls

Equipment and facility controls are meant to ensure that a company's equipment and facilities are qualified (i.e., they are suitable for their intended purposes), and that standard operating procedures have been designed, implemented, and enforced for all equipment and facilities managed by the company. Qualification of equipment involves its installation, ongoing operations, preventive maintenance, and the overall validation of its outputs and related processes. This subsystem applies to equipment and facilities involved in design, production, and post-production activities. These controls allow the company to determine if any quality events are

related to equipment at a particular facility so that equipment changes can quickly be made (when needed) to address a quality event.[22] On a practical note, early-stage companies often use outside services, vendors, or manufacturers for various aspects of product development. Sometimes choosing contract partners with established equipment and facility controls, and that are familiar with the quality requirements of the medical device space, can help in the long-run with quality assessments related to regulatory and manufacturing processes.

Material controls

Whether they are related to design, production, or post-production activities, all materials used in a medical device must be carefully controlled. Medical device companies must maintain processes to track all materials and their associated suppliers to ensure the quality of those materials and that the final product satisfies the design specifications. All suppliers must be rigorously screened and able to demonstrate that their materials are traceable to qualified and appropriate sources. Detailed records (including traceability of material to suppliers and specific delivery lots) must also be maintained so that any problems that arise can be tracked at the materials level.[23] In addition to thinking about materials from a quality standpoint, innovators should think carefully about the materials they choose for practical reasons, especially if these materials will come in contact with or be implanted or used in the human body. There are key requirements for the **biocompatability** of materials, so choosing materials that are medical grade and may have already been used in other human applications can potentially have a significant impact on the cost and timelines of regulatory processes and product qualification.

Records, documents, and change controls

This subsystem is focused on ensuring that medical device companies maintain a secure, comprehensive, and centralized approach to managing all records and documents related to their quality systems.[24] Along with design controls, this is one of the first, most important subsystems for innovators to implement because it affects early product development activities, as well as those that come later as product development progresses. For example, maintaining a DHF is essential. Clearly defined protocols should be put into place to track changes to processes, policies, and the products themselves, manage version control, and make necessary documentation accessible to those who need it during design, production, and post-production activities. Another key principle is that all parties involved agree on how work will be done. When changes to these original work agreements are required, they must be formally evaluated and confirmed.

Implementing a quality system

Implementing a quality system can be time-consuming and resource intensive, as detailed processes and procedures must be carefully orchestrated and then documented. While regulatory bodies require that quality systems are in place, these requirements focus on the goals of these systems and not on *how* the procedures must be implemented. Therefore, designing a quality system can be somewhat of a creative exercise (and, as mentioned earlier, the company's interpretation becomes the standard against which it is regulated). On the one hand, this allows a company to iterate and develop a system that works with its particular needs and fits the company culture. On the other hand, the degree of interpretation and analysis required to make "appropriate" decisions that are likely to achieve compliance can be challenging. As quality consultants tend to point out, many "gray areas" exist when it comes to achieving compliance.

Another problem that companies struggle with is getting and keeping management's attention when it comes to the quality system. Too often, over-extended managers have a habit of only devoting their attention to the quality system after a problem has surfaced. This is due, at least in part, to the fact that it is so difficult to quantify the value of a quality system that works, whereas the cost of a quality problem once it emerges is all too obvious. However, given the growing emphasis on designing and implementing quality systems as a part of an overall risk management strategy, executives

should recognize that these practices are invaluable to the health of the overall business. Management commitment and attention is essential to making sure a quality system is supported and maintained by employees throughout the organization. Given that executives have to "sign off" on most aspects of the quality system as part of the management controls subsystem and, thus, share responsibility for its outcomes, it is in their best interest to ensure that a sound quality system has been designed and implemented. Careful attention to implementing management controls early in the design of a quality system can help in this regard.

A third issue that many companies face is characterized by a reactive versus a proactive approach to quality management. Especially with start-up ventures, too many medical device companies postpone or overlook the need to develop a quality system and fail to adequately document their work according to the procedures outlined in the quality plan. As a result, they are forced to scramble when problems arise and have to retrospectively "fill in the blanks." The quality system can be viewed as onerous, or as a system that supports the ultimate goal of the company – to design and produce an innovative, safe product. Viewing it as the latter yields the best systems in which compliance is part of everyday work life, rather than an additional burden. Moreover, innovators must remember that it is illegal to bring a medical device to market in the US without having the supporting quality system in place and working properly. Table 5.5.2 summarizes these and other common implementation pitfalls that can jeopardize the effectiveness of a quality system and its return on investment.

Table 5.5.2 Common mistakes to avoid when implementing a quality system.

Common mistakes when implementing a quality system
Viewing the requirements as a burden, rather than a mechanism for increasing firm effectiveness.
Entrusting management of the quality system to employees who do not have thorough training and experience in quality systems.
Making quality an isolated, non-essential function rather than integrating it into the business via cross-functional and senior management involvement.
Being too prescriptive early on and not considering the stage of the product development or the team.
Not including quality professionals in system design AND not including all of the system users in the system design.
Not thinking about how the quality system will need to scale and grow to keep pace with growth in the rest of the business.
Not training all personnel on the overall quality system, as well as their essential role(s) in making the system work.
Designing and implementing a quality system, but not maintaining it (which ultimately renders the system useless).
Ineffective and/or untimely action to deal with problems within the system – poor use of corrective and preventive action systems.

Again, senior management sets the tone for quality system design and compliance. If the management team approaches quality as an essential, important, and value-added activity toward the organization's goals, the system is more likely to be valued, followed, maintained, and improved over time to service the company's growth and expansion. By implementing just the most relevant components of a quality system when the company is first starting out (usually management controls, design controls, and records, documents, and change controls), management may be able to get greater company-wide buy-in than if it tries to implement everything at once.

When developing and implementing a quality system, companies usually begin by naming an executive to be in charge of quality (often the vice-president of R&D in small companies). This person will sponsor the quality work stream and work with executives and managers in other parts of the business to ensure cross-functional support. A quality engineer, preferably with QSR experience, is also hired to lead the tactical development of the appropriate processes, protocols, and documentation,

again with cross-functional involvement. Sessions to educate employees about the quality system, including its importance and specific requirements that affect their work, are another important early step. Then, the company can begin to hold regular review meetings to ensure that it is achieving desired performance levels.

Keep in mind that the US Supreme Court has allowed criminal penalties to be imposed on corporate officers who were in a position to prevent or correct violations, even if they may not have known about or participated in any illegal conduct:[25]

> *The [Food, Drug and Cosmetic] Act imposes not only a positive duty to seek out and remedy violations when they occur but also, and primarily, a duty to implement measures that will insure that violations will not occur. The requirement of foresight and vigilance imposed upon responsible corporate agents are beyond question demanding and perhaps onerous, but they are no more stringent than the public has a right to expect of those who voluntarily assume positions of authority in business enterprises whose service and products affect the health and well-being of the public that supports them.*

Implications of an increasingly tough enforcement environment

When considering the best approach to implementing a quality system, it is important for innovators to recognize that, in recent years, both the FDA and public have become increasingly conservative and risk-averse when it comes to medical devices. One example of how the FDA has been more vigilant about exercising its authority over companies and individuals that fail to meet QSR requirements can be found in the story of the 2007 FDA raid on Shelhigh Inc., a manufacturer of heart valves and other implantable devices for heart surgery. FDA investigators and US marshals seized all of the company's devices after finding what the FDA deemed to be significant deficiencies in the company's manufacturing processes.[26] According to an FDA statement, the **seizure** followed an FDA inspection of the Shelhigh manufacturing facility, as well as meetings with the company at which the FDA warned Shelhigh that failure to correct its violations could result in an enforcement action. The FDA also alerted the company to its manufacturing deficiencies and other violations in two warning letters.[27]

Another example that illustrates the potential severity of FDA actions to enforce QSR is the story of C.R. Bard Inc. In 1995, the company was found guilty of unlawfully selling and distributing unapproved heart catheters. The company was forced to pay record criminal and civil fines totaling $61 million. It was also required to implement stringent measures to prevent such illegal activities from occurring again.[28] In addition, three former senior Bard executives were convicted of conspiring to defraud the FDA. The three officials were found to be aware of the serious patient complications that resulted and of the company's efforts to change its products without FDA clearance. These men each received 18 months in prison.[29]

Stories such as these demonstrate why the collective attitude about quality is shifting toward increased prevention. These issues are also driving an increased focus on post-market quality, not just premarket quality requirements.

Quality system regulations in the medical device industry: QSR and ISO

The two most dominant quality systems in the medical devices industry are FDA's QSR and **ISO** 13485. **ISO 13485** was developed by the International Organization for Standardization and is required for devices marketed in the European Union (EU) and other countries recognizing the **CE mark**. Depending on the target market for their products, companies will follow one or both of these standards. The two systems have elements in common, but are fundamentally separate and regulated differently.

When the FDA began to regulate medical devices in 1976, the agency developed what it called good manufacturing practices (**GMP**) to set forth quality requirements for device manufacturers. In 1997, the FDA

revised and expanded the device quality regulations under the QSR rubric (although the term "GMP" still lingers in the device field). The FDA moved to QSR in order to enforce regulation that was more focused on prospectively ensuring quality (QA) as opposed to retrospectively catching quality problems (QC). QMS and its subsystems (detailed earlier in this chapter) meet the basic QSR requirements. Of importance to early-stage innovators, one of the notable changes with the new approach was the introduction of design controls into US quality regulations.

The second important change in the shift from GMPs to QSR was driven by the emergence of **ISO 9001** certification in the late 1980s and early 1990s. The ISO 9001 system was considered a best-in-class model for quality management that was applicable to any industry in any country in the world. In 1994, ISO introduced supplementary guidelines (EN46001) to be used in combination with ISO 9001 to address unique quality requirements for medical device manufacturers. As medical device companies began adopting ISO certification on a voluntary basis, along with the required GMP standards, the FDA recognized the merits of taking a systems-based approach to quality. This realization dovetailed with the overhaul of GMP and stimulated the FDA to make its approach more systems-oriented and consistent with the ISO 9001 standard.

In 2001, ISO 13485 superseded the combination of ISO 9001/EN46001 and was launched as a worldwide quality management system designed specifically for medical device manufacturers. ISO 13485 was subsequently updated in 2003 and again in 2012 (though the 2012 update included no changes to the text of the global standard from 2003 and only had revisions to the foreword and annexes). Based on the same basic principles as ISO 9001, ISO 13485 is often seen as a crucial first step in ensuring design and manufacturing processes consistently produce high-quality products that meet international regulatory requirements.

Importantly, ISO 13485 dictates that risk management must be thoroughly documented and conducted across all stages of a product's lifecycle, but it leaves the specifics to a related standard, ISO 14971: 2001, Application of Risk Management for Medical Devices. ISO 14971 outlines the steps that must be taken by management to fulfill device-related risk requirements. Companies pursuing ISO 13485 certification are not formally required to be 14971 certified. However, compliance with 14971 can aid in the attainment of 13485 certification.[30]

Although not required in the US, ISO 13485 certification is a prerequisite for achieving regulatory approval in the EU, as well as marketing in Canada, Australia, and Japan.[31] In other countries with regulatory systems that are still taking shape or being modernized, such as China or India, specific quality system requirements may be less well defined or in flux. Innovators working in these countries are encouraged to seek out consultants or firms with knowledge of the regulation landscape to understand current requirements. Regardless, by proactively following the principles embodied by ISO and/or QSR standards, innovators can help ensure that they are prepared for whatever requirements they may face.

Primary differences between QSR and ISO 13485

The FDA participated in the harmonization of QSR with the European ISO standards, but stopped short of adopting the ISO standards outright. The biggest difference between the two systems is that ISO is a voluntary standard in the US and QSR is not, which makes the compliance process a very different experience for companies. The conventional wisdom is that ISO standards are more stringent and rigid than QSR, but they do not necessarily ensure QSR compliance. A sample of other high-level differences is provided in Table 5.5.3.

An important requirement for US companies is to determine where they intend to market and manufacture the device – in the short term and the long term. They must consider whether to build a quality system that is both QSR and ISO compliant, or just compliant with one or the other. Any distribution of the device in the US

Table 5.5.3 Important distinctions between the QSR and ISO quality systems.

	QSR	ISO 13485
General Requirements/ Provisions	"Each manufacturer shall establish and maintain a quality system that is appropriate for the specific medical device(s) designed or manufactured, and that meets the requirements of this part."	"The organization shall establish, document, implement, and maintain a quality management system and continually improve its effectiveness in accordance with the requirements of this International Standard."
Link to Regulatory Approval	Required in the US for all **Class II** and **III** medical devices (as well as some **Class I** where general controls are required).[32]	Voluntary in the US but required in the EU and Canada as a prerequisite for regulatory approval and increasingly in other countries combined with other country-specific requirements.
Auditors	FDA inspectors.	Conformity assessment bodies (**CABs**) in EU or other third-party ISO-accredited inspectors elsewhere in the world.
Audit Frequency	Generally, every two years, but this timetable is rarely maintained by the resource-constrained FDA. Safety-related concerns will merit more frequent visits.	Companies generally follow an annual or semi-annual "maintenance" audit procedure.
Audit Scheduling	Audits can be announced or unannounced.	Audits are scheduled in advance.
Cost	There is no cost for an FDA audit beyond the costs the company faces in implementing and maintaining the quality system, dedicating personnel to the audit process, and addressing required corrections.	Costs of initial certification can exceed $30,000 to $40,000, in addition to annual maintenance fees. Cost depends on the size of the organization, as well as the chosen registrar.
Audit outcomes	FDA has enforcement power over the organization and audit findings must be acted upon.	Because ISO is voluntary, an "unsuccessful audit" simply results in postponed certification.

requires QSR compliance and, in general, if a company is to be registered with the FDA it should follow QSR requirements (unless it has an exempt Class I device). However, a company's strategy might involve early clinical work performed outside the US (i.e., in the EU or other foreign countries). If this is the case, ISO compliance may precede QSR compliance. Or, if a company leads with US marketing but intends to later expand to the EU (or beyond), it would be wise to build a system that is both ISO and QSR compliant. Many quality professionals have experience in building such hybrid systems. If an element of one system does not apply at the current time, it is not necessary for all elements to be turned "on" at once. A framework can be established and necessary elements can be brought "online" as needed.

For additional information about ISO 13485 see online Appendix 5.5.2. An interpretive summary of the FDA's QSR is provided in online Appendix 5.5.3.

The story of Sympara Medical illustrates how one **medtech** start-up company approached the process of implementing a quality system.

FROM THE FIELD SYMPARA MEDICAL

Setting up a quality system

As Sympara Medical, a venture-backed start-up in San Francisco, California, started working on an innovative device to treat hypertension, the founding team realized that it needed to think about quality management early in the development process. Although the company was not sharing the details of its technology at the time of this writing, co-founder Kevin Ehrenreich offered that, "Because we have a much different design compared to most other medical devices, we have the opportunity to move quickly into the clinic, without going through many of the traditional phases of the design process."[33] This accelerated development and testing schedule caused Ehrenreich and team to begin thinking about how to establish a quality system soon after the company's initial founding in order to most efficiently manage risk and prepare the device for human studies.

One of the main goals of Sympara's Series A funding was to launch a First Human Use study in the clinic within one year. To achieve this milestone, the company had to immediately rent manufacturing space and begin preparing to obtain its California Medical Device Manufacturing License, which would allow the team to manufacture the regulated medical products for use in its clinical study. The Cal-State license, as it is commonly known, requires an inspection of the facility and at least one of the following items: an FDA-issued biologics license, an FDA-approved investigational device exemption (**IDE**), a copy of a federal inspection completed in the last two years, or proof of compliance to ISO standards.[34]

As a first step, the leadership team brought in an external quality consultant who spent approximately six months learning about the company and its device so that he could help design and implement a quality system that was tailor-made to Sympara's requirements in the near-term, but that would also provide a solid foundation from which the company could expand over the next five years. Accordingly, they used a combination of the FDA's quality system regulation and ISO 13485, which have significant areas of overlap. QSR and ISO both provide medical device manufacturers with guidance to help them design and implement a quality system that meets essential regulatory requirements, but the standards also give companies the flexibility to customize their approach based on the unique characteristics of the device and what is most needed to ensure it is safe. "We didn't just want to release a quality system for the Cal-State inspection, we wanted to be actually testing the system to make sure it worked for the type of device we were building," said Ehrenreich.

While the old approach to quality management was grounded in a compliance mentality, Ehrenreich indicated that the new trend is to consider the quality system as a mechanism for risk management. Early on, the Sympara team made a list of all of the **stakeholders** that would interact with its device, including manufacturers, physicians, nurses, pharmacy staff who stock the device, patients, and so on. "We actually put up photos of these stakeholders," he said. Then, with representatives from all functional areas across the organization, the team thought of all the ways its device could potentially create harm for each stakeholder group at every step in the **cycle of care**. Through this exercise, the company identified critical risks and related hazards that it would seek to mitigate through design, development, and quality management. "The earlier a company starts thinking about risk analysis, the earlier it will be able to set the appropriate specifications for the device and focus on achieving them to keep the patient safe," Ehrenreich stated.

In terms of actually designing and implementing the quality system, "The team's key consultant led our initial focus towards developing basic quality procedures and a quality manual," he continued. "The way to get started is to think about what's value added to the company at the given stage of development and what doesn't need to come online until later." Working with the quality consultant, the Sympara team identified 10–12 core aspects of the blended quality system requirements that needed to be in place early in the development process; for instance, management controls, design controls, records, documents, and change controls, validated testing methods, and part identification. Then, as development progressed and the company moved closer to the clinic (and eventually to market launch), they would integrate more advanced features into the quality system. "Having a flexible quality system that can accommodate the development needs of the company is key," Ehrenreich noted. "You don't want to over build the quality system before it's necessary, but many of these requirements add a lot of value during the early stages of development."

With guidance from Sympara's quality consultant, the team was encouraged to write and release quality system components such as standard test methods with the expectation that they would improve and revise them over time. As Ehrenreich explained, "The first time you write it, it's not going to be perfect, it might not even be good. But go ahead and write it and release it, and try to build or test parts using that documentation. Then, don't be shy about editing it. The first time, you may make 50 percent changes to the document or process. But by the third or fourth time, it will be good enough. Remember that the enemy of good is perfect," he added.

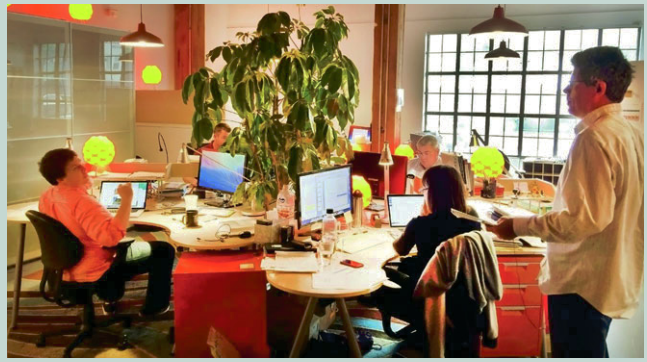

FIGURE 5.5.3
"Symparians" at work (courtesy of Sympara Medical).

Of course, this work should be conducted in collaboration with the quality consultant. In fact, Ehrenreich advised innovators to consider working with dual consultants who bring different points of view to the company. "Get two consultants who know the subject matter really well – one who's conservative in their view of quality systems and one that's more liberal – and *work with them* to settle on the best approach for the technology and the company," he elaborated.

Ehrenreich also strongly recommended keeping everyone in the organization involved in building out the quality system by discussing case studies that are grounded in the company's real-world experiences. For example, he said, "Have someone from the clinical team bring a clinical challenge and talk about how the quality system can help address it." Ultimately, the best quality systems are those that are based on the needs and input of the entire cross-functional team (see Figure 5.5.3).

Finally, Ehrenreich commented, "Remember that risk analysis is key. That's what gets you to the clinic and allows you to show that your device is safe, which is the whole reason to have a quality system."

Quality systems audits and what to expect

An important component of the regulation of medical devices is the performance of inspection audits of the quality system. Any company that manufactures or processes an FDA-regulated product may be audited every two years, although the actual interval between inspections is often longer. Preliminary audits are triggered by regulatory submissions and/or applications to use a device in humans. Following regulatory approval or clearance, most inspections are routine, although the FDA also conducts audits for cause as problems come to light.

To economize resources and maximize the value of its audits, the FDA has developed the Quality Systems Inspection Technique (**QSIT**). This process is based on a "top-down" approach to inspections, placing executive management at the core of the quality system. Rather than starting an audit by looking at any specific quality subsystem or potential non-conformance problems ("bottom up"), QSIT begins with an assessment of the company's total system. Then, QSIT sets forth specific guidelines and processes for the evaluation of the four primary subsystems within the company's overall quality system described earlier in this chapter (management controls, design controls, P&PC, and CAPA).[35]

The tone of a quality audit is often set by the company being audited, not the auditor. The FDA inspector has a job to serve the public by ensuring that companies are compliant with QSR. In turn, companies have the obligation to demonstrate to the FDA that they are, in fact, compliant with these regulations. This is largely determined through documented evidence, as well as some facilities inspections. The duration of quality audits depends on the nature and cause of audit, as well as the size of the firm, with brief audits lasting one to two days and lengthy, complex audits requiring one to two months. Auditors typically spend 80 percent of their time during an audit performing records review (looking for proof that the company's quality system requirements are consistently followed). The remaining 20 percent of the time is spent conducting interviews and observations of processes.

When contacting the company for a QSIT inspection, the auditor will generally request a copy of the firm's quality policy, as well as high-level quality system procedures, management review procedures, quality manual, quality plan, or other equivalent documents. (Note that QSIT inspections techniques only apply to preannounced audits, but not all audits are preannounced.) The company is *not* required to supply this documentation. However, the audit will typically progress more quickly if this information is provided in advance and the company assumes a cooperative posture with the FDA. All documentation is returned at the time of the inspection.[36] Within a company that has a well-designed quality system, compiling this documentation should be an efficient, simple, and straightforward process.

Each FDA quality inspection is designed to begin and end with an evaluation of the management control system. Upon the initiation of an audit, the first thing inspectors will likely do is to meet with the executive responsible for quality within the company to get an overview of the quality system and to verify that appropriate management controls are in place. Typically, the inspectors will then select a single design project to evaluate through the end-to-end design control process. At times, the inspection assignment will direct the inspectors to a particular design project (i.e., as part of a "for cause" inspection – an audit triggered by some evidence suggesting non-compliance in a particular area). Otherwise, they will select a project that provides the best challenge to the firm's design controls system. This project will be used to evaluate the process, methods, and procedures that the firm has established to implement the requirements for design controls outlined in Table 5.5.1.[37]

Based on a discussion with management, inspectors will also choose a manufacturing process to evaluate that seems to be a likely candidate for production deviations. They will then review the specific procedure(s) for the chosen manufacturing process, as well as the methods for controlling and monitoring the process. Their objective is to verify that the process is well controlled and actively monitored.

The agency will also seek to verify that CAPA system procedure(s) have been defined and documented, appropriate sources of product and quality problems have been

identified, and data from these sources are analyzed to identify existing product and quality problems that may require corrective action. The inspection also seeks to confirm that the defined CAPA processes are followed when problems arise.[38]

During the audit, employees may be coached to answer only the questions asked by the inspector and not to offer up additional information. It is the auditor's responsibility to follow whatever leads it encounters regarding potential quality problems. An audit potentially can be prolonged by an unraveling of issues, and no company wants the FDA on its premises longer than necessary since audits are time-consuming and disruptive to the organization. They can also be intimidating to employees. However, a company that has implemented effective, comprehensive quality systems from its inception should have nothing to hide from the FDA. Similarly, a well-designed quality system should be easily and successfully audited. In no case should the company try to hide anything. It is far worse to be caught trying to conceal information (which is illegal) than it is to receive a finding that will help improve the system.

The second case example illustrates effective practices for managing an FDA quality inspection to achieve a positive end result. For more information about compliance actions and enforcement, including responding to audit results and important information about product recalls, see online Appendix 5.5.4.

FROM THE FIELD DIASONICS AND OEC MEDICAL SYSTEMS

Strengthening quality systems to improve business performance

Allan May joined Diasonics, as its senior vice president of business development, just as the company was embarking on a major turnaround. According to May, "Diasonics was the company that introduced real-time imaging to the medical device markets. Until then, if you wanted an image, you had to go to the radiography suite or another location where the images could be taken. The idea that you could look at a dynamic image during surgery didn't exist." By introducing innovative new imaging technologies, such as ultrasound and fluoroscopy, the company grew rapidly from its inception in 1978 to its highly successful initial public offering (**IPO**) in 1983. However, shortly thereafter, it faced a series of performance problems that necessitated the formation of a turnaround team.

When May joined the company, Diasonics was a conglomerate of four or five businesses, each with its own technology. One of the issues facing the turnaround team, he said, "was how to harvest more value out of these various pieces to increase returns to shareholders." May continued, "OEC Medical Systems was the crown jewel of this corporate group. The trouble was that Wall Street wasn't giving Diasonics credit for what we felt was the real value of OEC." OEC specialized in making fluoroscopy C-arms – mobile machines that could be moved into the surgical or special procedures suite for real-time imaging during various laparoscopic or endoscopic procedures (see Figure 5.5.4). "That market was very small in the 1970s," he commented, "but it exploded in the 1980s with the proliferation of minimally-invasive procedures."

The OEC product initially had a reputation for being costly and over-engineered with "needless features." "Fluoroscopy was a Volkswagen market, and OEC was building Mercedes," recalled May. "But as these procedures caught on and the market really started to take off, you had longer procedures, like minimally-invasive cardiac or neurology procedures, that placed new demands on the equipment. Those over-engineered features became critical, and OEC's competitors couldn't duplicate them because they didn't have the more advanced architecture. The new requirements couldn't just be added on as a feature set," he explained.

FIGURE 5.5.4
An OEC® C-Arm, similar to the products produced by OEC when it was part of Diasonics. OEC was later acquired by GE (courtesy of Acclarent, Inc.).

This allowed OEC to capture approximately 70 percent market share against competitors such as GE, Siemens, Philips, and Toshiba. "So here was this little dinky company in Salt Lake City, Utah," said May, "competing globally against these major corporations. Every few years, they would appoint vice presidents to study and crush this little start-up, but they never broke it. And we held that market share despite their increasing attempts."

In the midst of OEC's unprecedented growth, the company experienced an unannounced FDA audit. "This was right about that time that a couple of high-profile problems hit the FDA and our sense was that the division offices had been told to step up their inspections," May noted. "The FDA inspector came into the OEC plant in Salt Lake City, inspected it, and said that, in his opinion, it looked like the plant might have to be shut down." During this same period, the US plants of several major competitors had been shut down or their imports restricted.

The FDA's report addressed a series of issues, but primarily focused on complaint handling and the company's corrective actions and procedures. "To be fair," May said, "the regulations were really just being put into place when this happened.[39] But the concept of an effective complaint handling system didn't exist at OEC. Basically, someone would complain and one of the engineers would look into the problem and try to fix it. There was no senior level involvement or review, few defined processes, and no comprehensive complaint handling system tied to corrective action loops. Most problems were considered 'unable to duplicate or verify' and so little was done to redesign the product or change production processes to prevent the problem from recurring. I also don't think we had manufacturing process instructions on the floor. We were making the best product in the world – number one in its class. Everybody knew how to do their specific job. But it didn't occur to people that, gee, if someone got hit by a bus, no one else would know how to do what they were doing."

News of the inspection results were received by employees in the plant with what May described as "outrage" and the perception of "bureaucratic make-work." "Many employees were in just a complete state of denial, or didn't understand what this was all about. So, our first challenge was to get to the core of the problem. We went to the FDA immediately and got involved with the agency. We wanted to make it very clear to them that we were not going to be confrontational. We intended to be completely cooperative in understanding and fixing our problems and would be inclusive of them in our discussions about what to change. Then, we had to go back to the plant and really patiently explain from the top of the organization down through every layer why we needed to do things differently and what those things were," he said. "The key was getting people's attention and focusing them on understanding the real problem. We couldn't just let them slough it off like, 'Okay, we have to fill out a bunch of paperwork, but we're right and the FDA is wrong.'"

As May and team began to investigate the FDA's concerns within the plant, it became increasingly clear that these quality issues were directly linked to the

company's business performance. "Our service calls on the equipment had crept up from one or two a year to 10 to 12 per year," May recalled. "Our customers were seeing our technicians more than our sales people. We recognized that there were some problems with the equipment but, since it had such a tailwind of being the dominant product in this particular sector, we failed to appreciate the extent to which customers were putting up with it. But they were really starting to grumble. On top of that, our margins were decreasing because it was costing us so much to service the equipment."

Over the next 18 months, OEC launched an expansive root-cause analysis to identify all potential sources of product failures. Based on the outcome, the company completely revamped its quality systems, implementing comprehensive new processes and thorough documentation. They reorganized their entire manufacturing facility and changed many of their process and systems, as well. When the FDA reinspected the plant, it was found to be in full compliance. Moreover, said May, "We ended up getting those service calls back down to one or two a year and driving down our costs. We also dramatically improved the quality of the product, our reputation with customers, and the satisfaction of our customers."

When asked for his advice to innovators implementing quality systems, May commented, "You have to completely forget the idea that this is about paperwork. You can't hire a consultant to draft a bunch of documents that you put in a drawer somewhere. Your quality system is totally about the mentality you use to design and manufacture your product. And I believe a hundred percent that if you do what the quality regulations say, and really understand them, you will design and manufacture a better product with fewer problems that will lead to improved financial performance."

Reflecting further, May added, "Quality should be understood at the top of the organization. When we were going through this, we had a slew of meetings where everyone, right up the board of directors, had to be involved. The higher you get in the organization, the more people may gripe about this sort of thing. But senior executives can't just delegate this and expect it to be done right. Upper management has got to stay personally involved. The phrase we repeated most often was, 'Quality is a journey, not a destination.'"

Overall, May stressed, the strength of a company's quality systems can either help or hinder the attainment of its strategic goals. In this particular case, Diasonics' senior management team had developed a corporate strategy to spin out OEC (along with two other operating companies) to help "unlock" additional value in the market. However, until OEC's quality issues were addressed and its risk of being shut down by the FDA was eliminated, "We had to keep OEC underneath the protection of the corporate shell," May recalled. This delayed Diasonics' ability to implement its significant corporate restructuring plans. However, sometime later, after OEC was found to be in full compliance with the FDA's requirements, Diasonics did, in fact, spin out OEC onto the public markets. Not long after, OEC was able to execute one of the larger corporate exits in the medical device field.

Online Resources

Visit www.ebiodesign.org/5.5 for more content, including:

- Activities and links for "Getting Started"
  - Identify quality needs and decide on an approach
  - Hire a quality professional
  - Engage executive and cross-functional management and define quality policies
  - Build a "shell" of a quality system and develop elements as the product progresses
  - Assign cross-functional champions to monitor and maintain quality system
  - Anticipate and prepare for audits
- Videos on quality management
- Appendices that provide additional information about:
  - Medical device reporting
  - ISO 13485
  - 21 CFR 820
  - Compliance actions and enforcement

CREDITS

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29 Ibid.

30 "ISO 13485," ISOConsultants.com, http://www.iso-consultants.com/iso_13485.htm (February 26, 2014).

31 "Management System Certification for Medical Device Manufacturers," www.sriregistrar.com, http://www.sriregistrar.com/A55AEB/sricorporateweb.nsf/layoutC/078690568D3D722586257299004F9FC4?Opendocument&key=Standards (February 3, 2014).

32 For a list of exempt devices, see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/315.cfm (February 3, 2014).

33 All quotations are from interviews conducted by the authors, unless otherwise cited. Reprinted with permission.

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36 "Guide to Inspections of Quality Systems," op. cit.

37 Ibid.

38 Ibid.

39 Recall that the FDA's good manufacturing practices for medical devices were not issued until two years after the Medical Device Amendments of 1976 were enacted. It then took quite some time for these guidelines to have an effect on the processes used to produce products that were already in the market.