Understanding Barriers to Medical Device Quality

Oct. 31, 2011

Contents

EXECUTIVE SUMMARY

This report is the result of an initiative launched by the United States Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), as part of an effort to assess and understand gaps in medical device quality. The work focuses on marketed product quality assurance, rather than pre-market activities. Its purpose is to provide a perspective on the state of medical device quality, as well as the challenges and opportunities for improvement.

The work was conducted with input from several sources: interviews with internal and external quality experts; a set of blinded industry interviews, a scan of databases, relevant articles, and conferences; and an outside press search.

These inputs uncovered several key facts about marketed medical devices as well as potential catalysts for quality improvement.

1. The **medical device industry has enjoyed tremendous growth** in both revenues and the technical complexity of the products that it produces over the past 10-20 years.
2. **Serious adverse event reports related to medical device use have outpaced industry growth** by 8% per annum since 2001.[1]
3. **Quality risk is not evenly distributed** across the industry. This reflects the heterogeneity and complexity of the devices, manufacturers, and use environments. Cardiovascular, in vitro diagnostic (IVD), and general hospital/surgical devices account for nearly 60% of adverse events reports. Only **20 of the 1189 active product codes account for 65% of all serious adverse events reports** between 2005 and 2009.
4. An analysis of root cause data reveals that **failures in product design and manufacturing process control caused more than half of all product recalls**. The **root causes of quality issues are tied closely to device type**. Therapeutic area was not as strong a predictor for recall root cause.
5. There are **seven major opportunities for improving quality within the industry**:

    Enhanced operating systems

    a. **Design and reliability engineering –** specifically, validation of actual product use, design-for-reliability and manufacturability, and software robustness.

    b. **Robust postproduction monitoring and feedback** into design and manufacturing that goes beyond base compliance requirements.

[1] For purposes of this report, the term “serious adverse events” encompasses death, life-threatening events, hospitalization, disability, congenital anomalies, and/or required interventions, and disabilities. This term should not be confused with the regulatory definition of “serious injury,” which is defined under the medical device reporting regulations (21 CFR Part 803.3).

c. **Supplier management processes**, particularly in material and process change controls.

Enhanced management infrastructure

d. **Quality metrics and measurement systems** that go beyond regulatory compliance measures.

e. **Quality organization** that integrates cross-functionally throughout the organization, rather than solely focused on compliance.

f. **Performance management,** where those in key roles associated with quality outcomes, like design engineers, are measured and incentivized around quality performance.

Enhanced mindsets and behaviors

g. **Quality culture** can be improved where companies have experienced severe quality-related issues.

6. Broadly, companies are experiencing three key challenges related to improving quality:

    a. **Low quality transparency,** driven by a lack of information for consumers and decision-makers around comparative quality (*i.e.*, quality differences among competitor products), time to market competition, and cost pressures, limits significant quality upgrades. **However, the economics of quality may be changing** as risks and costs of poor quality increase and transparency into comparative quality increases.

    b. **Increasing complexity of medical devices and usage environments** is straining the current quality system infrastructure. Companies report that they have not systematically upgraded their quality infrastructure due to the unclear economics and concerns about regulation.

    c. Companies perceive that **the regulatory framework is misaligned with assurance of quality outcomes,** in that compliance with regulations does not ensure quality, and that current intervention practices may de-incentivize improved quality.

7. Interviews and analysis also **identified several steps the FDA can take to accelerate momentum around adoption of quality best practices**. These steps should address seven key themes:

    a. **Focus regulatory efforts** to address industry quality gaps

    b. **Enhance visibility of comparative quality** to harness market forces to drive quality

    c. **Optimize consistency and clarity of Agency** expectations and requirements

d. **Learn from practices of regulators** of similar high-tech and complex industries

e. **Bolster data collection and analysis** to maximize potential impact

f. **Leverage wealth of Agency data and analysis to continuously refine FDA's compliance initiatives**

g. Increase level of engagement and **collaboration with industry** around enhancing product quality

INTRODUCTION

The United States Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), is charged with regulating firms that manufacture, repackage, re-label, import, and distribute medical devices sold in the United States. Compliance activities occur simultaneously within several CDRH offices, with the Office of Compliance taking the lead on medical device compliance.

The Quality System Regulation, Title 21, Code of Federal Regulations (CFR), Part 820, issued on October 7, 1996, delineates current good manufacturing practice for medical devices. This regulation has served as the guideline for the Agency as well as manufacturers on quality systems requirements such as design controls, document controls, and production and process controls, among other topics.

In recent years, the number and complexity of medical devices has grown rapidly. The medical device industry is a quickly evolving, innovative space with both small and established players competing to bring new, life-enhancing innovations to market. The increased complexity of new innovations has been driven by factors including the advent of combination drug-device products and the evolution of highly automated and wireless technology in medical devices. In parallel, the medical device supply chain has become increasingly cost competitive, globalized, and tiered, with companies routinely dealing with multiple layers of thousands of raw material, component, and sub-component suppliers, all of whom potentially impact final product quality and performance.

The assurance of continued medical device quality in this context requires a thoughtful and adaptive approach. While medical device flaws may vary by device, some sources of error are pervasive throughout the field. Identifying and addressing systemic barriers to medical device quality may yield improvements in medical device quality on a large scale. CDRH is tasked with overseeing an ever-increasing number of firms and devices, relying on finite resources; focused efforts to transform systemic drivers are an efficient and powerful way to drive quality.

This report is the result of a detailed look at the current state of medical device quality, highlighting the challenges to achieving optimal quality. The work focused on marketed product quality assurance rather than pre-market activities. The report draws on a variety of sources and explores challenges that exist within the medical device industry as well as challenges intrinsic to FDA.

METHODOLOGY

This report was generated with inputs from three main sources.

- **Analysis of existing FDA databases**. The team performed analysis of adverse event information from FDA's Manufacturer and User Facility Device Experience (MAUDE) database (approximately 1.2 million records from 1998 through 2009). Data were cleaned to ensure that only unique medical device adverse events were tallied in the analysis. As many entries had more than one patient outcome, for purposes of this report, a hierarchy was assigned to determine a single outcome per entry: 1) Death; 2) Life threatening; 3) Disability; 4) Hospitalization; 5) Congenital anomaly; 6) Required intervention; 7) Other. Death, life threatening, disability, and hospitalization were identified as a subset of "serious" adverse events.

  The team also analyzed recall information from the Recalls-CDRH database (RECS) and the recall enterprise system-ORA database (RES). Data were available from 2003 to 2009 and consisted of 10,980 z-codes or model recalls. Model recalls were grouped and counted by RECS case code; z-codes that lacked a RECS case number were grouped according to RES case number. Root cause information was taken from root causes assigned in RECS. Product codes were assigned based on FDA product codes.

- **Interviews with thought leaders.** In consultation with FDA staff, the team developed interview guides and identified interviewees. The team conducted interviews with FDA officers, industry leaders, and internal experts. Roughly 50% of the Agency interviews and 25% of the industry interviews were conducted face-to-face. All interviewees, both from the Agency and industry, were assured that their names and, where applicable, the names of the companies they represented, would be kept strictly confidential.

  a. **FDA leadership.** From the Agency, the team spoke with 22 leaders from various offices within the CDRH as well as from the Office of Regulatory Affairs (ORA) and the Center for Drug Evaluation and Research (CDER).

  b. **Industry leaders.** The team spoke with 23 executives across a broad cross section of companies in the medical device industry. These leaders represent a cross-functional view of areas impacting medical device quality, including heads of quality, regulatory, R&D, manufacturing, supply chain, business units and CEOs. The companies consisted of both public and private enterprises and ranged in size from several thousand employees and billions of dollars in revenue to two hundred employees with revenues of approximately one hundred million dollars. These companies covered a variety of therapeutic areas and product segments: orthopedic

implantables, cardiovascular implantables, diabetes care equipment, diagnostic imaging, hospital and surgical supplies, and healthcare informatics.

The interviews with the identified set of thought leaders covered three broad areas: (1) The relationship between quality and compliance in the medical device space; (2) Major quality risks/gaps in the industry value chain; (3) Suggestions to address these gaps, both within the industry and the Agency (see Exhibit 1).

Exhibit 1: Outline of Interview Guide

Context	FDA CDRH has undertaken a program to perform an in-depth diagnostic review of the challenges to adopting quality best practices that industry faces and development of detailed strategies and action plans to help overcome these barriers. We define quality best practices as best practices to assure patient safety
Approach	Industry will be engaged through a set of interviews across Quality, Operations and R&D executives. In parallel, we will be conducting a set of interviews within the FDA to understand their thoughts and perspectives from the regulator's standpoint
Discussion overview	Topics that we would like to cover today: 1. Understanding the relationship between Quality and Compliance 2. Areas of focus, risk and opportunity within Quality Landscape (QL) • What are the most important pieces of the QL? • What are the best practices? • How are resources deployed against elements of the QL? • What are the key issues and risks seen across the QL? • What are the root causes of these key issues and risks? • How does or could the FDA enable and/or encourage best quality practices? 3. Drivers and root causes of gaps in industry quality & compliance approaches 4. Implications for driving quality improvements

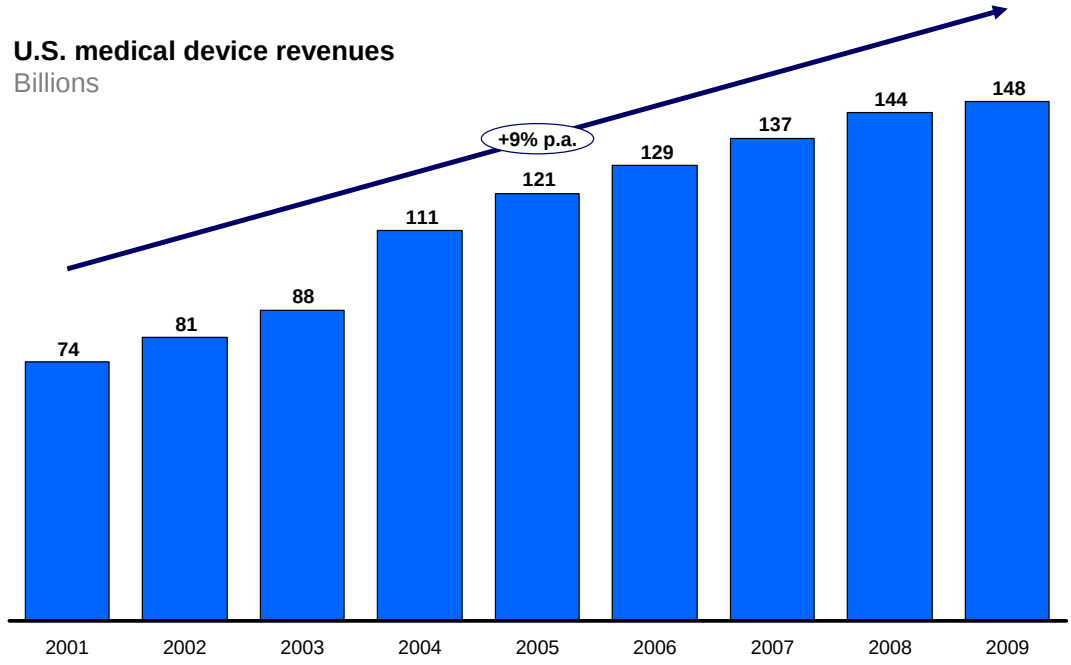
¶ **Data mining within additional resources.** The team performed an extensive search of databases, including case study libraries, benchmarking efforts, articles, survey databases, and conference presentations. The team additionally conducted several interviews with global leading industry experts in strategy, research and development (R&D), operations, quality, and product development across medical device and other industries, as well as experts on the FDA and on other agencies that regulate high-risk industries, such as nuclear power and airlines. Experts shared their knowledge and perspectives from many years of experience dealing with key decision-makers in industry.

MACRO TRENDS IN THE MEDICAL DEVICE INDUSTRY

In the past ten years, the size of the U.S. medical device industry has nearly doubled. In 2001, annual revenues were approximately 73.6 billion; by 2009, that figure had reached 147.6 billion, for a compound annual growth rate of 9% (see Exhibit 2). While part of this growth was due to increasing uptake of medical devices already in use, a large portion was driven by innovation. Between 2001 and 2009, nearly 30,000 devices were cleared via the 510(k) premarket notification pathway and more than 303 new devices received original premarket approval (PMA). Of note, supplements to PMAs grew by an average of 11% per annum between 2001 and 2009, while 510(k) clearances dropped by 2%.[2] (see Exhibit 3 and 4)

Along with this growth in the number of cleared or approved medical devices, devices have grown increasingly complex and sophisticated. For example, an insulin pump in 2001 could be programmed to deliver varying amounts of insulin throughout the day. Now, a more compact pump communicates via radio frequency to a continuous glucose monitor and suggests insulin dosing using an algorithm. Surgical tools now include endoscopes and robots in addition to scalpels. Modern stents and gauzes deliver drug therapy while providing mechanical support.

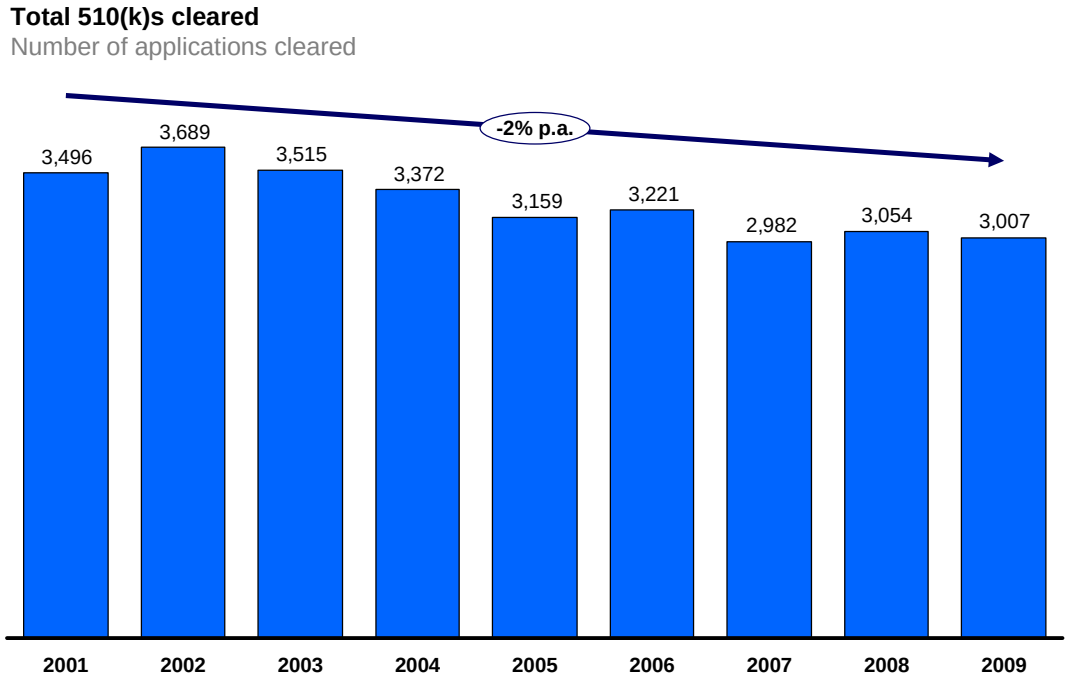
Exhibit 2: U.S. medical device revenues, 2001-2009



[2] 510(k) clearance is reserved for devices demonstrated to be substantially equivalent to a device legally marketed prior to May 28, 1976, that are not subject to a PMA. Premarket approval is the most stringent review process and is required for most Class III devices (high-risk devices that pose significant risk of illness or injury) and devices found not substantially equivalent to a class I or II predicate (i.e., novel devices).

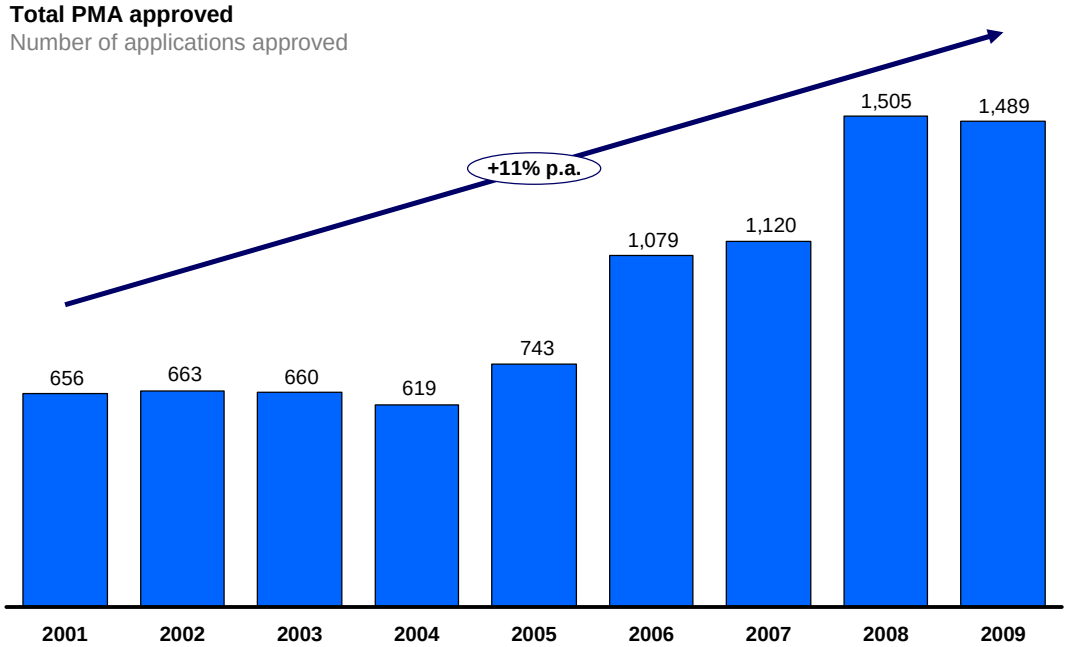
Source: HRI MD&D Reports

Exhibit 3: 510(k) approvals, 2001-2009



Source: Public database available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm; accessed November 2010

Exhibit 4: PMA approvals including supplements, 2001-2009



Source: Public database available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm; accessed November 2010

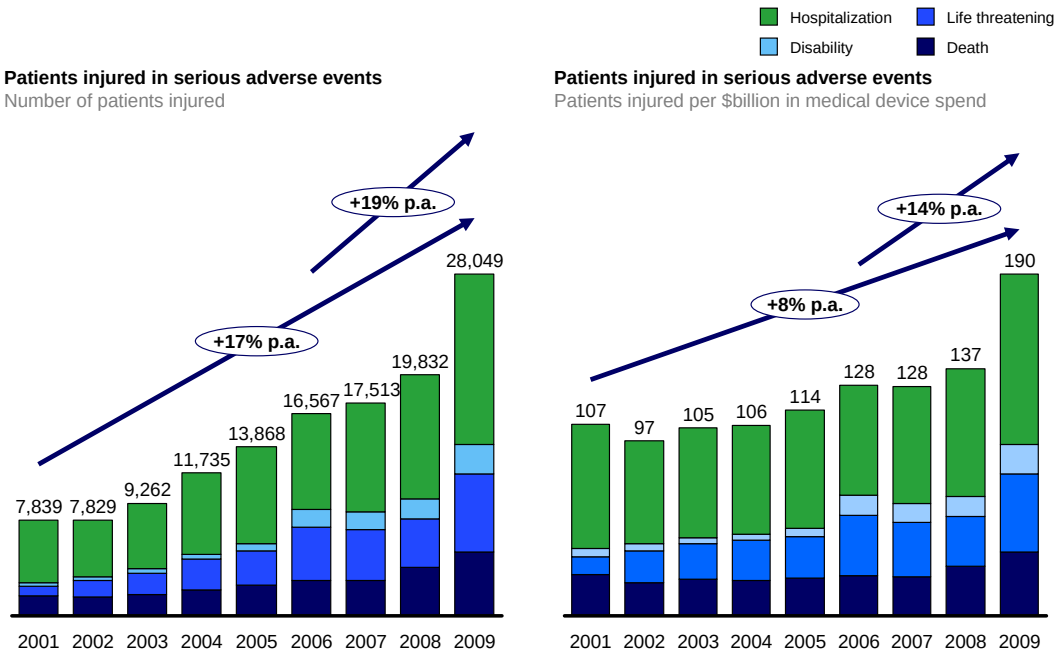
TRENDS IN MEDICAL DEVICE ADVERSE EVENT REPORTS AND RECALLS

FDA has long recognized that a subset of adverse event reports and recalls may reflect quality manufacturing system concerns.

The number of adverse event reports has increased dramatically and outpaced overall industry growth by a wide margin. Recalls have kept pace with industry growth. Likewise, while Class III devices have grown as a share of overall adverse events, they account for a decreasing proportion of total recalls.

¶ **The volume of adverse event reporting is on the rise.** Between 2001 and 2009, adverse events reported to the MAUDE database increased an average of 15% per year, from approximately 57,000 reported events in 2001 to more than 207,000 reported events in 2009.[3] From 2005 to 2009, the rate of reporting increased significantly to 22% per year. The subset of "serious" adverse events—with outcomes classified as death, life-threatening, disability, or hospitalization—rose 17% during that time, from 8,000 in 2001 to 28,000 in 2009 (see Exhibit 5).

Exhibit 5: Total serious adverse event reports adjusted for med device revenues



* Includes death, life threatening events, hospitalization and disability
Source: Manufacturer and user facilities device experimental (MAUDE) database

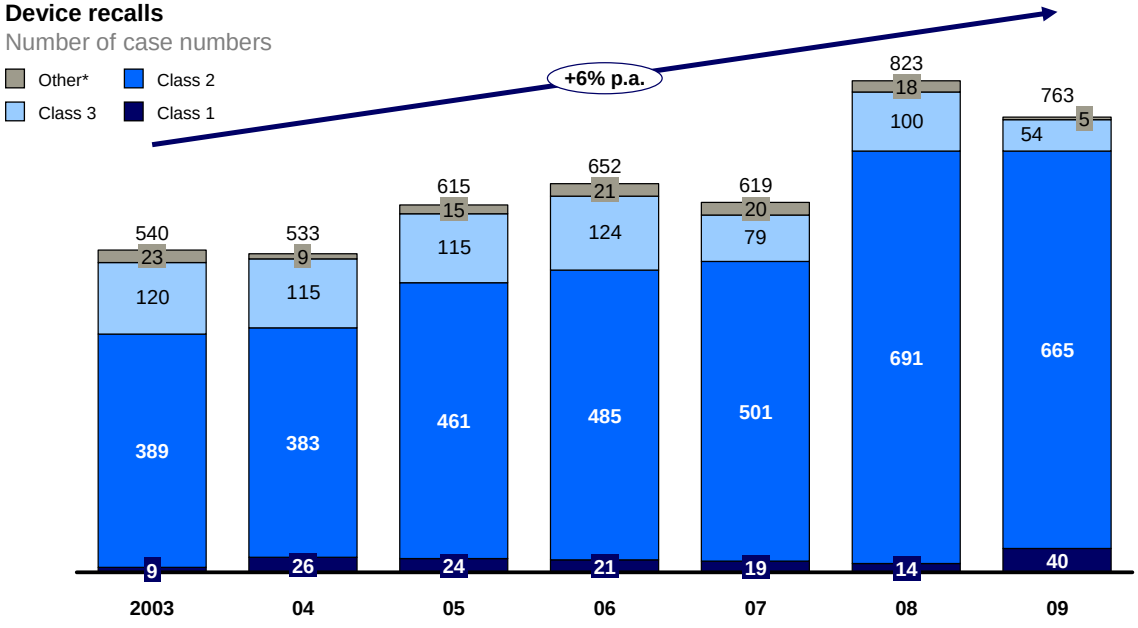
[3] Adverse event analysis includes data from the MAUDE database, but excludes data from special exemption summary reporting, such as the Alternative Summary Reporting (ASR) database, the Postmarket Spreadsheet Reports, and Remedial Action Exemptions. Manufacturers may provide batch summary reports to these databases only in certain circumstances; these databases do not include the level of detail included in the primary MAUDE database. If the ASR data had been included here, the combined annual growth rate (CAGR) would have been 24% between 2001 and 2009. Note: "p.a." means per annum, i.e., per year

U.S. medical device revenues nearly doubled during this period. Even controlling for this growth, however, serious adverse event reports grew at a rate of 8% per year, with a sharper increase of 14% per year since 2005 (see Exhibit 5).

Several factors may contribute to the growth in the volume of adverse event reports. These include greater outreach by FDA emphasizing reporting requirements, along with greater manufacturer sensitivity to reporting requirements following notable recalls. Some of this growth may also be due to growth in the number of medical devices in use.

¶ **Recalls have risen slower than adverse events, but have matched industry growth.** In 2003, there were 540 recalls; by 2009, this number increased to 763 for a rate of annual increase of 6% (see Exhibit 6). Like adverse event reports, some of this growth may be due to greater FDA emphasis on recall reporting requirements.

Exhibit 6: Total recalls 2003-2009

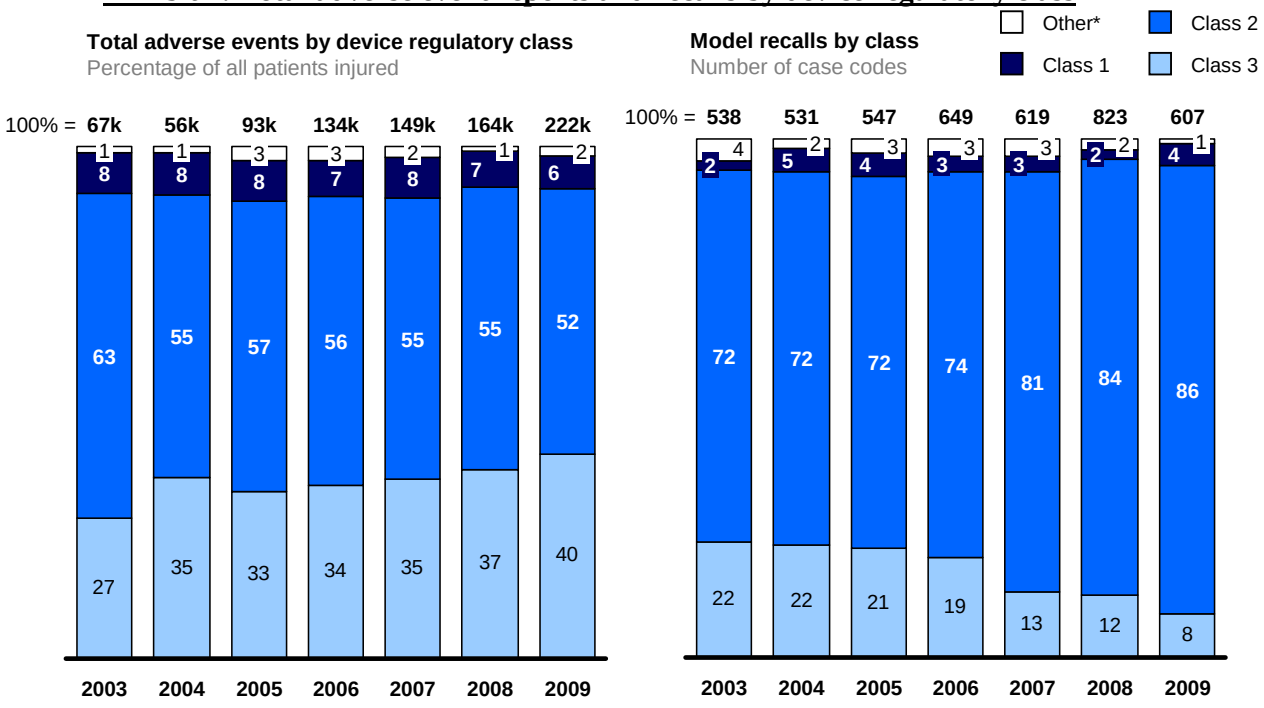


* Other: "Market Withdrawal" or "Safety Alert"

Source: Data from RECS database

¶ **In general, critical, life-sustaining devices are responsible for a growing share of adverse event reports, but not of recalls.** In 2003, 27% of adverse event reports were associated with Class III devices; by 2009, this figure had grown to 40%, even as adverse events overall increased. Conversely, recalls of Class III devices have shrunk from 17% of total recalls in 2003 to 7% in 2009 (see Exhibit 7).

Exhibit 7: Total adverse event reports and recalls by device regulatory class



* Other: Adverse Events: 3 (513(f)(1)), “Not Classified", or “Unclassified", or missing information

* Other: “Market Withdrawal,” “Non-Concur”, “Safety Alert,” or “Stock Recovery”

Source: Data from MAUDE database, data from RECS database

HOT SPOTS FOR PATIENT RISK

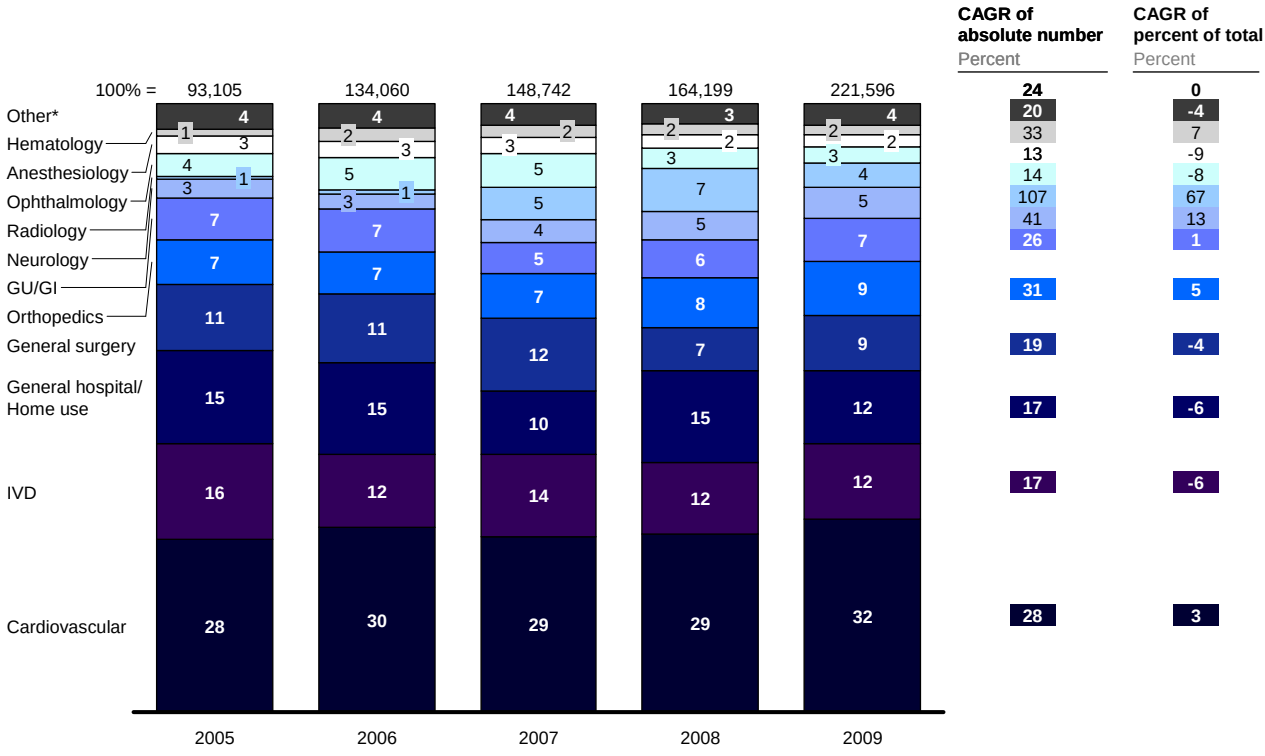
The risk of adverse events is not evenly distributed across the industry. Certain therapeutic areas and product segments comprise a larger share of total adverse events; others have attributable adverse events growing at a faster rate than average. Following are relevant findings.

¶ **Cardiovascular, IVD, and general hospital/surgical devices make up most adverse event reports.**

a. **These three therapeutic areas capture the majority of total adverse event reports.** Nearly 60% of adverse event reports are associated with cardiovascular, in vitro diagnostics, or general hospital/surgical devices. The share of adverse event reports attributable to each therapeutic area has remained relatively constant over time, with some exceptions. Cardiovascular devices have increased from 28% of the total to 32% of total; in vitro diagnostics have decreased from 16% of the total to 12% of the total from 2005-2009 (see Exhibit 8).

Exhibit 8: Total adverse event reports by therapeutic area

Percent of total adverse events



Other* <1% total: Unknown, Dental, General Hospital, ENT, OB/GYN
Source: Data from MAUDE database

b. **General hospital/surgical and cardiovascular devices account for more than half of reported serious adverse events.** For the subset of serious adverse event reports, more than half are associated with cardiovascular or general hospital/surgical devices. Cardiovascular devices have increased as a share of total serious adverse event repoorts even faster than for adverse events overall. Cardiovascular device-related adverse event reportss jumped from 31% to 42% of all serious events, while general hospital/surgical and IVD-related serious adverse event reports shrunk as a proportion of the total.

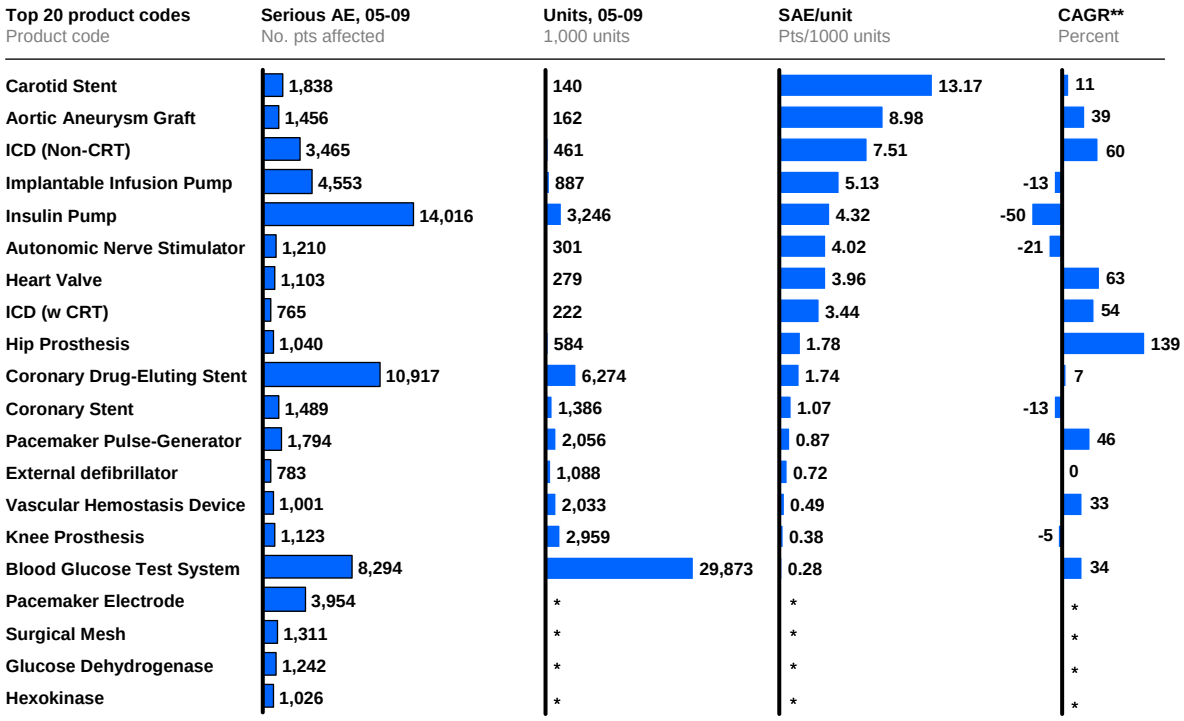
c. **Radiology (diagnostic imaging) and neurology are the areas growing most quickly.** On average, adverse events grew at an annual rate of 24% between 2005 and 2009, but some therapeutic areas grew more quickly. Cardiovascular devices grew at 28%, orthopedics at 31%, neurology at 41%, and radiology at 107% over five years. Adverse event reports related to general hospital/surgical, IVD, hematology, and anesthesiology devices grew more slowly than average.

¶ **Taken together, the top 20 product codes with the most serious adverse event reports between 2005 and 2009 account for 65% of all serious adverse event reports in this time period.** The top 20 product codes were determined by tabulating the number of patients affected by serious adverse events by product code before adjusting for units sold. The 20 product codes most frequently implicated in adverse event reports were then adjusted for number of units sold annually to determine a hierarchy within these top 20 codes.

¶ **Eleven of the 20 product codes with the most adverse events between 2005 and 2009 were related to cardiovascular devices.** Adjusted for number of units sold annually, carotid stents, aortic aneurysm grafts, and implantable cardioverter defibrillators without cardiac resynchronization therapy amassed the highest number of serious adverse event reports between 2005 and 2009. Insulin pumps, coronary drug-eluting stents, and blood glucose test systems had a high number of serious adverse event reports, but adjusted for units sold were lower in the top 20 product codes with the most serious adverse events (see Exhibit 9).

¶ **Recall focus has been elsewhere.** The top 20 most frequently recalled product codes are more heavily focused on radiology devices, which comprise seven of the top 20 product codes (see Exhibit 10). Only one of the product codes in the top 20 most frequently recalled devices pertains to cardiovascular devices.

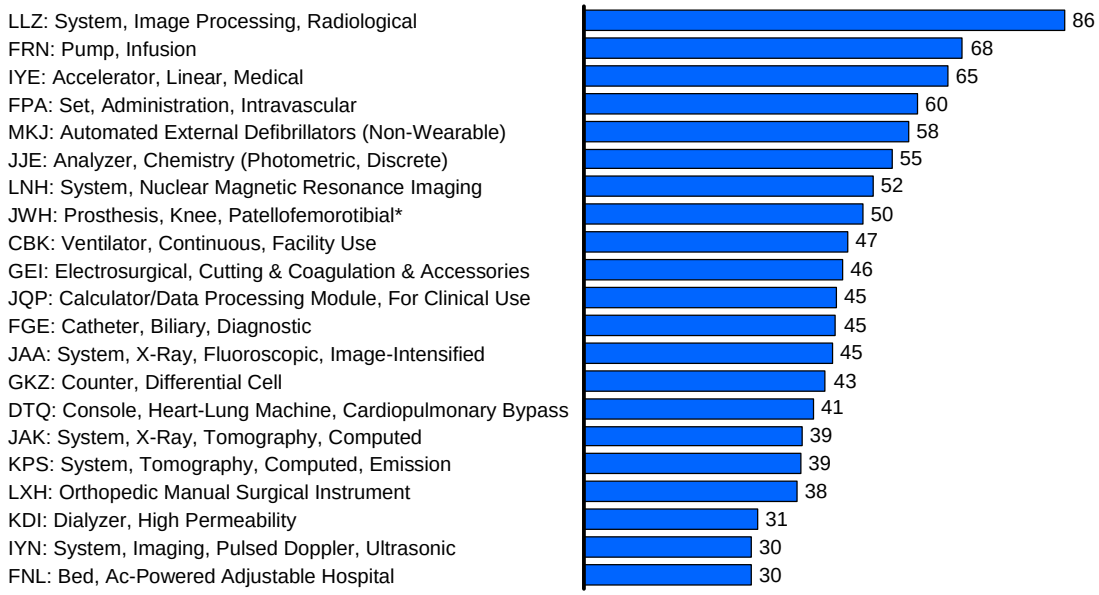
Exhibit 9: Top 20 product codes with most adverse event reports, 2005-2009



* Data not available ** CAGR of SAE/units 2005-2009
Source: Data from MAUDE database

Exhibit 10: Top 20 product codes with most recalls, 2003-2009

Recalls by product code, 2003-2009 (N=5,649 codes available, 1,189 used over time period)
Number of case numbers (N=4,314)



* Semi-constrained, Cemented, Polymer/Metal/Polymer
Source: Data from RECS database

QUALITY RISK EXTENT AND ROOT CAUSE VARY BY DEVICE TYPE

Systematically analyzing and understanding quality risk root causes may help guide FDA on how to focus its industry intervention and guidance efforts. The Agency designates one of 36 root causes for each recall initiated.[4]

Overall, nearly one-third of recalls are due to design flaws and almost another quarter are due to issues with manufacturing. On the product attribute side, almost one-third are due to hardware (see Exhibit 11).

Exhibit 11: Recall case codes by root cause

Model recalls (case numbers), 2003-2009, N=4,391

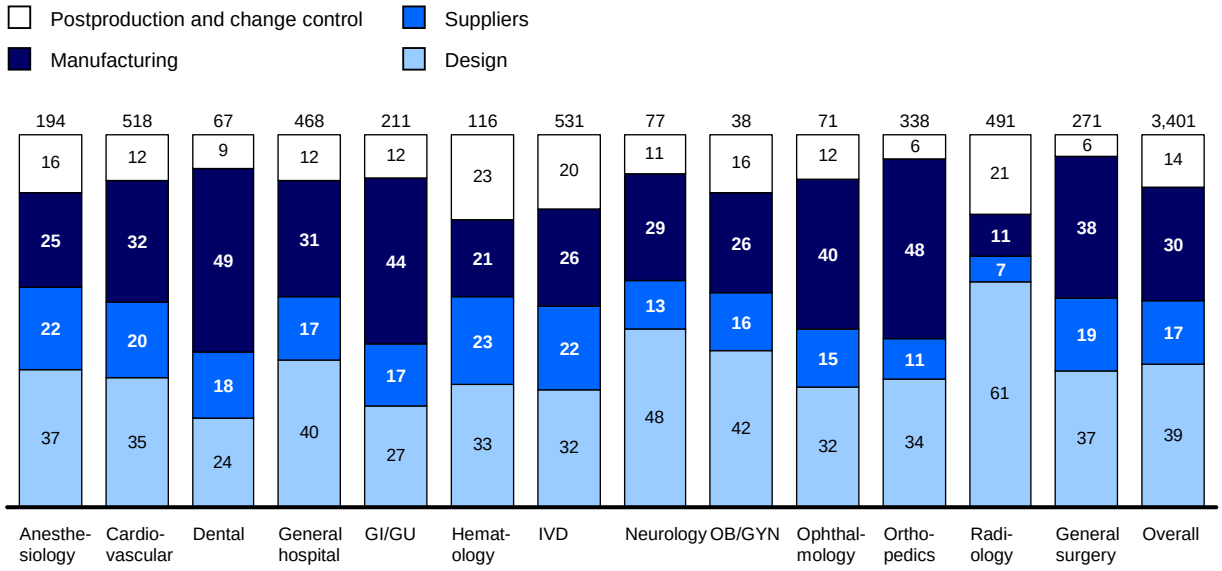
	Design	Suppliers	Manufacturing	Postproduction & change ctrl	Other	Unknown	Total by product attribute
Hardware	15%	12%		2%			29%
Software	8%			7%			15%
Labeling	4%		3%	1%			8%
Packaging	1%		3%				5%
Process	3%	2%	18%	1%			24%
Regulation					1%		1%
Other					9%		9%
Unknown						9%	9%
Total by value stream	31%	14%	24%	12%	10%	9%	100%

Source: Data from RECS database

Not surprisingly, however, this root-cause distribution differs by subset. A high-level breakdown of all recalls into 13 therapeutic areas shows considerable variability, with the share of recalls attributed to design ranging from 24% (dental) to 61% (radiology) (see Exhibit 12).

[4] These 36 root causes can be grouped by where the fault occurs along the value chain step/value stream step: design; suppliers; manufacturing; post-production; and change control. Alternatively, the root causes may be grouped according to which aspect of the product is affected: hardware; software; labeling; packaging; and process control.

Exhibit 12: Recall root causes by value stream and therapeutic area



Source: Data from RECS database

Even within devices in a given therapeutic area, there is great variability in root cause. In contrast, when devices are grouped by device type, root causes are more similar.

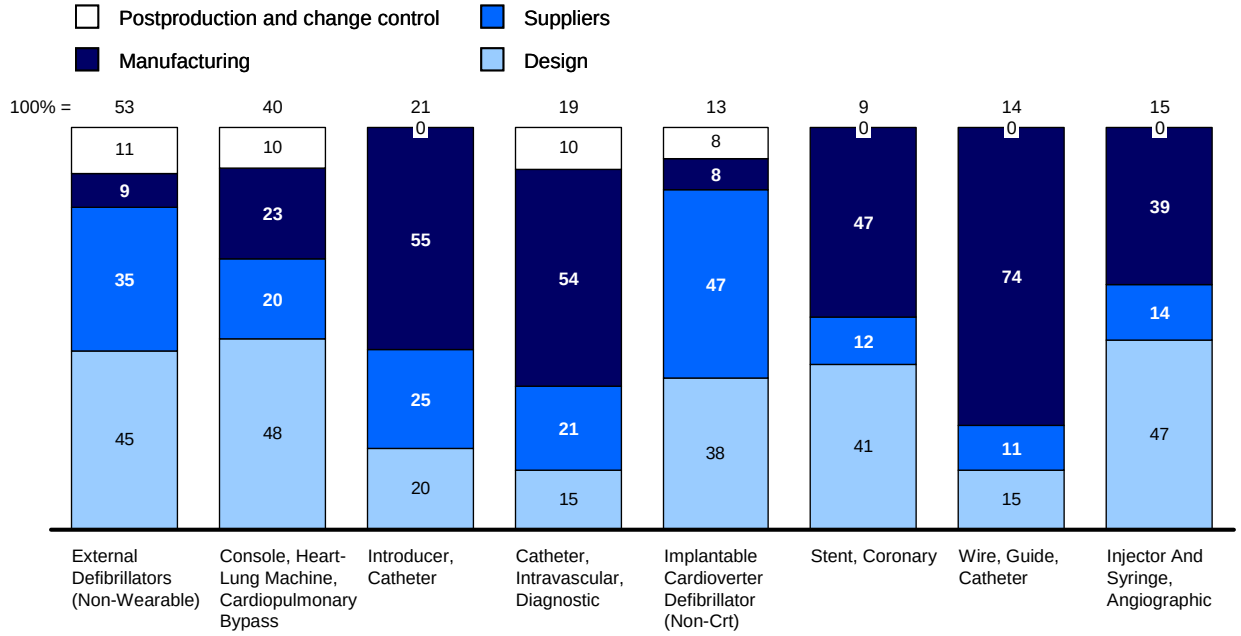
¶ **Recall root causes within therapeutic areas.** Perhaps due to the great variability in device types, there is relatively great heterogeneity in recall root causes both by value stream step and product attribute. The exception to this is radiology, which has a narrower profile of device types and consequently features more similar root causes across devices recalls.

a. **Breakdown by value stream step.** For instance, a closer look at cardiovascular devices reveals significant variability in the root cause of recalls (see Exhibit 13). While 74% of recalls of catheter guide wires are due to a manufacturing problem, only 8% of recalls of implantable cardioverter defibrillators occur for this reason. This type of variability is present in anesthesiology, orthopedics, general hospital devices, in vitro diagnostics, and general surgery. The average variability (as measured by standard deviation) in recall root cause by value stream step was 14%. Devices within radiology have similar root cause profiles, with most devices recalled for design issues.

b. **Breakdown by product attribute.** Similarly, hardware issues account for 68% of recalls of implantable cardioverter defibrillators, but as little as 15% of catheter guide wires (see Exhibit 14). Again,

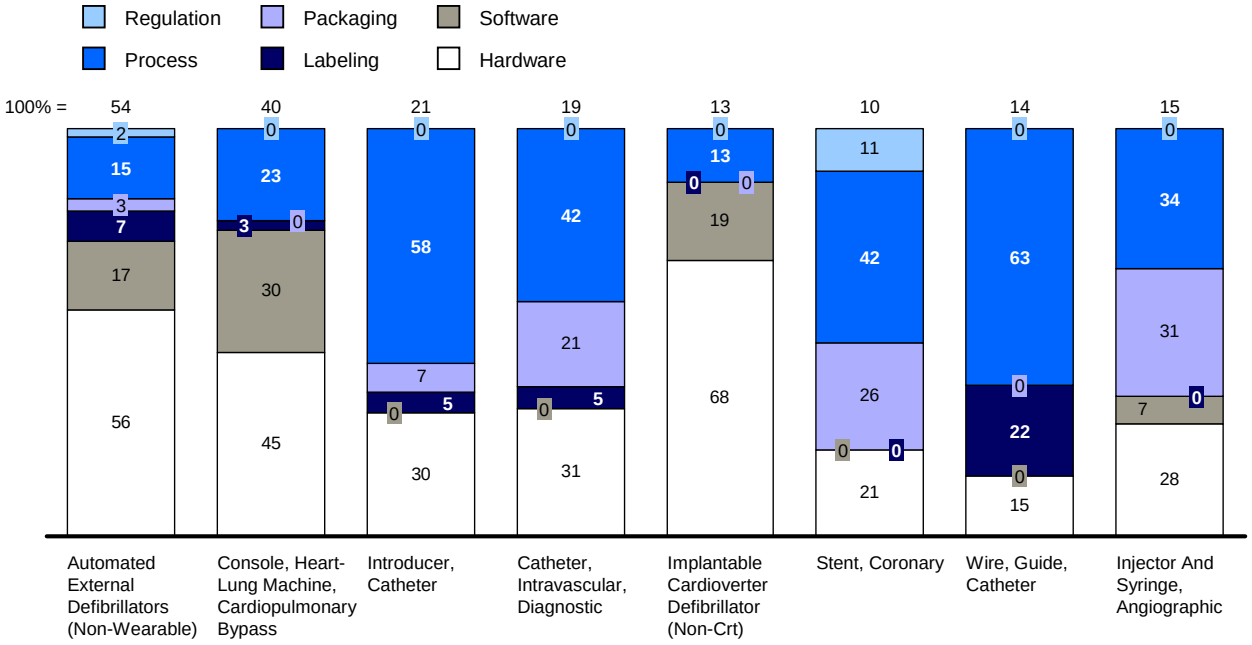
this pattern holds in most therapeutic areas, but in radiology most devices are recalled due to software flaws. The average variability (as measured by standard deviation) in recall root cause by product attribute was 13.4%.

Exhibit 13: CV recalls by value stream



Source: Data from RECS database

Exhibit 14: CV recalls by product attribute



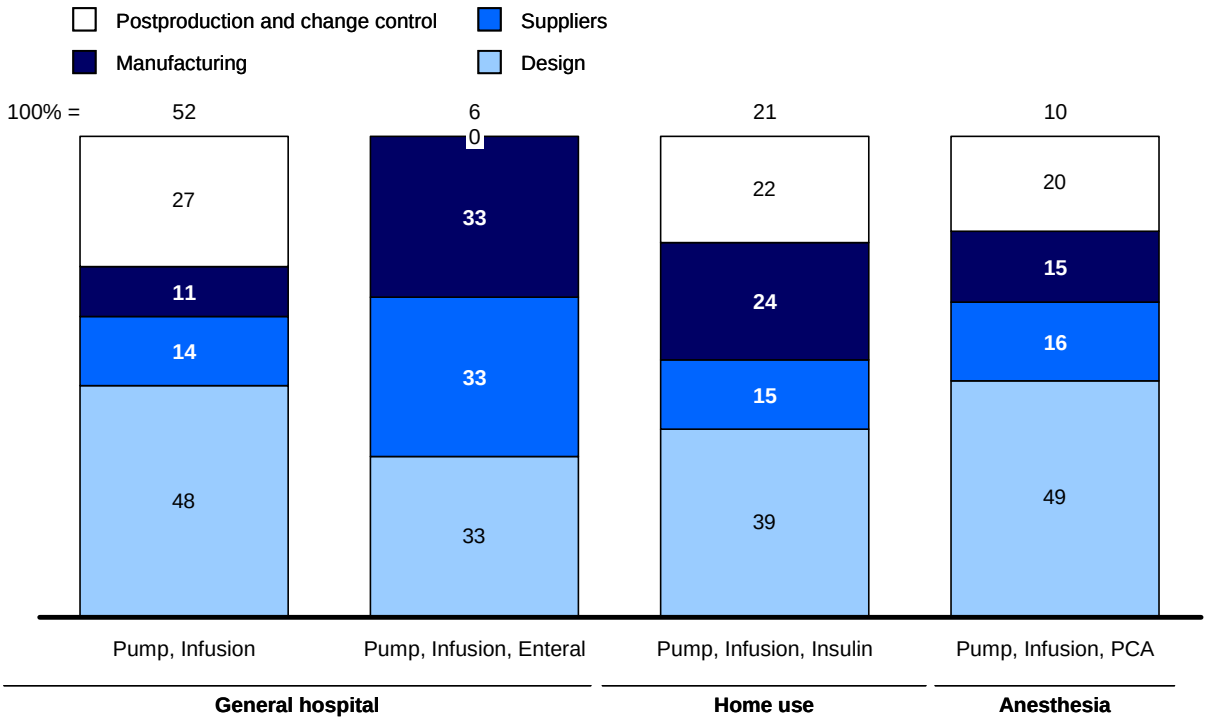
Source: Data from RECS database

¶ **Recall root causes within device types.** In contrast, devices with similar functions seem to have more similar root cause profiles.

a. **Breakdown by value stream step.** For instance, in "catheter" products—including biliary catheters, cardiac catheters, and general hospital catheters—the majority of recalls are due to manufacturing issues. "Pump" products universally suffer most from design issues (see Exhibit 15). The average variability for similar type devices (as measured by standard deviation) in recall root cause by value stream step was 10%.

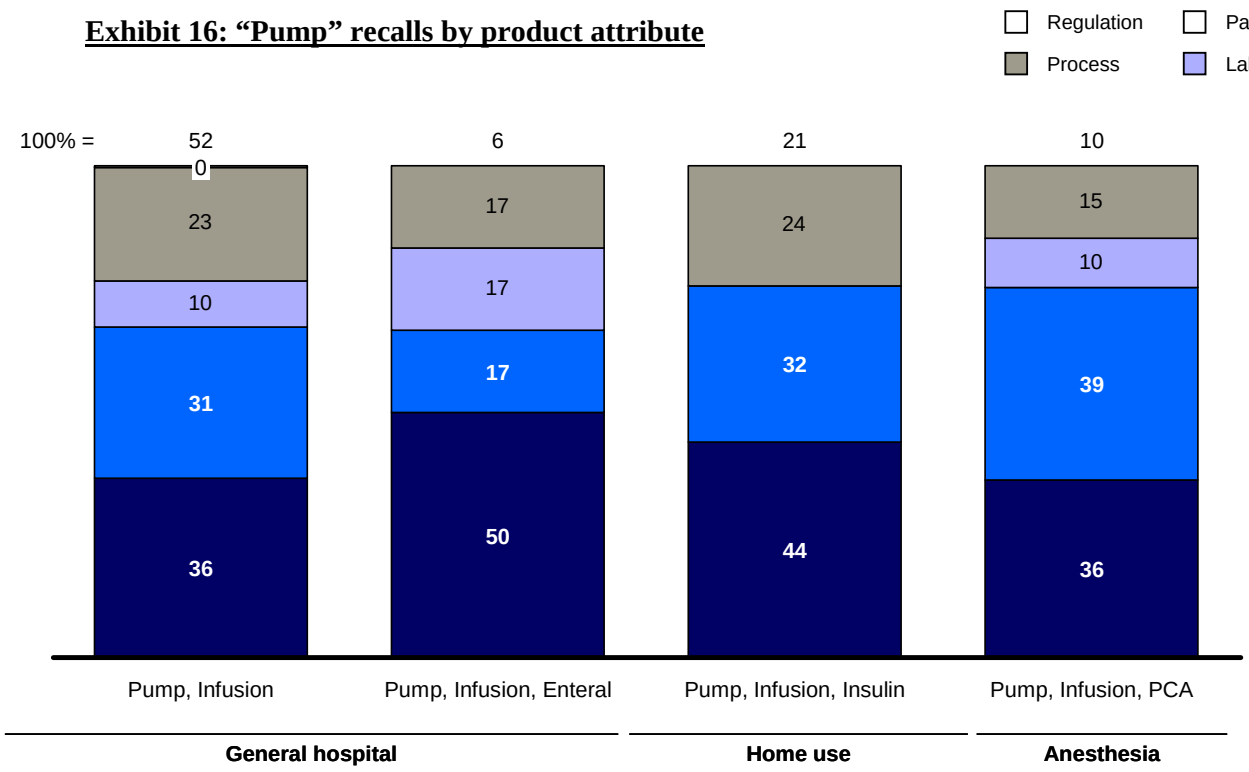
b. **Breakdown by product attribute.** The areas of product weakness are likewise similar across device types (see Exhibit 16). For catheters, most recall root causes relate to process defects. For pumps, hardware and software together capture more than half of root causes. The average variability for similar type devices (as measured by standard deviation) in recall root cause by value stream step was 7%.

Exhibit 15: "Pump" recalls by value stream



Source: Data from RECS database

Exhibit 16: "Pump" recalls by product attribute



Source: Data from RECS database

If product failures indeed vary in a predictable way, then analyses of these failures could inform FDA pre-market and inspection activities as well as resource allocation.

OPPORTUNITIES FOR IMPROVING QUALITY WITHIN THE INDUSTRY

There are several opportunities to improve quality assurance and reduce risk across the medical device industry. These draw on examples of best practices from within and outside the industry. To explore the strength of the quality infrastructure in the medical device industry, we examined quality processes along the value stream, considering product/process design, supplier management, manufacturing, and post-production activities in turn.

At each of these steps along the value chain, we examined quality support from within three domains: operating system, management infrastructure, and mindsets and behaviors. The operating system includes the way resources are configured and optimized for delivery of product in an efficient way. Management infrastructure refers to the formal structures, processes, and systems through which the operating system is managed to deliver business objectives. Mindsets and behaviors, the third critical piece of the quality landscape, encompasses the way people think, feel, and conduct themselves in the workplace (see Exhibit 17).

Exhibit 17: Overview of the quality landscape

	Quality		
Value stream steps	**Operating system**	**Management infrastructure**	**Mindsets & behaviors**
Product/process design	**"The way value streams and resources are configured and optimized for safe and timely delivery of customer demand at lowest lifecycle cost"**	**"The formal structures, processes, and systems through which the operating system is managed to deliver the business objectives"**	**"The way people think, feel, and conduct themselves in the workplace, both individually and collectively"**
Supplier management	• Continuous flow of material and information throughout value stream • Institution of standard operating procedures for each process step focusing on value-added • Scheduling of capacity to meet demand • Focus is on eliminating waste, variability, and inflexibility • Implementing learnings from market feedback	• Performance management including Key Performance Indicators (KPIs), metrics, target setting, reporting, and monitoring • Talent management/HR including clear roles, responsibilities, and accountabilities • Organization design (e.g., aligning the organization with the value stream) • Monitoring market feedback	• Leadership alignment and role-modeling • Clear direction and compelling purpose • Discipline, collaboration, and trust • Conformance to internal quality guidelines (e.g., SOPs) • Continuous-improvement and quality mindset
Manufacturing			
Post-production activities			

Operating systems

¶ Design and development engineering

a. **Defining and validating usage requirements.** Many companies interviewed spoke of significant difficulties in designing medical products for actual, and not merely intended, use. Firms struggled with designing and validating devices for the diversity of applications and environments in the field. Others struggled with translating customer and market requirements into effective "critical-to-quality" parameters that can be controlled and monitored within the product value chain to ensure quality. A primary reason for this gap is the lack of effective feedback mechanisms from the field into the product and process design stage. A few examples of best practices do exist; some companies use formal statistical tools to translate customer requirements into accurate technical specifications. Other firms used panels of medical device experts – academics and leading clinical practitioners – to achieve the same end.

b. **Designing for reliability and manufacturability.** Some executives acknowledged that their development process focused on designing complex, innovative products at the expense of long-term reliability or ease of controlled manufacture. Consequently, such companies have not developed sufficient expertise in reliability engineering and manufacturability. There exists tremendous opportunity to adopt learning and best practices from the automotive and aerospace industries that are far more advanced in this domain.

c. **Software development.** Most companies attributed poor software quality to challenges around "developing comprehensive test cases to simulate the effects of field usage." Software products are operated by a diversity of users, in various applications and environments. In addition, companies often have older "legacy" software platforms in their products that require significant investments in time and money to replace completely. Adding patches and workarounds to these systems often increases the likelihood of failure. For example, a robotic surgery device suffered unintentional performance issues caused by software fixes that were implemented to address a different problem altogether. In the face of such complexity, many medical device firms struggle to effectively scope, design, and validate software systems. Few firms that we interviewed followed formal software development models (e.g., Capability Maturity Model or equivalent). The Federal Aviation Administration (FAA) and Nuclear Regulatory Commission (NRC) regulate industries that produce complex software technology to work in high-risk environments. These industries provide best-in-class examples for developing quality, reliable software that could serve as a template for medical

devices. For example, aerospace manufacturers regularly use sophisticated software quality tools like assurance and safety cases to ensure fail-safe software operations.

- **Post production monitoring and feedback.** Interfaces between quality elements across the value chain are critical to effectively drive good quality. One critical interface involves post-production monitoring and feedback of field learning to improve design and manufacturing processes. The difficulty that some companies face in understanding end-user environments suggests that this is a gap.

  a. Many companies recognize a need to move beyond mere complaint handling mechanisms for feedback, especially since the "quality of complaints data often depends on what questions your customer interfaces are asking."

  b. Companies that have proper mechanisms for monitoring and feedback based on field usage are better able to define critical performance parameters in the device design, which helps with process and supplier controls. These mechanisms also serve as a basis for continuously refining device risk assessments and assessing the baseline level of quality for new devices.

  c. **Best practices.** There are examples of best practices within the industry. For instance, some companies use predictive analytics to build field performance predictor models before production and marketing, which are subsequently refined based on actual performance.

- **Supplier management**

  a. Supplier monitoring and management is widely identified as a continuing source of significant quality risk in the value chain. Risks are primarily around uncontrolled material or process changes, particularly when suppliers have an imperfect understanding of how their components affect end-product quality.

  b. Supplier management is a challenge particularly when dealing with a large, globalized supply base. For instance, one medical device company interviewed deals with close to 4000 individual suppliers across North America, Europe, China, East Asia, and India.

  c. **Best practices.** Companies that manage their suppliers well do so through a number of best practices. They carefully select and contract with their suppliers, often with deep involvement from the internal quality organization, and they identify vendors that deal with the most critical aspects of their product and invest heavily in training and monitoring them. Finally, they are highly disciplined about cutting off even preferred suppliers once it is clear that quality performance has dropped. They also recognize that resources for

supplier management often do not reduce with improved quality, unlike in manufacturing, for example. In addition, multiple interviewees suggested establishing an industry certification and shared auditing program for suppliers to drive quality and standardization.

Management infrastructure

- **Limitations in quality metrics**

  a. Many of the companies interviewed, both large and small, faced challenges around developing and tracking appropriate quality-related metrics through various stages in the value chain. For example, companies struggled with identifying quality metrics during product design, despite this stage being a key determinant of eventual product quality. Additionally, very few manufacturers indicated use of relevant metrics to track software quality, another significant source of quality issues. A number of companies focus instead on purely compliance-related metrics (e.g., CAPA time to closure and volume of complaints handled) that have limited bearing on quality.

  b. **Best practices.** Companies that define quality metrics early in the design stage saw a number of benefits. For some, quality metrics at the design stage allowed focused resources on the most critical elements downstream in the value chain, especially when managing supplier quality. Others indicated that tracking metrics was a key success factor in driving an effective mindset around quality – one company with an excellent recalls record had in place a dedicated 'measurements science' group with responsibility for developing and tracking quality and performance metrics across the organization.

  A few companies used in-process "leading quality performance metrics" that provided early signals of product and process quality, enabling the organization to identify and correct issues further upstream in the process. For example, tracking the number of non-conformances on the manufacturing floor could effectively identify any trends towards process nonconformance and loss of control. Leading metrics were put in place to measure quality performance in areas besides production – design, supplier management, and continuous improvement systems, for example.

- **Compliance-focused quality organization.** Quality is sometimes addressed as a separate function of the organization, rather than integrated cross-functionally throughout the organization. For instance, very few firms interviewed involve quality assurance personnel in the supplier selection process; supplier quality came up often as a significant source of quality risk within the industry. Additionally, very few of those

interviewed involve quality assurance substantively into the product and process design activities.

a. **Best practices.** Within companies that do well on quality, everyone through the value chain accepts ownership for quality. Additionally, the quality organization maintains a high-level, strategic focus on quality, which "alerts the company to changes in the external environment that require a shift in systems or actions," and "develops and maintains a system of checks and balances – quality audits." This results in a quality function that is integrated into the fabric of the organization, not an add on "quality check" function.

¶ **Performance management gaps around quality.** It is common in medical device companies for only the quality organization to be measured and rewarded based on quality performance. In fact, some interviewees reported performance incentive structures that inadvertently resulted in a disincentive to quality performance, particularly in R&D and product development functions, as well as business unit leadership. For example, design engineers are commonly measured on time to market, with no incentives tied to the actual quality of the products or manufacturing processes.

a. **Best practices.** Leading companies that integrate quality measures into their performance management and measurement systems have been able to achieve measurable improvements in actual quality performance for their enterprise.

Mindsets and behaviors

¶ **Quality culture.** Virtually every industry interviewee emphasized the importance of culture in driving a quality mindset through the organization. Companies that experienced quality-related issues in the past cited significant opportunities to improve quality culture. They highlighted two areas of quality culture gaps within organizations:

a. **Opportunity for top management to emphasize importance of quality.** Interviewees whose companies experienced quality issues typically did not track quality metrics at the executive level, and quality was considered the domain of a specific organization rather than a CEO-level agenda item. Regular management visibility into key quality (not merely compliance) metrics was considered vital to embedding a quality-centric culture for two reasons: first, such metrics provide management an opportunity to engage on quality issues; and second, to signal that top management believes quality is a high priority.

b. **Tendency for siloed focus.** Interviewees reported that a lack of involvement of the quality organization at all stages in the value

chain can lead to the mindset among frontline employees that quality is not their responsibility. Interviewees suggested that the most effective way to communicate the importance of quality was to link incentives to quality performance.

c. **Best practices.** Some of the companies interviewed intentionally embedded a strong quality culture within the organization. One executive at a large medical device company described the effect of tying performance incentives to product quality to underscore the firm's commitment to quality. Another executive, to turn around a poor quality and compliance record, reported directly to the CEO, thus enhancing his organization's credibility and status.

PERSPECTIVES ON CHALLENGES TO ADDRESSING QUALITY GAPS

In addition to an assessment of the biggest quality risks across the value chain, three broad themes emerged from our interviews with the industry.

First, many executives noted that, without greater transparency around competitive quality performance, the market rewards rapid product innovation and low cost, but not better quality performance. Second, executives acknowledged the increasing complexity of end-user environments and the sophistication of the products that operate in this environment. Finally, they spoke at length about the misalignment between quality outcomes and pure regulatory compliance.

¶ **Impact of low quality transparency**

a. **Lack of visibility around comparative quality.** For many device types, consumers, healthcare providers, and payors do not have an independent, reliable source of information on device quality, organized by manufacturer. This, in turn, means that the market is unable to reward manufacturers for quality improvements, reducing their incentives to do so. Analysis in other industries has shown that, where readily available, accurate information on quality has a strong influence on buying choices.

b. **Time to market competition.** Many companies believe that there is significant pressure to enter a device market early to maximize payoffs due to intense competition. Coupled with the perception that innovation and speed, rather than quality and reliability, reap rewards in the market, companies cite pressures to accelerate product launches instead of ensuring high quality before launch. Interviewees shared concerns that the primary focus for R&D is on timelines and that R&D is not incentivized on embedding quality.

c. **Cost pressures.** As healthcare consumers and payors look to curtail rising health costs, device makers are driving to push down their price points and costs. In turn, companies are searching for low cost suppliers and forcing existing suppliers to cut costs. This often has unintended consequences for product quality, for example, when a maker of implantable devices switches to cheaper raw materials that reduce product life.

d. **Consolidation.** As large medical device companies make acquisitions to enter new markets or obtain proprietary technology to maintain a competitive edge, they often absorb older, legacy designs and systems. This results in multiple design platforms for similar devices within the same company, and disparate quality systems. For example, one interviewee described how a large manufacturer had vastly different quality and inspection processes for what were

essentially identical products made by different subsidiaries of the company.

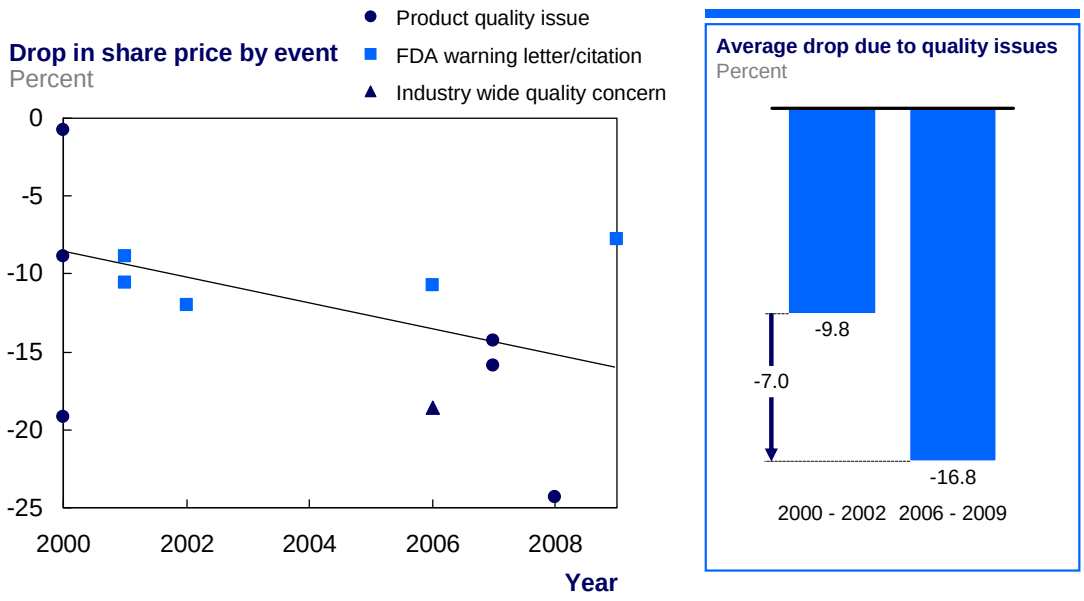
Economics of quality are changing

In the past, these factors meant that the benefits of launching a product in the market early were far greater than the costs of doing so without high levels of quality performance and reliability. However, this may no longer be the case for three reasons:

a. **Increasing risk of quality failure**. The increasing complexity of devices and user environments has in parallel increased the likelihood of significant negative quality events.

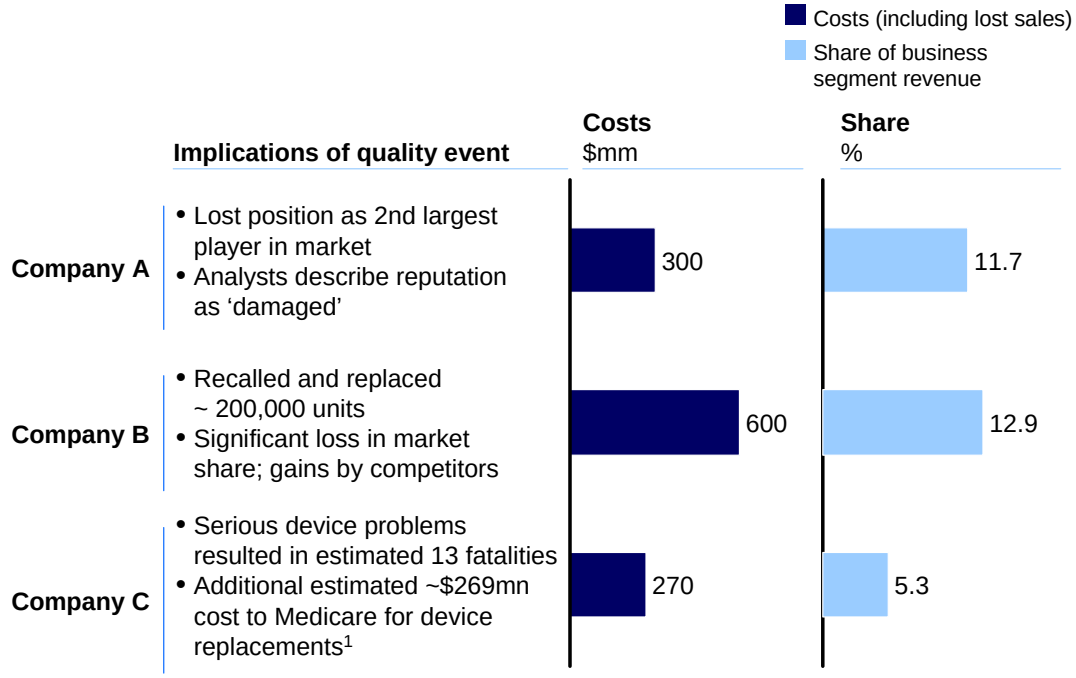
b. **Increasing cost of quality failure.** The costs of negative quality events have risen due to increasing regulatory, legal, and media attention. Exhibit 18 shows that the average drop in company share price following select quality incidents was quite significant and increased over the last decade. Exhibit 19 provides a few recent examples of costly quality events.

Exhibit 18: Size and trends in medical device company share price drops following specific major quality events



SOURCE: Manufacturer financial statements; Factiva; team analysis

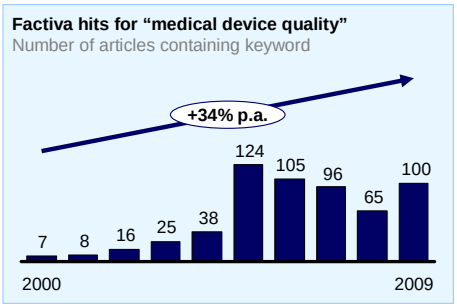
Exhibit 19: Examples of financial impact of select quality incidents

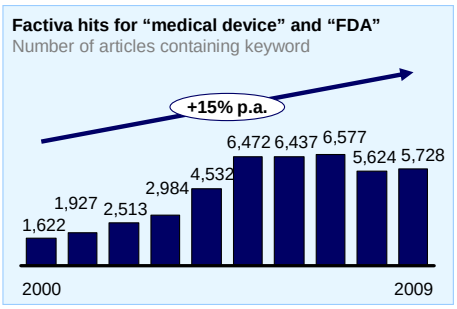


1 Based on independent research study

Source: Factiva; team analysis

Exhibit 20: Increasing media focus on medical device quality





Sample headlines

More Oversight Due For Infusion Pumps

New York Times, 24 April 2010
Federal regulators say they are moving to tighten their oversight of medical devices, including one of the most ubiquitous and problematic pieces of medical equipment -- automated pumps that intravenously deliver drugs...

Stent Concerns Are Galvanizing Plaintiffs' Bar

The Wall Street Journal, 8 December 2006
WHILE A PANEL of experts from the Food and Drug Administration weighs the safety of a popular heart device at a meeting concluding today, another group is paying close attention: personal-injury lawyers.

Risk Management for Software Design in Medical Devices …

Business Wire, 29 March 2011
Software quality for safety-critical medical devices has been at the center of discussion for industry experts and especially the FDA. In 2010, 39 of medical device recalls (500 total recalls over the past 7 years) were reported to be related to software defects and malfunctions. According to an FDA survey, this equates to approximately 8% of device failures.

Source: Factiva, team analysis

c. **Increasing transparency into quality**. The trend toward comparative effectiveness research will also promote greater visibility into device performance and quality. The American Recovery and Reinvestment Act of 2009 directed $1.1 billion to expand comparative effectiveness research at the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health (NIH). Head-to-head comparisons of therapy options that stem from this research will highlight the quality and safety of specific medical devices. The FDA Sentinel Initiative, an effort to leverage large, existing databases to automate collection of adverse event data via public-private collaboration, will further drive awareness of adverse events and device flaws.

The combination of these factors may constitute a tipping point in favor of ensuring high levels of quality and reliability at the expense of early revenues.

¶ **Increasing complexity of medical devices and user environments**

a. **Sophistication and complexity.** Medical devices have become increasingly sophisticated over the last decade. As one executive said, "Thirty years ago, the medical device industry essentially made simple tools." Today, new innovations are becoming increasingly complex, driven by the advent of new technologies**.**

b. **Quality tools and processes.** The sophistication of tools and practices used to drive quality and reliability through the medical device value chain does not appear to have kept pace with the increase in device complexity. With a few exceptions, most companies interviewed either do not implement quality processes at the same level of sophistication as other industries or are in the very early stages of doing so. While product design, defining critical-to-quality metrics, and post-production monitoring were commonly cited as areas of quality risk, few companies used formal statistical tools like quality function deployment in a disciplined way to accurately capture critical requirements. Risk assessment tools like design and process failure mode and effects analysis (FMEAs) are often not developed, applied appropriately, or updated frequently enough to incorporate substantial post-production feedback from the field. Also, very few companies interviewed had in place sophisticated reliability engineering practices like accelerated life testing analysis or life data and failure analysis. All of these tools are used routinely in the automotive and aerospace industries for product development and process control.

c. **Risk assessment and mitigation expertise.** Some medical device companies lack expertise in developing risk assessment and

mitigation plans during the product development phase. This significantly impairs their ability to monitor and control quality through the manufacturing and the post-production phases. Many interviewees within the Agency believe that these companies consequently lack the ability to identify existing and emerging risks in the broader market associated with their devices. Nor are they aware of applicable best practices in use within the industry.

d. **Quality investments.** Many companies interviewed recently began investing in upgrading their quality organizations, but believe that tangible benefits are still a few years away, making it harder to justify such investments in the current economic climate. A quality head at one large manufacturer indicated that one of the biggest challenges was "managing expectations around payoffs to the investment."

e. **Regulatory disincentives to innovate around quality.** Some companies are innovating with processes to drive quality. One large medical device manufacturer was evaluating advanced "process signature" methods in its plants to catch process non-conformance early. Another incorporated the use of "spiral modeling" techniques to quickly develop error-free software for its devices. However, both companies indicated that substantial effort was involved in educating the Agency to accept such process innovations. In general, companies believe that the current regulatory framework slows process innovation around quality.

¶ **Regulatory framework misaligned with assuring Quality outcomes**

Relationship between quality and compliance. An overwhelming majority of companies interviewed believe that maintaining compliance with FDA regulations does not ensure good product quality. Some interviewees indicated that they were aware of facilities that were highly compliant but produced low quality products or, the opposite case, products that were produced to high quality standards and achieved excellent performance but did not maintain good compliance standing.

In general, interviewees agreed that achieving compliance in the "right way" (e.g., through a focus on mature, embedded quality processes) moves organizations in the right direction and may deliver a baseline level of quality. However, some thought it possible, and perhaps not uncommon, to achieve satisfactory compliance without installing mature, embedded quality processes. Most companies define "quality" much more broadly than "compliance." Quality is defined as products and services that deliver intended performance, safety, and customer satisfaction, while compliance is defined as meeting regulatory requirements. These concepts are quite distinct in most industry leaders'

minds and, in fact, are often embedded even in industry organizational structures where compliance and quality functions are separate.

Specific issues related to the regulatory regime concerned: (1) an over-emphasis on pure compliance versus quality outcomes, (2) barriers to implementing safety related improvements; and (3) lack of enforcement specificity on highest-risk areas within the medical device space.

Exhibit 21: Industry perceived criticality of quality risks within medical device industry

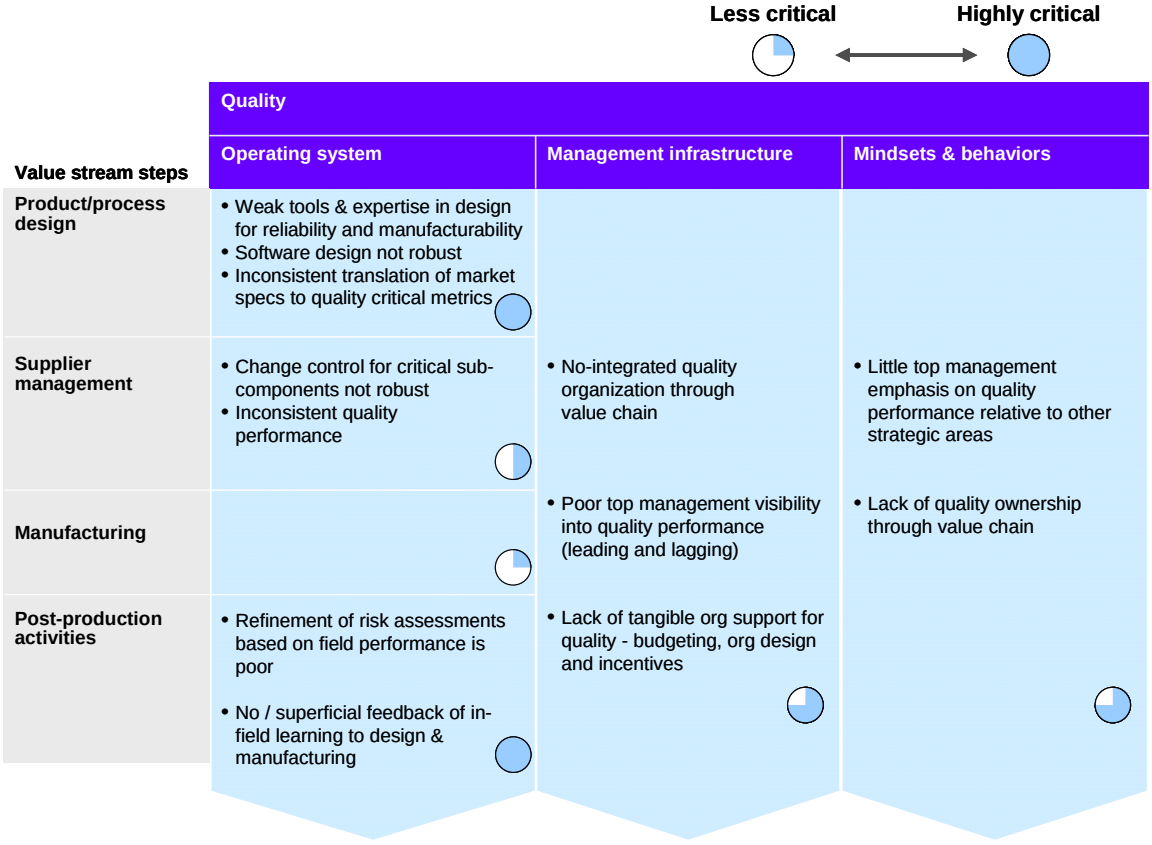
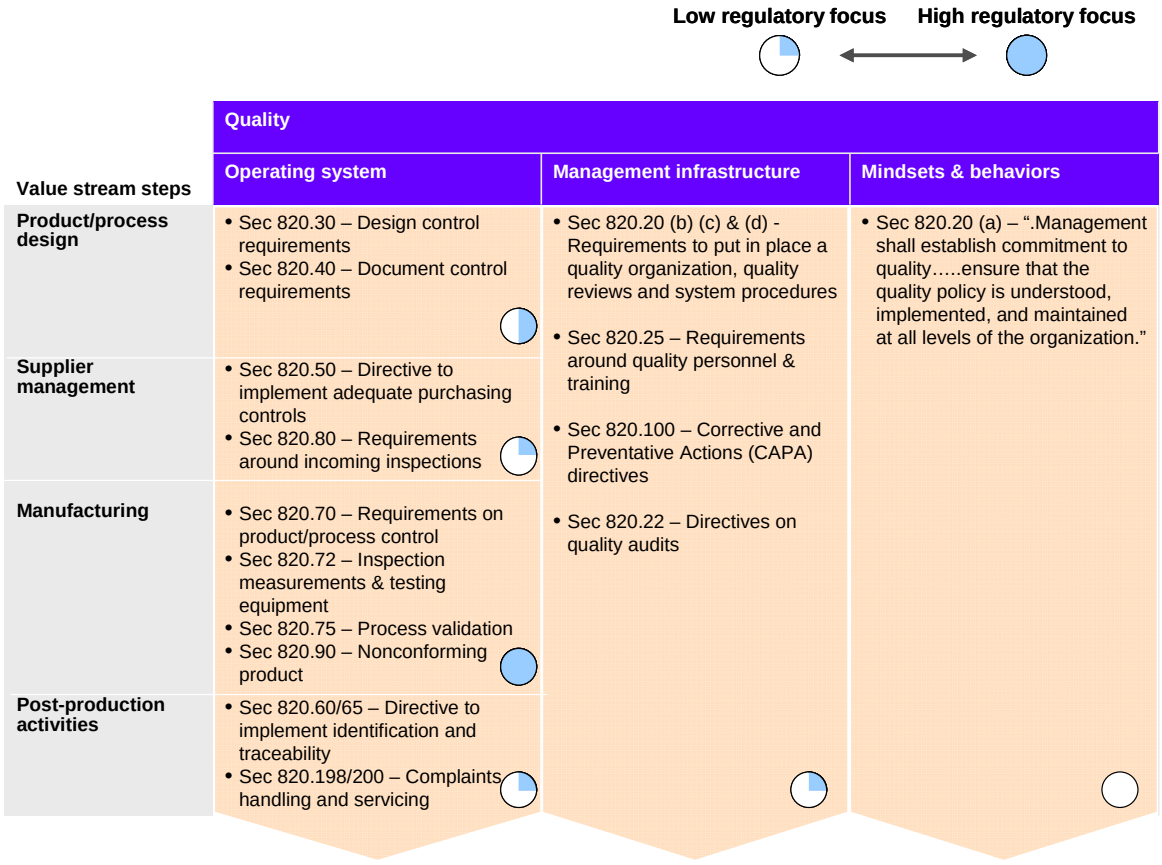


Exhibit 22: Industry perceived areas of regulatory focus



a. **Highly compliance-focused, inconsistent enforcement.** Virtually all companies interviewed shared their perception that the Agency has of late become highly focused on enforcement at the expense of cooperating with industry on delivering quality. These quality leaders indicated that an excessive focus on compliance often diverts resources and management attention away from investments in quality towards compliance activities like documentation, which do not directly lead to improved quality outcomes. This is particularly true for smaller companies for whom adverse regulatory action could threaten their very existence. One executive told us that, in her company, "it was hard for the leadership not to calibrate success based on Agency inspections." Another executive told us that the Agency "needs to change its paradigm from being like a 'policeman' and work with the industry." The situation is made worse by industry perception that the Agency inconsistently interprets and enforces regulations. One quality executive described how management focus completely shifted to ensuring that inspections were tightly managed after the company received adverse publicity for multiple citations following a plant inspection; this was particularly surprising since that same plant had been inspected just six months prior with no issues found. Other executives gave examples of differences in

interpreting regulatory codes across investigators and even across district offices. Executives also felt that there was inadequate transparency into how investigators arrived at specific decisions and dealt with specific cases.

b. **Disincentives to develop safety-related quality improvements.** A number of companies believe that penalties exist for making safety-related quality improvements because the Agency often requires an update to, or recall of, the existing device in light of the safety improvement. This raises the concern that some in industry may think twice before taking warranted action because of the potential repercussions.

c. **Lack of enforcement specificity on high risk areas.** Further, industry concerns involve FDA's measurements of, and accounting for, the areas of highest device quality risk across the industry. "Neither the industry nor the Agency has an effective way of determining a proper quality baseline, which must take into account, number of installed devices, [and] number of previous failures," said a business unit head of a major medical device company. A lack of focus on true areas of quality risk impairs quality outcomes in two ways. It leads to Agency resources spent on investigations that hunt for very broad compliance gaps, and it leads to a perception within the industry that the Agency is unfocused and "heavy-handed," forcing companies to devote resources to activities that do not bear on quality. Executives believe that, while systems like "Sentinel" are a step in the right direction, they still fall short because assessing quality risks requires active surveillance and monitoring of more than purely clinical outcomes.

¶ Interactions between FDA and industry

Many executives believe that the Agency should rethink its interaction with the industry. They make the case that stricter enforcement and stronger compliance focus from FDA does not help, and could potentially hurt, quality outcomes because, as noted above:

a. They believe that a highly compliance-focused environment diverts management attention and limited resources away from real quality investments.

b. The industry pursues an innovation paradigm based on incremental improvement of existing devices and enhanced regulatory oversight slows the rate of product improvements.

c. In an environment in which the Agency is seen as not tracking specific areas of high device risk, industry views stronger enforcement as unfocused and unnecessarily heavy-handed.

Executives spoke at length about a “policeman mentality” driven by negative views of the industry within the Agency, which prevents substantive cooperation around achieving high quality; many contrasted the FDA with EU regulatory agencies, whom they claimed have a more collaborative and mentor-like approach, as well as investigators who pay more attention to overall quality outcomes.

IMPLICATIONS AND POTENTIAL AVENUES TO ADDRESS CHALLENGES

In order to address the major barriers to quality that exist, the Agency should consider a comprehensive program centered on three parallel and overlapping agendas: (1) Aligning compliance focus to address industry quality gaps; (2) Enhancing transparency and visibility of performance to drive quality; and (3) Increasing industry engagement. The Agency should establish an implementation team to advance these agendas.

1. **Align compliance focus to address industry quality gaps**
    a. Interview findings reveal the two biggest areas of perceived quality risk as (1) device design and development, and (2) post production feedback, followed closely by supplier management. Within the quality system regulation (QS reg), however, there is strong focus on production and process controls, including purchasing controls, receiving and in-process acceptance activities, control of inspection, testing and measurement equipment, and process validation.
    b. A lack of alignment between regulatory focus and areas of current quality would misdirect the Agency's enforcement resources and education and outreach efforts. Consequently, there is a strong case for aligning Agency focus to deal with specific areas of quality risk like design for reliability and software development. For instance, given an increasing reliance on software and the advent of wireless communications, the Agency should consider equipping investigator and reviewers with appropriate tools to determine and enforce the quality of devices that incorporate these technologies.
    c. Overall, interviewees within the Agency also suggested that the link between compliance gaps and quality issues is often not apparent. Consequently, the current compliance regime does not encourage investigators to go beyond regulations to actively seek out quality issues. Making this link more transparent to both the investigators and the company being investigated could enable more efficient, focused enforcement.
    d. Actions that FDA could undertake to shape its compliance focus to better address industry quality gaps include:
        i. Perform a detailed internal diagnostic and gap analysis across CDRH and ORA to determine the allocation of resources, level of knowledge, knowledge management practices and scrutiny and oversight of quality relative to the

industry quality gaps and quality landscape presented in this document. Analysis should include evaluation of both system design and execution.

ii. FDA should seek to understand and learn from best practices of other regulators and industries. The Agency could undertake a program to understand, and compare and contrast, the approach of other regulators, with the aim of identifying best practices to align compliance policy with industry quality gaps.

iii. The output of these efforts should include a crystallized set of issues for the Agency to address, possibly including: industry interface, resource allocation, internal and external training and knowledge, internal procedures, and industry guidance or regulatory changes. An action plan should be developed to address these issues.

2. Enhance transparency and visibility of Agency data to drive quality

a. Examples from other industries prove that greater customer visibility into manufacturer quality performance (e.g., through quality surveys, reviews, and awards) strongly influences sales and improves market presence. However, in many device categories, such quality performance information is not readily available to buyers, who then often make purchase decisions based on brand image, price point, and marketing message.

b. FDA possesses a wealth of data pertaining to medical device quality. Unlike individual players in the medical device space, FDA has a uniquely broad view of quality and risk across many product types, therapeutic areas, and manufacturers. Though adverse events are thought to be underreported, the Agency receives reports on many adverse events and maintains documentation of all recalls and inspections. This data may be used to quantify the magnitude of medical device quality problems and to better understand the root causes of these problems.

c. Bolstering the data that FDA currently collects with a few key additional pieces could greatly increase its utility and provide a fuller view of medical device quality. Gathering additional risk data from companies will likely paint a clearer picture of the associated level of risks for devices. Additional data points include:

– Device usage. The Agency should consider adjusting absolute numbers of adverse events and recalls for “device usage,” or the number of devices on the market. Annual unit sales are a reasonable

proxy for many device, but to optimally understand these data, FDA could consider requiring manufacturers of durable devices to report installed base of a given device on an annual basis or when making a report of an adverse event or recall.

- Root causes of adverse events. The MAUDE system currently tracks device "problem codes," but does not incorporate codes specific to describing the root cause of adverse events. The 989 problem codes available describe generally what happened to signal that the device failed without giving a more in-depth root cause. Providing a focused list of root cause codes and eliciting these from manufacturers could generate data to prevent future adverse events. If no root cause is determined, then manufacturers could have the option of selecting "unable to determine root cause."
- Device failure modes. Particularly useful would be information on possible device failure modes, probabilities, and severity – available in standard FMEA documentation – and information on the size and growth of the installed base, which would help better assess the overall level of risk associated with field quality issues.

d. Actions that FDA could undertake to enhance transparency and visibility of performance to drive quality include:

   i. Construct and routinely report industry-wide and product-category wide quality and patient outcome information. In addition, publish a synthesis of causes and trends of adverse events and product recalls overall and by product class.

   ii. Spotlight companies that have best-in-class systems that result in excellent quality. Examples of high-quality manufacturers could serve as "case studies" for companies that are faced with quality and compliance challenges. Interviewees within the Agency indicated that smaller medical device firms, "typically know what needs to be done, but aren't sure how to do it." These firms would benefit from case studies on implementing best-in-class quality management systems.

   iii. Utilize quality and compliance analyses to focus FDA efforts in pre-market review, inspection, and industry engagement, for example:

      - Learnings from pre-market review of critical-to-quality product attributes could be fed forward into post-market monitoring efforts. Similarly, findings from post-market monitoring of root causes of quality events could be fed back into the pre-market approval process to ensure maximal

alignment between review process emphasis and medical device risk.

- Therapeutic areas/product codes. Areas of focus and resource allocation might be informed by therapeutic areas and product codes responsible for a quickly-increasing set of adverse events or recalls. For this in particular, regular analysis would be essential for timely detection of problem clusters.
- Root cause targeting. Information about where faults cluster in a given device type—either by value stream step or product attribute—could be applied to pre-market evaluation or provided to field investigators. For instance, the knowledge that radiology devices suffer disproportionately from software design issues could drive a renewed focus in this area.
- Facility inspections could be targeted to focus on known quality failure root causes specific to the products made at the facility and any company-specific quality weaknesses.
- FDA could systematically determine where individual products or product classes have quality challenges and engage industry and third parties to provide tools and assistance to address these challenges. A model for this is FDA's infusion pump improvement initiative, in which the Agency responded to sector-wide quality failures with measures such as a letter encouraging manufacturers to submit their software for review by FDA software experts prior to premarket review.
- Expand the use of pre-market data into post-market surveillance to further target risk assessment. While post-market data may inform pre-market and inspection activities, the reverse is also true. If manufacturers are able to provide additional information about common failure modes, post-market surveillance may be tuned to certain signals and pick up early problems.

e. The trend in health care toward real world and comparative effectiveness research could also drive greater visibility into device performance and quality. For example, data from Sentinel could potentially be mined and analyzed to find comparative performance of competitive products and performance anomalies. These findings could be published.

3. Increase industry engagement

a. FDA remains one of the best among global health care regulators. With that reputation comes great credibility and influence to shape industry behaviors and attitudes around quality. The actions described above will help to capitalize on this to improve quality. However, there are some additional considerations for FDA on how to better engage industry around quality.

b. Enforcement consistency and transparency. Most companies we interviewed had directly faced FDA inconsistencies in interpreting and enforcing the QS regulation. We found that this created a climate of resentment, which impedes meaningful cooperation between the Agency and the industry around improving quality outcomes. Many interviewees within the Agency were aware of the issue and attributed this inconsistency in part to a high attrition rate among inspection and investigation personnel and Center staff. There is also a view from within the Agency of some inconsistency across district offices, and some companies perceive inconsistencies within districts.

c. In particular, greater transparency and clarity is needed around two aspects of the regulatory process: (1) predictable and reliable benchmarks of quality system compliance and (particularly for smaller companies) guidance on how to reach them; and (2) updates to the company involved on the status of enforcement cases in process. Many executives complained that information about these topics was unavailable to them despite directly contacting the Agency. Others hesitated to even contact the Agency to avoid "drawing attention to what could potentially be a non-compliance issue."

d. FDA can potentially learn from practices of regulators of similarly high tech and complex industries:

- Federal agencies like the Federal Aviation Administration (FAA) and the Nuclear Regulatory Commission (NRC) regulate high risk industries characterized by interactions between humans and complex technology; there exist opportunities to adopt best practices around how these agencies deal with the industry to promote and maintain a high level of safety and quality.

- Collaboration. The FAA, for example, collaborates closely with the aircraft manufacturers and airlines to identify and monitor areas of risk by using mechanisms such as "air worthiness directives" that warn aircraft owners and operators of safety issues, and force compliance before using the equipment. The FAA also collaborates with select industry members to understand broad strategic and

technological trends within the industry, allowing the Agency to keep directives and regulations relevant.

- Rigorous training and certification for critical functions. The NRC has rigorous certification processes for engineers and nuclear power plant operators. Training programs are as long as 24 months, and are continuously refined through job analysis and feedback. Similarly, the FAA provides training, certification and re-certification for pilots and maintenance technicians, ensuring a high degree of standardization around equipment use, maintenance, troubleshooting and issue reporting.
- Innovative quality systems and tools. Both the FAA and NRC encourage the use of innovative engineering and systems tools to ensure quality. For example, manufacturers of aircraft and nuclear reactor systems are skilled in advanced reliability analysis and accelerated life testing, ensuring that equipment continues to perform optimally well past its standard operating life. The use of assurance cases in avionics software and redundancy principles in nuclear reactor control systems ensures quality and failure proof technology systems.
- European Union regulatory agencies. European Union inspectors were said to be collaborative and to act as unofficial "mentors" to smaller firms. In addition, investigators were described as highly consistent, very knowledgeable in engineering and technology, and also attentive to overall quality outcomes.

e. Steps FDA should consider to increase industry engagement on quality:

- Initiate a program in conjunction with industry to align on and document a set of FDA endorsed practices and standards for achievement of quality and compliance. These would need to be detailed practices that describe acceptable methods and documentation that meet the requirements of the QS regulation.
- These practices should then be imbedded into the FDA's internal procedures and training program for staff.
- CDRH should undertake a program to understand the similarities and differences and related pros and cons of its approach versus the approach of comparable medical device regulators and, potentially, regulators of other select high tech industries. The outcomes of this program could be a set of learnings that CDRH adopts to better assure product quality.

ESTABLISH AN IMPLEMENTATION TEAM

- FDA should establish an implementation team within CDRH, potentially led by the Office of Compliance, to set the three agendas described above in motion.
- Potential key indicators of implementation to be achieved within the next year could include:
  - Delivery of an “action plan” to address industry quality gaps
  - Organization and periodic external publication of industry quality measures
  - FDA-Industry engagement to align on and document a set of FDA endorsed practices and standards for achievement of quality and compliance

CONCLUSION

In recent years, a growing number of patients have suffered from adverse events due to medical devices. To better understand the reasons for these lapses in quality and safety, we conducted interviews with medical device industry thought leaders and FDA leadership and in parallel analyzed FDA adverse event reports and recall data.

Our efforts revealed that there are systemic gaps within the medical device industry's quality approach that result in these issues. Attempts to improve quality are hindered by challenges within the industry as well as specific aspects of the Agency's regulatory approach. Moving toward greater visibility into device quality and properly aligning FDA's regulatory approach will be important to catalyzing industry movement towards improved device quality. Investment by FDA now in a holistic quality infrastructure will support a next generation of medical devices that are as safe and well made as they are innovative.

APPENDIX

Recall root cause categorization matrix

CAUSE_CODE	CAUSE	Value Stream Assignment	Product Dimension Assignment
C1	Mix-up of Material/Components	Supplies	Process
C2	Material/Component Contamination	Supplies	Process
C3	Release of Material/Component Prior to Receiving Tes	Supplies	Process
C4	Nonconforming Material/Component	Supplies	Hardware
C5	Counterfeit	Supplies	Hardware
D1	Device Design	Design	Hardware
D2	Component Design/Selection	Design	Hardware
D3	Packaging Design/Selection	Design	Packaging
D4	Labeling Design	Design	Labeling
D5	Software Design(Device)	Design	Software
D6	Software Design (Process)	Design	Software
D7	Process Design	Design	Process
E11	Component Change Control	Postproduction and change control	Hardware
E12	Finished Device Change Control	Postproduction and change control	Hardware
E13	Packaging Change Control	Postproduction and change control	Packaging
E14	Labeling Change Control	Postproduction and change control	Labeling
E15	Software Change Control	Postproduction and change control	Software
E16	Process Change Control	Postproduction and change control	Process
E18	Vendor Change Control	Postproduction and change control	Process
L1	Labeling False And Misleading	Design	Labeling
M1	PMA	Other	Regulation
P1	Process Control	Manufacturing	Process
P10	Environmental Control	Manufacturing	Process
P11	Storage	Postproduction and change control	Process
P12	Error In Labeling	Manufacturing	Labeling
P13	Packaging	Manufacturing	Packaging
P2	Packaging Process Control	Manufacturing	Packaging
P3	Equipment Maintenance	Manufacturing	Process
P7	Reprocessing Controls	Manufacturing	Process
P8	Manufacturing Material Removal	Manufacturing	Process
P9	Labeling Mixups/Errors	Manufacturing	Labeling
T1	Employee Error	Other	Other
UI	Under Investigation by the Firm	Unknown	Unknown
UK	Unknown/Undetermined by the Firm	Unknown	Unknown
X1	Expiration Dating	Manufacturing	Labeling
X2	Radiation Control for Health and Safety Act	Other	Regulation
Z1	Other	Other	Other

Other = Failure to submit and/or obtain PMA or 510(k) approval, Noncompliance with Radiation Control for Health and Safety Act