Making Regulatory Compliance a Core Process
Director and Officer Liability Exposure

Chaos and complexity theories underlie the “new” science of organizations. Chaos theory posits that a butterfly flapping its wings in Brazil could cause tornadoes in Texas. An organization has to wrestle with the complexity of adopting evolving technologies and selecting adaptive systems with the “new science” models as it seeks to harness its company’s institutional values and organizational structures into capabilities that will unleash the human potential within. New models also incorporate emerging technologies into innovative operational concepts that produce synergy.

Companies are seeking new tools that minimize the negative repercussions of decision making. Those risk management tools evolved out of the financial sector, out of the tools we use, and from a strict application of game theory to the challenges of chaos theory; essentially, risk management is built on a foundation of elementary probability theory. Probability theory dates back to 17th century European mathematical development and to one ingenious idea on top of another combined with ideas from other disciplines.

Quantitative techniques for managing risk enhance the quality of our lives and accelerate the tempo of modern times. These methods allow people to take more risks than they otherwise would — a benefit to society, which cannot progress without risk takers (1).

Economic theory suggests that the higher the risk, the greater the potential return. Risk is inherent in any enterprise, and risk management has evolved into a separate and distinct discipline. The discipline of risk management, however, focuses on financial concerns — that is, on concerns that are generally measurable, based on actuarial data, and use statistical models for decision making. The concept of quality malpractice risk management is considerably more difficult to quantify and somewhat obscure to financial analysts. In this article, we link cataclysmic changes in operational environments and recent developments in FDA enforcement practices with risk management concepts to postulate a new risk management process for senior management — regulatory compliance.

Controlling Risk
Against the uncertainty of the future, business strategy must create options and identify choices. Because resources are finite, trade offs and changing commitments are inevitable. Corporate governance in successful companies means developing well-defined control cultures that allow management and employees to embrace corporate values and to be pragmatic in controlling today’s business risks. These companies have dispelled the myth that internal control is a bureaucratic, police-like process. For them, control is a proactive attitude embraced by all employees to achieve corporate objectives across the entire business. These companies secure the right leadership, ensure individual accountability, develop risk management as a strategic priority, and influence behavior through human resource reinforcement.

Risk in the News.
Last year, two major corporations — Ford Motor Company and Firestone Tires — were facing government scrutiny at home and abroad. The CEOs of both companies testified before the U.S. Congress, and both companies have been named in lawsuits in several countries. At issue is whether the companies and their executives had knowledge (or should have had knowledge) of a safety problem, and whether, upon realizing a safety problem existed, they acted in time to prevent a tragic outcome — injury and death — to an as-yet-unknown number of customers. At the core of this investigation are the companies’
Risk in health care. Nowhere is risk better recognized and regulated than in the health care industry where quality assurance (QA) practices are mandated by FDA regulations. Defects can originate in a therapeutic’s conception, design, manufacture, storage, or instructions for use, and companies go through lengthy and formal steps, defined by regulations, to establish the safety and efficacy of their products. After a drug development cycle that can last seven to 15 years, only one out of 12 new drugs successfully makes it to market.

QA requirements for drugs and devices ensure that responsibility is assigned and traceability is captured throughout the development cycle. Risk assessments are specifically required as part of FDA’s quality systems regulations (2). Those regulations (presently applicable to medical devices only) control a product throughout its life, extending through manufacturing to as long as the product is marketed — from cradle to grave. Future drug regulations will likely follow this quality systems model. Under the strict liability standards that adhere in FDA laws, management intent is of no relevance.

Regulating Risk
FDA is the nation’s oldest consumer protection agency, overseeing almost 100,000 facilities that produce commercial products valued in excess of $1 trillion. It has been a scientific agency since 1862 and a law enforcement agency for over 90 years (3). Regulations that mandate accountability and traceability throughout the drug development and marketing process are the foundation of FDA’s enforcement power. In the pharmaceutical sector, regulatory risks affect a company directly with FDA 483s, warning letters, and consent decrees. Those enforcement tools can result in nonapproval of a pending new drug submission, delayed approval of a new product, or loss of a government contract.

Legal risks for pharmaceutical companies include injunctions from manufacture, searches of premises, seizure of products and records, and prosecution — corporate or individual, civil or criminal. Blood bank personnel found this out when FDA held laboratory managers individually responsible for their actions. Regulatory penalties can include individual or corporate fines, sanctions, and imprisonment. Businesses can lose market share or their good name while bearing the cost of litigation or remediation, and particularly severe penalties can put a company out of business. Individuals can lose even more.

Personal responsibility is a hallmark of the Food, Drug and Cosmetic Act (4). FDA’s compliance and enforcement policy allows individuals who actively participate in unlawful conduct, who allow unlawful conduct to happen by passively tolerating violations, or who fail to take steps to learn that violations are occurring in their companies to be prosecuted. Company executives react with surprise and sometimes anger at being associated personally with the wrongdoing that brought their company to court, believing that violations are only a corporate problem, which should not affect them directly. FDA has defended its policies three times in the Supreme Court and has prevailed each time (5).

Risk Management Perspectives
The disconnect between management objectives and line employees’ understanding of those goals was made apparent in a PriceWaterhouse Coopers survey (11).

• Virtually all CEOs (95%) stated that they “truly have an open door policy and will reward employees who communicate potentially bad news.” However, half of all employees (48%) stated “the messenger of bad news takes a real risk in my company.”

• Nine of every 10 senior executives in the survey agreed that internal control is critical to effective management. Yet, 80% of that same group agreed, “when it comes down to compensation, making the numbers is what really matters.” This type of thinking creates powerful disincentives that undermine effective control cultures.

• Three-quarters of the chief executives surveyed answered “no” when asked whether their employees intentionally circumvent cumbersome corporate policies. Yet, half of the non-CEOs surveyed indicated that such circumvention is common.
The body of regulations is dynamic, changing as products and technologies evolve. Different regulations address different stages of a pharmaceutical’s life cycle: good laboratory practices (GLPs) cover discovery and preclinical development (6), good clinical practices (GCPs) regulate clinical trials (7), and good manufacturing practices (GMPs) focus on postapproval manufacturing and distribution (8). (Applied together, the regulations are referred to as GxPs). Interpreters. With the regulations thus defined as applying to different stages of a product’s development, it would appear easy to nestle the isolated regulations into their functional silos. Realistic and integrated risk assessment is not that simple, requiring cross-functional interpretations (that is, where GLP + GCP + GMP = GxP). Although regulations provide a framework for quality systems, many aspects of a complete quality system require expert judgment. There are many regulation “interpreters” in industry and in government, but there is no quantifiable model with which to assess their performance. Often, interpretation is an amalgamation of knowledge, experience, and serendipitous timing. Disagreements on interpretation can hurt reputations, profits, and shareholder confidence. No “ideal” model of clinical research or manufacturing exists. Depending on the experience and the interpretation of the inspectors, improvements can always be deemed necessary. The risk resides in those requested improvements escalating into an inspection failure — stopping part of a company’s operations.

FDA enforcement is predicated on human efforts and consequently follows discernable patterns. Particular functions of primary interest to inspectors (such as validation, adverse event reporting, and equipment cleaning, among others) are identified and targeted. Inspectors then attempt to unearth examples and obtain evidence of violations within those functions. Until the mid-1990s, the maximum fine levied by FDA was $202,000. That almost insignificant sum dared senior management to make “business decisions” without regard to regulatory compliance. After all, compliance programs generate costs, and their benefits seldom appear on accounting ledgers. Excessive emphasis on managing downside issues can limit a company’s ability to pursue the upside. This is especially true when penalties imposed are perceived to cost less than the rewards from reduced compliance expenditures. In the mid-1990s, however, amidst a flurry of consent decrees, a medical device company made headlines with a $61 million fine and prison sentences for its senior executives.

In November 1999, FDA raised the bar again. The agency filed a complaint for injunction and a consent decree of permanent injunction in the U.S. District Court for the Northern District of Illinois. Listed, by name, as defendants were the CEO of Abbott Laboratories and the president of the Abbott Laboratories Diagnostics Division (9). Two provisions make the consent decree particularly interesting. The injunction requested a one-time Abbott payment to the U.S. Department of the Treasury of $100 million, an amount derived not by mathematical calculation, but because “FDA believed the amount to be large enough to attract industry’s attention . . . and to serve as a useful deterrent.” That penalty represented a significant portion of Abbott’s profits generated from the sale of violative products (5).

Lost in the shadow of the fine were additional punitive damages and the as-yet-to-be-determined cost of remediation for the products taken off the market. Abbott was required to either validate its manufacturing processes and improve its corrective and preventative action system within FDA-approved time frames or pay substantial fines. In addition, Abbott was required to pay a fixed percentage of its gross revenues generated by the sale of any “medically necessary” products not validated within one year of the decree entry. In 2000, FDA imposed a $30 million fine and consent decree on Wyeth-Ayerst, and most recently reached a $500 million agreement with Schering Plough. Today several large companies face an increasing number of warning letters; speculation on the identity of the next consent decree recipient is rampant.

RICO. In the early 1990s, FDA was at odds with another large pharmaceutical company. Discussions were going nowhere; then FDA raised the specter of a Racketeer Influenced and Corrupt Organizations (RICO) accusation (10). The company ceased arguments, closed down several facilities, and undertook voluntary efforts to resolve its problems. The 1970 RICO law has the goal of busting “criminal enterprises.” RICO allows the plaintiff (the U.S. government) to
receive triple damages, and it extends the statute of limitations to 10 years after a crime is committed. RICO was designed by Congress to crack down on organized crime, drug dealers, and smugglers. More recently, it has been used to indict street gangs, HMOs, tobacco companies, law firms, and medical practices. The rules have changed. These examples show that FDA’s rules of engagement have changed and that management needs to recognize the developing trends. Increasing demands on regulatory agencies (and the global harmonization and “leveling up” of requirements) make the core operations of pharmaceutical manufacturers increasingly vulnerable. Corporations, directors, officers, and executives are increasingly at risk, individually and collectively. Shareholders, regulators, and society expect certain standards of conduct, and they are willing to promulgate these expectations into legal proceedings. Shareholder derivative suits are routinely targeted at officers and directors. Managers are now held to higher expectations and are beginning to suffer swift, personal consequences for their failures. This is a particular dilemma for the pharmaceutical industry in which the costs of compliance are receiving increased scrutiny from investors while regulators gather at the gate.

Controlling Costs
In the search for greater efficiency and increased economies of scale, management consultants create visions of future operating environments with increased control spans, well-suited for outsourcing and downsizing to “correct” organizational deficiencies resulting from overstaffing, over-managing, and redundant headcounts. Management seized the opportunity to make leaner companies, better focused on their activities. Cost and personnel reductions are commonplace, and new technologies are offered as solutions to every corporate difficulty. Initial returns from these measures were promising, and metrics (such as shareholder value) trumpeted the successes.

The reality, however, is that those measures were valid only where inefficiency existed; the syllogism ultimately fails on its own logical precept. In operations, where management directives are translated into activity, capacity is finite and resources are usually constrained. At this level, the paradigm promises not unlimited potential, but diminishing returns and possibly — the ultimate failure — collapse. Operations management is then compelled to devise local solutions for accommodating the overloads and shortages, usually by prioritizing purchases and personnel according to the most immediate and pressing problem. With this cost cutting, organizational charts no longer remain hierarchical structures with layers of reporting relationships. Suddenly, managers have 10–15 people reporting directly to them, and such managers begin to lose the day-to-day control that the hierarchical structure had provided. This ensures that only the proverbial squeaking wheel gets oiled. “Do more with less” is a recurring theme throughout industry during the past decade. The risk and liability assumed by the enterprise, its senior management, and even its outside directors escalate in direct proportion to the actions of its line managers.

Risk management plans. A 1999 PriceWaterhouseCoopers survey of senior executives found that in better-controlled organizations, the management and control of financial and business risks for all operating units are a strategic priority of the board and senior management (11). The survey identified the need for effective risk management integrated throughout the enterprise by aligning objectives, risks, and controls. Implementation starts at the top: Boards and CEOs must clarify and prioritize their business objectives, then each successive management layer must establish and prioritize objectives that are synchronized with the company-wide plan.

After a risk management plan is in place, the next step is to identify and prioritize related risks. With clarified objectives and prioritized risks, the adequacy of existing controls can be determined and necessary improvements designed. Risk and control alignment plans require regular reassessment by the management and employees of each unit. In doing so, staff assumes “ownership of the process.” Periodic reviews by auditors, regulators, and compliance personnel are not a substitute for company reassessments. This same process is applicable to regulatory control and compliance initiatives within the pharmaceutical and medical device sectors. The PriceWaterhouseCoopers survey found a clear divergence in perceptions about risk management control held by different levels of management and nonmanagement employees (11). In general, boards of directors and top management set appropriate business objectives and hold the right values. But such leaders fall short in creating corporate cultures in which all employees understand the objectives and execute their day-to-day tasks in accordance with those values. That disconnect between upper management and line staff is explored in the “Risk Management Perspectives” sidebar.

Preventing Quality (Mal)Practice
Conducting internal quality assurance audits is an established practice within the pharmaceutical industry and is recognized under U.S. regulations. Beyond the requirement to establish procedures for and
to conduct such audits, management has the responsibility to review audit results. When audits reveal situations that fail to comply with quality system requirements, corrective action must be taken. Quality system regulations (QSRs) require management with executive responsibility to establish a company-wide commitment to quality. Manufacturers are required to provide adequate resources (including internal quality audits) to meet the expectations of the regulation. QSRs require verification or validation that corrective and preventive actions are effective. FDA inspectors are trained to solicit information (during routine investigations) regarding the involvement of a company’s senior management. Clearly, FDA expects executive management to be involved with and responsible for all aspects of the quality system.

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**Quality audits.** Most pharmaceutical companies perform quality audits of their suppliers, contractors, and internal operations. Additionally, many businesses and consultants provide professional, independent third-party audits. Quality audit practices are well recognized within the industry, and such inspections follow the systematic approach laid out in the “Quality Audits” box.

Quality audits are focused in both their performance and their application. The results are exempted from regulatory inspection unless FDA alleges in its request to view internal audit findings that it is doing so “for cause.” Seldom do internal audit findings leave the protection of the operations department, and rarely are they reviewed by the company’s executives — the very individuals who are on the liability firing line.

Management’s task is to effectively bridge the gap between its objectives and values expressed at high levels and the processes and behaviors exercised at lower levels. Management needs to be aware of the regulatory dangers inherent in their business (as described in the “Danger! Danger!” sidebar). When the risks are enumerated and the gap between objectives and processes rectified, the strategy should be written into a coherent compliance risk management plan. A successful plan must ensure that the company and its people are protected from regulatory sanctions.

**Electronic compliance.** The enactment of the Electronic Records; Electronic Signatures rule adds further risk exposure (12). FDA’s enforcement policies on electronic records and signatures are largely undefined, and the industry has spent two years pretending the rule doesn’t apply. The regulation, however, sets forth specific controls on the use of electronic records and includes strict administrative controls on electronic signatures. FDA has stated publicly that the risks of falsification, misinterpretation, and data changes that leave no evidence trail are higher with electronic records than paper records. Therefore, FDA requires specific controls that prevent such tampering.

Companies that use electronic modalities to capture information are required to have those protective controls in place, but the nature of those controls — the logical, procedural, and physical methods that meet those requirements — are not strictly specified in the rule. Clearly, the regulators have expectations of the industry and have placed the burden on the companies to develop and establish appropriate controls to maintain record and signature integrity.

**Protective Compliance**

Proof of compliance with regulatory requirements and with ethical standards needs to be visible to the boards of directors and senior executives of the industry’s companies because increasingly they are being held accountable and personally liable for violations. In complex and decentralized business environments, companies must institute consistent, enterprise-wide compliance policies and procedures to prevent litigation and damaged reputations. Shareholders, legislators, investors, regulators, customers, and the public demand accountability and effective controls. Proactive risk assessment and sound risk management enable companies to protect their market position. The challenge is to focus compliance on actual danger points in a company’s processes, avoiding expensive blanket coverage for every risk.

Regulatory risk assessment is set within the context of broader business risks, risks such as product recalls, key development failures, process quality in remote locations, and marketing practices that fall below industry standards.

**Compliance specialists.** Because companies are “doing more with less” (and thus increasing their risks), regulatory compliance specialists are often needed to perform independent risk exposure assessments. Specialists can assess regulatory adherence and quickly identify gaps that, when corrected, significantly reduce risk exposure. Unfortunately, large pharmaceutical companies often feel that they have the internal resources to manage their operations. As a result, the company’s culture drives the risk management process, and the company can expose itself to increased regulatory risk without realizing it. Smaller companies often lack the knowledge or the resources to make the necessary risk assessments. In both cases, third-party compliance specialists can be effective and cost efficient.

**Liability coverage.** Independent assessments make particular sense when companies seek recall, liability, or director and officer insurance coverage. Liability carriers need to be aware of the changing regulatory environment in the pharmaceutical industry, and they must have some means of assessing a company’s ability to bridge its high-level objectives with its lower-level execution. The benefits from routine use of regulatory specialists and the inclusion of regulatory assessments in risk management coverage are self-evident and highly recommended.

Large pharmaceutical companies are often self-insured. Financial risk management in these companies is well-established, and officers and directors...
frequently oversee a vast network of treasury set-asides and insurance funds. They are not, as Abbott’s experience shows, immune to liability, and boards of directors would be well advised to seek independent verification of their exposure. Smaller companies, especially new start-ups, are not so fortunate. They lack the deep pockets of big pharma, and they may lack the sophisticated risk management tools used by their more established competitors. The more prudent companies pay risk management experts and liability carriers to protect them from their liabilities; the less prudent run the risk gauntlet at full speed, often ignorant of their status.

The concerns that must be addressed are not whether underwriters appreciate the new environment and incorporate new regulatory compliance paradigms into their underwriting process. The proper implementation of those baseline concepts should identify a GxP compliance program that ensures control over operations, sufficiently documents these operations, and guarantees the integrity of the data generated. With changing risks come changing needs that protect against negative consequences. FDA’s emboldened enforcement following Abbott’s consent decree puts industry on notice that fines and penalties directed against individuals are the “sanction du jour.”

If a company does not control its processes, those processes will almost certainly go out of control. As a corollary, if a process is out of control, an FDA inspector will eventually find it. Compliance is a serious and significant aspect of what pharmaceutical, biopharmaceutical, and medical device companies do. It is a fundamental part of business and one that can have far-reaching consequences for the financial health of a company. Compliance is a business component that deserves as much attention, excellent planning, and flawless execution as any other. Done well, the controls offer competitive advantage, company growth, and financial health for shareholders. Done poorly, the lack of controls can interrupt a company’s supply chain to its customers, cause long-term decline of its credibility, and in extreme cases, result in the ultimate demise of the business enterprise. The companies that emerge as winners in the new millennium will be those that embrace compliance as a core business process.

Suggested Additional Reading

References
(3) “Creation of the Food and Drug Administration,” online course (Medical Research Management, 2001), www.cratraining.com/online/chapter1new/maintext.asp.