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If a process is out of control, an FDA inspector will find it, eventually. Companies that emerge as winners will be those that embrace compliance as a core business process. Systems models provide strategic competitive advantage.

## Beyond QSIT

In January 2001, FDA began piloting a new “systems approach” inspection program. Much like the Quality System Inspection Technique (QSIT) program for medical device inspections conducted under Center for Devices and Radiological Health (CDRH), the aim is for faster, better-focused, and more efficient GMP audits. Under the pilot, investigators perform “abbreviated” inspections that audit companies’ quality systems and one or more other systems. In the face of shrinking field resources that make it impossible to inspect drug makers every two years as required by law, FDA is considering adoption of the CDER pilot program for all districts.

FDA’s rationale is simple: to promote faster, more efficient inspections — and, based on preliminary metrics, more effective inspections as well. Agency officials evaluating the program found that the six district offices were able to inspect 17% more drug manufacturing facilities during the first six months of 2001 than in the same period in 2000. In addition, inspections under the pilot took less time, averaging 12 fewer hours per inspection. Twenty-three percent (35) of the pilot’s 155 inspections fell into FDA’s most serious category — Official Action Indicated (OAI); 62 were classified as “Voluntary Action Indicated” (VAI); and 58 were coded as “No Action Indicated” (NAI). Normally, OAI inspections are only about 5% of all inspections (1).

The systems approach, however, is much more than a force-multiplier for FDA. It serves as a tool for companies to use to their advantage. The systems paradigm is a way of thinking about the strategic environment: how to develop processes that achieve strategic goals. This paradigm is a tool that forward thinking organizations can use to design their capability to analyze tactical and strategic environments; develop and enact strategies in response to environmental demands; and sustain an adaptive and productive organizational culture.

This article highlights some of the strategic leadership opportunities that organizations can use to enhance their

knowledge gathering to ensure compliance in the new environment.

### **Systems: Essential Properties**

A system is a set of two or more elements that satisfies three conditions: The behavior of each element affects the behavior of the whole; the behavior of the elements and their effects on the whole are interdependent; and subgroups are formed, each of which affects the behavior of the whole and none of which independently affects it.

The essential properties of a system taken as a whole derive from the interactions of its parts, not the actions of the parts. A system cannot be divided into independent parts. Every component of a system has properties that are lost when separated from the system, and every system has some properties — its essential ones — that none of its parts do. Thus, when a system is taken apart, it loses essential properties and because of this — and this is the critical point — a system is a whole that cannot be understood by analysis alone.

The key to systems thinking is *synthesis* or *synergy* — putting things together — just as *analysis*, or taking them apart, was the key to Industrial Age thinking. They are complementary processes. Analysis focuses on structure; it reveals how components work. Synthesis focuses on function; it reveals why components operate as they do. Synthesis looks out of components, and analysis looks into components. Analysis yields knowledge; synthesis yields understanding. This is the classic difference between deductive and inductive reasoning. Systems thinking essentially reverses the three-stage order of analytical thinking, namely, decomposing that which is to be explained; explaining the behavior properties of the parts taken separately; and aggregating these explanations into an explanation of the whole (a synthesis).

In contrast, the three steps of a systems approach call for identifying a whole (the system) of which the component to be explained is a part; explaining the behavior or properties of the containing whole; then

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**CONTRASTING PARADIGMS**

**Old Paradigm: Analysis**

- Restricts collaboration
- Reinforces the past
- Dehumanizes
- Delivers data
- Obscures operations
- Reinforces status quo
- Isolates the company
- Generates big learning curves

**New Paradigm: Synthesis**

- Enables collaboration
- Enables continuous transformation
- Empowers
- Delivers know-how
- Generates insight
- Forces the pace of change
- Opens into the world
- Eliminates learning curves

explaining the behavior or properties of the component in terms of its role(s) or function(s) within its containing whole.

These two approaches (see “Contrasting Paradigms,” above) should not — but often do — yield contradictory or conflicting results: They are complementary. The performance of a system depends more on how its parts interact and interrelate than on how they act independently of each other.

Development of this complementarity is a major objective of systems thinking. If each part of a system, considered separately, is made to operate as efficiently as possible, the system as a whole may not operate as effectively as possible.

**FDA Systems**

FDA offers the following scheme of “Systems for the Manufacture of Drugs and Drug

Products” and references specific statutory sections of the regulations. The overall theme in devising this scheme of systems is the subchapter structure of the CGMP regulation, 21 CFR 211. Efforts were made to group whole subchapters together in a rational set of six systems that incorporates the general scheme of pharmaceutical manufacturing operations: quality, facilities and equipment, materials, production, packaging and labeling, and laboratory control systems.

**Quality.** This system assures overall compliance with CGMPs and internal procedures and specifications (subparts B, E, F, G, I, J, and K).

**Facilities and equipment.** This system includes the measures and activities that provide an appropriate physical environment and resources used in the production of the drugs or drug products (subparts B, C, D, and J).

**Materials.** This system includes measures and activities to control finished products; components including water or gases, which are incorporated into the product; containers; and closures (subparts B, E, H, and J).

**Production.** This system includes measures and activities to control the manufacture of drugs and drug products including batch compounding, dosage form production, in-process sampling and testing, and process validation (subparts B, F, and J).

**Packaging and labeling.** This system includes measures and activities that control the packaging and labeling of drugs and drug products (subparts B, G, and J).

**Laboratory control.** This system includes measures and activities related to laboratory procedures, testing, analytical methods development and validation or verification, and the stability program (subparts B, I, J, and K) (2).

**Into the Future**

Good systems provide standardized and structured information flow and certain attributes that are particularly desirable to organizations. When properly implemented, systems function as a memory device that removes the frailty of human memory as a process variable. Systems also function as a buffering device to ensure continuation of the process at a defined or desired rate rather than allowing it to fluctuate with demand or the rate of input. By functioning as a queuing mechanism, systems allow pertinent data/information to be input without regard to ongoing processes. Another important

attribute is what the visual display systems afford to their users. The ability to see structured data allows individuals to organize their work efficiently.

Good systems are neither rigid nor self-limiting. They are dynamic, they are designed to handle “overload” conditions, and they can be adjusted. Systems should be designed to permit “omissions”: the simple rejection or nonacceptance of input. Adjustments vary

with particular circumstances. Faced with surges of demand or input, system owners can create new waiting lines or increase operating channels. Input can be filtered and/or prioritized to expedite more critical needs, and aggregating information according to predetermined arrangements can expedite some processes.

Change rather than stability engulfs us. We face endless demands for reinventing

and reinvigorating processes. These changes in the environment have strategic implications far beyond the realm of a single decision maker or even a top management team. The systems paradigm prompts management to analyze its organization’s ability to respond to issues. Each issue has a unique set of environmental factors that affect a company’s organizational system. Here are some points to consider.

- Which parts of the organization are designed to detect and analyze those factors?
- In light of these issues, can greater efficiencies be derived for analyzing inputs such as funding, raw materials, and human capital?
- Will the challenges posed by the changing environment require radically different transformation processes to generate and sustain the desired level of compliance and capability?

The answers to these questions depend on how you frame organizational capability. If you view the organization as a structural design, you won’t understand how processes are translated into capability. “Thinking” must be adjusted to a systems perspective to bring out those dynamics. From a systems perspective, organizations are collections of human and physical capital that exchange and process information, transform physical objects, and make decisions for the purpose of achieving some set of objectives related to their external environment. Systems should enhance existing processes in the organization and identify the need for additional environmental analysis to maintain the organization’s viability. If they don’t, they need to be redesigned.

At the strategic decision-making level, organizations are interpretation systems. This is better understood as *the process of translating events and developing shared understanding and conceptual schemes among members of upper management*. This necessarily goes beyond bureaucratic “staffing.” Organizations support leaderships’ interpretations by creating and maintaining their capability to gather information about environmental threats and opportunities and efficiently analyzing, evaluating, and internally synthesizing that information to support the decision-making process. Organizational interpretation processes are valuable to strategic decision makers on two counts. First, they reduce the ambiguity of

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strategic issues by analyzing data from the environment. Second, such processes reduce the uncertainty associated with strategic issues. The ultimate benefit to decision makers is that they can respond to issues more quickly, with higher quality decisions.

**A Core Process**

Compliance is a serious aspect of what pharmaceutical companies do — a core process — to remain in business. It is a fundamental part of the business process and one that can have far-reaching impact and influence on the financial health of an enterprise. It is a component of the business that deserves excellent planning and flawless execution. Done well, such controls provide competitive advantage, growth, and financial health for the shareholders. Done poorly, they can mean interruption of supply chains to customers, long-term decline of a company's credibility, and in extreme cases, the ultimate demise of the business enterprise.

Systems are a unifying force that facilitates the exchange of information between diverse and disparate disciplines. If an organization does not control its processes, they will almost certainly go out of control. As a corollary, if a process is out

of control, an FDA inspector will find it eventually. Those companies that emerge as winners in the new millennium will be those that embrace compliance as a core business process. Systems models provide strategic competitive advantage.

The systems paradigm is a "macro tool" to help make an organization successful. It provides an approach to analyze organizational capability by examining processes that occur in organizations. Applying this tool may be difficult for some to master, but it has value for many organizational issues in the strategic environment. It raises the level of requisite thinking from mere "quick fixes" to a structured evaluation of long-term impact. Emphasizing system concepts as a tool places greater responsibility on leadership to use that tool to achieve strategic outcomes efficiently and favorably for the organization.

**Reference**

- (1) Center case management and guidance branch chief F. Blumenschein at a Parenteral Drug Association (PDA) regulatory conference in Washington DC, 10 September 2001.
- (2) Center for Drug Evaluation and Research, *Compliance Program Guidance Manual for FDA Staff: Drug Manufacturing Inspections Program 7356.002* (FDA, Rockville, MD, February 2002). Available at [www.fda.gov/cder/dmpq/compliance\\_guide.htm](http://www.fda.gov/cder/dmpq/compliance_guide.htm). **BP**