Advantage Management

Shortening the Time to Decision as a Way to Shorten Time to Market

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Reducing the time, money, and personnel expended in developing new drugs is a perennial discussion topic among pharmaceutical industry thought leaders. New products are estimated to cost developers between $350 million and $500 million, and each day's delay in securing regulatory approval reduces future revenue by an estimated $1 million. The steps toward achieving competitive advantage by reducing cycle time and aligning concurrencies at each phase of the development process are categorized under the umbrella of time-to-market. The need to manage that process is mandated if not intuitive. Those who recognize trends and technological applications early and position themselves to participate throughout the power curve will reap the greatest rewards. So, here—based on new enabling technologies—we propose time-to-decision as the optimum response (Figure 1).

Organizations that manage knowledge and technological advantage effectively can shorten their time to decision and thus shorten their product's time to market.

Trumpeted by consultants as the true metric of performance, time-to-market is readily accepted by senior managers as a convenient benchmark to parade before analysts and shareholders. It is the subject of complex methodologies, risk management models, and numerous cookie-cutter business process solutions. But the reality is that this metric is neither conceivable nor measurable to the very employees charged with translating strategic objectives into direct action. To them, time-to-market is a series of arbitrarily assigned milestones posted on a Gantt chart. Compounding this operational difficulty is the reality that these milestones are usually unrealistically backfilled and aggressively assigned by successive layers of management using only best-case scenarios.[1] We know of one project for which the projected NDA (new drug application) filing date became so unrealistic that it lowered the morale of the project team to the point that they began working on other projects.

Time-to-decision

Time-to-decision is a concept based on existing processes and new technologies. It approaches time-to-market from a different perspective, concentrating on the process from within and focusing on improving the decision process at each successive control point. Control points are characterized by decisions and the information upon which those decisions are made. The timeliness and the accuracy of the data can expedite, impede, or, in some cases, negate the critical response. The organization that best manages the process, associated systems, and organizational culture by enabling and empowering decision makers with each successive individual decision achieves true competitive advantage. Time-to-decision is, therefore, a significant critical success factor in time-to-market. The imperative is to accelerate that process by providing the necessary tools for individuals to reach each step of the decision-making process.

Data is the asset. The average new drug application (NDA) can contain up to 300,000 pages or more of information. That information is accumulated during a 12- to 15-year development program for a new drug. In the past, the data generated during clinical research was recorded on paper or through hybrid paper-electronic systems. With the advent of 21 CFR 11, the landscape has changed and will continue to change markedly as more and more electronic capture takes place.[2] This is true for every section of an NDA—preclinical, toxicology, chemical development, metabolism, product development, clinical, chemistry, manufacturing and control, and regulatory. It will require that organizations reevaluate their information processes and controls, and their documentation of the process and controls, to demonstrate to the FDA that they have confidence that data submitted electronically is no less reliable than data on paper. This can be illustrated by looking at the clinical development and data capture process in depth.

Clinical development has one fundamental objective—to generate data to support an application. Data is the fundamental building block of information, which through appropriate communication becomes knowledge. Starting in the preclinical laboratories, computer-based models and instrumental analyses fuel the decision to move forward with clinical trials. During the trial, clinical observations, tests, and analyses establish safety and efficacy. During the postmar-

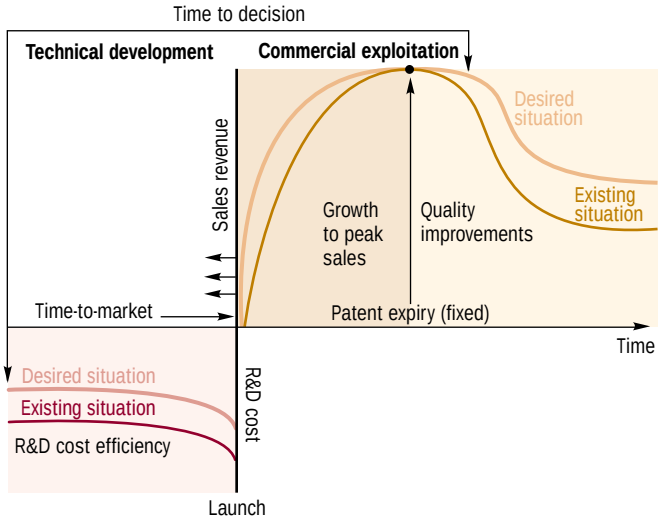

Figure 1. Advantage management can reduce R&D costs and can increase revenue by moving the launch forward, achieving faster growth to peak sales before patent expiry, and improving quality after patent expiry.

keting approval period, sponsors review manufacturing and analytical data along with adverse event reports and postmarketing study data to continually assess product performance and safety.

Until a few years ago, pharmaceutical companies relied almost exclusively on data from studies monitored by internal clinical staff. Generally, the data was created in diverse operational databases and stored with neither a metadata structure nor a standardized facility for searches and/or archiving. Lacking standard security controls, those records now fail the FDA usability criteria established by 21 CFR 11—the 1997 rule covering electronic records and electronic signatures.[2]

Clinical data capture

Clinical trials are about capturing data. Specifically, data capture is the process by which clinical researchers gather, review, and correct clinical data, which is then inserted into a database. To date, most data capture has relied on traditional methods that involve keypunch or scanned entry into defined fields. Emerging technologies—Internet data collection systems, handheld computers, voice recognition, wearable monitoring devices—are becoming alternatives for collecting clinical data. The perceived need for multiple studies and the increasing use of multinational megatrials are combining to produce nearly unmanageable quantities of data that must, nevertheless, be managed to produce the end product—the NDA.

Traditional data capture uses ink and paper with double-entry keystroke data entry. Remote data entry uses various electronic technologies, such as data-fax, interactive voice response, and notebook/laptop collection. Emerging technologies are enabling direct capture using Internet and intranet connectivity. Quality, speed, and cost are the variables that must be optimized.

Today's technologies can capture disparate data from multiple sources—laboratory instruments, graphical interfaces, documents, and more—and make that data usable. Generally identified as SDMS (scientific data management systems), these systems extrapolate data from a multitude of applications; store real, machine-readable electronic records; transform that data into human-readable reports; and store those reports in searchable databases. The software is designed to enable scientists to capture data from a range of instruments, lab applications, work stations, and controllers and then store it in a central database. It also aids in the collection, storage, search, retrieval, and compilation of electronic data. We propose extending this technology into the "total data" environment of drug development. The organization that most efficiently and successfully captures data and uses new technologies to produce its NDAs will be managing its competitive advantage.

21 CFR 11 is both the gatekeeper and the enabler of the electronic clinical data submission process (Figure 2). It not only places stringent controls on the use of electronic records and signatures, it also defines the requirements to make the capture, storage, retrieval, maintenance, and security of data acceptable to FDA. It is important to note that FDA also issued a guidance document (Computerized Systems Used In Clinical Trials) in April 1999 that explains how to meet FDA data quality standards when using computerized systems. It expands upon 21 CFR 11 by defining what SOPs should be available onsite, data entry requirements, suggested system features, security safeguards, system dependability (including validation of the software), system controls, personnel training, and records inspection. The introduction to the guidance indicates that it is intended for clinical sites, CROs, data management centers, and sponsors. Most experts agree that the guidance effectively adds another layer of documentation to the current clinical trial process.

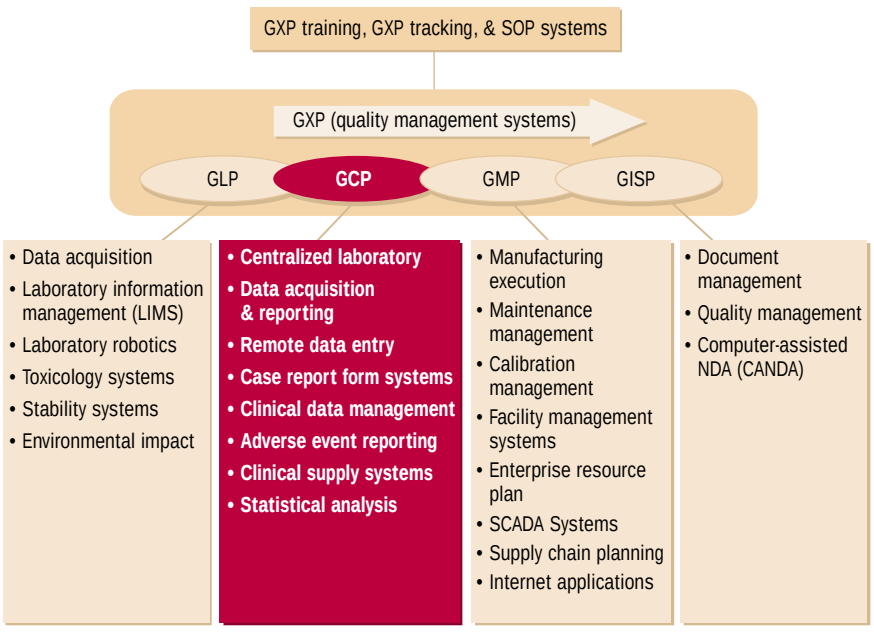

Figure 2. Applicability of 21 CFR 11 to GXP systems, including GISP (good information system practices).

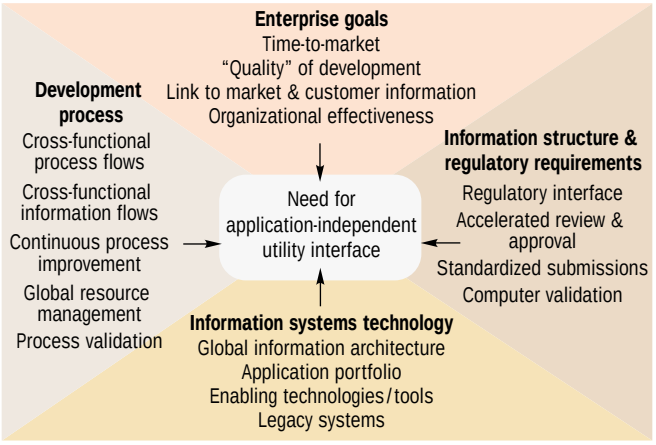

Figure 3. Formulate an information strategy with a universal, application-independent, clinical data interchange.

A second gatekeeper is an organization's knowledge architecture—that is, the way it transforms data into transferable information. Data is the fundamental building block of information, which becomes knowledge through communication. Currently, data is retrieved from operational databases, is generally unstructured (that is, stored in a variety of formats with incompatible encoding structures), and is stored with neither a metadata structure nor a standardized facility for searching or archiving. Industry formerly relied almost exclusively on data generated under its direct control, but today it more realistically relies on a mixture of internal and external data sources. In a very real sense, data is the commodity underlying alliances and outsourced services. Data is increasingly the commodity and asset upon which business relies. It is imperative to understand that the paradigm has already shifted.

The challenge

In recognition of that shift, organizations must establish knowledge architecture that acknowledges changing needs, meets regulatory compliance requirements, and paves the information superhighway for the new paradigm. Only then can organizations make full use of data acquired through CROs, joint ventures, strategic alliances, cross-licensing, other outsourcing arrangements, and outright purchases.

By itself, data is not readily usable. It must be searchable and retrievable regardless of its origin, and organized into a format that can be used to deal with the crisis of the moment. Organizations no longer have the luxury of spending inordinate amounts of time searching for information with nothing more to go on than someone's recollection that "we had a similar problem with a compound in development a few years ago." Nor can industry allow individual filing systems in departmental silos to become barriers to the free flow of necessary information. A 1 January 2000 *Wall Street Journal* article on Peter Drucker indicates that turnover in the pharmaceutical industry—relatively nonexistent in the recent past—has now reached 30%.[3] The fact that organizations may no longer be able to use people to retrieve information as they have in the past means that they must develop new ways of thinking. Information is power, but in the new competitive environment, the data, not the person who controls the information, is the real asset.

The major challenge of this decade for best practice organizations will be to capture and organize all of the information required for an NDA and change their organizational cultures to more openly share information on widely accessed systems. Open sharing of information raises other issues. Paramount among these is maintaining the security of sensitive information. 21 CFR 11 is very specific with regard to security controls—physical, logical, and procedural—and sets minimum requirements for electronic records and electronic signatures. Someone said that the information age is upon us. To stay competitive and improve time-to-market we must now manage the information age.

Application-independent data repositories

Traditionally, data has been stored in formats defined by commercial data management systems—which invariably use differing logical data models and thus make data interchange difficult. Most systems were optimized for double data key entry, not for integrating data from the emerging data-capture tools. Adding to the transfer and integration challenge is variation in design and nomenclatures between companies, countries, drugs, and even individual studies for the same drugs. Currently, the drive to an information strategy solution indicates the need for a universal clinical data interchange (Figure 3).

Such a solution is twofold. An organization must first structure itself to learn, then it must identify and use technologies that can help in unifying information from diverse origins.

Structuring to learn. Knowledge management is about thinking better, learning faster, and sharing information. The objective is to increase organizational effectiveness and create new synergies by increasing intellectual understanding and sharing on a timely basis—by identifying, optimizing, and extending an organization's ability to act decisively in each functional area by giving decision-makers more rapid access to expertise and information. To be effective, an organization must enable performance, reduce rework, improve focus, and eliminate work that can be automated.

Finding and using new technologies. Organizations must then identify and use technologies capable of unifying information from diverse systems of origin—possessing the ability to integrate, store, access, and manage dissimilar data within a single reservoir from anywhere in the corporation (in compliance with 21 CFR 11). This involves more than simply managing documents and storing information. Data resides everywhere today: internally and externally, in the laboratory and on the manufacturing floor, on network drives, in legacy systems, and on individual PCs. Diverse information systems and software applications cannot be easily integrated, accessed, or managed.

Someone must individually query the various systems for specific results or findings, then manually generate reports in a cut-and-paste manner—all while company resources continue to be diverted into the time-consuming efforts required to maintain and use disparate computerized systems. In practical terms, the information access and data management nightmare delays timely integration of information, thus increasing individual times-to-decision. The additive result is protracted time-to-market.

Managing organizational memory. The three main benefits of managing organizational memory are reduced time-to-decision,

improved processes, and enhanced decision-making.

Information software applications currently being deployed in analytical laboratories and manufacturing environments have the potential to manage organizational memory across an organization's value chain. Such an enterprise-wide solution can be the innovation that captures and harnesses an organization's data to drive the market process and thus create "advantage." The tenets of this new standard must be to

- enhance the organization's ability to capitalize on information generated in laboratories, clinics, and offices—both internally and externally—and readily access it through a standard format and central repository.
- improve the decision-making process while fostering a true enterprise of knowledge through effective management of scientific and business data.
- simplify regulatory compliance and meet internal and external reporting and auditing requirements.
- strengthen the competitive position of science-based companies by automating current practices to improve efficiency, accuracy, and quality.

Knowledge is an asset unlike any other—rather than succumbing to diminishing returns, it builds upon itself and generates ever-increasing future returns.

The path forward, as in any new endeavor, is not clear, but the process is easily configurable as a project. The acceptance of a framework and the commitment of senior management to the concept are the prerequisites for implementation.

A four-stage approach could provide a sequenced and orderly introduction.

Assess. During the first stage, "assess," detailed assessments of the organization, facility(ies), products, technologies, processes, and systems are performed. Analysis of this information, in relation to industry standards and the current regulatory environment, yields a deliverable that is, in turn, used to generate essential elements of information for the subsequent stage.

Articulate. This stage continues the discovery with focused data collection and detailed process mapping to provide a clear picture of the *as is* condition and to define a target, the *to be*, which will enable the project objectives. Typical deliverables define roles and missions within the scope of the organization's vision, identify functional interaction nodes for inter- and intra-company project management, propose realistic processes to implement compliance risk strategy, and identify performance measures and targets.

Authorize. This third stage transforms the recommendations into actual practice. It is during this stage that the organization implements the actions necessary to achieve the target environment.

Advance. During the final stage, periodic reassessment ensures continuing benefits to the organization.

Effective knowledge management

In nature, evolution of a species is normally a slow process. It occurs over many generations and is rarely discernible between consecutive generations. It is a series of minor changes or alterations, each of which is individually insignificant but in combination, can be dramatic. Dramatic changes in the landscape or the environment can expedite the process, but only with equally traumatic implications for existing organisms. Business organizations have many similarities to biological organisms. They are complex adaptive systems dealing with new technological landscapes and an increasingly competitive environment. Their evolution to meet new demands must be swift—and more importantly, it must be correct.

Value created by the generation of knowledge is rarely captured on corporate balance sheets. Yet, the use of processes, systems, and technology to spread information and best practices across a company transforms corporate fortunes in many tangible ways. Knowledge is an asset unlike any other. Rather than succumbing to depreciation or diminishing returns, knowledge builds upon itself and generates ever-increasing future returns. Unlike material goods, it does not change hands—it remains for everyone to share and use. There must, therefore, be a strategy in place to ensure its appropriate cataloging, storage, retrieval, and distribution through efficient communication.

Knowledge may be power, but it is a raw material that must be synthesized and processed to acquire value. Value is derived when knowledge is rooted in functional, well-organized, easy-to-manage information—structured secure data. The ability to reduce the manual labor required to support laboratory notebooks, clinical case report forms, nonclinical laboratory records, batch records, and regulatory filings and communications in the 120 countries where drugs are marketed would result in major process improvement and cost savings. Organizations that improve their processes will reap the rewards of effective knowledge management by improving time-to-decision across the organizational expanse and thus shortening time-to-market.

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