IBM Global Business Services

IBM Institute for Business Value

Pharma 2010

Silicon reality

Life Sciences and Pharmaceuticals

The IBM Institute for Business Value develops fact-based strategic insights for senior business executives around critical industry-specific and cross-industry issues. This executive brief is based on an in-depth study created by the IBM Institute for Business Value. This research is a part of an ongoing commitment by IBM Global Business Services to provide analysis and viewpoints that help companies realize business value. You may contact the authors or send an e-mail to iibv@us.ibm.com for more information.

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Introduction

Technology has long played an important role in the pharmaceutical industry (Pharma), but over the past five years the landscape has been transformed. In "Pharma 2005: Silicon Rally," the report IBM Global Business Services published in 1999, IBM examined various opportunities for automating the drug discovery and development process.[1] Web-based search portals and e-business were then in their infancy, the human genome was still being mapped, and the blockbuster model reigned supreme. Today, thanks partly to a massive increase in computing power, the human genome has been fully sequenced, and researchers are steadily unraveling the subcellular mysteries of man's life.

The molecular sciences will ultimately enable Pharma to change the very nature of the medicines it makes. But if the industry is to capitalize on the understanding of disease that is now starting to emerge, it will have to invest in new tools. This paper identifies the seven key technologies that IBM believes will drive innovation in the life sciences over the next decade. All seven technologies once belonged in the realm of science fiction, but they are fast becoming fact – the "silicon reality" to which the title of our report refers.

A proper return on investment

The emphasis that Pharma places on technology is obvious from the money it spends. Technology research firm META Group estimates that it invests between 4 and 5 percent of its annual gross revenues on hardware, software and related services.[2] Given global sales of an estimated US$492 billion in 2003, the industry's total expenditure on information technology (IT) is between US$19.7 billion and US$24.6 billion a year.[3]

Big sums are at stake – and they are rapidly increasing. Market analyst Datamonitor predicts that the top 11 pharmaceutical companies will collectively spend almost US$7.4 billion on IT in 2005, up from US$5 billion in 2000. Their overall IT expenditure over the same period will increase at a compound annual growth rate of 6.5 percent worldwide, peaking at 8.5 percent in North America.[4]

The scale of Pharma's IT expenditure is not a problem, as long as it delivers a positive return on investment. Yet few pharmaceutical companies can claim to have realized the full benefits of the money they have spent. This is sometimes true because they have focused on the wrong goal – they have looked for technologies that will do more things rather than technologies that will help them make sense of

the data they possess. Alternatively, they have failed to set clear strategic objectives, integrate applications or even explain how to operate a technology to the people who must actually use it.

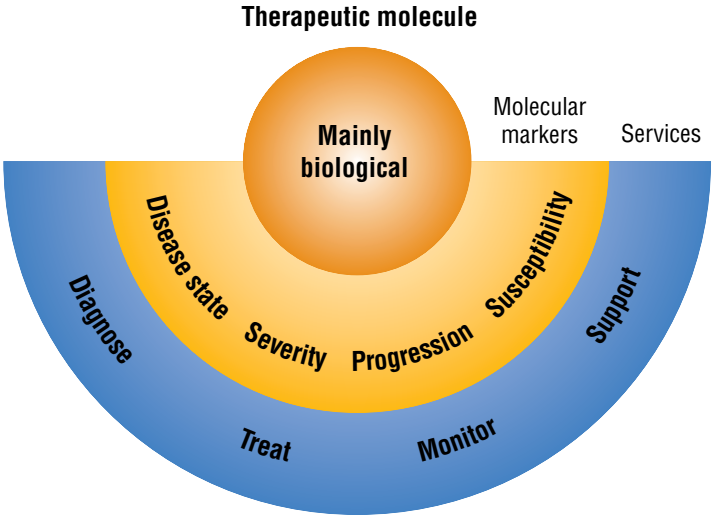
However, the situation is now changing. As Ludwig Siegele, the technology correspondent of *The Economist*, recently observed, "Companies everywhere are rationalizing their existing IT infrastructure and keeping purse strings tight."[5] Pharma is no exception. Most drugmakers have become much more cost-conscious, not least because they are under enormous pressure to deliver better returns for shareholders, who have seen the value of their stock plummet over the past few years. If they are going to invest billions of dollars in technology, then, they want to ensure that money is not misdirected.

The rise of targeted treatment solutions

It is already possible to spot the most promising source of future revenues. In "Pharma 2010: The Threshold of Innovation," IBM described how the molecular sciences will help the industry define diseases more accurately and create healthcare packages for patients with specific disease subtypes, rather than making one-size-fits-all drugs for patients with similar symptoms but essentially different diseases.[6]

These "targeted treatment solutions," as the report called them, will be mainly biologics. They will be made using biological methods of discovery and development, and they will be aimed at specific patient subpopulations – including, where appropriate, people who would benefit from prophylactic medication. They will measurably modify the diseases for which they are prescribed. And they will include a network of services for diagnosing, treating, monitoring and supporting patients (see Figure 1).

Figure 1. New definitions of diseases will result in the development of targeted treatment solutions.



Source: IBM Global Business Services analysis.

Targeted treatment solutions will also be manufactured, marketed and sold very differently from traditional, one-size-fits-all drugs. Biologics are more difficult to make than conventional chemical compounds, so much more care will be required in the manufacturing and distribution of such products. Moreover, demand for biomarkers and medicines that are targeted at patients with specific disease subtypes will be much smaller than for mass-market drugs, so they will have to be made in much smaller batches. In addition, the range of formulations and packaging will vary widely.

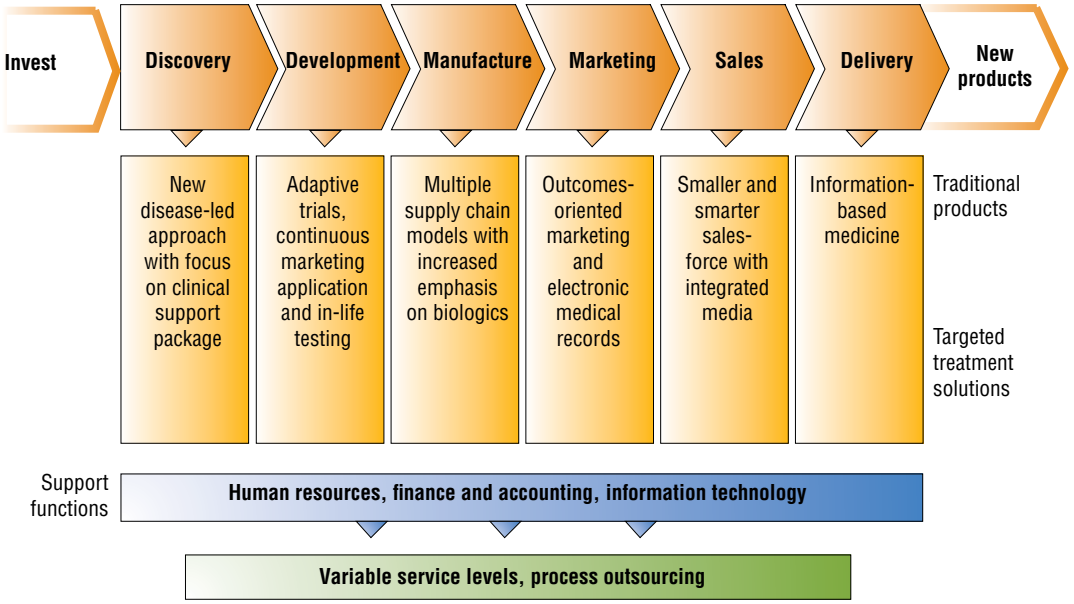
Similarly, the way in which targeted treatment solutions are priced and promoted will differ from the techniques that are used with traditional medicines. Targeted treatment solutions will be priced according to the clinical results they deliver; they will cover both the primary- and secondary-care markets; and a substantial part of their value will reside in the services that come bundled with them.

The need for such medicines is now widely recognized. Allen Roses, worldwide vice-president of genetics at GlaxoSmithKline, acknowledged as much when he noted in a recent newspaper interview, "Most drugs work in 30 to 50 percent of people. Drugs out there on the market work, but they don't work in everybody."[7] Dr Roses clearly believes, as IBM does, that the future of Pharma lies in being able to target drugs to a smaller number of patients with specific genes and disease subtypes, rather than in selling as many drugs as possible to as many patients as possible.

The need for a new business model

Although it is anticipated that targeted treatment solutions will eventually generate most of the industry's revenues, the transition will take some years. In the meantime, most companies will have to manage multiple product types. They will also need to adopt a new business model that requires changes at every stage in the value chain (see Figure 2). This model will not only affect their critical operations, it will entail new ways of performing daily activities such as accounting, human resources and IT. At present, the emphasis is primarily on transaction-processing, but most such support functions will ultimately be centralized or outsourced.

Figure 2. The new business model.



Source: IBM Global Business Services analysis.

Some companies have already begun to prepare. For example, in November 2003, Johnson & Johnson announced plans to consolidate the back-office operations of its five major pharmaceutical and biotechnology subsidiaries. The group also intends to divide the five subsidiaries into two streams: traditional drugs and biologics.[8]

Thus, one of the main challenges Pharma now faces is identifying which technologies are a prerequisite for making targeted treatment solutions, and which are essential for managing in the interim. In other words, what are the technologies on which Pharma *should* be spending its money? The next section of this report discusses the seven technologies that IBM Global Business Services thinks will be vital during the coming decade. The section after that elaborates on how these technologies will help the industry. The final section examines the changing role of IT.

Seven key technologies

IBM believes seven technologies will be key to Pharma:

- Petaflop and grid computing
- Predictive biosimulation
- Pervasive computing
- Smart tags
- Advanced storage solutions
- Process analytical technology
- Web-scale mining and advanced text analytics.

Some of these technologies have already reached the market, although they are not yet mature; others are still emerging. However, all of them should soon be available. These technologies are discussed below.

Petaflop and grid computing

Petaflop and grid computing are technically very different, but both will give the industry access to unprecedented levels of computing performance. The theoretical measure of a computer's speed is floating operation points per second (FLOPS). The fastest machine on earth today – the Earth Simulator at Japan's Marine Science and Technology Center – can perform over 40 teraflops, but this is nothing compared to the computing horsepower in the pipeline (see **Gene machine** sidebar).

A new generation of petaflop computers will enable Pharma to start doing large-scale biomolecular simulations. For example, the computation effort required to study protein folding is enormous. Proteins fold very rapidly, some as fast as a millionth of a second (microsecond). Although this is quick in human terms, it is a very long time for a computer to simulate. Even using a petaflop machine, it would take about three years to simulate 100 microseconds.[9]

Gene machine

In December 1999, IBM announced plans to build a supercomputer that will help biologists model the folding of human proteins. A prototype with only a fraction of the processing power that the final version will possess ranked 73rd on the list of the world's top computers in November 2003. But when Blue Gene® is completed in 2005, it will be 6 times faster and 10 times more compact than today's fastest supercomputers, and consume just one-fifteenth of the power per computation.

Among other things, Blue Gene will explore how proteins sometimes fold the wrong way. Scientists have found that when some proteins fold incorrectly, they aggregate and form fibrils. Alzheimer's disease, new variant CJD (the human form of mad cow disease) and cystic fibrosis are among the illnesses associated with protein misfolding.

Home remedy

Smallpox can be prevented with vaccines, but some people experience dangerous side effects. Since there is no treatment for anyone who has the virus, a third of all patients with smallpox die. The Smallpox Research Grid is a collaborative effort to find a cure. Launched in February 2003, it makes use of idle time on more than two million home computers. Volunteers from over 190 countries have already contributed over 39,000 hours of computing time. Thirty-five million potential drug molecules have now been screened against eight models of smallpox protein to see whether any of the molecules will bind to the protein and render it inactive. The results have massively narrowed the field of molecules that can be considered lead candidates for the next phase of research.

Petaflop computing involves bringing different processes together in one huge machine. Grid computing works the opposite way; it splits a computing task into discrete packages, which are distributed to numerous computers. The answers are then posted back to a controlling hub. This approach harnesses the idle computing power locked in a company's many desktops and servers or in computers linked to the Internet. Therefore, it is a very economic means of solving problems that can be broken up into millions of tiny parts. It also provides a cost-effective base infrastructure for connecting research scientists working at different sites and enabling them to share data.

One of the best known applications of grid computing is SETI@home, which uses computers to analyze data from radio telescopes to look for extraterrestrial civilizations. After funding for SETI, which stands for Search for Extraterrestrial Intelligence, was cut, researchers sought a new way to get the computing power they needed. More than four million subscribers now participate in the project.

Pharma is also tapping into the potential of grid computing to analyze sales and marketing data in realtime, perform protein-folding predictions, screen for DNA sequence matches and run sequence comparison algorithms. So, for example, Find-a-Drug is working on treatments for cancer, HIV and Severe Acute Respiratory Syndrome (SARS); Drug Design and Optimization Lab is screening target proteins for anthrax, Ebola and other infectious diseases; Compute against Cancer is studying the structure and behavior of cancer cells; and the Smallpox Research Grid is seeking a cure for smallpox (see **Home remedy** sidebar). IBM is also in the process of building the World Community Grid, which will be open to scientists around the world.

Predictive biosimulation

Predictive biosimulation is the use of computer modeling to put all the pieces of the biological puzzle together in a dynamic model that shows how they interact and work as a whole. It goes hand-in-hand with high-performance computing because it requires enormous computing resources.

A model cell

Indiana University's Center for Cell and Virus Theory is currently developing a computational model of the behavior of a cell and its response to chemical disturbances, gene deletion or mutation, and the presence of other cells. Karyote, as the model is known, includes genomic, proteomic, metabolic, and other experimental data and can be tailored to different cell types. It can be used to predict the speed with which a cell will react, its bioelectricity and pumping, and other membrane-localized processes.

Genomics, genetics, proteomics and metabolomics have generated vast amounts of data, but it is not yet possible to integrate this material in comprehensive models of human organs or bodies. Scientists can correlate changes in gene expression and protein synthesis with a particular disease state, but they cannot distinguish changes that *cause* a disease from those that are *caused by* the disease. Nor can they predict how those changes will affect the system as a whole. In short, they lack the biological context in which to interpret the data.

Predictive biosimulation addresses this problem by using *in silico* – literally, "in computer" – modeling to integrate all the relevant data, reproduce the control principles of a biological system and simulate how it will respond. Such models enable researchers to test hypotheses by "playing" with numerous permutations. Then researchers can identify potential molecular targets and compounds as candidates for treating disease.[10]

A number of organizations, mainly academic rather than commercial, are currently building biological models of cells or organs (see **A model cell** sidebar). But the development of industrywide standards – like Bio Sequence Markup Language (BSML), Micro Array and Gene Expression Markup Language (MAGE-ML), and Health Level Seven Clinical Document Architecture (HL7 CDA) – will make the integration of data from a wide variety of sources much easier.

Pervasive computing

Pervasive computing was famously first defined by the late Mark Weiser, former chief technologist at the Xerox PARC computer science laboratory. In 1991, he wrote: "The most profound technologies are those that disappear. They weave themselves into the fabric of everyday life until they are indistinguishable from it."[11]

Smarty pants

Electronics giant Philips has developed a prototype wearable monitor that can warn patients with health problems and even call for help if it is linked to a wireless technology like Bluetooth. The device can be built into common items of clothing like bras, pants and belts. It is designed to be worn continuously, tracks a particular body signal (such as the heart rate), and can store up to three months' data. All the active electronics are incorporated in a small module that slips into a pocket in the garment and can be removed for washing.

Meanwhile, Triumph International is developing a special bra with a "pulse beat." Vivometrics, a U.S. start-up, has designed a lightweight "Life Shirt" that contains electrodes and physiological sensors that can record more than 40 vital signs, including fluid in the heart, breathing rate and oxygen consumption. Sensatex, another U.S. operation, has designed a similar product – a shirt made of an electro-optical fabric that transfers data from the wearer to the garment. A transceiver on the shirt records the information and sends it to a wireless gateway, from which it can be transmitted to a doctor.

Weiser envisaged an era in which everyone and everything would be connected through numerous intelligent devices linked to an all-embracing communications network. Some of those devices would be the thousands of computers people access in browsing the Internet. Others would be embedded in walls, furniture, equipment, cars, clothing and even the human body. Today, man is close to fulfilling Weiser's vision. Forrester Research estimates that about 870 million embedded devices will be hooked up to the Internet by 2006 – rising to 14 billion by 2010.[12]

A growing number of "smart" healthcare devices are already reaching the market. Bang & Olufsen, for example, has developed a "pill box" that reminds patients when to take their medicine. AARDEX has developed a bottle monitor that records the date and time the bottle is opened and measures how well a patient has complied with his or her drug regimen. Vitaphone has designed a mobile phone that simultaneously functions as a heart monitor. Given Imaging has developed a wireless digital camera so small it can be swallowed. And several companies are experimenting with intelligent biomedical clothing (see **Smarty pants** sidebar).

The networks that are needed to transmit the data that such devices collect are also becoming much more robust. The first, third-generation (3G) networks offer an enormous increase in bandwidth and theoretically can transmit data at a speed of as much as 2 megabits per second (Mbps). Wi-Fi (the wireless network protocol known formally as 802.11) runs even faster – the most common standard can transmit data at a blistering 11 Mbps. Access is limited except in large urban areas, and the encryption system is relatively easy to break. But both these problems should soon be resolved.

In the longer term, ultra wide broadband (UWB) – a technology that uses brief, lower power pulses across a wide spectrum – could dispense almost entirely with the need for wires. UWB is still in its infancy, but it provides a bandwidth of many hundreds of Mbps at short distances and uses very little power. Hence, it is ideally suited for portable devices.[13]

Smart tags

Smart tags – or radio frequency identification (RFID) tags, as they are sometimes called – enable physical objects to be identified at any checkpoint in the value chain. A microchip containing product information that includes a unique identification number and a tiny antenna is attached to an item. The data it captures is then transmitted via radio waves to a reader, which converts the data into a form that can be passed on to a safeguarded database and accessed through the Internet.

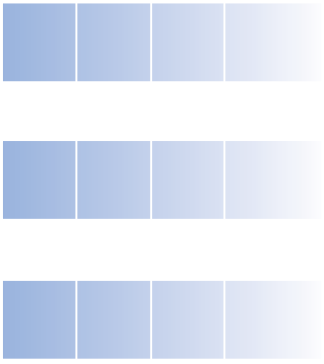
Smart tags are thus far more than glorified bar codes. They can be read as long as they are within range of a reader, rather than having to be swiped by a scanner. They can hold hundreds of characters of information, whereas bar codes can only hold 12 to 15 characters. And they can be used to trace the entire lifecycle of the goods to which they are attached – including how and where those items were made, shipped, consumed and disposed of.

The technology is proven but has not yet been fully exploited, partly because global software and network standards are still being developed, and tags and readers are still quite expensive. However, several organizations, including EPCglobal, are already tackling these difficulties.

Greater government interest and endorsement from leading retailers are also likely to fuel its popularity. U.S. Health and Human Services Secretary Tommy G. Thompson favors using new technologies to track dispensing. Wal-Mart, which operates the fifth largest pharmacy chain in the United States, has announced that it will require its top 100 suppliers to tag all the pallets and cases they ship to its distribution centers and stores by January 2005. And Forrester Research estimates that, by the end of the same year, about five billion consumer products will carry smart tags – with high-value healthcare products being among the first items to which the technology is applied.[14]

Advanced storage solutions

Pervasive computing and smart tags will generate enormous quantities of data, as will some of the other technologies identified. Fortunately, new storage media and systems will provide the means to keep such information.



Magnetic media (ferrous or nickel oxides) are both cheap and reliable, but there is a limit to the volume of data they can hold because the individual particles that store the bits become so condensed that the laws of physics break down; this problem is known as superparamagnetism. The limit of ferrous magnetic media storage is thought to be about 100 gigabytes (GB) of data per square inch, although most commercial products are currently only capable of holding about 25 GB per square inch.[15]

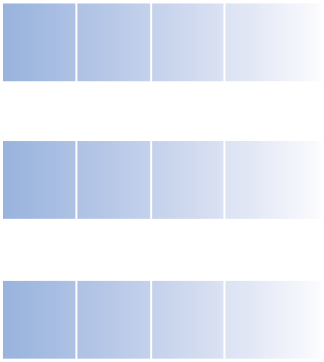
Optical storage (CDs and DVDs) has more potential, and some companies have experimented with holographic storage, but plastic media offer even greater promise. One such instance is Millipede, which was developed by IBM Research, although it is not yet commercially available (see **Back to the future** sidebar).[16]

Back to the future

Millipede uses thousands of tiny needles to make marks little bigger than an atom on a thin plastic film; the presence or absence of a pinpoint corresponds with the ones and the zeros used to store binary digital data. The result is akin to a nanotech version of the data processing punch card developed more than a century ago, but with two crucial differences: the Millipede technology is rewriteable for up to 10,000 read/write cycles (which is about 10 years of service), and it can store one terabyte per square inch – the equivalent of putting 25 million printed pages on a surface the size of a postage stamp.

New tools for handling large volumes of data are also emerging. They include storage area network (SAN) file servers, storage virtualization systems and storage grids. SAN file servers enable users to access information regardless of where it is located and how it was generated. In other words, they function as a common "language" through which files that have been produced on incompatible operating systems can be read. Storage virtualization separates the function of data storage from the procedures and physical process by which the data is stored. Some of the systems currently on the market are based on storage pools and disk-like interfaces. Users simply request the disk space they need from the pool, while the intervening layers of software and hardware manage the system so it functions like a single attached disk. Storage grids take the concept of virtualization a stage further by integrating internal and external storage facilities in a virtual storage pool.

Similarly, smart enterprise suites, as technology research firm Gartner has dubbed them, provide a consolidated approach to content management both within and between organizations. They incorporate content management systems, portals, and knowledge management and collaboration tools in one powerful, integrated system rather than using separate solutions, as is largely the case today.[17]



Two regulatory changes also may help fuel development of more sophisticated content management and archiving technologies. The FDA has introduced a new science- and risk-based approach to the regulation of pharmaceutical manufacturing and product quality, which will massively increase the amount of manufacturing data that must be captured, processed and interpreted. Meanwhile, the Sarbanes-Oxley Act of 2002, billed as the most sweeping reform of the U.S. securities laws since the 1930s, imposes much stricter reporting requirements on all public companies. Among other things, they must now retain all relevant audit and review "records" – including electronic communications such as e-mail and instant messages – in unaltered form for five years.

Process analytical technology

The FDA's new initiative, "Pharmaceutical cGMPs for the 21st Century," also accounts, in part, for the significance of process analytical technology, or PAT. PAT is comprised of testing equipment that allows manufacturing companies to monitor their manufacturing processes continuously both *in situ* and in line.

Pharmaceutical companies have traditionally manufactured drugs within specific tolerances and performed regular quality checks with laboratory testing of batch samples. But the FDA is now encouraging (and may eventually stipulate) the use of PAT – which it defines as "timely measurements…of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality."[18]

Monitoring the critical attributes of a manufacturing process with PAT verifies that the process is stable and will produce the desired results. It also has various advantages over conventional offline laboratory testing. It enables a company to test the quality of the manufacturing process in realtime rather than historically and to test continuously rather than intermittently via samples and post-manufacturing quality controls. This ultimately saves money because it is cheaper to adjust or stop the production line immediately than to discard goods that have fallen outside the agreed tolerances.

PAT requires sophisticated instruments (such as in-line chromatographs, near infrared, Raman and mass spectroscopy). It also requires realtime analysis and decision-making software as well as immense data storage facilities. Continuous realtime or near-realtime monitoring generates vast quantities of data, and, in the case of pharmaceutical manufacturing, those data must be preserved for many years.

Web-scale mining and advanced text analytics

The last key technology discussed here is Web-scale mining – using intelligent algorithms. A new generation of data- and text-mining tools is being designed to enable organizations to scan the entire World Wide Web. These tools will trawl through every public source of digital information, including bulletin boards, chat rooms, news groups, personal Web sites and electronic media, as soon as it becomes available.

The Internet contains billions of pages and is growing at a rate of about 50 million pages a day. Eighty percent of the data come in unstructured formats like e-mail, spreadsheets and graphics – which is why extracting useful insights from the Web has been compared to trying to drink from a fire hydrant.[19] But these new data-mining tools will read and understand text, and use natural language to make correlations between words. They will be able to extract trends, patterns and relationships; track topics of interest; and pick up on "buzz" – the groundswell of opinion that suggests something is happening before it becomes very visible.

Early testing of one such tool shows just how powerful it can be (see **WebFountain** sidebar). A global energy company beta-tested an application designed to help it manage its corporate reputation. The company monitored the Web on a monthly basis to identify and track emerging global and local issues that could affect its business. The information it derived gave it a comprehensive view of how it was perceived and helped it determine how best to deal with important issues.[20]

WebFountain

WebFountain exemplifies the power of mining the Internet to pick up marketing and business intelligence. It combines supercomputing with advanced text analytics and sophisticated information management software to identify useful information from the vast quantities of data on the Web. The system has already indexed over three billion pages and stored two billion pages in multi-terabyte data stores. It covers most of the languages used on the Web, can mine 20 million pages a day and it is anticipated that it will have mined the entire Internet by the end of 2004!

But the potential benefits of text mining are arguably even bigger for Pharma. For example, one new text-mining tool has made it possible to analyze and mine MEDLINE, the U.S. National Library of Medicine's bibliographical database of references to articles in over 4,500 biomedical journals published throughout the world. The development of intelligent bioinformatic algorithms has also produced programs like Genes@Work, which analyzes patterns in gene array chip data, and the software used by deCODE Genetics, the Icelandic population-based genomics company, to identify disease genes. Tools that can map the genes associated with susceptibility to particular illnesses will be vital in developing targeted treatment solutions.

The implications for Pharma

This paper has identified the seven key technologies that IBM thinks will be critical for producing truly innovative medicines and securing a competitive advantage in the marketplace during the next decade. Let us look at the collective impact of these technologies on the life sciences industry.

Predictive discovery at the speed of light

Pharma has traditionally relied on academia for information about how specific diseases work and used knowledge that is in the public domain as its starting point for making new medicines. But the development of targeted treatment solutions hinges on a much more precise understanding of disease, including the mechanisms and pathways involved in particular disease states and the differences between related disease subtypes.

Therefore, companies will have to "own" all there is to know about specific diseases. They will have to mine increasingly numerous and disparate sources of information, using a wider variety of data forms, and they will have to search both inside and outside the traditional corporate boundaries. So, for example, when a company wants to identify candidate drugs, genes and proteins associated with a particular disease, it will need core text analysis and text-mining tools to search the patent registrations and medical literature for information about competing products (see **Mining and pattern recognition tools** sidebar). If a novel gene or protein sequence is involved, it will also need document clustering tools to search the gene banks and literature for cell functions associated with those sequences.

Mining and pattern recognition tools

Core text analysis: Extract and categorize terms, term relations and document contexts

Text search: Index and search for documents containing terms and relations

Document clustering: Browse search result documents based on topics

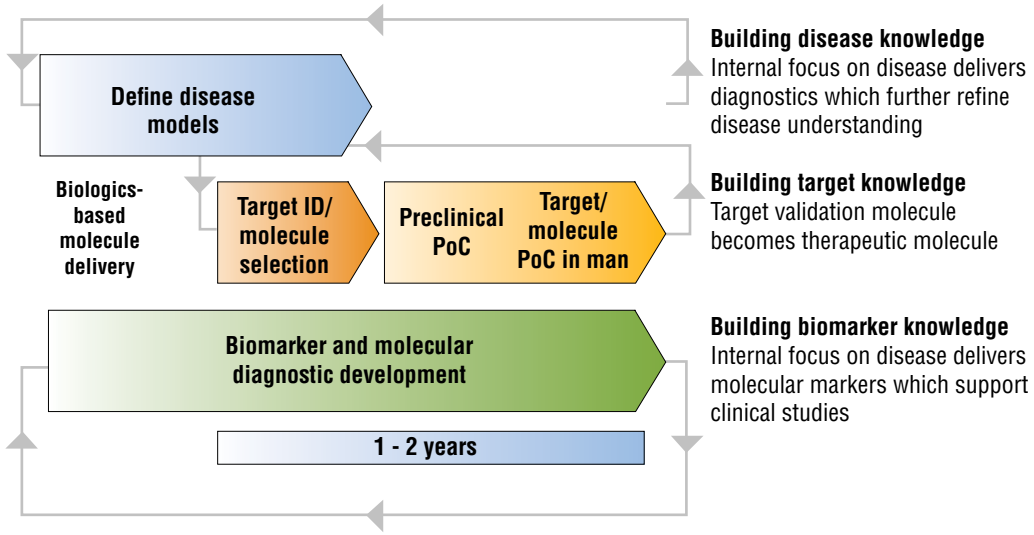
Text mining: Mine and view associations between categories of terminology

Similarly, when a company wants to model the interactions between a given compound and various genes or proteins, it will need core text analysis, text search, document clustering and text-mining tools to retrieve the relevant literature on micro array experiments and so forth. And when it wants to test a drug, it will need core text analysis and text-mining tools to correlate the outcomes with genomic and clinical data on individual patients.

One organization that is already using some of these techniques is the Translational Genomics Research Institute (TGen). As its name implies, TGen focuses on "translational research" – a relatively new field employing genome-wide array technology and computational biology to provide the data and tools necessary to identify the genes that play a role in hereditary susceptibility to disease. Together with its partners – Arizona State University, the International Genomics Consortium and IBM – and using Genes@Work, TGen has implemented a powerful supercomputing infrastructure that will allow it to map the molecular markers of cancer. In one of the first phases of the project, researchers will analyze the cells of cancer patients who were treated and responded well, and compare them with the cells of those who did not. The ultimate goal is to distinguish between genes in diseased and healthy cells.[21]

Proprietary knowledge about how specific diseases work will be vital. But if Pharma is to produce targeted treatment solutions, it will also have to adopt a *biological* approach to discovery – where it simultaneously accumulates knowledge about different disease pathologies, molecular targets and biomarkers (see Figure 3). Petaflop computing, grid computing and advanced storage solutions will be essential technologies in this respect. They will enable companies to use advanced data integration and middleware technologies to integrate and manipulate multiple, disparate sources of data and perform predictive biosimulation.

Figure 3. The discovery process of the future will be biologically based.



Source: IBM Global Business Services analysis.

Virtual phenotype

Biotechnology firm Virco has developed a drug-resistance test for HIV which works by creating a computer model of a patient's phenotype. The test reads the genetic sequence of the specific HIV virus with which an individual is infected, searches a large database of genotypes and phenotypes for samples with the same mutations, and uses the phenotypic data for the matched genotypes to produce a virtual phenotype. The phenotype is then used to predict which drugs will be most effective in fighting the virus.

Other industries have already learned the advantages of *in silico* modeling. Boeing famously developed the 777 jet using an online electronic prototype and only performed physical tests on the aircraft when it was ready to fly. Similarly, carmakers use crash dummies to test new car designs. Volvo, for example, has created the world's first "virtual" mother-to-be, which it is using to study what happens to pregnant women and their unborn babies when a collision occurs.

But Pharma has been slow to follow such leads. As Tom Paterson, co-founder of systems biology firm Entelos, put it: "If Boeing developed aircraft the way the pharmaceutical industry develops drugs, [it] would develop ten very different aircraft, fly them, and the one that stayed in the air would be the one [it] would sell."[22]

Of course, modeling the subcellular structure of the human body is an even bigger challenge than modeling the inner workings of an aircraft. Nevertheless, predictive biosimulation has a vital role to play in pharmaceutical discovery and development. It will enable companies to simulate the way in which diseases act and evolve, identify drug targets and pathways, and test drug candidates for efficacy and toxicity on large-scale computer models.

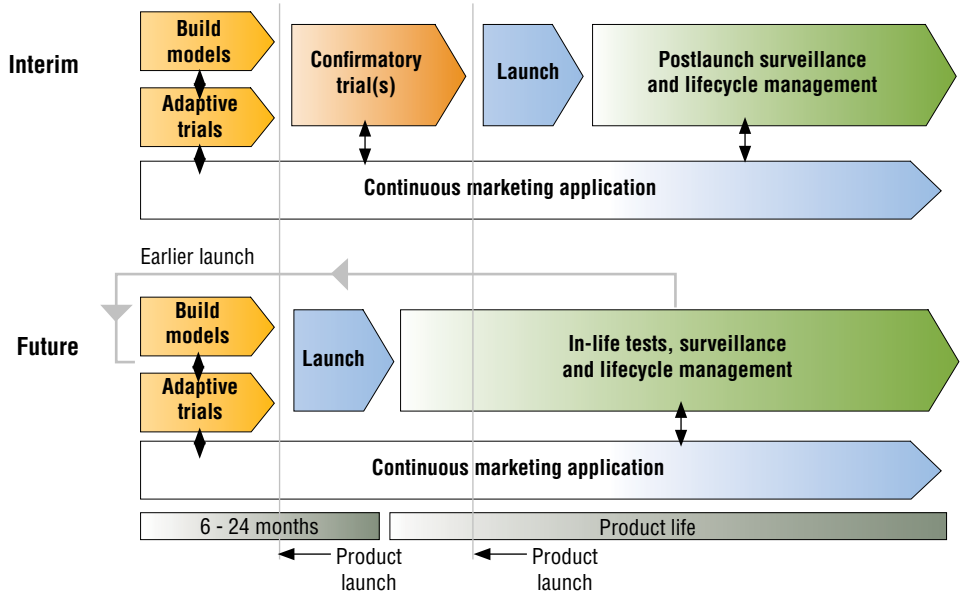
The industry leaders will probably build their own models so they can better understand the specific disease mechanisms on which they are working. But few, if any, smaller companies will be able to afford the considerable costs involved. Those with promising drug candidates will therefore have to test them by "renting" time on models that are designed and maintained by universities or specialist companies with an appropriate combination of life sciences and IT expertise.

In the long term, Pharma should be able to design and test drugs almost completely *in silico*. Predictive biosimulation will enable researchers to work with virtual patients and "tune" specific variables in a biological model to reflect common genetic polymorphisms or differences in lifestyle (see **Virtual phenotype** sidebar). Virtual patients will thus become the crash dummies of the life sciences industry. They will improve target validation, reduce lead times and attrition rates, and help make testing in man very much safer – both in the laboratory and in life.

The pervasive reality of clinical development

Clinical development will also undergo a huge transformation, and the new technologies will play a big part in facilitating the change. The many limitations of large-scale confirmatory trials – including timely patient recruitment, cost, inefficiency and inaccuracy – have been thoroughly documented. Fortunately, genetic stratification, adaptive trials, electronic data capture (EDC), in-life testing and continuous marketing applications will reduce or eliminate these problems (see Figure 4).

Figure 4. The development process of the future will include adaptive trials, conditional approvals and in-life testing.



Source: IBM Global Business Services analysis.

Clinical genomics (the diagnosis of patients based on genotypic and phenotypic data) and translational medicine (bench-to-bedside research, in which clinical science investigators use a discovery in the laboratory to diagnose, treat or prevent a specific disease) will make it possible to segment patients for trials. That, in turn, will promote the evolution of targeted treatment solutions.

Several major medical institutions are already building systems that will allow them to identify potential trial patients very rapidly. The Mayo Clinic has created an electronic archive of more than four million records from informed, consenting patients. UK Biobank aims to track the lifestyles and medical histories of 500,000 people in what will be the world's biggest resource for the study of the role of nature and nurture in health and disease. And deCODE Genetics has devised an integrated approach to drug discovery and development using population genetics to discover disease susceptibility genes and validate potential drug targets or diagnostic markers. With sophisticated data-mining tools and advanced data management systems capable of performing complex cross-patient correlations across demographics, diagnostics and laboratory results, these institutions will be able to help Pharma find patients with the "right" genotypes and disease subtypes for the treatments they are testing.

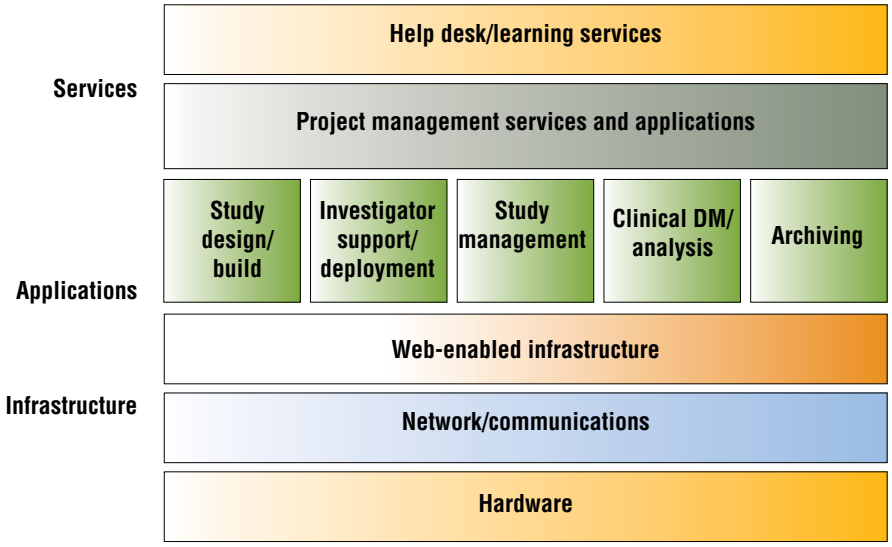
Meanwhile, the transition to adaptive trials will help ensure that patients, clinical supplies and clinical data are used as effectively as possible. In conventional clinical testing, data obtained during a trial are used to design and administer *subsequent* trials. In adaptive trials, by contrast, the data are run through numerous simulations to optimize the course of the *same* trial without jeopardizing its statistical integrity.

Adaptive trials will, in turn, necessitate the use of EDC to facilitate the rapid integration of the data thus produced and support the modeling and decision-making required to determine how the trials should proceed. Although the earliest EDC systems were developed approximately 20 years ago, relatively few pharmaceutical companies have successfully explored their potential in a clinical setting. CenterWatch estimates that only 24 percent of clinical trials conducted in 2002 used EDC, up from 12 percent in 2000.[23] Yet the evidence in favor of EDC is compelling: One analysis of 10 Phase III studies involving 6,700 subjects shows a dramatic reduction in the percentage of queries raised when using such techniques.[24]

The barriers to widespread use of EDC include the high cost of conducting pilot studies and installing an electronic infrastructure across numerous sites. But one way of solving these difficulties is to adopt an on demand infrastructure, where a company purchases computing and software services from a specialist provider on a pay-per-use basis, as and when it needs them. On demand computing converts fixed costs into variable costs and removes the need for a large, up-front capital investment. It also affords much greater flexibility because the service can rapidly be scaled up or down.[25]

So, for example, in a clinical trial, a pharmaceutical company could appoint a third party to manage the hardware and software – including equipping the trial sites with computers, loading the software, providing technical support and collecting the computers afterward. It could then run a help desk for trial investigators and patients, and manage the project and applications itself (see Figure 5). Alternatively, it could subcontract everything except the applications or globally source the entire trial to an IT supplier working with a contract research organization. Ultimately, it could even delegate its clinical data management operations to a long-term partner – an approach that is known as clinical transformational outsourcing.

Figure 5. EDC on demand.



Source: IBM Global Business Services analysis.

The shift to "in-life" testing – using a variety of remote monitoring devices equipped with 3G or Wi-Fi technologies to track how patients respond to new drugs in an everyday context – has other implications and, clearly, pervasive computing will play an essential role in the transition. It will change both the way in which new medicines are tested in man and the way in which healthcare is delivered.

The nature of the disease and biomarker that are tracked will determine whether a particular device should function on a constant or intermittent basis. For example, a device that monitors the heart rate in a patient with a history of cardiac events must be constant, whereas one that monitors lipid levels in the bloodstream of a patient who has high cholesterol need only be intermittent. Meanwhile, advances in microfluidics will provide the means with which to perform remote biochemical assays (see **Diagnosis at a distance** sidebar).

Diagnosis at a distance

One of the new disciplines that will help promote pervasive healthcare is microfluidics, sometimes known as "lab-on-a-chip" – a branch of physics that studies the behavior of fluids on microscopic levels. A miniature chemical vessel extracts a tiny amount of fluid that is thousands of times smaller than a droplet. The fluid passes via a nano-scale loading pad to a reaction chamber and capillary pump, where its composition is analyzed *in situ*.

Microfluidics is already used for separating and analyzing genetic sequences, but it has numerous other potential applications including biochemical assays on blood, saliva or urine to diagnose patients at a distance. Rather than having to visit a physician for a test and wait for the results, patients will eventually be able to test themselves and send the data directly to their healthcare providers.

But in-life testing also requires the ability to integrate and manage the data that are collected, and distribute the correct data to the correct people – including patients, healthcare providers, clinical staff at the company conducting a trial and the regulators. It is easy to imagine the hubbub that would ensue if confidential information about patients fell into the wrong hands or preliminary data about a drug were accidentally released to the regulators before verification.

This is where the clinical information exchange (CIE) has a role to play. The CIE is a portal that integrates all the different pieces of data required to perform clinical development – be they trial data, clinical supplies data, details of trial investigators, financial records or anything else. It aggregates, centralizes and filters the data, and it verifies the appropriate level of access to authorized users.

One of the two main technological components of a CIE is a clinical data repository, which provides a central pool where computer applications can store their data and retrieve information placed there by other applications. The second main technological component of a CIE is an investigator relationship and trial management system, which can be used to recruit trial investigators with particular qualifications or skills and patients with particular genetic profiles, and provide them with the support they require.[26]

The shift to rolling dossiers and continuous marketing applications has other implications. The FDA and the European Medicines Evaluation Agency are currently installing systems that can handle electronic versions of the Common Technical Document – the standardized framework for drug applications devised by the International Conference on Harmonization. This is likely to be followed by the introduction of rolling dossiers, where pharmaceutical companies submit clinical data to the regulators on an ongoing basis. The logical extension of the rolling dossier is the continuous marketing application, where the right to market a drug is subject to continuous reassessment, with regular reviews that are even more demanding than the FDA's annual adverse-event reporting checks.[27]

Both rolling dossiers and continuous marketing applications will require an "always-on," electronic connection between individual pharmaceutical companies and the regulators. Therefore, it is essential that such connections are completely safeguarded and that a company has full control over the visibility of its data.

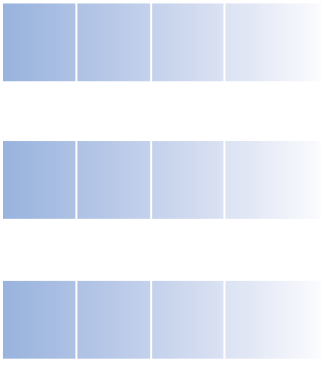
Development of advanced systems for compiling dossiers and annotating and viewing regulatory submissions will also facilitate greater interconnectivity between the industry and agencies. For example, at present, dossier management systems typically work like conveyor belts; each unit adds a piece of information to the folder that eventually culminates in a drug dossier. In the future, however, such systems will probably function more like shopping trolleys, and a regulator will pull the relevant sections when it wants them. That, in turn, means pharmaceutical companies will have to use security-rich information lifecycle management systems so they can manage the publication of regulatory documents and data sets through a tightly controlled process.

A quantum leap in product development and manufacturing

The move toward targeted treatment solutions (and the technologies enabling that transition) will have an equally profound impact on the pharmaceutical supply chain. Indeed, it will require a huge improvement in the caliber of the industry's product development and manufacturing processes.

Biologics are more fragile and more difficult to scale up than small molecules, often involve novel drug delivery techniques and are more vulnerable to impurities in the manufacturing process. Making biologics is thus a far more complex business than making conventional chemical compounds, and it takes much longer to set up the plant.

The range of products that are manufactured will also vary much more, as will demand for those products. It will still be necessary to make traditional, mass-market drugs in large batches, but biomarkers and medicines targeted at patients with specific disease subtypes will obviously have to be produced in much smaller batches. They will have to be formulated and packaged more variously, too, with a corresponding increase in the number of stock-keeping units to be tracked.



Companies manufacturing targeted treatment solutions will therefore need to become much more flexible. They will need to reduce packaging changeover times from hours to minutes and package to order rather than stock to avoid accumulating costly inventory. They will also need to improve their quality management. Six Sigma, the definitive methodology for measuring and reducing product variation, sets a target of six standard deviations between the mean and the nearest specification limit. But IBM estimates that most pharmaceutical companies are still functioning at two sigma – far from the level they will need to achieve.[28]

Again, other industries have something to impart. One of the most important development concepts used in the consumer packaged goods, automotive, electronics and aviation sectors is product lifecycle management (PLM) – the management of a product from initial idea through design, launch and production to marketing and sales. This definition of PLM is foreign to Pharma, where the term is used only in a marketing context to describe the management of a drug from the point at which it is launched to the point at which there is generic competition.

Companies like Proctor & Gamble design for ability to be manufactured. Similarly, many automakers use common platforms and components for models in the same series. They also actively encourage their suppliers to design and build integrated components and even to work alongside them on the factory floor.

Conversely, a pharmaceutical company typically develops a new drug in one country and manufactures it at plants in several other countries. But the development function rarely consults the manufacturing function to ensure that a formulation is fit for large-scale production. Data related to new drugs are not shared electronically, and none of the manufacturing systems at the different production sites are integrated. In addition, the sites themselves are fixed rather than interchangeable because a drug manufacturing set-up in one country is not automatically validated in another. Any company that wants to overcome these issues will need to install an electronic backbone that spans everything from early development to marketing and sales, and that allows information to travel in both directions (see Figure 6).

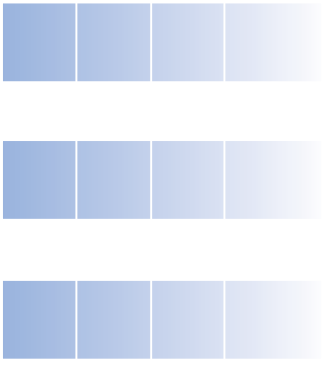
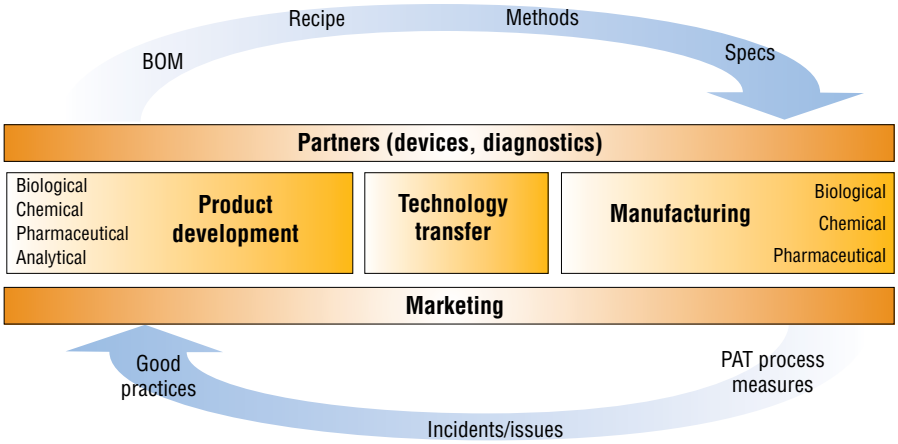


Figure 6. The product lifecycle management loop.



Source: IBM Global Business Services analysis.

Earlier and greater collaboration between the product development and manufacturing functions should ensure fewer hitches on the production line. Earlier collaboration should prevent design features that make the manufacturing process unnecessarily difficult and should produce design features that have greater flexibility. Companies will be able to decide at the last minute where they want to manufacture a particular product and change the manufacturing site at any point in its life. They will also be able to pass feedback from marketing and sales back into early development to make products that better meet the needs of the marketplace. The use of advanced collaboration tools and traditional enterprise resource planning (ERP) solutions within pharmaceutical development will form the baseline for PLM.

But PLM is only one of the elements that will transform product development and manufacturing – a second element is PAT. The FDA traditionally performed spot checks and issued a letter of warning if Good Manufacturing Practices (GMP) were violated. It now proposes to focus on three things: a risk-based approach, GMP systems-based inspections, and science-based policies and standards. This new agenda will drive the industry into using compliance-centric processes and applications architectures.

The FDA reasons that concentrating on GMP systems rather than products or profile classes will enable it to monitor companies more effectively with the resources it has at its disposal, because the systems are generally used to manufacture many different kinds of products. So, if the FDA finds a problem with a particular system, it

Data, data everywhere

Celera Genomics, which helped to sequence the human genome, has at least 110 terabytes of data in its computer farm. The most sophisticated high throughput screening facilities generate an annual output of about 350-400 million data points. And if the medical images produced each year were stored electronically, they would consume about 150 petabytes of memory.

Combinatorial chemistry, high throughput screening, high throughput sequencing, X-ray crystallography and other technologies have added to this vast data load, and the data are massively varied. They include textual data, spectra, genomic sequences, chemical structures, molecular conformations and protein crystal structures.

But this is only a fraction of the data Pharma will soon have to hold. Genetic profiling will generate about two terabytes of data per person. In-life testing will produce a continuous stream of data from hundreds of thousands, if not millions, of patients. And in-process monitoring of manufacturing systems will produce numerous data points for *every* batch that is made.

can shut down the whole plant or, indeed, multiple plants if a company is using the same system elsewhere. It has also encouraged the use of PAT as part of an overall shift from periodic inspections and batch reporting to continuous monitoring and reporting.

This, alone, will dramatically improve manufacturing quality by providing the means with which to perform in-line, online quality checks. Measuring and monitoring equipment will be incorporated in the process control systems and overarching manufacturing execution systems that a company uses, in order to record and control production. It will be supported by data-mining tools and statistical pattern recognition techniques.

The introduction of PAT will have an enormous impact on how quality control departments operate and how software providers develop integrated manufacturing applications. It represents a huge challenge – both to implement in the manufacturing process and to integrate with the product development process. But, together with PLM, it will help the industry raise quality levels in pharmaceutical development to three sigma, and quality levels in pharmaceutical manufacturing to four sigma. Higher quality levels will, in turn, enable companies to achieve better average order lead times and plant utilization levels.

The introduction of Corporate Information Asset Management (CIAM)

The sheer volume and variety of data that Pharma has to handle is already a major problem, but the situation will soon become much worse (see **Data, data everywhere** sidebar). Predictive biosimulation, clinical genomics, in-life testing, PAT and Web mining will generate vast quantities of additional information. If the industry is to manage all these data and ensure that it complies with the regulators' requirements, it will need to switch from manual, paper-based records management to digital records management and adopt appropriate solutions for organizing, retaining, restoring and utilizing electronic data over extended and indefinite periods of time.

The new storage media, virtualized storage solutions and storage grids that are now being developed will help Pharma cope with the data explosion. On demand storage also has a role to play, especially in managing periods of peak demand. A company can decide whether it wants to store data in its own facility or use a "storage farm" owned by a trusted third party and pay a unit price for each gigabyte it stores. The latter is a particularly attractive option for small biotechnology operations, which cannot always afford the capital outlay required to build a large data repository.

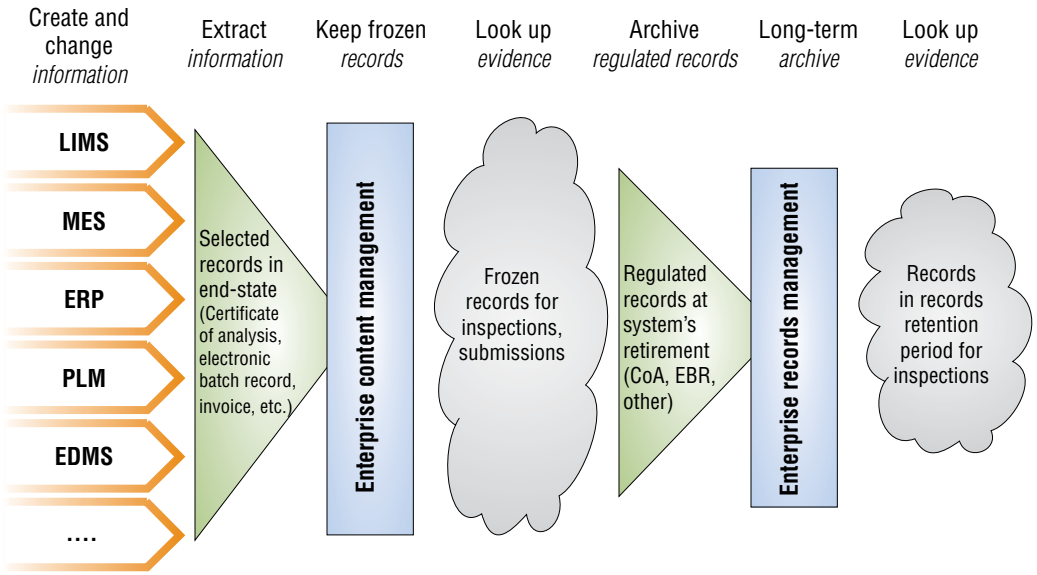
However, all pharmaceutical and biotechnology companies must also maintain formal records of specific transactions throughout the value chain to satisfy the regulatory requirements, and the incentive to comply is growing rapidly. The FDA now plans to apply the doctrine of strict liability, under the Federal Food, Drugs and Cosmetics Act. The doctrine states that individual executives have a duty to prevent corporate violations from occurring and can be held criminally liable for such violations, regardless of any awareness of wrongdoing. The Sarbanes-Oxley Act likewise makes CEOs and CFOs personally liable for their companies' accounting practices, with large fines and jail sentences for failure to comply.

This trend is driving the transition to digital records management – the better to manage risk. Increasingly stringent regulatory requirements, patent infringement or patent interference suits, and product liability suits will stimulate the development and governance of digital record management systems that help companies comply with the regulations, protect their intellectual property and limit their financial exposure.[29]

The systems themselves will need to be consistent throughout the value chain, including research and development, manufacturing, and finance and accounting. They will also need to be transparently linked to the source processes or applications that generate the records they manage, thereby providing what could be described as "in-process" records management.

So, for example, the systems that control the manufacturing process all generate data sets that need to be retained for regulatory reasons. With in-process records management, these can be automatically collated in an enterprise content management system, "frozen," cleared for archiving, and transferred to a data repository either onsite or offsite and either in-house or out-of-house (see Figure 7). The supply chain is one area of business where in-process records management will prove invaluable. In-process records management will also help companies fulfill the terms of the Sarbanes-Oxley Act regarding the retention of audit data.

Figure 7. In-process records management.



Source: IBM Global Business Services analysis.

Archiving is yet another challenge. Most pharmaceutical companies have different local systems for archiving clinical, manufacturing, financial and regulatory data. They also archive obsolete data manually rather than automatically; someone must physically key in instructions to transfer data that are no longer used to an online warehouse or arrange for the data to be copied and stored offline.

Many companies now recognize the need for a flexible electronic archiving process that is fully integrated with their day-to-day data, content and records management applications – a seamless facility that automatically identifies the point at which information is no longer being used, confirms its status and moves it offsite. But even this is not enough. If a company wants to change its systems, for example, it must either keep the system on which it originated the data so the data can still be read or adopt some sort of long-term records management system.

Unfortunately, creating a "data museum" is usually very difficult because large pharmaceutical companies use so many applications. However, the most advanced electronic archiving systems can now read frozen files, regardless of the application that was used to produce them and whether the data are structured or unstructured. Historical records stored in such systems can thus be traced, reconstructed and examined at any time in the form in which they were initially produced.

IBM calls the integration of in-process records management, content management, electronic archiving and virtualized storage systems Corporate Information Asset Management (CIAM). CIAM has numerous benefits. It is designed to enable pharmaceutical companies to use and share their information assets more effectively and optimize the value of those assets, greatly reduce the total costs of storing and archiving information, and provide consistent enterprisewide policies for managing sensitive information assets over the long term.

Smart products in a smart value chain

If CIAM has applications in numerous areas of business, so do smart tags. Their usefulness in managing the pharmaceutical supply chain is obvious: They can be used to track the passage of each unit, bottle or blister pack through the manufacturing process and hold information on batch records, storage conditions and shipment history. This information is particularly important for biologics, which are highly sensitive to extremes of temperature and movement since excessive heat or violent jolting can change the way a protein folds.

Apart from making products much easier to trace, smart tags can help deter counterfeiting, tampering and parallel importing; enhance brands; and generate rapid top-line growth. They can be used to manage inventories, locate products, validate the fulfillment of prescriptions and automate payment of over-the-counter medicines.[30] In fact, smart tags have potential across the pharmaceutical value chain (see Figure 8).

Figure 8. Potential uses of smart tags across the pharmaceutical value chain.

Discovery	Preclinical	Clinical	Supply	Delivery
Identification of sample containers and well plates Container environment history Lifecycle tracking (e.g., biological/ radioactive samples)	Animal identification and tracking Identification and tracking of laboratory samples	Patient identification Document tracking Laboratory specimen identification and tracking Materials and supplies tracking	Inventory management Gray-market tracking Counterfeit protection Product recall/expiry management Manufacturing line management	Sample tracking Patient identification Smart package inserts Materials and supplies tracking Compliance monitoring Device tracking

Source: IBM Global Business Services analysis.

Mirror writing

Philips Electronics has developed a bathroom mirror that can surf TV channels, trawl the Internet or check your blood pressure while you brush your teeth. Called Mirror TV, it has a built-in LCD display that can be switched on and off. Philips is also road-testing a more advanced model that can be linked via wireless connections to healthcare devices such as bathroom scales; it should be ready for the home market in 2005.

Moreover, the smart value chain will not stop at the factory gate. It will extend to the pharmacy and, ultimately, to patients' homes. Smart package inserts will obviate the need for multi-lingual prescription guidelines, for example. A chip in each box or package will enable the pharmacist to download and print out the instructions in the relevant language. Alternatively, when a patient takes a drug out of his or her bathroom cabinet, the dosing instructions and details of any potential side effects or contrain-dications will appear on the bathroom mirror (see **Mirror writing** sidebar). In addition to being more convenient for patients, the elimination of traditional inserts will cut manufacturing and packaging costs by simplifying the packaging process and reducing changeover times.

Mining for patient insights

This paper has thus far discussed the attributes required to discover, develop and manufacture targeted treatment solutions. But targeted treatment solutions will also be marketed and sold quite differently from traditional, one-size-fits-all drugs. They will be priced according to the outcomes they deliver; they will cover both the primary- and secondary-care markets; and they will be supported by a network of services for patients.

One of the core technologies required for marketing and selling targeted treatment solutions is pervasive computing. In-life testing and surveillance will provide the outcomes data on which pricing negotiations with governments and healthcare payers are based, while the advent of electronic medical records (EMRs) will help ensure that such information is readily available to the various parties who need it.

Obviously, access to EMRs must be carefully controlled to avoid any abuse of patient privacy. One way of addressing these concerns is to put the data in the hands of a trusted third party that can manage them on behalf of everyone – much as the banking cooperative SWIFT manages messaging services for the financial services sector.

Phone a friend

In May 2003, Roche and health call center specialist International SOS launched the UK's first ever helpline to encourage patients to keep taking their drugs. Patients prescribed Roche's obesity treatment Xenical can call in for assistance. But in the first service of its kind, patients will also be called regularly by trained healthcare professionals offering support and advice. Roche is now thinking of offering an email-based service for male patients who are reluctant to talk on the phone.

The advantages of ready access to patient records are considerable. It will help facilitate the transition to "information-based medicine" – the marriage of information technology with pharmaceutical research and the practice of medicine to provide personalized healthcare. The integration of outcomes data, genotypic and phenotypic data, genealogical data, population profiles, epidemiological studies and the like will help enable the medical community to diagnose patients more accurately, identify people at risk of experiencing drug reactions and tailor treatments for a variety of diseases. It will also change healthcare from a primarily episodic approach to illness into a form of disease management that includes pre-symptomatic treatments, therapies and lifestyle adaptations.

Pervasive computing will play an equally important part in providing the support services that are intrinsic to targeted treatment solutions. With portable devices, it will be possible to monitor patients as they go about their daily lives. With mobile communications and Internet connections, it will be possible to give patients advice and encouragement – including news about relevant medical advances, recommendations regarding diet and exercise, and reminders and alerts. One example of this approach is the pilot scheme for patients taking Xenical, which Roche recently launched (see **Phone a friend** sidebar).[31]

In short, pervasive computing will help pharmaceutical companies build a long-term relationship with the patients who are taking their products, and the development of sophisticated contact management tools will reinforce this trend. Customer relationship management systems will help companies manage key accounts and support prescribing physicians with patient compliance programs, while patient relationship management systems will help them personalize their communications with patients. Together, these tools will allow pharmaceutical companies to manage their relations with healthcare providers, patients and payers much more actively.

But pervasive monitoring is not the only technology that will play a major role in marketing and selling targeted treatment solutions. With core text analysis and text-mining tools, companies will be able to monitor drug effects and adverse reactions in the real world and track the reputation of their products via disease Web sites, patient chat rooms and other information published on the Internet. They will also be able to use such knowledge to promote their products. Suppose, for example, that a company has just launched a new drug. It could collect information on the level of interest from patient chat rooms, advertising sites and competitor sites, which it could then use to position the drug as effectively as possible.

A new era in information management

Thus far, this paper has examined the seven core technologies that IBM believes Pharma will need to make innovative new treatments in a manner that complies with the regulators' requirements. This paper has also discussed how these technologies collectively will transform the various parts of the value chain. Next, let us examine the scientific and commercial advantages that flow from using these technologies, together with the change in the role of IT.

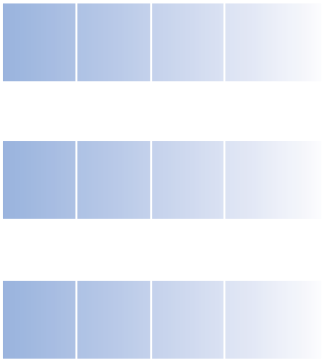
At present, the industry spends a fortune on IT, but it rarely reaps the full rewards of that investment. Moreover, much of its expenditure is devoted to technologies that improve transaction processing. The technologies identified in this paper will deliver much more – they will further the industry's strategic goals.

These new technologies will provide a much better understanding of patients. They will help to identify the genes that correlate with common diseases, the dynamic interplay between different genes, and the relationship between nature and nurture – the insights that are needed to make targeted treatment solutions. These new technologies will also revolutionize the economics of making new drugs by reducing prelaunch drug development costs to as little as US$200 million (a quarter of the current average cost per drug); reducing lead times from 12-14 years to between 3-5 years; and increasing success rates from first human dose to market dramatically – as indicated in IBM's publication, "Pharma 2010: The Threshold of Innovation."[32]

In addition, these new technologies will enable individual pharmaceutical companies to differentiate themselves much more effectively, because the skills required to develop and produce biologics that depend on complex, heavily regulated manufacturing techniques will be difficult to replicate. Finally, the new technologies will help the industry raise quality levels in pharmaceutical development to three sigma and quality levels in pharmaceutical manufacturing to four sigma. Attaining these levels will allow companies to aim for order lead times of as little as one day and plant utilization of as much as 80 percent.

Flexible delivery and financing

But few, if any, pharmaceutical companies can simply afford to jettison the technologies in which they have already invested. Assuming that most such companies have centralized or outsourced the majority of their transaction-oriented processes, the first challenge facing the chief information officer is to make the most of the existing infrastructure – to reorganize it both to provide much greater flexibility and to control costs.



Creating a flexible infrastructure that can be scaled up or down as necessary is essential to accommodate future expansion or shifts in direction. Cutting costs is essential to release capital for investing in the technologies required to develop the targeted treatment solutions that will deliver that growth.

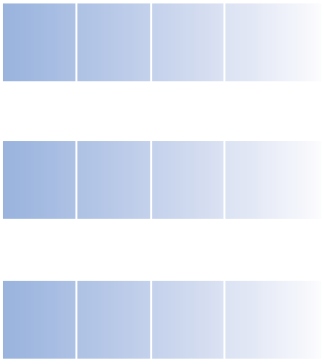
One way of introducing greater flexibility and simultaneously securing economies of scale is to consolidate servers and storage platforms, thereby improving the overall performance of the IT infrastructure and potentially reducing the total cost of ownership. This enables companies to start using more flexible modes of delivery. A second approach is to harmonize applications throughout the business and to delegate part or all of the responsibility for implementing and running key application areas like SAP, JDE or content management applications to an external IT provider that can execute them more economically and efficiently.

Getting a specialist to take full responsibility for the implementation, maintenance and upgrading of complex solutions has several major advantages. It allows a company to focus on its core activities. It provides greater flexibility in terms of both the infrastructure that is used and how it is financed. Payment typically is made in installments or based on use rather than up-front license fees. Also, it generates savings through the use of outsourcing, industry templates, shared equipment and so forth. In fact, in IBM's experience, outsourcing responsibility for an SAP or JDE system can reduce the total cost of ownership by as much as 30-35 percent over five years. IBM's expertise in this area is virtually unrivalled as we have invested heavily in developing on demand solutions and a supporting supply infrastructure.

Component business modeling

Once a company has reduced its IT costs and released funds for investing in new technologies, it must identify the areas of business – and, in turn, the specific technologies – on which it should to be spending its money. The most successful organizations focus their financial, intellectual and technological resources on what differentiates them and drives margins in their business. They consolidate or use outsourcing for all those components that support the business but do not generate innovation and growth.

Some companies use outsourcing only for management of the computing resources they need. Others outsource entire business processes, a route that can reduce the overall cost of performing a particular process by another 30-35 percent in addition to the savings from turning over management of specific applications such as SAP to an external specialist.



Component business modeling (CBM) provides a framework for making these decisions. CBM involves breaking a business down into its logical components to establish which processes can really help it stand out from the competition and which processes are what it has to do to keep the doors open and the lights on. In other words, it provides a way of looking at an enterprise as a collection of building blocks that erase the boundaries created by geography, structure, product streams, customer channels, data sources and the like.

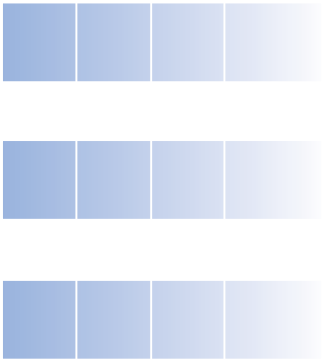
When a company analyzes itself in these terms, it can identify the strategic activities that offer significant potential for differentiating the business and generating better margins over time. It can then determine which technologies will best support those activities. It can also identify where its costs reside and where greater efficiency or variability would yield major savings. Finally, it can rank the changes it wants to make in order of priority.

Taken to its logical conclusion, CBM results in what IBM calls an "on demand business." An on demand business is an enterprise, the business processes of which are integrated end-to-end across the company and with key partners, suppliers and customers, enabling the enterprise to respond with speed to virtually any customer demand, market opportunity or external threat. CBM also allows such an enterprise to concentrate on the activities, processes and technologies that will generate the biggest returns on investment.

Open standards and layered architectures for universal collaboration

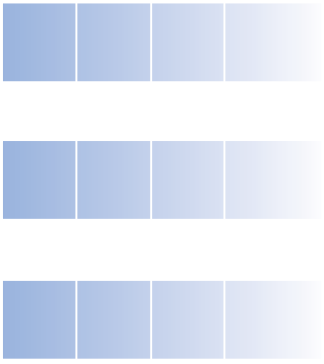
There are two other features that every pharmaceutical operation should bear in mind when selecting new technologies: open standards and layered application architectures. Open source software and standards (such as Linux, XML, OGSA, SOAP and WDSL) reduce the costs of integration and customization, and provide greater flexibility and scalability. But they are also vital for building collaborative networks.

As we have already indicated, pharmaceutical companies will increasingly have to share information with their partners in discovery, development, manufacturing, distribution and sales and marketing. However, they will have to extend collaborations with numerous other entities, too. Healthcare is gradually becoming an ecosystem that includes pharmaceutical and biotechnology firms, governments and healthcare payers, regulators, the medical community, and patients and their families. The various entities in this ecosystem are starting to work together in new ways in order to improve human health.



Moreover, some forms of collaboration will see data generated by multiple parties. This is true of three areas in particular; accessing patient records for evidence of outcomes; submitting dossiers to the regulators; and tracking products through the value chain to ensure they are properly manufactured, distributed, delivered and used. IBM envisages that virtual information brokers will emerge to manage such data, thereby helping to ensure that data from different countries, organizations and systems can be compared and that the data are available to all authorized users in a safeguarded environment.

A layered application architecture – in which universal access, business process management, end-to-end process integration, security services, functional application engines and data storage are layered like a sandwich – is equally important on several counts. It allows people to access the system, no matter what device they are using. It also allows them to use the same transaction management, security management, records management and archiving applications rather than separate applications in different parts of the business, as is currently often the case. And it enables a company to specify, activate, control and change the processes that are used. Therefore, it is an ideal means of helping to ensure the compliance of regulated processes – a particularly important issue given the FDA's new systems-based inspections approach.

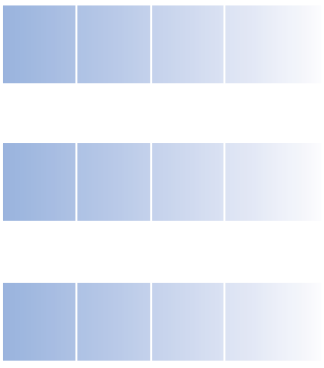


Conclusion

To sum up, the technological advances of the past few years have huge implications for Pharma. The "silicon rally" that lay on the horizon at the start of the decade has turned into "silicon reality." It has produced, or is about to produce, the key tools for discovering, developing, manufacturing and selling targeted treatment solutions – the primary source for creating future shareholder value.

However, it also heralds a new era of information management in which the IT function performs a totally different role. Today, most pharmaceutical companies devote most of their IT resources to support services and the supply chain, and focus mainly on technologies that cut costs. But as computing turns into a true utility, it is anticipated that they will increasingly use outsourcing for their day-to-day computing requirements. Many of the routine tasks that currently consume the bulk of their time and money could be transferred to external technology providers.

The chief information officer's traditional empire will change accordingly; that empire will become smaller but it will also become much more important. The IT function will become an integral part of the core value-making activities of the business. It will focus on the technologies that enable the company to make better treatments for patients and better understand the needs of those patients, for it is those technologies that will drive future growth.



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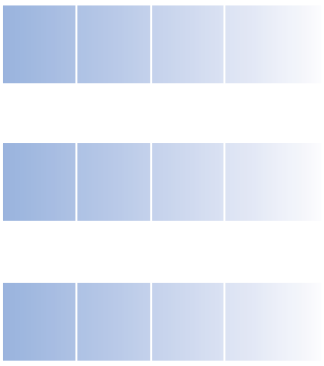

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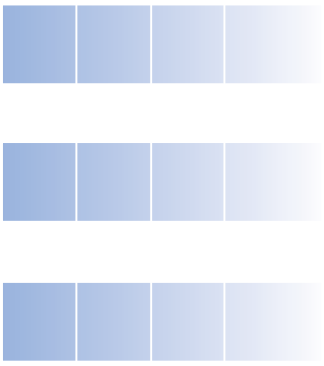

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