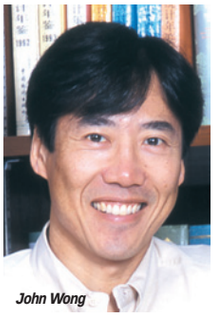

## Opportunities and Challenges for PHARMA R&D IN CHINA


John Wong

*By investing more heavily and in more complex areas of R&D in China, a multinational pharma company can signal its commitment to the Chinese market and strengthen relationships with key opinion leaders, says John Wong, Senior VP and Regional Chairman of The Boston Consulting Group's Asia-Pacific Region.*

China will likely surpass many Western European markets to emerge as the world's fifth-largest national market for pharmaceuticals by 2010. Biopharma research and development in China are also on the rise. Stimulated by government spending, leading multinational pharmaceutical companies are playing a key role by outsourcing chemistry-based R&D to China. These companies must now decide whether to raise the stakes, say consultants from The Boston Consulting Group (BCG) in a recent report, A Game Plan for China.

China's R&D expenditure boasted a compound annual growth rate of 24% during the four-year period from 1999 through 2003, more than double that of India.

During that same four-year period, pharma patent applications from local Chinese companies rose from 283 a year to 1,696 a year. Today, about 30 innovative drugs are in preclinical development or clinical trials in China.

But relocating R&D operations to China won't necessarily result in major cost savings for global biopharma companies.

"Not only is there a cost incurred by relocating Western staff and importing research equipment and supplies, but there are inherent costs in lost productivity as the leaders of new lab sites negotiate language, cultural, and regulatory differences," says Kim Wagner, a BCG VP and one of the report's authors.

## NOVARTIS EXCELS AT MEETING THE NEEDS of Managed-Care Pharmacy Executives

Novartis remained No. 1 overall for the seventh consecutive cycle in Verispan's fall 2005 Managed Care Pharmacy Executive Promotional Audit. Based on the responses of pharmacy executives, Verispan calculates overall ranking from four assessment categories.

Novartis ranked first among pharmacy executives in three of those areas: contracts, account personnel, and corporate approach. Pfizer retained the top spot in value-added services for the second consecutive audit cycle.

Novartis held an impressive lead, with 31 net points separating it from second-place Merck. Merck — which performed strongly in the areas of contracts, value-added services, and account personnel — jumped in overall ranking from seventh to second between the spring and fall 2005 audit cycles.

**COMPANIES THAT MEET THE NEEDS OF MANAGED-CARE PHARMACY EXECUTIVES**

**OVERALL RANKING**

| COMPANY | FALL 2005 RANK |
|---|---|
| Novartis | 1 |
| Merck | 2 |
| Novo Nordisk | 3 |
| GlaxoSmithKline | 4 |
| Wyeth | 5 |

Source: Verispan's Fall 2005 Managed Care Pharmacy Executive. For more information, visit verispan.com.

## CROs Expand Capacity of PHARMA'S DEVELOPMENT PIPELINE

Over the last five years, the proportion of resources involved in pharmaceutical product development has shifted from drug and biotechnology companies to contract clinical research organizations (CROs). This realignment has increased the speed and efficiency of the industry's product-development pipeline while maintaining clinical-trial data quality and high levels of regulatory compliance.

These are the findings of a survey conducted by the Tufts Center for the Study of Drug Development (CSDD) on behalf of the Association of Clinical Research Organizations (ACRO) to examine the contribution CROs make to the pharmaceutical industry's overall development capacity and to assess the impact clinical outsourcing has on development-project performance.


Candace Kendle

*The insight provided into current outsourcing trends will stimulate further dialogue on the benefits of outsourcing and the value CROs bring to biopharmaceutical customers, says Candace Kendle, Pharm.D., Chair of ACRO, and Chairman and CEO of Kendle.*

The study's key findings include:

- Since 2001, spending by pharma and biotech companies on contract clinical research services has grown 15% annually, outpacing the 9% annual increase in overall development spending.
- From 2001 to 2004, head count among major CROs grew 6% annually, while project-sponsor head count remained flat.
- Drug companies reported that, typically, projects that relied heavily on CROs submitted data to regulators more than 30 days closer to the projected submission date compared with projects with less CRO participation.
- Even larger, more complex trials are completed more quickly when they have a high degree of CRO involvement.

## Dramatic Changes Proposed for CLINICAL-TRIAL PROCESS

The pharmaceutical industry is trapped in a deepening productivity crisis. While the discovery and preclinical development process is highly productive, a fraction of candidates make it through the subsequent clinical-evaluation process.

Currently, about 30% of new molecular entities fail in Phase I clinical testing, and close to 50% fail in Phase III trials. Of all compounds that begin human clinical testing, more than 80% fail because of either efficacy or safety issues. For those candidates that made it to U.S. pharmacy shelves, no fewer than 10% faced market withdrawal or severe use restrictions between 1975 and 2000.

A new CHA Advances report says the way human trials are designed and conducted makes significant contributions to the delays, failures, and exploding costs.


Mike Goodman

*The current model for conducting clinical trials is unsustainable; too many companies are chasing too few patients at too high a cost, says Mike Goodman, General Manager of CHA Advances Reports.*

The report, entitled New Paradigm for Clinical Development: The Clinical Trial in 2015, proposes that a bidirectional approach is needed to accelerate the clinical process and make it more effective. The report suggests revamping trial design and including truly pervasive modeling and monitoring, driven by information technology.

According to the report's author, Mike Goodman, general manager of CHA Advances Reports, emerging developments — biomarkers, offshoring of trials, EDC, computer simulations of the "virtual patient," and Bayesian techniques for adaptive trial design — are poised to address these challenges. The issue now is for companies to integrate these technologies and practices in an efficient manner.

If the report's proposed changes were to be made by 2015, there could be dramatic changes in the world of drug development. The pre-approval clinical trial phase might be shortened to about three years, and 40% to 50% of all candidate compounds that enter this stage could be completed — with the majority of the failures occurring in the early human validation phase.

## GROWTH IN U.S. PHARMA MARKET is Predicted


Diana Conmy

***The U.S. market's continued success this year will depend largely on enrollment in the new Medicare benefit, the ability to overcome safety concerns, and new product launches to make up for the higher level of patent expirations, says Diana Conmy, Corporate Director of Market Insights, IMS Health.***

U.S. prescription drug sales grew 5.4% to $251.8 billion in 2005, compared with $238.9 billion in sales the previous year, according to IMS Health. Last year the volume of total U.S. dispensed prescriptions increased significantly over 2004, growing 4.7% after adjusting for longer-duration mail-order prescriptions.

Biotech products remained a major growth engine in 2005, with sales increasing 17.2% to $32.8 billion. Within the biotech market, a number of new rheumatoid arthritis drugs were launched successfully over the last few years, and growth within this product class is expected to continue.

Generics also posted strong 2005 sales growth of 20.6%. Analysts suggest this growth demonstrates the increasing influence third-party payers are exerting on patients' therapy options.

Other factors influencing 2005 pharma market performance include fewer new chemical entities (NCEs) approved than expected; fewer and lower-performing product launches; the decreasing use of COX-2 class products; and more aggressive generics launches.

Also, U.S. seniors continued to grapple with multiple Medicare discount card choices in 2005, leading to low participation in the program. But IMS reports that the cards were effective in lowering users' prescription costs, achieving $601.1 million in savings.

IMS forecasts that the U.S. pharmaceutical market will continue to grow at a compound annual growth rate of 5% to 8% over the next five years. This growth will be sustained by new product launches, recovery from COX-2 withdrawals, and increased utilization through Medicare Part D.

## Resistance to Change Affects E-CLINICAL TECHNOLOGY ADOPTION

With life-sciences and pharmaceutical companies showing a definite inclination toward electronic technologies and investing substantial amounts in transitioning from paper-based to electronic processes, Frost & Sullivan analysts expect revenue in the e-clinical trials (eCT) market to increase from about $210 million in 2004 to $357.4 million in 2011.

But the adoption of e-clinical technologies currently remains largely confined to pilot projects, barring a few implementations by some major pharmaceutical companies. Resistance mainly stems from life-sciences research scientists who are reluctant to accept newer electronic processes.

According to Frost's report, World eClinical Trials Market, shifting to e-clinical technologies would not only mean adapting to more technically sophisticated processes but also could require a complete redistribution of roles and responsibilities.

The major task at hand for eCT technology vendors is to convince all stakeholders in the clinical-trials process to adopt and integrate these technologies across all teams within the organization. The real challenge is to provide a compelling return on investment (ROI) to life-sciences and pharmaceutical companies.

Regulatory acceptance of clinical data standards also is helping promote the uptake of eCT technologies by allowing greater integration of data standards. Additionally, the growing number of strategic alliances between eCT technology vendors and contract research organizations also reflect the increasing adoption of these tools in drug development.

## FAST-TRACK DRUG DEVELOPMENT PROGRAM Firmly Established

Fast-track drug development, introduced in the United States in 1997, has become an important element of the nation's drug-development landscape, according to analysis from the Tufts Center for the Study of Drug Development (CSDD).

Between the start of 1998 and the end of 2005, nearly 500 fast-track designations have been granted by the U.S. Food and Drug Administration (FDA), accounting for about 20% of all active investigational compounds in clinical development programs worldwide during that time.


Christopher Milne

***The fast-track program has had a significant public-health impact by speeding access to drugs to treat AIDS, breast cancer, leukemia, and other diseases that afflict millions of patients, says Christopher Milne, Assistant Director, Tufts Center for the Study of Drug Development.***

The Tufts CSDD analysis also found that cancer-related programs today account for 40% of all fast-track designations. Although HIV/AIDS accounted for about 20% of all fast-track designations in 2001, it now accounts for 8%.

Total development time for fast-track products is eight years on average, which is about the same as for nonfast-track standard and priority review drugs. Additionally, total development times for fast-tracked products vary considerably by therapeutic area: nine years on average for cancer; five years for anti-infectives (mostly for HIV/AIDS treatments); and seven years for other indications (primarily rare diseases and orphan indications).

Tufts CSDD analysis also found that about one-third of all fast-track programs are currently struggling, with efficacy issues in late-stage trials being the major source of problems.

While a formal fast-track program currently exists only in the United States, international interest in similar fast-track mechanisms is growing in Europe, Japan, and China.

## Pharma Adopts Several STRATEGIES TO COMBAT GENERIC COMPETITION

Patents will expire on more than $80 billion worth of drugs by 2008, exposing top-selling brands to considerable generic competition. The generics industry, which accounts for 53% of all U.S. prescriptions, is expected to grow by at least 10% to 15% annually through 2008. The branded-drug industry, however, is expected to grow by only 6% to 9% during that time.

A new report from Cutting Edge Information finds that in the fight against copycat products, branded drug companies are considering a balanced array of legal, marketing, and science-based strategies.

New formulations are the most popular defense against generic competition. According to the report, Combating Generics: Pharmaceutical Brand Defense for 2007, 82% of the companies surveyed pursued new formulations to extend product life past patent expiration.

But drug companies need more than new formulations to fend off generics. The Cutting Edge report finds defensive pricing is the next most-used

strategy, with 70% of surveyed companies lowering prices or renegotiating purchasing contracts to fight generics.

Next-generation drug development is another, more risky strategy that companies are employing to protect revenues. Despite the risks, Cutting Edge analysts suggest that next-generation products can be one of the most effective means of protecting revenue streams from off-brand challengers.

Ultimately, companies balance their options among the most desirable and most reliable options. While R&D may work to develop a next-generation brand, marketing teams ramp up promotions and do their best to secure patient and prescriber loyalties.

## Report Predicts Growth
# TRENDS IN OUTSOURCING SERVICES


Steven Heffner

***As outsourcing becomes more widely accepted, concerns of intellectual property protection, trust, honesty, and transparency still remain obstacles, says Steven Heffner, Publisher at Kalorama Information.***

Outsourcing drug-discovery services — such as chemistry, biology, screening, and lead-opt — is expected to reach nearly $7.2 billion by 2009, according to a study from Kalorama Information.

Outsourcing in Drug Discovery, 2nd Edition, predicts that the swiftly growing market for outsourcing services, fueled in part by impressive advances in the Asian market, will increase at a rate of 15% from the current 2005 figure of $4.1 billion. In fact, upon discovering the benefits of outsourcing in Asia, many of the top pharma and U.S.-based contract research organizations (CROs) have opened their own operations there.

# AVIAN FLU THREAT
## Shakes Doctors' Confidence

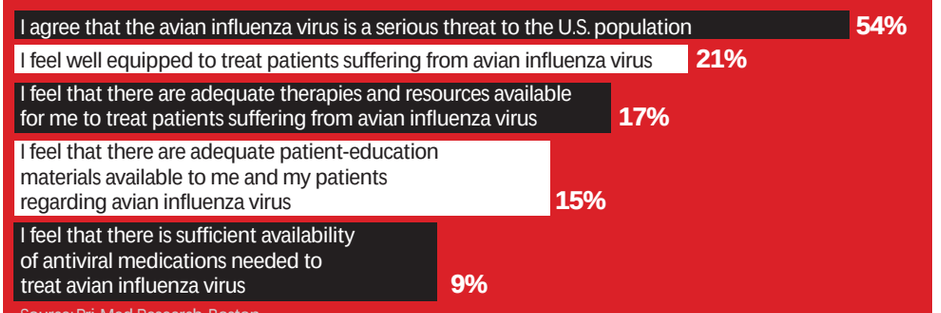

Anne Goodrich

***Primary-care practitioners clearly perceive the threat of an avian flu pandemic as real, says Anne Goodrich, Director of Pri-Med Research.***

Two-thirds of physicians are concerned about the threat of an avian influenza pandemic in the United States, and more than half believe an outbreak poses a serious risk for Americans. These are the findings of a nationwide survey of primary-care clinicians conducted by Pri-Med Research.

Fewer than one in five primary-care practitioners believe they are adequately equipped today to treat infected patients, and more than 50% of these physicians express little or no confidence in the government's ability to manage a flu pandemic at the local, state, federal, or international level.

**PRIMARY-CARE PHYSICIANS' CONCERNS REGARDING AVIAN INFLUENZA**




Source: Pri-Med Research, Boston.
For more information, visit pri-med.com.

Additionally, 91% of practitioners surveyed by Pri-Med believe that the current availability of antiviral medications is inadequate to meet an avian flu crisis.

"It's evident that practicing clinicians believe they need intensive preparation to respond to an avian flu outbreak in the United States, if one does occur," says Alan Lotvin, M.D., president of Pri-Med.

"They are beginning to take this threat seriously; more than 40% of primary-care practices in the United States have an emergency-response plan in preparation or already in place," he continues.

## Follow up

**THE ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS (ACRO)**, Washington, D.C., represents the world's leading clinical research organizations and aims to advance clinical outsourcing to improve the quality, efficiency, and safety of biomedical research. For more information, visit acrohealth.org.

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**CHA ADVANCES REPORTS**, Waltham, Mass., evaluates the latest advances in pharmaceutical R&D, their potential applications and business impacts, and their current and future positions in the marketplace. For more information, visit advancesreports.com.

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**FROST & SULLIVAN**, San Antonio, is a global growth consulting company. For more information, visit healthcare.frost.com.

**IMS HEALTH INC.**, Fairfield, Conn., provides leading-edge business intelligence products and services to the pharmaceutical and healthcare industries. For more information, visit imshealth.com.

**KALORAMA INFORMATION**, New York, a division of MarketResearch.com, supplies independent market research for the life-sciences industry. For more information, visit kaloramainformation.com.

**PRI-MED RESEARCH**, Boston, a division of M|C Communications, conducts research and provides continuing medical education programs for practicing physicians. For more information, visit pri-med.com.

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