GEN Clinical Research & Diagnostics

China Increases Healthcare Investment

Gov't Investment Is Opening Up Opportunities for Domestic and Multinational Firms

Qing Xia and Daming Chen

While the spring of 2009 has been difficult for most global industries, the Chinese healthcare sector seems to be an exception. Recently announced healthcare reforms that vow to bring wider insurance coverage to the country's 1.3 billion people as well as invest an additional $124 billion into the sector have opened up many opportunities for domestic as well as multinational firms.

While the $124 billion will be spread across China's healthcare industry, the vaccine sector is expected to garner significant benefit as the reform plan stresses the importance of preventive care. Even if all of the sectors benefit evenly, the reform plan translates to 30% CAGR for the vaccine industry over the next few years, to $1.7 billion, according to China Merchant Securities projections. The current vaccine market in China is valued at between $658 and $761 million. Most recently, the CAGR has been around 15%.

Vaccine Industry

China is currently the world's largest vaccine producer, producing more than one billion vaccine doses annually. But, given the huge population of China, analysts still consider the market underserved. According to the National Immunization Program (NIP), the 16 million infants born every year in China require 64 million doses of DPT vaccines (four immunizations in the first year), yet China currently only produces 18 million doses. The case is similar with MMR, hepatitis A, and other vaccines.

China's vaccine industry is heavily regulated and influenced by policy trends. The government-reimbursed NIP, in place since 1978, provides childhood vaccines free of charge. This program is responsible for the vast majority of vaccine consumption in China. The NIP covers a range of vaccines, some with a low profit margin, most from domestic manufacturers (*Table 1*). Multinational pharmaceutical companies, such as **GlaxoSmithKline**, **Novartis**, and **sanofi-aventis** also sell their vaccines in China, however most of their vaccines are not included in the NIP. This is because these multinational corporations (MNCs) tend to focus on so-called secondary vaccines such as flu vaccines, which claim a much higher profit margin.

Sanofi-aventis plans to produce 25 million flu shots annually at its Shenzhen, China facility.

Denis Félix/Corbis

The Chinese Center for Disease Control and Prevention (CDC) is responsible for purchasing and distribution of all vaccines covered by the NIP. For some provinces the CDC system covers non-NIP vaccines, as well. This makes the CDC highly influential in vaccine production, reimbursement, and distribution.

In the past, the vaccine industry in China had been monopolized by the China National Biotec Group, with regulatory barriers that excluded newcomers. The monopoly was loosened during the 1990s, and China now has more than 50 vaccine manufacturers (*Table 2 provides a partial list*). But the China Biotec Group remains an industry leader domestically.

In recent years, domestic vaccine makers have been trying to produce secondary vaccines outside NIP coverage, but their technology, product stability, as well as economies of scale have yet to catch up with that of their global counterparts.

Market-Oriented Reform

Though still heavily regulated, China's vaccine industry has also been through market-based reforms in recent years. In June 2005, China's "Guidance on Vaccine Distribution and Immunization" came into effect, which permits vaccine makers and distributors to directly sell vaccines not covered by NIP to the CDC, other vaccine distributors, and vaccine-consuming organizations. The new regulation breaks the CDCs monopoly and increased vaccine sales channels from 54 provincial CDC centers to over 5,700 sales terminals. While seen as good news to both domestic and MNC vaccine makers, it also increases competition.

The gradual market-oriented reforms also benefit MNCs that are mostly engaged in secondary vaccines. With better technology, wider sales networks, and brand image, they appeal to more affluent parents seeking comprehensive immunization for their children.

In 2008, sanofi-aventis finished first-stage construction of its flu vaccine production base in Shenzhen—a $94 million project that the firm said would produce 25 million flu shots annually for the domestic market.

Government Commitment

While economic reform and an open-door policy have brought decades of rapid growth, international travel has made disease control a more daunting task for Chinese authorities. This was made clear by the recent outbreaks of SARS and bird flu. In the more affluent coastal areas, keeping dogs as pets is also becoming trendy, which means greater demand for rabies vaccines. These factors are among the trends influencing the government's strong commitment to vaccine development.

In 2008, NIP coverage was expanded to include four additional vaccines, bringing the list of infectious diseases being immunized against to 15. The government's commitment is energizing domestic producers,

See Healthcare in China on page 54

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News Molecular Diagnostics

Ipsogen Licenses JAK2 Molecular Diagnostic Assays to ARUP

Ipsogen (www.ipsogen.com) penned a contract with ARUP Laboratories (www.aruplab.com) to offer JAK2 molecular diagnostic testing in the U.S. According to the terms of the agreement, Ipsogen grants ARUP nonexclusive rights for the U.S. territory to offer a complete range of assays for the molecular classification and screening of myeloproliferative neoplasms, a group of leukemias caused by JAK2 gene variations that affects more than 100,000 people in the U.S.

BD and Fujirebio Sign Alliance for Early Ovarian Cancer Detection

Becton Dickinson (BD; www.bd.com) and Fujirebio Diagnostics (www.fdi.com) signed a worldwide development and supply agreement for oncology diagnostic assays. The two companies will develop diagnostic products that incorporate Fujirebio Diagnostics' cancer biomarkers for use on BD's multiplex testing platform.

The initial products will be directed to the ovarian cancer biomarker, HE4, which is FDA-cleared for monitoring the progression or recurrence of epithelial ovarian cancer. Fujirebio Diagnostics also grants access to its other cancer biomarkers for inclusion in future multiplex diagnostic products to BD through the BD Diagnostics' TriPath platform.

Alethia Licenses Preclinical Cancer mAbs from the NRC

The NRC Biotechnology Research Institute is licensing exclusive, worldwide therapeutic and diagnostic rights to clusterin-specific antibodies to Alethia Biotherapeutics (www.alethiabio.com). The lead product, 16B5, is a humanized mAb in preclinical development.

Alethia says that it is primed to launch large-scale manufacturing of 16B5 to carry out toxicology studies in preparation for the filing of an IND soon. The acquired program includes mAbs that block the function of secreted clusterin, which seems to be a critical downstream effector of EMT, according to the company.

PGxHealth and U of Pittsburgh Ally for Anticancer mAbs

PGxHealth and researchers at the University of Pittsburgh Cancer Institute are joining forces to research genes that can be used to determine a patient's response to anticancer mAbs. The scientists will focus on the application of genetic variants in Fc gamma receptor genes, including FCGR3A. They will conduct a series of clinical programs to evaluate the response to Erbitux in the treatment of head and neck cancer.

Healthcare in China

Continued from page 52

which see growth opportunity in NIP-covered vaccines.

While the central government has expanded NIP coverage, some municipal authorities have also started to make moves to reimburse these secondary vaccines. For example, the Beijing municipal government has subsidized flu vaccines to Beijing residents since 2007, providing free immunization to over 1.85 million children.

Research Efforts

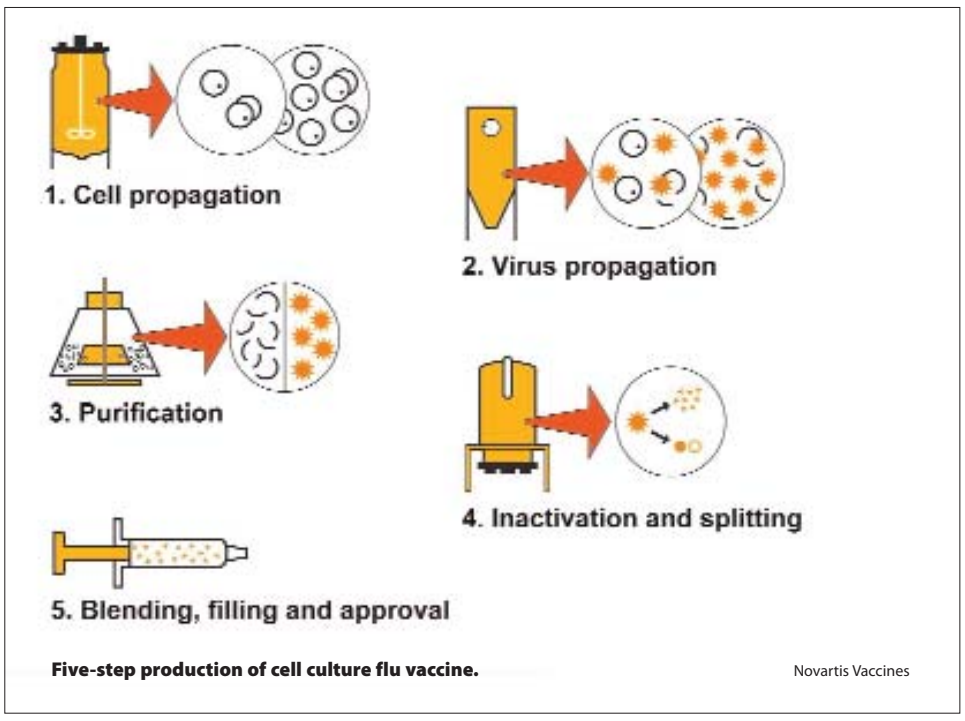
The government is not only subsidizing a wider range of vaccines, but it is also racing to invest in its own R&D. In 2006, The National Development and Reform Commission made new vaccine development a priority. The Ministry of Science and Technology has been providing funding for vaccine research via the National 863 Vaccine and Antibody program, the Pillar Program, and the National Innovative Drug Development Mega Project.

The National 863 program alone is putting nearly $30 million into vaccine R&D, and the Pillar Program is going to fund key platform technologies for vaccine manufacturing.

Recent success include approved vaccines against *Helicobacter pylori* and bird flu, and two late-stage therapeutic vaccines for hepatitis B. Progress has also been reported on vaccines against HIV, for which Phase II trials were initiated in March.

Distribution and Manufacturing

While the vaccine market is growing and research efforts are stepping up, concerns remain over manufacturing and distribution. Moving to a more market-oriented model for vaccine distribution has had a generally positive effect on the industry, but it makes regulation and quality control of the distribution process more difficult.



Five-step production of cell culture flu vaccine. Novartis Vaccines

As vaccine distribution demands strict cold-chain logistics, some worry that certain distributors may disburse the vaccines under room temperature and certain end-users may purchase from unqualified distributors to cut cost. The media is also becoming more sensitized to vaccine-related deaths, which are raising concerns over quality in vaccine manufacturing and distribution.

Industry insiders say that China faces a dilemma—concentration of distribution in the CDC system could lead to corruption while a loosening up of control may result in quality problems. With recent crackdowns on distributors related to vaccine scandals, China is expected to find a balance via trial and error.

Large-scale vaccine manufacturing in China is plagued with bottlenecks. Among the more than 50 domestic vaccine producers, only two are using bioreactors and these are relatively small (<100 liters). The rest of the industry is using roller-bottle manufacturing. The projected high growth of the vaccine industry in the next few years is expected to boost demand for bioreactors as well as services like cell-specific media development.

China's vaccine industry is expected to flourish as new healthcare reforms put more emphasis on preventive care. With strong government commitment, greater purchasing power, and market-oriented reforms, the vaccine industry in China is entering a phase of robust growth. Growing pains will accompany the process, but the modernization of the industry will likely benefit the Chinese population as well as domestic and MNC pharmaceutical companies seeking opportunities in the sector. GEN

Table 1. National Immunization Program (NIP) Coverage*

Calmette-Guérin
Polio
DPT
Measles
Hepatitis B
Hepatitis A
Meningococcal polysaccharide
Japanese B encephalitis
MMR
Hemorrhagic fever with renal syndrome
Anthrax
Whole cell leptospira

*Fifteen infectious diseases are being immunized against, some with combined vaccines that target more than one disease.

Table 2. Domestic Vaccine Producers

Company	Focus
China National Bio-Tec Group	Flu, Japanese B encephalitis, Measles, Hepatitis B, Hepatitis A , MMR, Rabies, HFRS, Whole cell leptospira
Sinovac	Hepatitis A
Beijing Tiantan	Tetanus, Diphtheria, Flu, Japanese B encephalitis, Hepatitis B
Changchun Changsheng	Rabies, Flu, Hepatitis A
Dalian Gaoxin Biologic	Rabies, Hepatitis B
Dalian Jingang Andi Biologic	Rabies
North China Pharma Group	Hepatitis B
Shenzhen Kangtai	Hepatitis B
Zhejiang Pukang	Hepatitis A
Zhejiang Tianyuan	HFRS, Flu
Chinese Academy of Medical Science	Hepatitis A, Polio