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## Vaccine Development in China

Improvements in China's regulatory and technology scenario are creating an optimistic outlook for its vaccine industry

The global vaccine market has grown phenomenally over the past decade and was estimated to exceed \$10 billion in 2006. [QA: Did the market exceed \$10 billion in 2006? Is it possible to give an estimated figure for 2007 instead?] With the world's largest population and 17 million newborn babies each year, China is the world's fourth largest vaccine market. In China, vaccines represent a market worth over 3 billion RMB (\$3.88 million), and this market is growing at 15% annually, reports Dr. Jianyuan Liu, associate director of National Vaccine and Serum Institute (NCSI) in the study, *Advances in Biopharmaceutical Technology in China*.<sup>1</sup> Today, China has the largest vaccine manufacturing capabilities and capacity in the world. Dr. Liu and his colleagues also predict that China's vaccine market demand will rise to 20% in the next few years. Recent improvements in China's regulatory, market, and technology scenario are creating an optimistic outlook for its vaccine industry.

### VACCINE CLASSIFICATION

In China vaccines are classified into two categories: government "planned immunization" vaccines and "nonplanned immunization" or "charged" vaccines (Table 1). The first category of vaccines is subsidized and ordered by the government, and eventually supplied to Chinese citizens (mostly children) at no charge. The second category is for-profit with high margins of 30-40% for imported vaccines and more than 50% for domestic vaccines.<sup>2</sup> These are "charged-for," or "non-planned" vaccines, produced by manufac-

urers based on the market demand. The charged vaccines may be purchased by consumers voluntarily. The market for the first category vaccines is controlled by the government and the second is open to domestic or international companies. These two markets are predicted to grow to roughly equal market shares.

### MARKET BACKGROUND

#### Large population, many newborns

China's population reached 1.3 billion in 2005 and will approach 1.4 billion in the next decade. The state has managed to control its birth rate to between 1.2% and 1.3%. Each year, approximately 17 million Chinese babies are born and all are suppose to receive vaccination. Based on this number, the following vaccine doses are needed each year for newborn babies:<sup>2</sup>

- Poliomyelitis vaccine 68 million doses
- Diphtheria-pertussis-tetanus vaccine 68 million doses
- Hepatitis B vaccine 51 million doses
- Measles vaccine 34 million doses
- BCG vaccine 17 million doses

#### Enhancing disease prevention awareness in adults

With the progress in public healthcare policy, hygiene education, and increased vaccine adver-

Table 1. Vaccine classification in China

Planned immunization vaccines (free)	Planned immunization vaccines	BCG, TOPV, DTwP, measles vaccine, hepatitis B vaccine
	Planned immunization managing vaccines	Japanese encephalitis vaccine, meningococcal polysaccharide vaccine, rubella vaccine, mumps vaccine, hepatitis A vaccine, etc.
Nonplanned immunization vaccines (market-demanded)	Varicella vaccine, pneumonia vaccine, influenza vaccine, typhoid vaccine, hemophilus influenza b vaccine, hemorrhagic fever vaccine, rabies vaccine, etc.	

tising programs operated by the government, an increasing number of Chinese are realizing the importance of preventive medicines. More Chinese are voluntarily spending on preventative vaccinations to reduce potential threats from prevalent diseases such as hepatitis B and influenza.

### SARS and bird flu have activated the market

The outbreak of SARS, avian flu, and the spread of hepatitis B across China have been directly responsible for energizing the vaccine industry in China. In addition, polio, which was almost eliminated, has reappeared in the country. The prevalence of measles is also increasing. China has set aggressive goals to eliminate diseases such as poliomyelitis in the country by 2012, and measles by 2010. Consequently, polio and measles vaccines are legally allowed a 20–60% price increase by the authorities. Moreover, new generations of traditional planned immunization vaccines may be reclassified as “charged” vaccines. This will permit manufacturers to raise their prices as much as ten times. These developments are fueling the expansion of the Chinese vaccine industry.

### Government protection and support

The Chinese government has considerably increased its investment in epidemic prevention systems after the SARS outbreak of 2003. The state invested 5 billion RMB (\$127 million) on anti-epidemic system in 2005, equivalent to the total investment for the previous five years. The year 2005 was a turning point in China’s vaccine development industry. In March of that year, the State Council issued “Administrative Regulations on Vaccine Distribution and Inoculation,” which became effective on June 1, 2005. For the

**Table 2.** Vaccine manufacturers in China

Domestic	
National Vaccine & Serum Institute (NVSI)	Shanghai Institute of Biological Products (SIBP)
Changchun Institute of Biological Products (CIBP)	Chengdu Institute of Biological Products (CDIBP)
Lanzhou Institute of Biological Products (LIBP)	Wuhan Institute of Biological Products (WIBP)
Beijing Tiantan Biological Products Co., Ltd. (BTBP)	Shenzhen Kangtai Biological Products Co. (SKBP)
Sinovac Biotech Ltd. (Sinovac)	Changchun Changsheng Life Sciences (Changsheng)
Changchun BCHT Pharmaceutical Co., Ltd. (BCHT)	Zhejiang Tianyuan Bio-pharma Co., Ltd. (Tianyuan)
Zhejiang Pukang Biotechnology Co., Ltd. (Pukang)	Nanjing Dalu Dekang Biotech Co. (Dalu Dekang)
Jiangsu Yanshen Biological Technology Co., Ltd. (Yanshen)	NCPC GeneTech Biotech Dev. Co. (GeneTech)
Hualan Biological Engineering, Inc. (Hualan)	Henan Puxin Bio-engineering Co., Ltd. (Puxin)
Beijing Hua-er-dun Biotech Co., Ltd. (Hua-er-dun)	Dalian Hissen Bio-pharm Inc. (Hissen)
Dalian Jingang Biological Products Co., Ltd. (Jingang)	Dalian Jingang Andi Bio-products Co., Ltd. (Andi)
Shenyang Baiao Biotech Co., Ltd. (Baiao)	Shanxi Institute of Biological Products (SXIBP)
Kunming Institute of Medical Biology (KIMB)	Yunnan Wosen Biotechnology Co., Ltd. (Wosen)
Chongqing Kangwei Biological Co., Ltd. (Kangwei)	Chongqing Jianchen Bioengineering Co. (Jiancheng)
Shenzhen Aokoo Biotechnologies, Ltd. (Aokoo)	Shanghai Fudan-Yueda Biotech Co. (Fudan-Yueda)
Shenzhen Neptunus Interlong Biotech Co., Ltd (Interlong)	Livzon Pharmaceutical Biotech Co., Ltd. (Livzon)
Foreign	
Shenzhen Sanofi Pasteur Biological Products Co., Ltd. (Pasteur)	Shanghai GlaxoSmithKline Biological Products Co., Ltd. (GSK)
Merck, Inc. (imported)	Chiron (Novartis Vaccine) (imported)

first time in history, the regulations dismantled the long-term market monopoly controlled by the provincial disease control centers. Sales outlets increased significantly from the former 54 provincial centers to 5,700 county-level anti-epidemic stations. Qualified drug wholesalers were also permitted to distribute “charged” vaccines. This has removed the supply-demand bottleneck, thereby giving a boost to the Chinese vaccine industry.

In the same year, the National Development and Reform

Commission (NDRC) published its China Bioindustry Development Strategies, which states: “to develop new types of vaccines to protect national public hygiene safety is the number one project in the biopharmaceutical industry.” The government will grant tax privileges to vaccine developers and manufacturers. NDRC is also planning to set up and subsidize special high-tech projects for vaccine development. As a result, the vaccine industry in China is poised to become the most promising

high-tech industry in China's biotech sector.

## MAJOR PLAYERS AND PRODUCTS

China is home to more than 30 vaccine manufacturers, which produce more than 1 billion dose units of vaccines each year, including 41 kinds of vaccines against 26 viruses. According to China's State Food and Drug Administration (SFDA) product database ([www.bioplanassociates.com/china](http://www.bioplanassociates.com/china)), there are more than 300 domestic and 130 imported vaccine products of various doses, forms, or specifications in the Chinese market. Although domestic companies have been protected by government policies and have thus dominated the planned immunization vaccines, imported products are becoming increasingly competitive in the charged vaccine market. For instance, all the influenza vaccines purchased by the Chinese Disease Control Center (CDC) in 2005 were imported products.<sup>2</sup>

The largest Chinese vaccine developer and manufacturer is the China National Biotec Group (CNBG), which controls six former state-owned biological product institutes in Beijing, Shanghai, Changchun, Lanzhou, Chengdu and Wuhan, and two biopharmaceutical companies in Beijing and Chengdu. CNBG employs nearly 10,000 people across China. The six institutes affiliated to CNBG currently supply 90% of planned immunization vaccines to the Chinese market, with an annual output of 300 million doses of vaccines.

Privately-owned companies such as Shenzhen Kangtai, Beijing Sinovac, Changchun Changsheng, and Zhejiang Tianyuan have been actively involved in charged vaccine manufacturing since the early 1990s.

**Table 3.** Major vaccine products in the Chinese market

Product Name	Manufacturers
Recombinant (yeast) hepatitis B vaccine	BTBP, Kangtai, Hissen
Recombinant (CHO) hepatitis B vaccine	LIBP, CIBP, Hua-er-dun, GeneTech, CDIBP, WIBP
Oral attenuated poliomyelitis vaccine	BTBP, KIMB, Pasteur
VAQTA (hepatitis A vaccine, inactivated)	Pasteur, Sinovac, KIMB, GSK
Live attenuated hepatitis A vaccine	GSK, LIBP, Changsheng, Pukang, KIMB, Yanshen
Combined hepatitis A and B vaccine	GSK, Sinovac
Purified rabies vaccine	Pasteur, CIBP, LIBP, CDIBP, WIBP, Yanshen, Puxin
Hemorrhagic fever with renal syndrome (Type I) vaccine	LIBP, SIBP, Tianyuan
Inactivated Japanese encephalitis vaccine	CIBP, BTBP, SIBP
Live attenuated Japanese encephalitis vaccine	CDIBP, WIBP, LIBP
Live attenuated rubella vaccine	Pasteur, LIBP, BTBP, SIBP
Live attenuated mumps vaccine	NIVS, WIBP, Yanshen, LIBP, SIBP
Measles, mumps and rubella vaccine	Merck, GSK, BTBP
Oral attenuated rotavirus vaccine	LIBP
Inactivated influenza vaccine	Pasteur, GSK, BTBP, LIBP, CIBP, Changsheng
Split influenza vaccine	SIBP, LIBP, CDIBP, CIBP, Changsheng, WIBP
Lyophilized live attenuated varicella-zoster vaccine	GSK, CIBP, SIBP
Inactivated forest encephalitis vaccine	LIBP
Live attenuated yellow fever vaccine	BTBP
Absorbed diphtheria vaccine	BTBP, SIBP, CIBP, WIBP, CDIBP, LIBP
Absorbed tetanus vaccine	CIBP, BTBP, SIBP, LIBP, WIBP
Absorbed diphtheria and tetanus combined vaccine	LIBP, BTBP, CIBP, SIBP
Absorbed pertussis and diphtheria combined vaccine	CIBP, LIBP
Absorbed acellular pertussis, diphtheria, and tetanus combined vaccine	BTBP, SIBP, CIBP, WIBP, CDIBP, LIBP
Absorbed pertussis, diphtheria, and tetanus combined vaccine	CIBP, WIBP, CDIBP, LIBP, SIBP
Absorbed diphtheria, tetanus, pertussis, and polio vaccine	Pasteur
BCG vaccine	CIBP, SIBP, LIBP, CCIBP
Tracheitis vaccine	LIBP, CIBP, SIBP, Yanshen, WIBP
Typhia vi polysaccharide vaccine	Pasteur, LIBP, CIBP, BTBP, SIBP, CDIBP, WIBP
Pneumococci polyvalent vaccine (Pneumovax 23)	Pasteur, Merck
Hemophilus influenza b conjugate vaccine	Pasteur
Furunculosis vaccine	SIBP, WIBP, Yanshen
Meningococcus group A polysaccharide vaccine	LIBP, CIBP, BTBP, SIBP, WIBP, CDIBP
Meningococcus group A plus C polysaccharide vaccine	LIBP
Oral bivalent live vaccine of S.flexneriza-S. sonnei capsule	LIBP
Live anthrax vaccine for scarification	LIBP, CDIBP
Live plague vaccine for scarification	LIBP, CIBP
Absorbed cholera toxoid vaccine	SIBP, CIBP

**Table 4.** Pipeline Products

Product	Developer	Clinical Trial
Therapeutic hepatitis B vaccine (synthetic peptide)	Chongqing Jiachen Biopharma	Phase 2
Therapeutic hepatitis B vaccine (Immune Complex)	Shanghai Fudan-Yueda & NVSI	Phase 3
AIDS vaccine	Changchun Baike	Phase 1
SARS vaccine	Sinovac & CDC	Phase 2
H5N1 Influenza vaccine	Sinovac & CDC	Phase 2
Helicobacter pylori vaccine	Chongqing Kangwei Biological	Phase 3
O1/O139 cholera bivalent vaccine (capsule)	Unknown	Phase 1
Group A.C.Y. W135 meningitis vaccine	NVSI, Hangzhou Tianyuan, Hualan	Preclinical trials
Polyvalent pneumococcus combined vaccine	NVSI, LIBP, CDIBP,	Preclinical trials
Cancer vaccine	Shanghai Zhangjiang Biotech Center	Phase 2
Cancer vaccine	First Hospital of Sun Yat-sen Univ.	Preclinical trials

These companies are becoming very competitive because of their flexible capital advantages and market awareness. Sinovac, for example, has taken the lead in developing vaccines for SARS and avian flu.

Because the Chinese government restricts foreign companies to set up vaccine manufacturing facilities or even seek Chinese contract manufacturing partners, so far, only two foreign vaccine manufacturers, Sanofi Pasteur and GlaxoSmithKline, have established repacking facilities in China. Other major vaccine importers include Merck and Chiron (Novartis Vaccine). Also, Pfizer is planning to enter the Chinese vaccine market after acquiring PowderMed in 2006.

Table 2 and Table 3 summarize vaccine manufacturers and products in China. Table 4 lists the major pipeline products.<sup>2</sup>

### MARKET PERSPECTIVE

In the current Chinese market, domestic products completely control the planned immunization vaccine market. Foreign companies

**The Chinese vaccine market competition is now transferring from the former price-competition model to a technology-competition model.**

are only permitted to be involved in the charged vaccine market. This has restricted the imported products market, which accounts for only 10% of the business. In terms of single product share, hepatitis B, hepatitis A, rabies, and influenza vaccines have the chunk of the market share in China. China's cur-

rent vaccine market size is RMB 3 billion (\$380 million) and is expected to reach RMB 10–15 billion (\$1.3 billion–1.9 billion) based on market growth trends. The market perspective is very promising.

Chinese domestic vaccine manufacturers are now facing challenges as a growing number of imported products are entering the market. Domestic vaccines have dominated the Chinese market for decades, thanks to government protection and lower prices. However, the vaccine market competition is now transferring from the former price-competition model to a technology-competition model. The question posed in China today is how competitive are its domestic vaccine manufacturers compared with the multinational giants.

“Which other country (than China) in the world would be able to satisfy the needs of vaccines for 1.3 billion people?” asked Dr. Weidong Yin, CEO of Sinovac Biotech. “Only we Chinese people can help ourselves. We will master core technologies and protect national security and public health...to prevent public crisis such as pandemic influenza, the key is to develop Chinese-owned vaccine products.” Sinovac spends 20% of its sales revenue on product research and development.

Given the demographics, health-care policy, and national needs, we believe there is a promising future for the Chinese vaccine industry. ♦

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