

## China's emerging vaccine industry

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The Chinese vaccine industry is developing rapidly due to an emerging and large market for current and new vaccines, a large potential for local vaccine manufacturing both in the public and private domain, and a governmental orientation towards national vaccine self-sufficiency. There are currently over 40 companies and institutions manufacturing a large variety of traditional (EPI) and some new vaccines. The innovative development capacity of state vaccine institutions is stimulated by significant government investments. Various Chinese influenza manufacturers were in 2009 among the first worldwide to obtain national license for their pandemic H1N1 flu vaccines. It is of interest to note that private but also governmental entities are committed to raise manufacturing quality standards to reach WHO prequalification. It is expected that WHO prequalification for at least one product from a Chinese manufacturer will have been obtained by 2011. This will open the door to the global market for Chinese vaccines.

### Introduction

The global human vaccine market is expected to grow rapidly in the coming decades, fueled by re-emerging vaccine preventable health threats such as pandemic influenza, an increasingly more coordinated international response thereto, and the availability of licensed new vaccines combined with several international philanthropically public private partnerships, such as GAVI. On top of this, countries with emerging economies are introducing these new vaccines in a more rapid pace than

ever. At the same time, equitable access to vaccines for the global community remains a subject of intensive international public health concern, as for example the recent case of pandemic influenza caused by the new H1N1 virus illustrates.<sup>1</sup> The importance of local or regional vaccine manufacturers, coordinated in the Developing Countries Vaccine Manufacturers' Network (DCVMN), to reduce this global vaccine inequity has been highlighted before.<sup>2</sup> The DCVMN ([www.dcvmn.com](http://www.dcvmn.com)) is a voluntary public health driven alliance of vaccine manufacturers in developing countries, under advocacy of WHO.<sup>2</sup> The members include vaccine manufacturers in developing countries, international organizations and resource institutions such as the Netherlands Vaccine Institute (NVI) and the Programme for Appropriate Technology in Health (PATH), based in Seattle, USA. The objective of the Network is to help the vaccine manufacturers in developing countries understand the most up-to-date status of vaccine development and assist them becoming a supplier to international markets, thereby improving the health of people in developing countries.<sup>2,3</sup> Members of the DCVMN include public and private manufacturers mainly from countries with fast growing emerging economies, such as Brazil, India and China.

It is remarkable that at the international level, little is known about the vaccine situation in China, a country with a very large part of the world population. Due to China's impressive economic growth figures in latest years, the Chinese market is becoming very attractive for pharmaceutical companies. Because of its huge population, national vaccination policies in China are influenced by the ability of

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**Table 1.** The Chinese national immunization program (CNIP)

Abbreviation	Vaccine	Year of Introduction	Remarks
HBV	Hepatitis B Vaccine	2002	
BCG	BCG Vaccine	1978	
OPV	Oral Poliomyelitis Vaccine	1978	
DTP	Combined Vaccine of Pertussis, Diphtheria & Tetanus	1978	
MV	Measles Vaccine	1978	
DT	Combined Vaccine of Diphtheria & Tetanus	2008	Booster for 6 year olds
DTaP	Acellular DTP Vaccine	2008	To replace DTP
HAV	Hepatitis A Vaccine	2008	
MenA/MenAC	Meningococcus Vaccine	2008	
JE	Japanese Encephalitis Vaccine	2008	
MMR	Combined Vaccine of Measles, Mumps & Rubella	2008	
	Hemorrhagic Fever Renal Syndrome Vaccine	2008	
	Anthrax Vaccine	2008	Only for certain risk groups in endemic regions
	Leptospira Vaccine	2008	

domestic manufacturers to supply needed vaccines at an affordable price.

This commentary aims to give a recent overview of the emerging human vaccine industry in China in view of the increasing global awareness of the importance of regional or local vaccine manufacturing to tackle international vaccine availability issues.<sup>4</sup> Although the focus of most Chinese vaccine manufacturers is at this moment their domestic market, they have a clear ambition and potential to play a role in the global market. This became apparent at the latest Annual Meeting of the DCVMN that was hosted by the China National Biotec Group (CNBG) in Beijing in September 2009. Currently 4 Chinese manufacturers are DCVMN members, including CNBG. CNBG's national status was actually reconfirmed end 2009, when China's State-owned Assets Supervision and Administration Commission (SASAC) announced a merger of the CNBG with the China National Pharmaceutical Corporation (Sinopharm). Sinopharm is one of China's largest pharmaceutical companies and is believed to become one of China's three giant pharmaceutical conglomerates over the next few years.<sup>5</sup>

### The National Immunization Program and Vaccine Markets

China, with its 1.3 billion inhabitants and over 17 million newborns annually, is the world largest vaccine consuming

country. The current vaccine market in China was valued in 2009 to be around \$700 million with a compound annual growth rate expected to increase from around 15% now to 30% over the next few years, thanks to recently announced governmental healthcare reforms that emphasize prevention and aim to bring wider insurance coverage to the population.<sup>6</sup>

The Chinese government has traditionally over the years managed a successful vaccine-preventable disease programme. Polio-eradication was for example already achieved in 1994 and childhood immunization continues to be a high priority.<sup>7</sup> A law was passed in 2005 ensuring provision of vaccines free of charge through the Chinese National Immunization Program (CNIP). The CNIP currently includes 14 (mainly pediatric) vaccines against 15 diseases (Table 1). Several new antigens including recombinant Hepatitis B were introduced since 2007.

Several vaccines in the CNIP are in short supply, for example the demand for Diphtheria-Tetanus-acellular-Pertussis vaccine (DTaP) was nearly 64 million doses in 2008, whereas manufacturers supplied only about 18 million doses, resulting in a market gap of 46 million doses in 2008. For MMR, the market gap is estimated at 23 million doses each year and there are also shortages for live attenuated hepatitis A vaccines, inactivated hepatitis A vaccines, and inactivated Japanese Encephalitis vaccines.<sup>8</sup>

The priority and cost-effectiveness of introduction of new vaccines such as conjugate Hib vaccine, pneumococcal and rotavirus vaccines, IPV replacement for OPV and combination vaccines to reduce the number of injections into this CNIP is currently actively being assessed in collaboration and consultation with international bodies such as WHO and GAVI.<sup>9</sup> These studies are expected to lead in the coming years to the uptake of new vaccines in the CNIP. Currently, the introduction of a cHib vaccine (widely promoted by GAVI) is seriously being considered by the Chinese authorities and several domestic manufacturers have already started to develop and manufacture this conjugate vaccine.

Vaccines used outside the CNIP in the private market are produced by manufacturers based on market demand (Table 3). Examples are seasonal influenza vaccines and rabies vaccines. These may be purchased by consumers on a voluntary basis.

### The Vaccine Regulatory Authority

Vaccines are regulated in China by the State Food and Drug Administration (SFDA). The SFDA with provincial FDA's supervises and controls throughout the country the entire vaccine supply chain, from production, trading, to supply and administration. Since China aims to produce and export vaccines, it is a prerequisite that China's regulatory authority,

the SFDA, is able to exercise the six regulatory functions that are recognized by WHO as essential to ensure that vaccines manufactured in China are of international assured quality. The Government has thus embarked since 2003 with WHO support on a programme to improve the vaccine regulatory capacity of the SFDA up to international standards.<sup>10</sup> Currently WHO is preparing for a re-assessment of the SFDA which is expected to take place by the end of 2010. A successful outcome of this re-assessment will start the process of submission to WHO of pre-qualification dossiers of vaccines made by Chinese manufacturers, which will pave the way of China's entry into the global market. One of the first candidate vaccines for WHO pre-qualification will be the Japanese Encephalitis vaccine made by the Chengdu Institute for Biological Products in collaboration with PATH.

### Vaccine Manufacturing in China

China ranks as the world's largest vaccine manufacturing country with an annual output of more than one billion doses.<sup>11</sup> The Chinese government has a policy to provide vaccines for the CNIP by Chinese manufacturers and, with the exception of BCG and OPV, does not encourage supply of CNIP vaccines by international vaccine manufacturers, according to a "Guidance Catalogue of Foreign Investment Industries" issued by the National Development and Reform Commission and the Ministry of Commerce in 2007.<sup>12</sup> Currently the website of the Chinese national regulatory authority (SFDA) lists 46 Chinese registered vaccine manufacturers, of public and private status, collectively manufacturing 24 licensed vaccines.<sup>13</sup> Table 2 shows an overview with an indication of the number of vaccines they each manufacture and their legal status.

**CNBG/Sinopharm.** It is interesting to note from this list that the six subsidiary manufacturers of the CNBG group, located in Beijing, Changchun, Chengdu, Lanzhou, Shanghai and Wuhan, have the widest diversity of vaccines as compared to the private manufacturers. Collectively they provide 90% of the doses of the 14 CNIP vaccines (Table 3). To bolster

innovative development capacity, CNBG/Sinopharm established in Beijing in 2004 a corporate R&D centre to maximize the synergies of the 6 Institutions. The construction of a New National Vaccine Engineering Research Center, China's first national-level research, development and industrialization base for new vaccines started in 2009 in Beijing. The center will aim to upgrade traditional vaccines and solve technical problems occurring during the R&D and industrialization of new vaccines, focusing on R&D including pilot scale production of new vaccines and biomedicines.

CNBG/Sinopharm has also interests in several private companies, for instance CNBG/Sinopharm is a majority shareholder of Beijing Tiantan Biological Products Co., Ltd., (nr 43 in Table 3).

Recently, multinational vaccine companies show an increasing interest in expanding their presence and are entering the Chinese market by taking majority shares in Chinese companies. GSK announced in 2009 to take a 65% stake in a joint venture with the Chinese firm Walvax (nr 24 in Table 3) for the development, manufacture and supply to China's public vaccine market of MMR. This followed GSK's earlier announcement of a 40% stake in a JV with another Chinese company, Shenzhen Neptunus Interlong Biotech Co., Ltd., (nr 42 in Table 3) to develop and manufacture flu and rabies vaccines. Sanofi pasteur has a majority in Shenszen Sanofi (nr 36 in Table 3) and has announced investments of over \$94 million (RMB 700 million) in a flu vaccine facility with a 25 million doses annual capacity. Novartis obtained in November 2009 a majority (85% stake) in Zhejiang Tianyuan Bio-Pharmaceutical Co., Ltd., (nr 20 in Table 3), subject to government and regulatory approval in China.

### Influenza Vaccines

**Seasonal influenza vaccines.** There is a big potential market for seasonal flu vaccines considering the current low vaccination rates and China's huge population. The overall seasonal flu vaccination rate in China was about 1.5% in the 2007–2008 season. For certain risk groups (the aged population) it was only about 0.3%.

Under the current SFDA regulation, provinces and municipalities can develop their own policies. This explains that regional differences on flu vaccination practices exist. For example, the Beijing municipality offered in the 2007/2008 season free flu vaccines to the registered elderly population, and half-price flu vaccines to students in primary and junior middle schools, totaling together over 1.5 million persons. Five flu manufacturers (Table 3; nrs: 9, 20, 26, 43 and 37) supplied seasonal influenza vaccines to this Beijing city programme. Obviously there is a marked interest by various manufacturers both domestically and internationally to obtain a market share of the influenza vaccine market in China, as is apparent from the relatively large number of influenza manufacturers in Table 3 as well as the interest of the international companies to get a stake in China's flu vaccine market.

**Pandemic influenza vaccines.** The recent global threat for a new avian flu pandemic and in particular the 2009 new (H1N1) influenza pandemic amplified galvanized the emerging Chinese flu vaccine industry. Due to very proactive pandemic vaccine preparedness decisions at the Government level, China made global headlines in 2009 becoming the first country to complete clinical trials for the new H1N1 pandemic flu, to approve domestically made pandemic flu vaccines and to start mass immunizations. The Chinese government's strategy was to vaccinate in 2009 five percent of the total population, or about 65 million people. By November 2009, SFDA had provided a national license to 10 Chinese manufacturers (see Table 3 nrs: 2, 3, 4, 7, 9, 20, 22, 26, 43 and 46). By February 2010, around 77 million people had received the vaccine. The Chinese vaccines were made in eggs with the NYMCMX-179A virus seed strain obtained from WHO. An extensive clinical study coordinated by the Chinese CDC in 7 provinces involving over 13,000 volunteers showed that a one dose regimen of a 15 ug split formulation without adjuvant yielded a protection of about 85%.<sup>14</sup> The Chinese government purchase price was set to about 22 RMB (2.2 EUR) per dose. The vaccines were provided to the public (especially high risk groups: public health workers, students and patients

**Table 2.** Chinese vaccine manufacturers registered at SFDA<sup>13</sup>

	<b>Vaccine Manufacturer</b>	<b>Location</b>	<b>Nr of products</b>	<b>Legal Entity</b>
1	National Vaccine & Serum Institute (NVSI)	Beijing	2	Public; Sinopharm
2	Changchun Institute of Biological Products (CIBP)	Changchun, Jilin	7	Public; Sinopharm
3	Lanzhou Institute of Biological Products Co., Ltd., (LIBP)	Lanzhou, Gansu	13	Public; Sinopharm
4	Shanghai Institute of Biological Products (SIBP)	Shanghai	3	Public; Sinopharm
5	Wuhan Institute of Biological Products (WHIBP)	Wuhan, Hubei	4	Public; Sinopharm
6	Chengdu Institute of Biological Products (CDIBP)	Chengdu, Sichuan	6	Public; Sinopharm
7	Hualan Biological Engineering Inc., (Hualan)	Xinxiang, Henan	7	Private
8	Yunnan Yuxishangcheng Biotech Co., Ltd.	Yuxi, Yunnan	1	Private
9	Sinovac Biotech Co., Ltd., (SinoVac)	Beijing	3	Private
10	Rong'an Pharma Co., Ltd., (RongAn)	Ningbo, Zhejiang	2	Private
11	Guangzhou Nuocheng Bio-product Co., Ltd., (Nuocheng)	Guangzhou, Guangdong	1	Private
12	Beijing Qiweike Biotech Co., Ltd.	Beijing	1	Private
13	Shanghai Zerun Biotech Co., Ltd., (Zerun)	Shanghai	1	Private
14	Tianshili Jinna Biotech Co., Ltd.	Tianjin	1	Private
15	Shandong Hengye Biotech Co., Ltd.	Qingdao, Shandong	1	Private
16	Henan Puxin Bio-engineering Co., Ltd., (Puxin)	Zhengzhou, Henan	1	Private
17	Changchun Institute Co., Ltd., of Biological Products	Changchun, Jilin	2	Private
18	Zhejiang Pukang Biotechnology Co., Ltd., (Pukang)	Hangzhou, Zhejiang	1	Private
19	Changchun Wei-er-sai Pahrma Co., Ltd.	Changchun, Jilin	1	Private
20	Zhejiang Tianyuan Bio-Pharma Co., Ltd., (Tianyuan)	Hangzhou, Zhejiang	4	Private (85% Novartis)
21	Dalian Kunyang Pharma Co., Ltd.	Dalian, Liaoning	1	Private
22	Changchun Changsheng Life Science (Changsheng)	Changchun, Jilin	7	Private
23	Luoyi Bio-pharma Co., Ltd., (Luoyi)	Wuxi, Jiangsu	1	Private
24	Walvas Biotechnology Co., Ltd., (Walvax)	Yunnan	4	Private (65% GSK)
25	Shenzhen Kangtai Biological Products Co., (SKBP)	Shenzhen, Guangdong	1	Private
26	Jiangsu Yanshen Biological Tech Co., Ltd., (Yanshen)	Changzhou, Jiangsu	4	Private
27	Xinkexian Biotech Co., Ltd.	Fuyang, Anhui	5	Private
28	Liaoning Yisheng Pharma Co., Ltd., (Yisheng)	Shenyang, Liaoning	2	Private
29	Liaoning Chengda Bio-tech Co., Ltd., (Chengda)	Shenyang, Liaoning	1	Private
30	Fu'er Pharma Co., Ltd., (FuEr)	Hebei	2	Private
31	Zhejiang Weixin Pharma Co., Ltd., (Weixin)	Ningbo, Zhejiang	2	Private
32	Shenzhen Qinghuayuanxing Bio-pharma Tech Co., Ltd.	Shenzhen, Guangdong	1	Private
33	Beijing Hua-er-dun Bio-tech Co., Ltd.	Beijing	1	Private
34	Dalian Hanxin Pharma Co., Ltd., (Hanxin)	Dalian, Liaoning	2	Private
35	Beijing Lvzhu Phama Co., Ltd., (Lvzhu)	Beijing	3	Private
36	Institute of Medical Biology, Chinese Academy of Medical Science (IMBCAMS)	Kunming, Yunnan	2	Public
37	Shenzhen Sanofi Pasteur Biological Products Co., Ltd., (Pasteur)	Shenzhen, Guangdong	4	Private; (Stakeholder Sanofi)
38	Jilin Yatai Bio-pharma Co., Ltd., (Yatai)	Changchun, Jilin	1	Private
39	Jilin Maifeng Pharma Co., Ltd., (Maifeng)	Changchun, Jilin	1	Private
40	Beijing Wansai Bio-Pharma Co., Ltd.	Beijing	1	Private
41	Huabei Pharma Jintan Bio-tech Co., Ltd., (Jintan)	Shijiazhuang, Hebei	1	Private
42	Shenzhen Neptunus Interlong Biotech Co., Ltd.	Shenzhen, Guangdong	1	Private; (JV 40% GSK )
43	Beijing Tiantan Biological Products Co., Ltd., (BTBP)	Beijing	3	Private (holding company of Sinopharm)
44	Shanghai Rongsheng Pharma Co., Ltd.	Shanghai	1	Private
45	Shenzhen Weiwu Guangming Bio-product Co., Ltd.	Shenzhen, Guangdong	1	Private
46	Dalian Aleph Biomedical Co., Ltd., (Aleph)	Dalian, Liaoning	1	Private

**Table 3.** Major vaccine products in China<sup>13</sup>

	Product Name	Nr of Manufacturers	Reference nr in Table 2
1	Recombinant HBV	8	2, 3, 5, 6, 25, 34, 41, 43
2	BCG	5	1–4, 6
3	OPV	2	36, 43
4	DTP	6	1–6
5	MV	5	3–6, 43
6	DT	6	2–6, 43
7	DTaP	7	2–6, 22, 43
8	HAV	6	2, 9, 13, 18, 22, 36
9	Meningococcus A and A + C Vaccine	9	2–6, 20, 23, 24, 35, 43
10	JE	9	1–6, 20, 29, 43
11	MMR	1	4
12	Hemorrhagic Fever with Renal Syndrome Vaccine, Inactivated	6	2–4, 20, 23, 31
13	Anthrax vaccine	2	3, 6
14	Leptospira Vaccine	3	4–6
15	Adsorbed Tetanus Vaccine	6	2–6, 43
16	Combined Vaccine of Hepatitis A and B	1	9
17	Rabies Vaccine	14	2, 3, 5, 10, 11, 16, 22, 26, 28–30, 34, 38, 39
18	Tracheitis Vaccine	4	2, 4, 5, 26
19	Typhoid Vi Polysaccharide Vaccine	6	2–6, 43
20	Tick-borne encephalitis vaccine	1	2
21	Split A (H1N1) Influenza Vaccine	10	2–4, 7, 9, 20, 22, 26, 43, 46
22	Seasonal Influenza Vaccine	11	2–4, 7, 9, 20, 22, 26, 37, 42, 43
23	Pandemic (H5N1) Influenza Vaccine	1	9
24	Brucella Vaccine	2	2, 3

NB. The first 14 vaccines are used in the Chinese National Immunization Programme (see also Table 1).

with chronic diseases) free of charge. The estimated national flu vaccine production capacity was estimated by the first quarter of 2010 at around 100 million doses.

### Concluding Remarks

The recent developments described here will lead to an increased uptake of traditional and new vaccines in the Chinese public immunization programme. In the years to come the domestic vaccine market in China will grow at an accelerated pace. Besides stimulating the domestic industry, this has attracted the interest of international manufacturers who are now engaging in China through different strategies, such as taking interests in Chinese private companies. This may lead to competitive supply of vaccines to Chinese markets including the EPI-markets. Because the Chinese regulatory authorities are striving to meet international criteria for vaccine

manufacturing and regulation, it may be expected that in the years to come the number of domestic vaccine companies will decrease, as they are forced to meet international quality standards. China's national policy to stimulate domestic vaccine manufacture is becoming more internationally oriented, as exemplified by the increasing presence of Chinese manufacturers in the DCVMN. Several Chinese manufacturers are making significant investments in their facilities to meet international GMP standards and regulations. CNBG/Sinopharm and others have embarked on an ambitious programme to meet WHO pre-qualification for one or more of their products opening the way to provide vaccines for the global market. The remarkable, very fast and significant up scaling of Chinese pandemic flu vaccine production capacity in 2009 illustrates the enormous potential and global relevance of the emerging Chinese vaccine

industry. This will in the near future no doubt benefit global access to vaccines.

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### References

1. Verweij M. Health Inequities in Times of a Pandemic. *Public Health Ethics* 2010; 2:207-9.
2. Jadhav S, Datla M, Kreeftenberg H, Hendriks J. The Developing Countries Vaccine Manufacturers' Network (DCVMN) is a critical constituency to ensure access to vaccines in developing countries. *Vaccine* 2008; 26:1611-5.
3. Poeloengan T, Raw I, Martinez LH, El-Abbadi M. Developing Country Vaccine Manufacturers Network (DCVMN), 26–27 April 2001, Bandung, Indonesia. *Vaccine* 2001; 20:285-7.
4. Milstien JB, Kaddar M. The role of emerging manufacturers in access to innovative vaccines of public health importance. *Vaccine* 2010; 28:2115-21.
5. Anonymous, Press Release. SASAC Announces Sinopharm CNBG Merger. *PRNewswire-Asia* 2009; www.transmedia-china.com.

6. Qing Xia, Daming Chen. China Increases Health Care Investment. *Genetic Engineering & Biotechnology News* 2009; 52-4.
7. Anonymous. Press Release. Sinovac establishes joint venture to expand human use vaccine development and manufacturing capabilities. *PRNewswire-Asia* 2009; [www.prnewswire.com](http://www.prnewswire.com).
8. Qiu Ying-ping. Domestic supply in vaccine-producing countries. *Health News (JianKangBao)* 2008; [www.jkb.com.cn](http://www.jkb.com.cn).
9. Eliza Yibing Zhou. The top-60 Chinese Biopharma Companies. [www.bioplanassociates.com](http://www.bioplanassociates.com) 2008.
10. Office of the WHO Representative in China. WHO-China Country Cooperation Strategy 2008–2013. 2008.
11. Han P. China's growing biomedical industry. *Biologicals* 2009; 37:169-72.
12. Man TY, Zeng Y, Jing Sun. Foreign Investment Industry Catalogue: New Revisions & Alignment with National Development Strategy. *China Law & Practice* 2007; 17-9.
13. State Food and Drug Administration (SFDA). Website. [www.sfda.gov.cn](http://www.sfda.gov.cn) 2010.
14. Xiaofeng Liang. Immunization Strategies in China. Oral presentation at DCVMN Meeting Beijing 2009.

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