BioPlan associates, inc.

Second Edition

Directory of Top 60 Biopharmaceutical Manufacturers in China

SECOND EDITION

Directory of Top 60 Biopharmaceutical Manufacturers in China

A comprehensive industry review: Profiles of established, and rapidly growing, facilities involved in biopharmaceutical manufacturing.

FEBRUARY 2017

BioPlan associates, inc.

DIRECTORY OF

Top 60 Biopharmaceutical Manufacturers in China

A comprehensive industry review: Profiles of established, and rapidly growing, organizations involved in biomanufacturing.

FEBRUARY 2017

BioPlan Associates, Inc.
2275 Research Blvd, Suite 500
Rockville, MD 20850 USA
301.921.5979
www.bioplanassociates.com

Directory of
Top 60 Biopharmaceutical Manufacturers in China

A comprehensive industry review: Profiles of established, and rapidly growing, organizations involved in biomanufacturing.

February 2017

BioPlan Associates, Inc.
2275 Research Blvd, Suite 500
Rockville, MD 20850 USA
301.921.5979
www.bioplanassociates.com

Authors: Vicky Qing XIA, Leo Cai YANG
Review: Donnie E. Gillespie, Ron Rader, and Eric S. Langer
Text design and Layout: ES Design, Arlington, VA
Cover Photo: Courtesy of Adam C. Kemp
ISBN 978-1934-106-31-1

Preface

This is the second edition of BioPlan Associates' facilities directory of major biopharmaceutical manufacturing facilities in China. In it, we cover China's major biopharmaceutical manufacturing facilities, particularly those with the most bioprocessing capacity (total bioreactor volumes), and those under active construction. Facility information includes company ownership, background, management and facility capacity and history.

This *Directory* is based on in-depth research, using public secondary and primary information resources. This on-going project is intended to provide in-depth information and insights into the rapidly growing and changing Chinese biologics industry. The original directory, published in March, 2008, included some facilities that have grown rapidly, and some that no longer exist. The landscape in China biopharma has evolved over the past eight years, so much that this update has become urgently necessary.

As the Chinese industry continues to expand, both in technical capabilities and commercial presence, the information in this directory will, necessarily, become outdated. As such, we will have on-staff researchers to keep it up-to-date. However, our readers' input will be invaluable in that regard. If you have comments or corrections, please forward them to us.

The ranking of companies is based on information publicly available. Factors in ranking each facility include aspects such as liter's' capacity, number of employees related to biologics production, number of products in commercial or clinical production. Financial estimates in some cases are derived from data such as the number of employees, facility size, and available partnership resources.

Because the Chinese biopharmaceutical industry is in a growth phase, some of the organizations profiled are emerging as industry participants. These companies may be included because, based on their human resources, their internal expertise, or their financial capabilities, they have the potential to rapidly enter this market with their own biological products.

We wish to acknowledge the contributions of many individuals in China, and around the world, who have reviewed and evaluated the content of this directory.

Without their support, this project would not have been possible.

Eric S. Langer
Managing Partner
BioPlan Associates, Inc.
February 2017

Photo with permission Tiantan Pharma Production Facility

Table of Contents:

Photo with permission Hisun Pharmaceutical Ltd., Zhejian

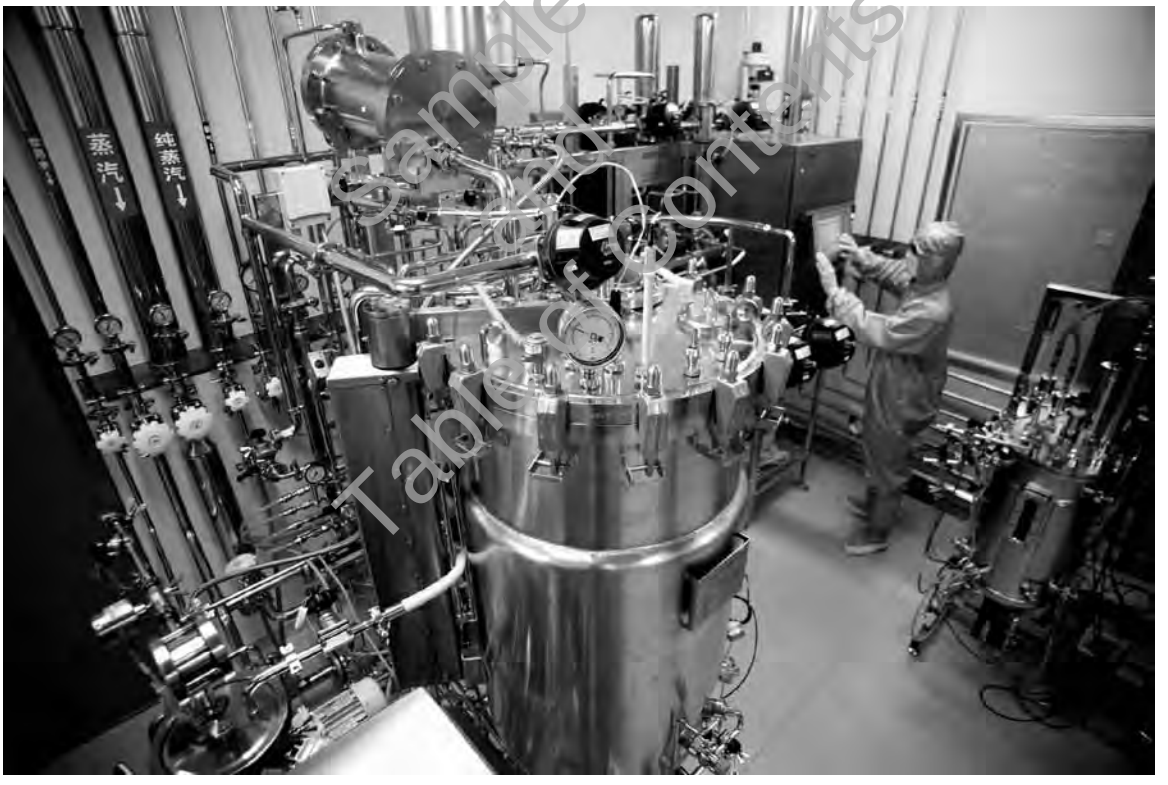

Photo with permission Hisun Pharmaceutical Ltd., Zhejian

1 China Biopharmaceutical Manufacturing

Introduction

Since 2000 China has placed biotechnology prominently in its 5-year Plans (guidelines). And the current Guidance makes the "*Made in China 2025*" a priority focus. The country is actively addressing nationally vital technologies, including biopharma, that lack a domestic core platform. Where Chinese products today are perceived internationally to be of inferior quality, investments are being made to address these shortfalls. This directory provides a perspective on how rapidly changes are taking place.

As revenues from biologics sales expand at double digit rates, both domestic Chinese, and global investors have recognized the potential for sustained growth and a global position for China in biotech. The Chinese government has invested heavily to expand Chinese companies and their innovations. Because biotechnology is a prominent part of China's 12th Five-Year Plan (2011-2015) for strategic economic growth and investment, the segment will receive major portions of the related $1.7 trillion available investment. Further, China's Minister of Health announced the country is spending an additional $11.8 billion to advance biopharma innovation through 2020.

Manufacturing has, and will continue to be a cornerstone of investment in China, and this 2nd Edition of our *Top 60 China Biopharma Facilities Directory* helps outline the current leading biopharmaceutical manufacturing companies and facilities that will lead China into the future. At present, investment goals include doubling the number of people in biotech, creating the needed staffing talent and educational infrastructure capable of "Nobel-level scientists by 2020", and establishing the facilities needed to succeed. The next 10 years will be quite exciting for this segment.

China's Biopharmaceutical Manufacturing

China's biopharmaceutical manufacturing segment includes 4 primary subsectors:

- mAb manufacturers
- First-generation therapeutic protein drug makers (insulin, TPO, EPO, etc)
- Biologics CMOs
- Vaccine/blood product manufacturers.

In our first edition of the *Top 60 China Biopharma Companies Directory, March 2008*, the companies in China at the time belonged primarily to just two categories: Makers of first-generation therapeutic protein drugs, and vaccine/blood products. The addition of competent manufacturers of mAbs, and biologics CMOs to the China market itself speaks volumes about how the industry has evolved over the past decade.

Monoclonal antibody maker and biosimilars

The Chinese pharmaceuticals market has a strong need for mAb products, and a large proportion of its mAbs currently are imported from developed countries. China imported USD$950 million in mAb therapeutics in the first half of 2015 according to *Medicine Economic Reporter,* and *Zhongkang CMH* similarly estimates that the total Chinese market of mAbs was worth USD$960 million in 2014. Naturally, many domestic drug makers see this as an opportunity for future growth. Many domestic industry observers believe that with the expansion of national health insurance in both coverage and increase in reimbursement rates, as well as the coming patent expiration of many of the mAb developed by multinational companies, the mAb market in China is going to increase rapidly in the near future.

According to CFDA insiders, close to 200 manufacturers had submitted applications for clinical trials in China (the Chinese equivalent of an IND) for mAbs by the end of 2015. It is estimated that over 600 companies in China are planning therapeutic mAbs in their pipeline. Many of those domestic applicants are new comers in the arena, as we can see that IND applications number 132 while only 11 mAbs from domestic companies are on the market (with other mAbs from multinational pharma). (See: Pharmacodia.com).

In our first edition of this *Directory*, we listed only a few monoclonal antibody makers (e.g., CP Guojian, Biotech Pharma). Now this segment has dozens of players, including new mAb makers founded within this decade, as well as established chemical drug and Traditional Chinese Medicine (TCM) makers venturing into this new field. While the newly founded mAb makers, such as Henglius Pharma, Genor Pharma, and Teruisi, are generally considered capable of more innovative drug development with their experienced returnee scientists, several domestic chemical drug TCM makers have successfully launched their own antibody therapeutics in recent years, including:

- Kanghong Pharma, a TCM maker in Sichuan, launched its bio-similar version of Lucentis in 2015
- Hisun Pharma, an important chemical drug maker and API exporter, launched Anbainuo, a recombinant human TNF-alpha receptor II:IgG Fc fusion protein this year.

Many more companies are building antibody production plants with state-of-art bio-processing equipment from international vendors. The manufacturing capacity of those antibody making plants, is usually in thousands, or tens of thousands of Liters with mammalian cell culture based system, which is significantly larger than that of the first-generation protein therapeutics makers, who often use bacteria-based systems.

From a sales point of view, currently CP Guojian and Biotech Pharma, the two mAb makers covered in the first edition, continue to grow. According to the CEO of CP Guojian, Mr. Wang Junlin, the company has around RMB 1 billion (USD$145m) revenue from sales of mAb in 2014 with an annual growth rate between 20%-30%. Biotech Pharma's Taixinsheng (nimotuzumab), had revenue of RMB 450 million ($65m) in 2013. Some optimistic analysts project that Langmu from Kanghong would attain sales of RMB 500 million (USD$72m) in 2016. Whether China will have a blockbuster 'made-in-China' mAb drug remains uncertain as the ones launched or under clinical development are mostly bio-similars (biogenerics, from a highly regulated market perspective) and some biobetter versions of mAbs developed by multi-national corporations (MNCs), which have a better quality image for biological drugs.

Biologics CMOs

The Contract Manufacturing Organization (CMO) sector in China started from being almost non-existent just 10 years ago, and is now a sector attracting multinational pharmaceutical companies' interest. At that time, CMOs were not permitted to operate in China, but rules have been changing. This sector has grown quickly thanks to strong international/domestic market needs as well as new reforms that open doors for biologics CMOs in China, *the Marketing Authorization Holder System*. In August 2015, the State Food and Drug Administration (SFDA) submitted a request to the State Council to launch a pilot Marketing Authorization Holder program in 10 provinces and municipalities. This essentially allows certain companies in certain areas to undertake biopharmaceutical-related CMO work, particularly involving manufacturing.

By the end of 2015, the Standing Committee of the National People's Congress had issued a decision to authorize the State Council to carry out the pilot program, providing policy breakthrough and legal basis for biopharma CMO to undertake domestic business. Under the Marketing Authorization Holder (MAH) system, a holder of the drug approval number could be a drug production enterprise, a research institute or a researcher, who are required to market the drugs on their own and take the responsibility for the drugs during their entire life cycles. Essentially, after receiving CFDA biologics approvals, the license holders are allowed to manufacture the products either on their own or use contract manufacturers instead.

Contract manufacturing will help separate drug marketing authorization holders from production enterprises and significantly contribute to CMO industry's growth. Prior to the trial of the Marketing Authorization Holder program, domestic (bio)pharmaceutical research companies had to develop their own production lines, perform all manufacturing themselves, and were not allowed to use contract manufacturers. This left the existing CMOs dependent upon revenue from international clients.

This shift in regulatory system, long anticipated by the industry, was made possible via close collaboration between Boehringer Ingelheim (BI) and local authorities. After BI made an investment to open a biologics CMO in Shanghai, under the MAH program, it soon received contract manufacturing deals from local biotechs, such as BeiGene and Zai Lab. Mabplex, a biologics CMO in Shandong, informed us that its business is showing strong growth potential just 10 months after its kick-off. In that time, it generated revenue of over RMB 100 million ($15 million). WuXi Biologics, which focuses on international clients, started contract manufacturing services in 2008. In 2015, the company began construction on a new $150 million biologics manufacturing facility in Wuxi City. When complete, this new facility will be the largest mammalian cell culture manufacturing facility using disposable bioreactors in the world.

Another biologics CMO, JHL Biotech, partnered with GE Healthcare Life Sciences to build a monoclonal antibody manufacturing plant in Wuhan, the first modular factory for biologics manufacture in China. The rapidly growing business of these companies is attracting more biologics makers to consider providing contract manufacturing services of their own. Teruisi, Innovent Bio, as well as 3S and Guojian, each with their own mAb pipeline under development, have all expressed interest in providing contract manufacturing services.

Vaccine Manufacturers

From a facility point of view, vaccine makers remain an important sector for bio-processing equipment, with usually thousands of liters of manufacturing capacity (bioreactor total volumes). This 2nd edition covers domestic vaccine makers as well as multi-national company Chinese vaccine facilities. Both GSK and Sanofi have facilities in Shenzhen, which use chicken embryos to manufacture seasonal influenza virus vaccines. GSK also acquired a vaccine facility in Hangzhou from Novartis China. The China National Biotech Group, which consists of the Chengdu, Wuhan, Shanghai, Changchun, Beijing, Lanzhou Institutes as well as Tiantan Biologics, remains the single most important group in vaccine manufacturing in China, as it is in charge of making vaccines for government-sponsored programs. In the past decade, two domestic vaccine makers, Hualan and Chengdu Institute of Biologics, have passed WHO pre-qualification in 2015 and 2013 respectively, the very first ones in China. Currently, the Shanghai Institute of Biologics, is also preparing for WHO pre-qualification. We expect to see more domestic vaccine makers getting this certification and tapping international markets in the future.

First-generation Therapeutic Protein Manufacturers:

China has many biopharmaceutical companies making first-generation (i.e., older, now generally off-patent, biopharmaceuticals developed in highly-regulated, developed countries, primarily U.S. and Western Europe, with these now often targets for biosimilars/biobetters/biogenerics development) therapeutic proteins, such as insulin, EPO, interleukins, interferons, growth hormones, etc. This is a crowded sector with relatively low industry concentration and small scales of production, but insulin makers are an exception with over 10,000L bioreactors. Insulin manufacturers also have made progress in cost-saving bioprocessing technologies, e.g., Gan & Lee utilizes 'intra-molecular chaperon' technology developed by its founder, Dr. Gan Zhongru, to optimize bioprocessing (they do the bioprocessing with about a dozen steps compared with about 30 steps used by multi-national company insulin makers) and cut manufacturing costs significantly. Another insulin maker, Tonghua Dongbao, claims that it has a unique technology for bioprocessing of insulin developed by the VP of the company, Mr. Leng Chunsheng, which can scale up the fermentation to 30 m^3 and reduce the cost significantly. Apart from the improvement in biomanufacturing, these manufacturers are also striving to develop pipelines of longer-acting therapeutic proteins using PEGylation, and some have already launched these products recently.

Growth, Changes and Trends in China:

Major events: A brief overview of the major events in the past decade (see also the appendix).

Strong Growth: China Biological Markets Projected to be Second Largest Globally: China's biologicals industry started rather late, but is making rapid progress. In 2014, the biologicals market in China was ~$5.0 billion, and was projected to be the 2nd largest biological market globally by 2020 (IMS Health). Other estimates from industry put the market size at $5.9 billion at the end of 2013, and projected it to grow to $21.0 billion towards 2020 at a CAGR of 20%. A rapidly aging society, expansion of national health insurance, and increase in GDP all contribute to the robust growth of the industry.

Fig 1. Biologics Market in China

Source: With permission, Livzon mAbPharm, Chinese Biologic Industry

Our primary research, as we compiled this directory, shows data consistent with the above-mentioned optimistic projections. Among the Top 60 companies we profiled, most have either upgraded/expanded their biologics manufacturing facilities in the past decade, or have biologics facilities under construction, are upgrading currently, or have plans to do so in the near future.

Trends:

a. ***Investment in bio-pharma industry on the rise***: This will continue as investors and companies see new business opportunities in the sector, and financing is more accessible via going public, secondary offerings, government funding support, etc.

b. ***Cross-border collaborations clearly on the rise:*** Our findings show Chinese companies are going overseas for pipeline, for manufacturing Our findings show Chinese companies are going overseas more for pipeline products, manufacturing technologies and equipment, as well as for recruitment of talent. Growth in domestic product marketers' revenue, helped by a rising RMB, makes cross border investment more feasible.

c. ***Innovation and progress in bioprocessing technology:*** In our first edition of the Top 60 directory, we predicted that innovation and outsourcing would become the major driver for industry growth. This has been the case, as we can see that domestic companies are moving from bacteria-based follow-on proteins to mammalian cell culture of mAbs; while the launched mAb products all belong to biosimilar/ biobetter category, with more innovative pipelines on the rise. Longer-acting therapeutic proteins are another direction where domestic drug-makers are making progress. Co-development/out-licensing deals between domestic companies and foreign pharmaceutical giants also show that domestic companies are making progress in innovation capability. In 2015, Incyte licensed exclusive development and commercialization rights to Jiangsu Hengrui Medicine's SHR-1210, an anti-PD-1 monoclonal antibody heading into proof-of-concept studies in

patients with advanced solid tumors. The deal could generate up to $795 million-plus for Hengrui. That same year, Innovent Bio signed a co-development agreement with Eli Lilly for development of a portfolio of potential cancer therapies, with value exceeding $456 million if an Innovent-contributed preclinical immuno-oncology molecule hits key milestones, while other projects in the collaboration could yield a biosimilar of the blockbuster Rituxan. Such collaborations would have been unimagined when the first edition was published, but now we expect more of this kind to come in the near future.

From a bioprocessing point of view, we also see clear signs of technology advancement. Domestic biopharma companies are shifting away from bacteria-based culture to mammalian cell culture. Titers and yield of protein are also on the rise. When CP Guojian launched its first mAbs, the titer was at ~1g/L. Currently titers below 2g/L would generally be considered as having no commercial value. Some domestic companies claim that they can obtain a yield ~5g/L. Our findings also show that while stainless bioreactors remain the mainstream choice for Chinese biopharma companies, single-use technology is beginning to get support mostly from mAb makers, especially the relatively young companies focused on mAb development and the biologics CMOs.

Companies like Henglius Pharma have stated that single-use technology can greatly reduce the time and cost for developing mAbs, such as completing 4 IND-enabling studies for mAb projects in 4 years with 30% less cost. WuXi Biologics recently established a biologics CMO solely dependent on single-use technology, the biggest of such kind in the world. Single-use technology-based modular factories, while regarded by many as too expensive a solution, are getting more business in China recently, including foreign companies building Western cGMP-compatible facilities. For example, Pfizer Hangzhou, IHL Biotech, and PnuVax, (SL Pharma's vaccine subsidiary in Canada), have all collaborated with GE to set up modular factories in the recent 3 years. We see a pattern that the older companies tend to remain with stainless steel, especially the established vaccine makers, while newer, more Western style companies in mAbs and CMOs, either founded by returnee scientists or with global talent, are more open to single-use technology and modular factories. At the same time, industry insiders also feel pressure from rising costs of downstream processing due to higher standards in product purity as more biological drugs receive approvals in China. At current stage, it is estimated that ~60% of manufacturing costs (which is ~20%-25% of the price of biological drugs) are related to downstream processing. This also creates strong needs for streamlined purification technology.

d. ***International certification and exploring of global markets:*** Chinese companies are also striving for international certification for future exploration of global markets. In 2013 and 2015, Chengdu Institute of Biologics and Hualan Biologics passed WHO pre-qualification, the first two in China. More companies are planning for clinical trials in regulated markets (US/EU) (please refer to the major event list). Some companies show interest in getting US/EU cGMP certification for their biologics facility, such as Gan & Lee, Generon, etc.

e. ***Multinationals making investment in China's biopharma:*** Besides GSK and Sanofi's vaccine facilities in China, other multinational companies are also making investment. Pfizer broke ground for its biologics center in Hangzhou in 2015 with an approximately USD$350 million investment, while BI's contract manufacturing of biologics has started test operation in Zhangjiang. Besides establishing facilities of their own, foreign multinationals are also making investment via venture capital funds, such as Lilly Asian Venture's investment in Innovent Bio.

Strength and Opportunities

a. ***Funding support***: Much investment is coming from the national, regional and local governments, as well as companies having better accessibility to financial markets. Chinese biopharma industry segments continue to receive funding support from government bodies. Our research shows that multiple companies have such current funding support for their process development and biologics pipeline, while both central and municipal governments have created funding opportunities dedicated to attracting overseas biopharmaceutical scientists to return to China. Multiple companies have benefited from staff recruited via these programs, such as 1000 Talents, Taishan Scholar, etc. The past decade also witnessed about a dozen domestic biopharma companies going public. These are noted in our directory. We even see multiple cases of companies listed on US stock exchanges going private, and then trying go public on the Hong Kong exchange, as the evaluation is higher at the latter (e.g., Simcere, 3Sbio). The Chinese NEEQ (Chinese version of OTCBB) also gives biotech companies a way to raise funds.

b. ***National health insurance increases domestic market demand***: China has been undergoing healthcare reform in the past decade. As a result, by the end of 2011 basic national health insurance has covered over 1.3 billion people. As *'Made-in-China'* biologics are considered as more likely to be covered by the national health insurance, such policy trends provide strong support for China's biopharma industry.

c. ***Western trained returnee scientists bring talent to the industry:*** Apart from the government sponsored programs, the industry, domestic and multi-national China subsidiaries included, are hiring more returnee scientists. Multiple multi-nationals have opened R&D centers in China. Many of these employees shift to local companies later, so the talent pool available for the industry is expanding.

d. ***Across the board 'Infrastructure' improvement:*** Investments continue, including in contract manufacturing, contract research, clinical trial, mammalian cell culture, increases in yield, animal test, etc.

Weakness and Threats

a. ***R&D capability and lack of pipeline:*** Though we see clear signs of improvement, weak R&D capability in developing truly innovative pipeline remains a concern with many industry insiders. Most of the *'Made-in-China'* biologics belong to the bio-similar/biogeneric category. China still needs to catch up in basic research in life science, as well as in finding new drug targets/mechanisms of action.

b. ***CFDA regulatory system not fully in line with US/EU practice***: Although this is changing, the CFDA evaluation process is still considered too slow. Until regulatory systems are better aligned, exports to Western markets of innovative biologics, or biosimilars will face significant hurdles.

c. ***Concerns regarding over-investment and over capacity:*** Industry analysts tend to have different opinions as to whether there is overheating in the Chinese biopharmaceutical sector. Some have expressed concern that there are too many biosimilar/biogeneric mAbs under development, while others show optimism. Many believe that biologicals, which comprise ~20% of the worldwide pharmaceutical market globally (but only ~10% in China), still has substantial opportunities in the sector. BioPlan expects that the industry will grow with increased industry concentration over the next decade. There may not be as many players in the future, but total revenue will increase with perhaps even the emergence of blockbuster, innovative biological drugs.

Government Initiatives

In 2010, the Ministry of Health adopted The Good Manufacturing Practice for Drugs (2010 Revision), which went into effect in March 2011. This new GMP standard, which is viewed as comparable to EU GMP, has raised the entry threshold for Chinese manufacturers. This will increase the industry concentration of China's biopharma sector (i.e., there will be consolidation among players), and improve the quality image of *'Made-in-China'* biologics. In 2015, long criticized for a too-slow drug evaluation process, CFDA also announced plans for reform to deal with this issue.

The intended reform includes CFDA setting priority lists for evaluation, as well as setting up an evaluation center in Shanghai to speed up the process of new drug evaluation and approval. The new site will bring additional staff working on pharmaceutical product evaluations. According to the plan, the Shanghai site will share the burden of evaluating new medicines with the current 120 CFDA staffers, theoretically enabling the regulator to shorten its notoriously long approval times. In 2015, CFDA also made an announcement which ask for all drug-makers awaiting NDA approval to conduct self-examination of clinical trial data. Drug-makers who found their NDA applications with data integrity issues are allowed to withdraw respective applications. These moves, welcomed by industry analysts, are seen as signs of China's regulatory system moving towards being more in line with their international counterparts.

2 Study Methodology

This unique facilities-specific directory includes information obtained through public secondary and primary research, including interviews with industry analysts and participants for relevant facility and company public information. Other commonly-used sources included:

- Company annual reports, prospectuses, websites, etc.
- Company financial statements
- Company press releases, announcements
- Stock analysts' assessments
- Vendor reports
- Trade periodical articles, industry media
- Chinese public environmental evaluation reports
- Facilities construction bidding advertisements (RFPs)
- Company marketing materials
- Local governments (Municipal Administrations of Industry and Commerce)
- Environment evaluation reports
- Bidding advertisement
- Presentations at industry conferences
- Networking (with other experts)

All of the information presented was obtained for publication through interviews, was extracted from public domain sources, or involved analysis of public information by our staff.

Coverage and Facilities' Ranking:

This *Directory* includes ≥60 entries for those biopharmaceutical manufacturing facilities in China ranked by BioPlan Associates as having the largest bioprocessing capabilities/ infrastructures. Facilities were ranked consistently using an algorithm that favors larger facility bioprocessing capacity, i.e., the reported (or as needed, the estimated) total volume (Liters) of the on-site bioreactors. Some facilities reported only their production or other largest bioreactors, and some cases 10%-15% additional capacity was added to account for other smaller in-house bioreactors, including feeder bioreactors, those used for process design, scale-up, preclinical manufacturing, etc.

Ranking a facility is done quantitatively based on factors including:

- Total in-use capacity, including equivalent capacity for manufacturing mAbs, (cumulative facility bioreactor volume in Liters) currently online;
- Capacity under active construction (not just planned);
- Total Bioprocessing-related staffing for biologics production;
- Marketed/approved products, in clinical, and in commercial scale. Marketing/ approvals can be in any country, and includes biogenerics distributed in lesser- and non-regulated international commerce;
- Clinical stage products; currently reported in clinical trials or with pending INDs.

These factors are evaluated, and a ranking number is assigned. Of course, all these are subject to change and relative ranking can shift rapidly. However, we believe aggregating these factors moderate the impact of any outlier data point, such as over staffing, or availability of legacy or unused capacity.

Products covered, considered in ranking and for which information is presented, are all biopharmaceuticals, particularly cultured therapeutic and prophylactic biologics. Thus, coverage includes recombinant and non-recombinant proteins, monoclonal antibodies (mAbs), vaccines, etc.

Blood/plasma-derived products, such as immunoglobulins, are not covered, nor are drugs (chemical substance-based pharmaceuticals), including no coverage of synthetic peptide drugs. Diagnostics are not covered at all, even if involving recombinant protein components. Cellular and gene therapies are within scope of coverage, but essentially none of these companies in China currently have enough manufacturing capacity to rank in the Top 60. Nearly all facilities are involved with recombinant protein, mAbs and/or vaccines. Products in preclinical stages are not included in the ranking mechanism, and are generally not individually cited within facility entries.

Coverage concentrates on the biopharmaceutical manufacturing aspects of facilities, and we present limited information about other non-biopharmaceutical manufacturing capacities or products at that same site. Coverage includes all types bioprocessing, e.g., both mammalian cell culture and microbial fermentation (with bioreactor volumes for these and all other products considered equal).

Most of the listed facilities are currently manufacturing one or more marketed/approved biopharmaceuticals, although a few product developers lacking marketed/approved products had enough pilot plant capacity to make the Top 60. Currently, no biopharmaceuticals manufactured in China have yet obtained U.S. or EU approvals, although many covered facilities are US/EU cGMP "compatible" or are working to become a fully US/EU cGMP facility. Readers should keep in mind that China still uses different, often lower, standards for product and facility approvals, compared to the U.S., Western Europe and other highly regulated markets. Thus, GMP approvals in China should not be interpreted as meeting other global standards.

Updates:

As with any directory, information becomes outdated virtually upon publication. To maintain currency, we are offering this directory online, as well. If you wish to indicate a correction or update, or for more information, please contact us at www.bioplanassociates.com.

Table 1: Facility Ranking and Data

Rank	Company	Number of Employees in Bioprocessing	Bioreactor Total Current Capacity	Bioreactor Configuration, under active construction	Number of Biologicals Marketed	Number of Clinical Biologicals in Pipeline
1	Tonghua DongBao	441	60000	10000	5	3
2	Tiantan Biologics	1500	18500	5000	24	12
3	CP Guojian	120	42000	2000	3	9

5 Profiles of Top 60 Biopharmaceutical Organizations in China

Photo with permission WuXi Biologics.

Beijing Tiantan Biological Products Co., Ltd.

Rank: 2

Basic Information:

FACILITY Name	Beijing Tiantan Biological Products Co., Ltd., subsidiary of Sino Pharm Group
Address	No.6 Boxing Er Rd., Yizhuang Development Zone, Daxing, Beijing, P.R. China 100176
Telephone & Fax	+86 10-60963333 (tel); +86 10-60963311 (fax)
Email	xxzx@tiantanbio.com
Website	http://tiantanbio.com.cn
Chairman; General Manager & CEO; Legal Representatives	Mr. Baokang Wei
International Business Contact	Mr. Xiang Ci +86 10 60963010 ttswdb@tianbaobio.com
Employees, Total	2750
Biomanufacturing Staff	1500
Employment Overview	All staff work in biopharmaceutical areas
Revenue, Total (million, USD)	~$37 million in 2015
Revenue Overview (million, RMB)	Revenue is from sales of vaccines. 2015 revenue is 248.9 Million RMB.

Company Overview:

Company Overview	The company is engaged in the manufacturing of vaccines, blood products, as well as diagnostic reagents. It went public in 1998 (initiated by Beijing Institute of Biologicals). The company has several subsidiaries involved with manufacture and marketing of blood products. The company has over 110 products, including influenza vaccine, Hepatitis B vaccine, etc. It is an important vaccine making company.

Biographies of Senior Executives	**Mr. Hui Wang** Vice General Manager 2014 – Present In 2009, appointed as the Assistant to General manager and QA manager. From 2003 to 2009 he was director of the 4th Vaccine workshop in Tiantan Bio. Served as vice director of development in Lanzhou Institute, 1997 to 2003. Worked at the Lanzhou Institute of Biological Products in the manufacturing and verification of virus vaccines, from 1985 to 1996. **Mr. Daoxing Fu** Vice General Manager 2016 – Present From 2012 to 2015 he was Vice general manager of Lanzhou Institute of Biological Products. Served as vice general manager of Chengdu Rongsheng Pharmaceutical, from 2004 to 2012. From 2001 to 2004, he worked as the director of manufacturing in Chengdu Rongsheng Pharmaceutical. From 1997 to 2001, he was vice head of the manufacturing department and head of blood products. From 1983 to 1997, he worked at the Chengdu Institute of Biological Products.

Manufacturing/Marketing Information:

Facilities Description	In 2010, the company moved its vaccine manufacturing facility to Yizhuang, Beijing. The company made RMB 2.66 billion investment to move and upgrade the facility. Charged with making 17 vaccines, the new facility occupies ~160,000 sq. m. of space and is the biggest vaccine making facility in China. The facility is claimed as US/EU GMP compatible. The Gates foundation gave the company a project fund to expand its OPV making plant in 2011, which is expected to get WHO prequalification in the near future. Beijing municipal government estimates that the Yizhuang facility will produce ~200 million injections of vaccines annually and bring RMB 2.03 billion in revenue. It is currently being upgraded, and expected to have an additional approx. 5000L.
Manufacturing Capacity (Biomanufacturing Liters)	18500
Manufacturing Capacity, Description	*Current total bioreactor capacity:* Bioreactor configuration: 1 x 50L, 1 x 500L, 2 x 5000L for making pertussis vaccine (GEA) Another 3 production workshops: 750L x 8 Yizhuang facility is estimated by Beijing Municipal government to produce ~200 million injections of vaccines annually and bring in RMB 2.03 billion in revenue. Note: Additional capacity is specified for seed, and other bioreactors.
Fill-Finish	On site fill-finish: ~200 million injections of vaccines annually
Facility's Growth	The company started moving and upgrading its facility since 2010. The upgrading is not completed finished yet.
Equipment Strategy	Stainless bioreactor from GEA
Bioprocessing technologies Used	Claims to have self-developed bioprocessing technology and bioreactor and patented it

Domestic GMP Certifications	Certified
International GMP Certifications	None, but claims to be US/EU GMP compatible; the OPV plant is planning for WHO prequalification with funding support from Gates Foundation
Number of Marketed Products	24
Marketed Biological Products, Descriptions	1. Diphtheria, Tetanus and Acellular Pertussis Combined vaccine. 0.5ml, 2015 2. Diphtheria and Tetanus Combined Vaccine, 5.0ml, 1998 3. Diphtheria vaccine, 2.0ml, 2015 4. Typhoid Vi Polysaccharide Vaccine, 5.0ml, 2015 5. Group A meningococcal polysaccharide vaccine, 5.0ml, 2015 6. Measles Mumps and Rubella Combined Vaccine, Live, 0.5ml, 2002 7. Yellow Fever Vaccine, Live, 0.5ml, 2015 8. Recombinant Hepatitis B Vaccine (Saccharomyces cerevisiae), 1.0ml, 2011 9. Japanese Encephalitis Vaccine (Vero Cell), Inactivated, 0.5ml, 2004 10. Japanese Encephalitis Vaccine, Inactivated, 5.0ml, 2015 11. Measles vaccine, live, 0.5ml, 2006 12. Measles and Rubella Combined Vaccine, Live, 0.5ml, 2002 13. Influenza Vaccine (Split Virion), Inactivated, 0.5mg/15ug, 2006 14. H1N1 Influenza A Vaccine (Split Virion), Inactivated, 0.5ml/15ug/injection, 2009 15. Influenza Vaccine (Whole Virion), Inactivated, 1.0ml/15ug, 2003 16. Poliomyelitis Vaccine (Human Diploid Cell), Live, 1.0ml, 2013 17. Poliomyelitis (Live) Vaccine Type I Type III (Human Diploid Cell), Oral, 2.0ml, 2015 18. Rubella Vaccine (Human Diploid Cell), Live, 0.5ml, 2015 19. Varicella Vaccine, Live, 0.5ml, 2009 20. Tetanus Vaccine, Adsorbed,0.5ml, 2015 21. Poliomyelitis Vaccine Candy (Human Diploid Cell), Live, 1g, 2015 22. Mumps Vaccine, 0.5ml, 2015 23. Human Serum Albumin 24. Human immunoglobulin for intravenous injection
Number of Clinical Phase Products	12
Clinical Stage Projects, Description	MMR and varicella Quad-components Vaccine, NDA approved rabies vaccine, IND approved High purity Factor VII virus inactivation in two steps: clinical trials phase III Inactivated Poliomyelitis Vaccine (IPV): clinical trials phase I Group A/C meningococcal conjugate vaccine: clinical trials Phase I. Group ACYW135 Meningococcal Polysaccharide Vaccine: clinical trials Phase I H7N9 Influenza Vaccine (Split Virion): clinical trials phase I. H7N9 Influenza Vaccine (Whole Virion, Inactivated): clinical trials Phase I. Quadrivalent influenza vaccines (Split Virion): applied for clinical trials. OPV, inactivated: entering into clinical trial I/III attenuated live OPV: NDA approved Blood coagulation factor VIII: clinical stage
Product Distributors	Direct sale to CDA via its sales network

Company General Business Objectives	To be a leading vaccine maker in China while exploring global markets
Future Plans and Objectives	Clinical development of biologics; Registration of its current marketed biologics in developing countries; WHO prequalification of its OPV plant; Finish upgrading the Yizhuang facility
Potential Partnering Objectives	In licensing and out-licensing; Co-development of drug projects, registration and distribution overseas
Company Strengths	A leader in China's vaccine market; Upgraded facility with greater manufacturing capacity and prospects of getting WHO prequalification
Challenges Ahead/ Company Problems	Government-imposed pricing constraints may affect sales; Facing substantial competition from domestic market including both multinational and domestic companies, which may lead to smaller gross profit margin; Investors uncertain about the company's future as the parent company may go public

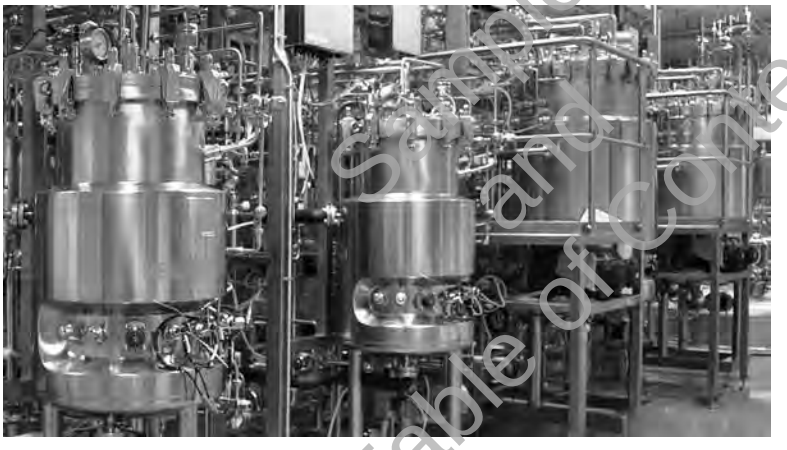

Photo Courtesy of Beijing Tiantan Biological Products Co., Ltd., subsidiary of Sino Pharm Group

Company Overview *(cont'd)*

CPGJ is equipped for world-class genetically engineered antibody research. It has established a 300L antibody cell culture pilot plant line with the highest scale and level in China, along with four 750L antibody cell culture production lines.

Two other 3000L antibody cell culture production lines have received CFDA GMP certification. The company is also equipped with a large-scale bioprocess purification system, a fluorescence-activated cell analyzer, etc. CPGJ's antibody manufacturing capacity is among the largest in China and looks to provide contract manufacturing of mAb services to other companies.

CPGJ has put IP protection on its upcoming agenda and has filed for over 100 patent applications and 27 trademarks by 2016.

Company History

Capabilities Timeline:

1998

Shanghai Zhangjiang Biotech Research Center established in December with 3 million Yuan registered capital

2000

Shanghai Lansheng Guojiang established in January with 120 million Yuan registered capital

Shanghai Zhangjiang Biotech Research Center restructured to Shanghai Zhangjiang Biotech Co., Ltd. in December

2002

Shanghai Lansheng Guojian Co., Ltd. signs an investment agreement with Hong Kong CITIC Pacific Ltd. to establish a joint-venture company in December

The company officially changes name to Shanghai CP Guojian Pharmaceutical Co., Ltd. in January

2003

SFDA approves Recombinant Human Tumor Necrosis Factor-alfa Receptor II for clinical trials in April

The 'Recombinant TPO for injection' and the 'Recombinant TNF-a II receptor-antibody fusion protein' are awarded as 'Achievements Transformation Projects' (both are in the A Class) by the Shanghai Municipality in July.

SFDA issues New Drug Certificate to "Recombinant Interleukin II for injection" in September

CPGJ's subsidiary, CPGJ Biotech Research Institute, is authorized by the Ministry of Personnel to set up a post-doctoral station

2004

Three products are granted "Patent Rights for Invention" by the Intellectual Property Bureau of the State (SIPO): Humanized anti-CD3 monoclonal antibody; Recombinant anti-human CD11a monoclonal antibody and manufacturing and the drug complex; and Humanized anti-endothelial growth factor monoclonal antibody and manufacturing and the drug complex

2005

Three patents ("Anti-CD20 humanized monoclonal antibody", "Humanized anti-HER2 monoclonal antibody and its manufacture process and medicine compound", and "Recombinant human blood platelet reproduction factor cDNA sequence and its applications") issued by State Intellectual Property Office of PRC

Company's two recombinant products (Recombinant human interleukin–11 for injection and rhTNFR:Fc Fusion Protein for Injection) attain production licenses issued by Shanghai Food and Drug Administration in April

The patent "The human melanoma monoclonal antibody and its preparation method and applications" issued by State Intellectual Property Office of PRC in September

BioPlan associates, inc.

Second Edition

Directory of Top 60 Biopharmaceutical Manufacturers in China

A comprehensive industry review: Profiles of established, and rapidly growing, facilities involved in biopharmaceutical manufacturing.

Tonghua DongBao
Tiantan Biologics
CP Guojian Pharmaceutical
Hualan / Xinxiang
Walvax / Yuxi
Sinobioway / Hefei
Shanghai Institute
AlphaMab
WuXi Biologics
Changchun Institute
Chengdu Institute
Qilu Pharma
Wuhan Institute
Sinovac / Beijing (Haidian)
Jiangsu Wanbang
Changchun Hi-Tech GeneScience
Gan & Lee
Zhifei / Beijing
Teruisipharm
Lanzhou Institute
Innovent Bio
BioThera Solutions
Yantai Rongchang (MABPLEX)
Genor (Walvax) / Shanghai
JHL biotech
3SBio
GSK / Hangzhou, Zhejiang
Sanofi / Shenzhen
Sinovac / Dalian
Amoy-Top Biotech (Tonghua Dongbao)
Livzon mAb
Mabtech Holding Ltd, (HK)
Harbin Pharma Bio
Biotech Pharma
CSPC Pharma
Hisun
North China
Shanghai United Cell / Shanghai
Tot Pharma
Anhui Anke Biotechnology
Zhuhai Essex
Hengrui Pharma/Suzhou
Henglius Pharma (Fosun Pharma)
Genor / Yuxi
Kelun Pharma
Chia Tai Tianqing
GSK / Shenzhen
Eastern Biotech
Four Rings
Shanghai Pharma
Celgene Pharma / Shanghai
Simcere Pharma / Yantai
Tasly
Hengrui Pharma / Shanghai
Boehringer-Ingelheim
Tri-Prime Gene
Akeso Bio
Lunan Pharma
Sinobioway / Tianjin
Pfizer / Hangzhou

ISBN 978-1-934106-31-0