

Current situation and development trend of biomedical industry in China

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Abstract. In recent years, China's biomedical industry has developed at an unprecedented speed, and China's biopharmaceutical market is in its early stage of development and has strong growth potential, which is ahead of the overall pharmaceutical market. In this article, we start with the background of the development of China's biomedical industry, elaborate the policy and investment environment for the development of China's biomedical industry, investigate the scale and development trend of China's biomedical industry, and deeply analyze the current situation and development trend of China's biomedical industry.

Keywords: Biomedical industry, Investment status, Development status

1. Introduction

In the light of rapid economic growth and the age structure change in China, demands for medicine and medical services are anticipated to experience continuous expansion. Besides the growing markets, several important factors are also hugely influencing the future of biomedical investments and corporations in China. The medical insurance reform and new governmental policies have promoted competition and price control on the market. The trade conflicts and new cooperation with different countries also impacted heavily on the overall industry. Aside from political perspective, the technology development also brings both the opportunity and challenge to biomedical investments and corporations. The commercialization of new genetic modification technologies, such as CRISPR (clustered regularly interspaced short palindromic repeats), have enabled the construction of more complex proteins for biomedical applications. Other materials such as biosensors and antibodies, have been further investigated in the past decades. Other than the bio-technology break through, another important factor is the application of big-data, computer science technology, as well as other information technologies in recent years. These new technologies can make access to valuable real-world data (RWD) as well as promoting the efficiency of the industry.

Compared with chemical drugs, biological drugs have higher efficacy and safety, and less side effects and toxicity. Because of their structural diversity, their ability to selectively bind to targets and better interact with proteins and other molecules, biologic drugs can be used to treat a variety of medical conditions that lack available therapies. With the remarkable development of biotechnology and the increasing r&d investment, economic development and the improvement of people's living

standards, the demand of China's medical market has increased significantly. Under the policy guidance of encouraging innovation and adjusting industrial structure, the bio-pharmaceutical industry will continue to develop rapidly.

Nowadays, the annual global economic growth rate is slowing every year, and even the global economy will shrink by 4.4% in 2020. The total GDP is expected to drop from \$87.75 trillion in 2019 to \$83.84 trillion in 2020, which is a decrease of \$3.91 trillion, equivalent to the annual GDP of Germany. But only the biopharmaceutical industry's economic growth rate reached 8%, while China's biopharmaceutical economic growth rate reached an unprecedented 20%, the gap between China's biopharmaceutical industry and developed countries such as Europe and The United States has also narrowed significantly. and will continue to grow steadily in at least the next decade.

2. Development and investment status of biomedical industry in China

2.1 Development status of biomedical industry in China

In recent years, China's biomedical industry has developed at an unprecedented speed, and China's biopharmaceutical market is in its early stage of development and has strong growth potential, which is ahead of the overall pharmaceutical market. Data show that in 2019, the scale of China's bio-drug market reached 317.2 billion yuan. China's biologic drug market is expected to further expand to 464.4 billion yuan by 2021 as affordability increases, patient population grows and medical insurance coverage expands. China began to appear in the field of biological vaccine segmentation, innovative vaccine pipeline also began to close to the world's top level. Vaccines in China are mainly divided into three categories: "antibody class", which mainly refers to autoimmune drugs, such as cancer vaccines; "Vaccine-based drugs class", such as Prevnar 13 and HPV vaccine; "Hormones class," for example, Insulin. At the same time, the proportion of biopharmaceutical industry is increasing year by year. China has also seen the emergence of a number of biopharmaceutical giants. For example, in the field of vaccine development, "Zhifei", "Kangtai", "Watson", "Changchun High-tech", as well as "Xinda", "Henrui", "Junshi", "Baekji Shenzhou" and other traditional biopharmaceutical companies. In 2016, the growth rate of China's pharmaceutical industry was the highest compared with the 12 industries that can be evaluated. Its main revenue profit and sales profit margin year-on-year growth in the 12 industries also ranked first, and starting to become the world's second-largest pharmaceutical market. According to statistics, as of December 30, 2020, a total of 11 enterprises on the list of listed enterprises in China's pharmaceutical and biological industry market value more than 100 billion yuan, two enterprises market value of more than 500 billion yuan. Hengrui Pharmaceuticals ranked first in the pharmaceutical and biological industry, with a market value of 60.0885 billion yuan. Mindray Medical ranked second with a market value of 508.232 billion yuan; Wuxi Aptec ranked third with a market capitalization of 317.728 billion yuan. The top 10 enterprises in market capitalization are: Aier Ophthalmology, Zhifei Biotechnology, Changchun Gaoben, Pien Tze Huang, Yunnan Baiyao, Tige Pharmaceutical, And Kangtai Biotechnology.

However, China's biomedical innovation still has a short board of original innovation, such as the phenomenon of innovative research and development clustering is becoming increasingly prominent. Sun Feihe, chairman of Jiangsu Henrui Pharmaceutical Group Co., LTD., said that China's innovative drug market has the problem of excessive duplication, such as PD-1, which is the most typical case. Regarding the termination of PD-1 drug development, The company said that based on clinical data of pD-1 monoclonal antibodies, it is expected that more than 20 PD-1 products will be launched globally in the next two to three years, and the market competition is becoming increasingly fierce. China is the region with the fiercest competition for PD-1. There are 154 PD-1 in the world, of which 85 are developed or co-developed by Chinese enterprises, accounting for 55%. It is worth mentioning that at present, besides PD-1, BTK, PARP and other hot targets are also the research and development clusters of domestic innovative pharmaceutical companies.

Secondly, there is a lack of industrial talents in the field of biomedicine in China, research and development is disconnected from industrialization. Due to the long training period of research and

development personnel, a large number of outstanding scientific research personnel stay abroad, and the lack of outstanding talents in China, especially the lack of technical and business talents. In addition, the existing biotechnology talents in China focus on theoretical research, and the industrialization talents are relatively lacking. In the development of biotechnology industry in China, it is often difficult to industrialize the scientific research results in the laboratory, or the industrialization cost is very high and there is no economic value.

At the same time, although many leading enterprises have emerged in China's biomedical industry, the fragmented situation has not been effectively improved. According to statistics, by 2020, the United States has a total of 841 biomedical research and development companies, their total sales of 451 billion US dollars, China's biomedical research and development companies about 4600, their total sales of 2.96 trillion US dollars. But U.S. nail biomedical research and development companies contributed about \$536 million, 5.76 times more than China. This fragmented situation leads to a lack of talent concentration, which leads to slow research and development, and is the main reason why China's biomedical market has not yet become a world-class market. As mentioned above, the phenomenon of innovation research and development cluster is also one of the serious consequences caused by the lack of talent concentration. This fragmented situation leads to a lack of talent concentration, which leads to slow research and development, and is the main reason why China's biomedical market has not yet become a world-class market. As mentioned above, the phenomenon of innovation and research and development cluster is also one of the serious consequences caused by the lack of talent concentration. Because of the small and scattered enterprises, there is a lack of overall spatial layout planning at the national level, leading to the emergence of a large number of biomedical industrial parks with the same industrial orientation and development direction across the country. Local level, due to lack of space layout of the whole province, the city or county level, the number, scattered, and on a smaller scale, the industry positioning, development direction and development mode, the lack of a clear distinction in terms of investment, the introduction of talent, low level repeated region and the surrounding area, and even lead to problems such as vicious competition.

2.2 Investment status of biomedicine in China

China's biopharmaceutical industry is undergoing a rapid development, with new policies, rules, and regulations being adopted at a breakneck speed. According to Chen, Xue, Lv, and Wang (2019), China's pharmaceutical industry strategy could be divided into two parts: First, the management of the pharmaceutical market, which contains approval of new drugs and market entrance. Second, the macro-level management of the pharmaceutical industry, which contains medicine pricing policy, regulatory industrial and layout policies, and policies on developing biomedical science and technology [1].

Chen (2014) [2] studies the procedure of new drugs' market entrance process, from the research development stage to the entry of national health-care system, which is summarized in Fig.1 flowchart. After submitting an application for a novel chemical medicine, it usually takes around 17-18 months to receive a clinical permit. Even though the new medicine is approved, it still needs to deal with some market access issues, including province access and hospital access. The new medicine's provincial access requires drug bidding that takes around 14 months on average among 31 provinces in China and is followed by the purchases made by the hospitals if winning the bid. It is required to enter the national and provincial health insurance directories if it is to become a new medicine that may be reimbursed. In general, the whole process would take about three years for new medications to be approved. Furthermore, the approval procedure for generic drugs is comparable to that for novel medications, and takes around three years, which is summarized in Fig.2 flowchart.

Starting from May 2016, the State Council issued a trail plan of implementing Drug Marketing Authorization Holder (MAH) system. Individuals and qualified drug R&D institutes in 10 pilot provinces could apply for a drug license and to become an MAH for certified medicines. The clinical trials, drug registration, manufacturing, and marketing processes would be the responsibility of the

applicants and holders, who could produce by themselves or outsource to a contract manufacturer. This new approach aims to encourage small and medium-sized research facilities (as well as individual researchers) and enterprises to invest in R&D by offering a clear path to financial reward.

Since 2016, the China Food and Drug Administration (CFDA) has approved several new regulations aimed at speeding up the clearance of important new drugs applications and tightening the requirements for generic drug approval.

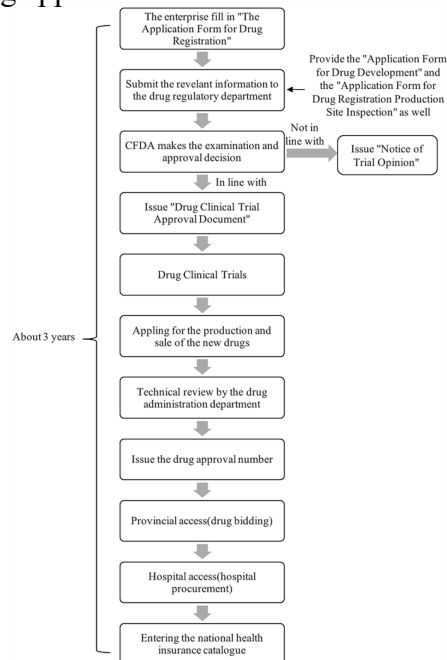


Fig. 1 Flow chart of new medicine listing in China [3]

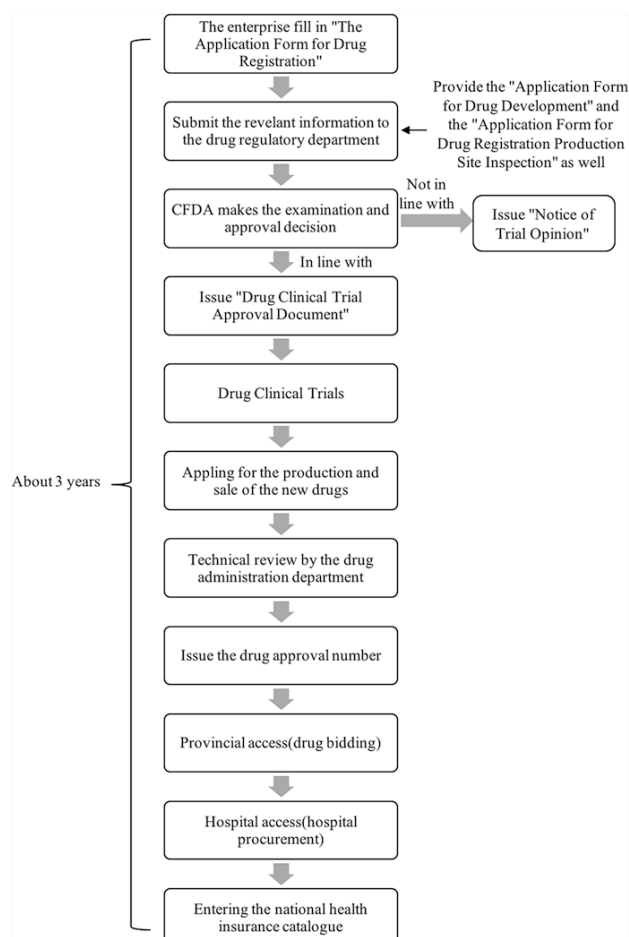


Fig. 2 Flow chart of generic medicine registration and approval in China [3]

2.3 Drug Pricing Policies

A joint program named the Opinions for Advancing Drug Price Reform is issued by several government institutions in May 2016, which contains the National Development and Reform, the National Population and Family Planning Commission, and Ministry of Human Resources and Social Security, aiming at eliminating government's direct price controls of all drugs except narcotics and class 1 psychoactive. In the meanwhile, the government attempted to approve a pricing-reform program that would remove hospitals' price markups as well. These changes serve to lower health-care costs, improve market competition in medication pricing, and restrict side payments, physicians' over-prescribing, and corruption. (Wong and Fei, 2016; China Guide 2016)

The following is the structure of China's medication pricing regime: (1) For medications reimbursable by the Basic Medical Insurance (BMI), BMI agencies shall create processes, bases, techniques, and other regulations for determining the payment standards, as well as establish mechanisms for rational market pricing, in collaboration with relevant departments; (2) a transparent negotiating framework for pricing setting with participation from different stakeholders should be practiced for patented and exclusively manufactured medicines; (3) prices for blood products not covered by the reimbursement list, and preventative vaccination, free AIDS treatments, and birth-control drugs and devices universally purchased by the government, should be established through purchase tenders or negotiation; (4) on the other hand, government remains responsible for setting the maximum ex producer and retail prices for class 1 psychoactive and narcotic medications; and (5) manufacturers should be able to determine pricing for other medications based on their costs, plus market supply and demand conditions.

In 2020, the medical reform would continue to be promoted. China's aging population would bring about a substantial increase in health-care expenditure. Cost control remains the main theme of the biomedical policy in China.

Volume-based procurement (VoBP or VBP) is a set of medicine procurement policies that mainly aimed at improving the low efficiency of health insurance funds in the field of generic drugs. More specifically, there are three major problems in China, namely, over-pricing of generic drugs, over-pricing of expired patented drugs and over-share of expired patented drugs. These three problems lead to the inefficient use of medical insurance funds in the generic drug field in China. Therefore, they have become the main direction for the implementation of medical insurance cost control after the establishment of the National Medical Insurance Administration (NMIA).

In 2018, only 25 medicines were assigned in the initial VBP experiment, which was conducted in 11 cities (the "4+7" cities). The scale of the price reduction, on the other hand, exceeded most people's expectations. One generic manufacturer slashed the price of Entecavir by 94% that brings shockwaves among the industry. Furthermore, VBP has expanded its scope and been implemented at a faster rate at the national and provincial levels. Four rounds of VBP were conducted at the national level, affecting approximately 150 medicines, the majority of which were loss of exclusivity oral tablets with quality consistency equivalence generics. Embracing the Change: Strategizing on Volume-based Procurement in China (2021)

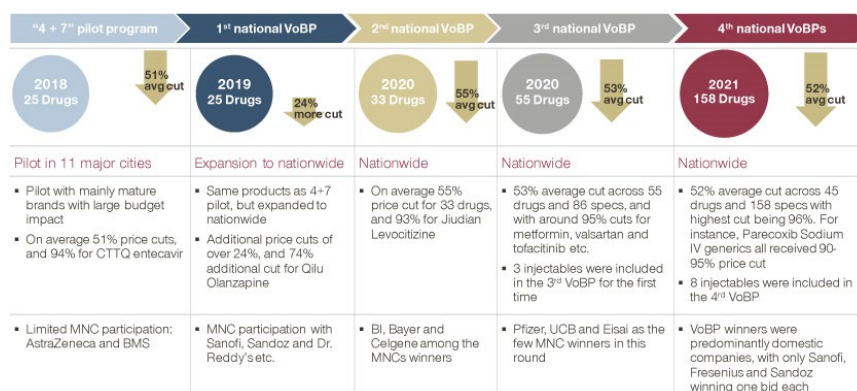


Fig. 3 National VBP Timeline to Date

Reconstruct the generic drug industry chain with VBP, and reduce channel costs. The original business model of generic drugs in China is similar to that of innovative drugs, with emphasis on marketing and high promotion costs and sales costs, with related costs reaching more than 50%. After the adoption of VBP, the marketing link of generic drugs is weakened, and the channel cost is significantly reduced, which leads to that the focus of generic drug companies has shifted from marketing to cost and quality control.

In this context, we believe that: (1) innovative drugs and devices with real clinical value deserve long-term attention; (2) with the growth of per capita disposable income in China, the demand for consumer medical care is growing rapidly; (3) characteristic APIs, which are difficult to generalize and have high added value, are growing rapidly. The plate immunization cost control policy that is worthy of an attention.

3. Development trend of biomedical Market

Before a new drug becoming mature and can be put into use, it needs to go through time-consuming and high-cost stages including drug discovery, Pre-clinictoxiology studies and clinical trials. According to Deloitte's data, it takes 800 million and more than 8 years on average for a new drug to appear on the market. However, the return to investment ratio is only 1.8%, which discourages many companies to invest on bio-pharmaceutical area. In order to facilitate the development of bio-pharmaceutical area, the emphasis should be put on reducing time and financial cost.

Drug discovery stage includes target verification, leading compound determination and refinement. Nowadays, most drugs are made to target on proteins with known structures. However, obtaining the structure of a protein is complex and difficult. Purification of a specific protein using wet-lab methods may take more than two years and the following 3-D structure rebuild is not easy as well. Fortunately, the recent success of AlphaFold2 in Critical Assessment of protein Structure Prediction shows possibility to largely shorten the process of target verification. AlphaFold2 can predict the structure of protein with high accuracy using amino acid sequence which is easily accessible. Another technology called docking can aid in leading compound determination. There are many docking platforms available online which can find compounds with high affinity towards the target protein. These platforms are also able to predict essential functional groups and then refine the compounds by adjusting other groups connected to the functional groups. Poonam et. Al (2020) used Glide module of the schrödinger suite to perform docking. They discovered a functional group, Hydroxyethyl amine, that have high affinity towards 3CLpro of SARS-COV-2. After that they do the refinement and predicted a potential drug that can treat SAR-COV-2.

The main purpose of Pre-clinical and clinical trials is to find out the efficacy and safety of the potential drug. Plenty of experiments are needed to be done in order to get sufficient data. This process can be significantly accelerated if some of the data can be obtained from existing data. That's why Real-World Data (RWD) becomes more and more popular. According to CB insights, the attraction of RWD increased constantly between 2016 and 2019 while increased exponentially in 2020. RWD is directly collected from real patients and medical institutions. Nowadays, RWD are becoming more and more accessible due to the development of data extraction and storage technology, digitalization of the database of various medical institutions and the popularization of online medical platforms. The biggest challenge of utilizing RWD is to extract valuable and high quality information from huge amount of RWD which is in a mess. Once this challenge is solved, RWD can contribute to the drug development of rare disease, can provide reference when adjusting the use of existing drug and can shorten the time for a drug to come onto market.

4. Conclusion

At present, China's basic research in the field of medicine has made rapid progress, but there is still a big gap compared with developed countries. Although the development of China's biomedical

industry has made remarkable achievements in recent 30 years, there is still an obvious gap compared with developed countries in technology development, human capital level, scientific research investment and industrialization level. This paper provides a reference for the development of China's biomedical industry by analyzing the current situation and problems of China's biomedical industry.

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