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Insight into Development of Solid Dosage Form Industry in China



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Overview

Based on the current situation of increasing aging and increasing of people's livelihood in China, the medical market in China is burgeoning. Solid dosage forms, as an important part of pharmaceutical market globally, with the advantages of good stability, low manufacturing cost, portability, easy administration and high patient compliance, have always occupied a high share in the pharmaceutical market of China. And it is expected that the market size of solid dosage forms will further expand to 988.7 billion yuan by 2025.The solid dosage form market in China is embracing a huge development opportunity.

China Solid Dosage Industry Development Insight is consisted of five chapters, which respectively analyze the solid dosage form market of China from 5 aspects, namely development of overview of pharmaceutical industry in China in 2024, scale and trend analysis of solid dosage form industry in China, status of industrial chain of solid dosage forms in China, application and trend of innovation model of solid dosage form industry and investment opportunities in solid dosage form market.

1 Overview of Pharmaceutical Industry in China in 2024

1.1 Analysis of macro environment of solid dosage form industry

1.1.1 Completion of main economic indicators in pharmaceutical industry

For the pharmaceutical industry, 2024 is a year full of opportunities and challenges, innovation and change. Against the backdrop of an optimized policy environment, rising quantity and quality of domestically produced innovative drugs, stable growth of the generic drug market, strengthened international cooperation, and equal emphasis on the cultivation and introduction of talents, the pharmaceutical industry will continue to innovate and change, and provide patients with more high-quality and highly effective medicines and services. medicines and services for patients.

According to the National Bureau of Statistics, from January to September 2024, enterprises above designated size in the pharmaceutical manufacturing industry realized operating revenue of 1844.7 billion yuan, up 0.2% year-on-year; total profit of 254.39 billion yuan, down 0.4% year-on-year. Especially in September, the pharmaceutical manufacturing industry increased by 11.0% year-on-year, showing growth potential. Among them, in the first three quarters, the production of crude chemical drugs reached 2.584 million tons, with a cumulative growth of 7.5%, maintaining a faster growth rate in production. In the nuclear medicine industry pipeline layout, the domestic nuclear medicine enterprises have 75 pipeline in the research, involving nearly 20 pharmaceutical companies, domestic and overseas development have shown a trend of diagnosis and treatment integration. In addition, more and more pharmaceutical companies are actively exploring overseas markets, some companies' overseas business has become an important driving force for growth.

1.1.2 Analysis of solid dosage form related policy

The industrial documents related to solid dosage forms are mainly represented

by the Pharmaceutical Planning in the 14th Five-year Plan Period issued by the General Office of the State Council. The pharmaceutical industry policy issued by the state shows that the government attaches great attention to innovative R & D in the pharmaceutical field, and the fact that the government proposes to safeguard the supply of drugs that are clinically necessary, easy to be in short supply and poor in substitution is the direction that solid dosage form enterprises can advance in the future; the state encourages the manufacturing of solid dosage forms and is committed to promoting the consistency evaluation of oral solid dosage forms. By the end of 2023, the State Drug Administration had released 74 batches of reference preparation catalogs with a total of 6,714 product specifications, and 4,552 acceptance numbers deemed to have passed the consistency evaluation of generic drugs (generic drugs approved according to the new registration classification of chemical drugs).

Overall, the policy in Pharmaceutical Planning in the 14th Five-year Plan Period regarding the solid dosage form industry showed the following trends: encouraging the innovation, research and development of innovative drugs of solid dosage forms, promoting the consistency evaluation in oral solid dosage forms, and encouraging independent innovation and industrial upgrading in solid dosage form equipment enterprises.

Drug market authorization holder stimulated the innovation vitality of solid dosage form industry

In August 2019, the drug marketing authorization holder system (MAH system) began to be implemented, allowing the owners of drug technology (drug development institutions or scientific research staff) to obtain drug marketing authorization and drug approval document number, market the products in their own name and enjoy the reward and income from drug marketing by law. Before the implementation of MAH system, China implemented the management model of bundling drug marketing authorization (drug approval number) with manufacturing authorization, while drug research and development institutions were disqualified for drug marketing authorization independently, so they could only transfer scientific research results to drug manufacturers, and could not obtain long-term considerable benefits, which was not conducive to the encouragement

of drug innovation. This bundling model will lead to the problem that the subject responsible for ensuring the safety and efficacy of drugs in the whole life cycle is unknown before and after marketing. The current MAH system has solved these problems to some extent, thus stimulating the innovation vitality of practitioners in the solid dosage form industry.

The policy attaches great importance to the consistency evaluation of oral solid dosage forms

At present, generic drugs occupy a large scale in the pharmaceutical market of China, and the consistency evaluation of oral solid dosage forms has attracted great attention. With the internationalization of pharmaceuticals in China, the National Medical Products Administration has joined International Conference on Harmonization (ICH), and the international standard of R&D and evaluation has been gradually implemented in China. For generic drugs and other varieties, the ultimate goal of consistency evaluation is to establish a sound quality assurance system to ensure that the whole product life cycle after approval is consistent with the quality of the original drug or reference product, so as to better serve the public health.

The development of greening and environmental protection requires accelerating elimination of outdated production capacity and optimizing the industrial structure

In recent years, the Chinese government has issued many policies to strengthen the environmental protection regulation of pharmaceutical industry. The increasingly stringent environmental protection requirements will promote the development of enterprise manufacturing in the direction of energy conservation and environmental protection, and eliminate many enterprises with substandard environmental protection requirements. Meanwhile, the green transformation has increased the operating costs of pharmaceuticals, which made some small-capacity enterprises gradually withdraw from the market, and the industry concentration and production quality have been continuously improved. Changes in pharmaceuticals will be transmitted to the pharmaceutical equipment industry, and the new requirements for green and environment-friendly development are often accompanied by equipment upgrading. In order to adapt to the new environmental protection standards, solid dosage form manufacturers need to upgrade their equipment and reduce the use of raw

materials with high pollution intensity.

Affected by policies such as procurement with target quantity and "two-vote system" and under the background of fierce competition of solid dosage form market currently, the demand of solid dosage form manufacturers for pharmaceutical equipment has also changed, such as production capacity and cost, which puts forward new requirements for solid dosage form equipment enterprises: first, they should continuously improve the quality and safety and improve the product quality in key areas; second, they should promote the digital transformation of the industry, empower pharmaceutical research and development with a new generation of information technology, promote the deep integration of information technology and production and operation, and actively develop new models and new types of business. Third, they should improve green manufacturing, implement carbon emission reduction actions in the pharmaceutical industry, so as to continuously improve the solid dosage form production capacity of enterprises and help pharmaceuticals achieve green, digital and smart manufacturing.

1.2 Characteristics and status of the industry of solid dosage forms

1.2.1 Definition of the industry of solid dosage forms

Solid dosage forms are the dosage form with extensive application and a great variety in the pharmaceuticals, occupying an important share in the pharmaceutical industry. The common characteristics of solid dosage forms include: compared with liquid preparations, they have good physical and chemical stability, low manufacturing cost, easy to take and carry, and the pretreatment of the preparation process undergoes the same unit operation to ensure the homogeneous mixing and accurate dosage of the drugs. Moreover, there is a close relationship between the dosage forms, and the drug can only cross the physiological membrane and be absorbed into the blood circulation after first being dissolved in the body. According to the dosage form, commonly used solid dosage forms can be divided into bulk drugs, granules, tablets, capsules, dropping pills, film agents, etc. [1].

1.2.2 Characteristics of the industry of solid dosage forms

The solid dosage form industry is directly related to the safety and physical fitness level of the citizens, and China has always implemented a very strict market entry and supervision system for this industry. The production and operation of solid pharmaceutical products need to go through multiple stages, including research and development, clinical studies, clinical trials, pilot-scale production, large-scale production, and product sales. The technical requirements are high, the capital investment is large, and the approval and study cycles are long. The development of new drug products also requires a large amount of investment in funds, talents, and equipment. Therefore, overall, the solid dosage form industry is a high-tech, high-profiting, high-risk, and high-investment industry.

1.2.3 Status of the industry of solid dosage forms

In the context of volume-based procurement (VBP), the production of

domestic generic drugs is tending towards intensive production, and large-scale generic drug manufacturing companies depend on low-cost and multi-variety to survive, but the estimated value is not high. Due to the core technologies owned by innovative drugs, high production barriers, and relatively low level of competition, profits can be better guaranteed for these drugs. Therefore, domestic pharmaceutical companies, which traditionally focus on the production of generic drugs as their main products, have begun to transform their strategies towards developing innovative drugs so as to improve market competitiveness and seek long-term development. In the past decade, there have also been pharmaceutical companies that specialized in the research and development of innovative drugs, and these enterprises also have had multiple new drugs successively approved for marketing. Pharmaceutical companies specializing in developing innovative drugs have attracted increasing attention in the domestic pharmaceutical market and they are playing an increasingly important role in improving the accessibility of drugs to more patients.

1.3 Opportunities faced by the industry of solid dosage forms

With the implementation of the 14th Five-Year Plan, the increasing importance of online retail, the continuous increase in Chinese residents' income, the expansion of medical insurance coverage, the gradual improvement of medical payment capacity, and the increasingly obvious aging population and the increases in policy support have become the driving force that push the solid dosage form market to enjoy a broad growing space in the future.

The opportunities for the development of the solid dosage forms industry are as follows:

- The cancellation of the policy of "drugs for healthcare" and the rise of online retail are expected to expand the sales channels of solid dosage forms.
- The increase in residents' income and the expansion of medical insurance coverage will enhance the medicine's affordability for the citizens.
- The increase in income level will drive

the upgrading of residents' consumption demand, thereby driving the market demand for pharmaceuticals and health products.

- There is still room for improvement in China's healthcare expenditure, which will provide a broad space for the development of solid dosage forms.
- The aging population and the increasing incidence rate of chronic diseases drive the increasing demand for medicine.
- Government policies support the development of Traditional Chinese Medicine, and traditional Chinese patent medicines will become a new growth point of the solid dosage form industry.

According to the "14th Five-Year Plan for the Development of Traditional Chinese Medicine", by 2025, the high-quality development policies and system of Traditional Chinese Medicine will be further improved, and the unique advantages of Traditional Chinese Medicine in the construction of a healthy China will be fully utilized. According to statistics, in 2021, there were 430 applications for Traditional Chinese Medicine registration, a year-on-year increase of 40.07%, higher than the growth in that for chemical medicine registration (27.5%). During the "14th Five-Year Plan" period, Traditional Chinese Patent Medicines, as an important part of the Traditional Chinese Medicines industry, will usher in major development opportunities. According to the M2 statistics, nearly 70% of Traditional Chinese Patent Medicines will be solid dosage forms. In the future, the Traditional Chinese Patent Medicines market will strongly promote the development of the solid dosage forms market.

1.4 The main problems and challenges confronted in the development of the solid dosage form industry

1.4.1 Solid dosage forms are difficult to pass the consistency evaluation, and the entry threshold is constantly increasing

In March 2016, the General Office of the State Council issued the "Opinions on Conducting Consistency Evaluations of Quality and Efficacy of Generic Drugs" (hereinafter referred to as the "Opinions"), which required that generic drugs that

have been approved for marketing should undergo quality consistency evaluation in stages and batches based on the principle of consistency with the quality and efficacy of the originators and the quality and efficacy of the generic drugs must be consistent with those of the originators. Consistency evaluation is required for generic drugs that have been approved for marketing. If solid dosage forms want to pass the consistency evaluation, there are high requirements for the formulation, production process, product quality, etc. of the manufacturing enterprise. Moreover, the "Opinions" stipulated that after the first variety passes the consistency evaluation, the consistency evaluation of the same variety of other drug manufacturing enterprises should be completed within 3 years in principle, otherwise, the drug will not be registered again. In view of this situation, the entry threshold for China's solid dosage form industry is constantly increasing [2].

1.4.2 Excessive initial investment will increase business pressure in operation

Firstly, the solid dosage form industry belongs to the heavy asset industry, wherein a wide variety of raw materials are involved in the supply chain and the requirement for initial investment is high, moreover, the solid dosage form manufacturing enterprises must obtain certification from relevant authoritative institutions to enter the market. The NMPA and GMP have high requirements for the research and development, process, technology, and other strength of the manufacturing enterprises. Moreover, the evaluation cycle of drugs is long and the evaluation cost is high, requiring these enterprises to invest heavily in the long term[3]. Secondly, solid dosage forms include different types of dosage forms such as tablets, powders, and granules. If multiple dosage forms are produced using the same personnel, premises, facilities, equipment, etc., cross contamination, confusion, and human errors are prone to occur. Once a problem occurs, the enterprise will face long-term closure for rectification and re-review and re-approval, which will greatly increase the operational risk of the enterprise.

In addition, the heavy investment in the solid formulation industry is also reflected in the drug development process and large-scale production. In terms of research and development, the long research and development cycle of solid formulations is accompanied by continuous investment

in funds and talents, etc. In terms of production, on the one hand, investing in the production line takes a considerable amount of time. According to statistics, the construction of the production line can take up to 5 years to put into production, which requires sufficient funding as support. On the other hand, due to the strict standards set by the country for production, sufficient and sustained financial support is required in fixed equipment investment (regular equipment updates), operator training, and other aspects. Once the sampling inspection is unqualified and the production personnel operate irregularly, all previous achievements will be wasted.

1.4.3 Drug prices are showing a downward trend due to macroeconomic regulation, and profit margins are gradually being compressed

In recent years, due to a series of official policies such as the negotiation of national medical insurance drugs, the issuance of the "Notice on Printing and Distributing Opinions on Promoting Drug Price Reforms", and volume-based procurement, the coverage of the medical insurance drug list has expanded to almost cover all well-selling drugs, resulting in a downward trend in the overall price level of the drug market. For example, in July 2022, the seventh batch of volume-based procurement was completed, totaling 60 drugs, with an average price reduction of 48%. In addition, drug developers are the main beneficiaries of future drug profits, and most pharmaceutical manufacturing companies that contract manufacturing have relatively low profits, which further reduce the profit margin of solid formulation manufacturing enterprises.

1.5 Future Development Trends of Solid Formulation Industry

1.5.1 Continuously optimizing industry structure

In the context of the continuous promotion of medical reform policies and the rising cost of raw materials, solid dosage form manufacturing enterprises are facing significant pressure and they should develop towards the directions of

more efficient, economical, and flexible ways. In the future, if solid dosage form manufacturing enterprises want to achieve significant development, they must continue to explore and build scaled and green and lean factories, reduce cost inputs through taking measures such as scale effect and lean production, and ensure the stability in product quality, price, and supply. The industry environment is more conducive to the development of high-quality enterprises. A large number of small and medium-sized enterprises lacking core competitiveness will disappear or transform, and the concentration ratio of the solid dosage form industry will be further improved.

1.5.2 Enterprises seeking internationalization development strategy

With the continuous promotion of China's medical reform policies, the transformation and upgrading of the pharmaceutical industry, coupled with the impact of the epidemic, the situation faced by domestic pharmaceutical enterprises is far more severe than before. In this context, internationalization will be an important development direction for Chinese solid dosage form enterprises in the future.

1.5.3 The production of solid dosage forms is gradually developing towards continuity, digitization, and informatization

The digital development of the solid dosage form industry is a major trend in the future. With the breakthroughs made in artificial intelligence technologies, the importance of data and intelligence technology in the development process of the solid dosage form industry is becoming increasingly significant. By connecting the processes of pre-treatment, formulation mixing, granulation, tablet compressing/ capsule filling, coating and packaging through the MES, APS, and ERP systems, continuous manufacturing can be achieved, which can effectively improve production efficiency, shorten production cycles, enhance process monitoring and outcome feedback, thereby improving product stability, reducing production costs, improving approval efficiency, and increasing enterprise profits.

Moreover, with the launch of policies such as the "14th Five-Year Plan for the Implementation of National Clean Production" and the "14th Five-Year Plan for the Development of the Pharmaceutical Industry", clear requirements have been put forward for the green and low-carbon

development of the pharmaceutical industry. The basic principles and main goals for promoting key industries such as chemical raw materials and pharmaceuticals have been established, including the "one sector, one policy" green transformation and upgrading, accelerating the implementation of systematic clean production transformation in existing enterprises and parks, such as energy conservation, water conservation, material conservation, pollution reduction, and carbon reduction, building a green industry system, and improving the level of green manufacturing. This series of policies is of great significance for the transformation, upgrading, and sustainable development of the pharmaceutical industry of raw materials. It will further accelerate the high-quality development of the solid dosage form industry under the new situation and enhance the core competitiveness of the industry.

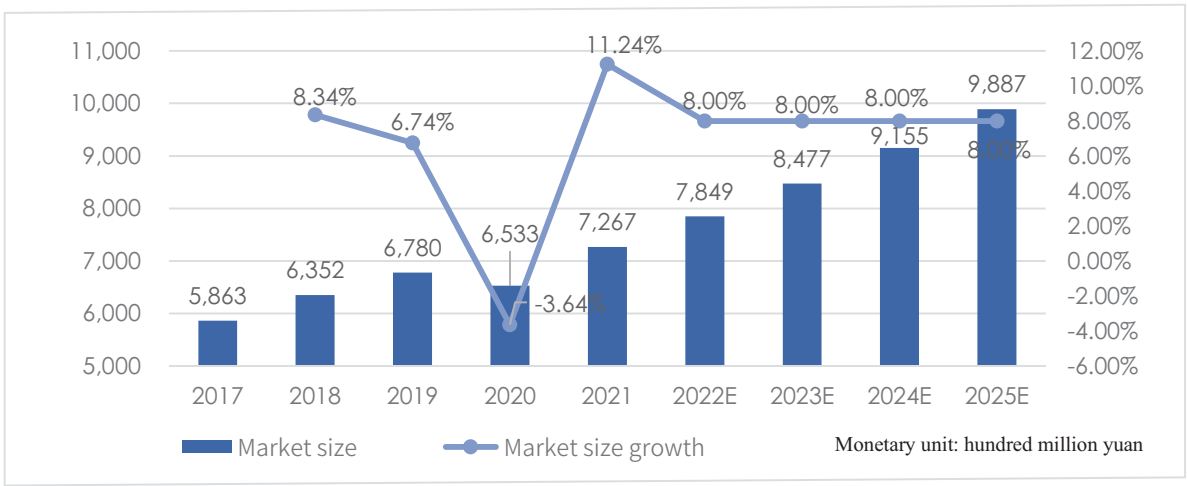
2 Analysis on Industrial Scale and Trend of Solid dosage forms in China

2.1 Solid dosage forms industry market size

Compared with other Asian countries, China 's solid dosage forms market has developed relatively mature, but there is still a big gap with developed countries, and there is still strong growth potential in the future. In 2021, the market size of solid dosage forms in China reached 726.7 billion yuan. With the improvement of residents' affordability, the growth of patient groups and the expansion of medical insurance coverage, the market size of solid dosage forms in China are expected to further expand to 988.7 billion yuan by 2025, with an average annual compound growth rate of 8%, as shown in Figure 1.

Figure 1

Sales volume and growth rate of solid dosage forms in China from 2016 to 2025



Note: In 2020, due to the new coronavirus pneumonia epidemic, the market size has declined significantly, and it is expected that the market will continue to grow steadily in the next five years with the normalization of the epidemic and the expansion of the scope of medical insurance

Source: National Bureau of Statistics, Research and Analysis of M2 Consulting

2.2 Solid dosage forms industry analysis

From the perspective of business scope, at present, among domestic solid dosage form enterprises, the first echelon is state-owned background enterprises, which are involved in the fields of chemical medicines, Chinese patent medicines and biological medicines, and form a complete industrial chain from drug research and development, raw material supply to drug manufacturing to drug sales. The second echelon is mainly listed companies, integrating R & D and production. In recent years, it has increased the investment costs in improving drug R & D, drug production technology and other aspects, and has laid out overseas and become an international large-scale enterprise. The third echelon is enterprises with contract production as the main business, such as Humanwell Pharmaceutical, specializing in drug contract production, drug packaging and other businesses.

The pharmaceutical industry in China is undergoing structural changes, and a number of enterprises focusing on R & D and emphasizing innovation take generic innovative drugs as a breakthrough, and focus on the investment at the production end, gradually form a relatively complete industrial chain integrating R & D, production and sales, and gradually separate from a single contract and single R & D model. Moreover, with the improvement of domestic regulatory requirements, some pharmaceutical companies have begun to directly build production lines that meet foreign requirements. In the future, the Matthew effect in the industry will be particularly obvious, head manufacturers will continue to earn high profits in the industry, the profit margin of small solid dosage form manufacturers lacking technology will be squeezed, and the industry concentration will be further improved.

3 Analysis on Industrial Chain of Solid dosage forms in China

3.1 Overview of solid dosage forms industry chain

The upstream of the solid dosage form industrial chain is the raw material end, including traditional Chinese medicinal materials, APIs and pharmaceutical excipients, the middle reaches are the equipment end, including drug pulverization equipment, mixing equipment, granulation equipment, drying equipment, compression equipment and packaging equipment, and the downstream is the preparation market, including chemical medicines, biological medicines and Traditional Chinese Medicines.

3.2 Solid dosage forms raw material development analysis

Solid dosage forms are mainly made of excipients and APIs (APIs). Excipients are substances added to pharmaceutical products that exert different functional and physiological activities, including fillers, binders, disintegrants, lubricants, taste-masking agents, stabilizers, backbone materials, and coating materials. The active ingredients of APIs are the basic substances constituting the pharmacological effects of drugs. APIs cannot be directly used by patients, and must be further processed into preparations through the addition of excipients and other links in order to be taken by patients. An intermediate, on the other hand, is a material produced in the API process step that must undergo further molecular change or refinement to become an API.

3.2.1 Green and low-carbon transformation at the raw material end, and the use of chemical APIs will closely follow environmental protection requirements

In recent years, the national requirements for environmental protection have gradually increased. Production and use of chemical APIs will closely follow environmental

policy requirements. In recent years, many API enterprises have stopped production and shutdown due to environmental protection problems. Under the current strict environmental protection policies, the pressure of API companies will gradually increase, but this will also promote Chinese APIs to strive for initiative in the construction of green production system and international competitive cooperation.

3.2.2 Under the opportunity of patent expiration, featured APIs and patented APIs have great market potential

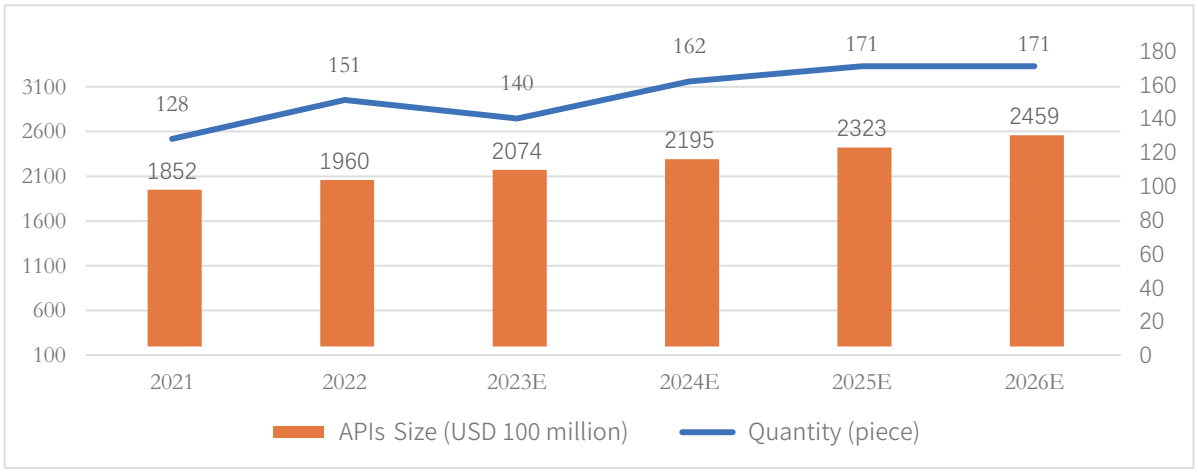
APIs are generally divided into three categories: bulk APIs, featured APIs and patented APIs. With the global industrial division of labor and the transformation of the business model of multinational pharmaceutical companies, the outsourcing market for patented drug APIs will be further expanded.

In the next few years, the number of global drug patents expired will usher in a wave of climax: 128 patents of patented drugs expired worldwide in 2021 and will increase year by year in the future, and more than 171 patents will expire each year by 2025 and 2026, as shown in Figure 2. It is expected that the development of generic drugs will spawn a huge demand for featured APIs and patented APIs in the next five years, which will trigger a major outbreak in the market size of generic drugs for downstream solid dosage forms. From 2021 to 2024, patented drugs with total sales of $145 billion are expected to expire, corresponding to about $14.5 billion to $29 billion in generic drug substitution space.

With the continuous improvement of policy support and supervision, the continuous expansion of procurement scope with quantity and the advent of patent expiration tide, as well as the promotion of new technologies such as continuous manufacturing technology, China's API industry will enter the stage of high-quality rapid development, the transformation will be upgraded and accelerated, and the industry concentration will be continuously improved.

Figure 2

Number of global drug patents expired 2021–2026



Source: Public data collation, Research and Analysis of M2 Consulting

3.3 Development and analysis of solid dosage forms manufacturing equipment

3.3.1 Development status of solid dosage form manufacturing equipment

In 2019, the integration of GMP standards into drug manufacturing licenses means that authorities are more stringent in the regulation of drug manufacturing and that the elimination of old manufacturing equipment is accelerating. At the same time, the epidemic situation in 2020 has promoted the acceleration of import substitution of domestic solid dosage form manufacturing equipment.

With the continuous improvement of domestic solid dosage form pharmaceutical equipment enterprises' requirements for their own sustainable development, intensifying the development of new products, continuously enhancing the scientific research level and design and manufacturing ability of enterprises, and continuously learning and absorbing foreign technologies and concepts, the technical level of equipment production

in the domestic solid dosage form pharmaceutical equipment industry has been greatly improved, and a number of advanced domestic solid dosage form pharmaceutical equipment manufacturers with high innovation level and recognized by the pharmaceutical industry have emerged, providing assistance for the development of the solid dosage form pharmaceutical industry in China.

For example, Beijing Goldenteam Technology Co., Ltd, with the vision of "making customer production simpler", has been committed to the field of pharmaceutical equipment for more than twenty years, and continues to propose efficient solutions around customer pain points along the direction of smart green manufacturing engineering of "Made in China 2025" by virtue of excellent expert teams and the original 5H concept. At the same time, entrusted by the National Development and Reform Commission and industry associations, Beijing Goldenteam Technology Co., Ltd has prepared five industry standards: JB/T 20049-2014 Pharmaceutical Vacuum Charger, JB/T 20165-2014 Pharmaceutical Tooth Pulverizer, JB/T20191-2018 Pharmaceutical Weighing and Compounding Device, JB/T 20192-2018 Pharmaceutical Helical Conveyor, and JB/T 20196-2020 Pharmaceutical Airflow Mixer.

After more than 20 years of innovative development, Beijing Goldenteam Technology Co., Ltd. has formed three major business modules: solid dosage forms, pretreatment of Traditional Chinese Medicines, and powder engineering. The solid dosage form module takes the "fully closed granule continuous manufacturing system" as the core product, including: dismantling, unpacking, dust-free feeding, dust-free pulverization, automatic compounding, wet mixing granulation, continuous drying, sieving to all links of the total mixing. Traditional Chinese Medicine pretreatment module takes "automatic fully closed grinding system of traditional Chinese medicinal materials" as the core product, including: error-free feeding, primary grinding, pre-mixing, secondary grinding, total mixing, and metering and bagging.

Powder engineering module is the core product of positive/negative pressure airflow transportation, ton bag metering bagging/unpacking feeding, small bag metering bagging/unpacking feeding, wet material transportation, which is applied to fully closed VC production system, API production system, etc. These modules

include specific equipment: NZQ series medicinal vacuum delivery system with independent property right, GDF dust-free feeder, DMA traditional Chinese medicinal material pulverizer, DMB medicinal tooth pulverizer, FC series hammer pulverizer, GSG granulator, GMP metering subassembly machine, MRS automatic batching system, GSM series air flow mixer, HLSG series wet mixed granulator, GWL horizontal continuous boiling bed, etc.

Beijing Goldenteam Technology Co., Ltd. successively delivered "smart, green and continuous manufacturing systems" to thousands of customers including Beijing Tong Ren Tang Group, Yiling Pharmaceutical, Yunnan Baiyao, Jiuzhitang, Northeast Pharmaceutical Group, North China Pharmaceutical and Jingxin Pharmaceutical. Help customers achieve the indicators of shortening the production cycle by 50%, reducing the production cost by 50%, reducing the ungood quality rate by 50% and reducing the pollutants by 20%, and promote the integration of domestic solid dosage form pharmaceutical equipment with the international advanced level. Beijing Goldenteam Technology Co., Ltd. has created high-tech products with "Chinese characteristics" with innovative development.

"Do not blindly imitate any product, foreign products are not all advanced, there will be defects. According to Chinese regulations, culture and management, we reinterpret the 'production process', reestablish the mathematical model, design more efficient equipment, help users reduce production costs and transmit value to customers. This is the root cause that Beijing Goldenteam Technology Co., Ltd. has been highly recognized by customers.

Traditional Chinese medicine (TCM) equipment must rely on us, and TCM is a unique drug in China that has been verified for thousands of years and has a complete theoretical system. Its process is much more complex than western medicine. We should use modern technology to continuously improve the progress of TCM production equipment and make it close to the level of Western medicine equipment."

Shao Tianjun, General Manager of Beijing Goldenteam Technology Co., Ltd.

3.3.2 Future development trend of solid dosage form manufacturing equipment

In recent years, the proportion of domestic solid dosage form pharmaceutical equipment has gradually increased, indicating that the independent R & D capacity of Chinese solid dosage form pharmaceutical equipment enterprises is gradually strengthening. Although the development of domestic solid dosage form pharmaceutical equipment industry to today's level is worth affirming, it should be seen that compared with foreign equipment, domestic solid dosage form pharmaceutical equipment technology still remains to be developed, which also promotes the domestic solid dosage form pharmaceutical equipment industry to accelerate innovation drive and promote the update and upgrading of domestic equipment.

The Outline of the Fourteenth Five-Year Plan for National Economic and Social Development of the People 's Republic of China and the Vision Goals for 2035 issued in March 2021 insists on accelerating the construction of manufacturing power and quality power. Emphasis should be placed on enhancing the competitive advantage of manufacturing industry and promoting high-quality development of manufacturing industry. This will enable more pharmaceutical companies to further develop and apply advanced manufacturing technologies and equipment from the source, more actively improve the use of key solid dosage form pharmaceutical equipment, promote continuous iteration of the equipment industry, and develop breakthroughs in digital, smart, and continuous manufacturing. Senior experts in the industry generally believe that "the next decade will be the golden period for the development of the pharmaceutical equipment industry", and the developed solid dosage form pharmaceutical equipment will become a new support for the continuous growth of the entire industry in the future.

3.4 Development analysis of solid dosage form R & D

With the growth of China's economic and scientific and technological strength and the continuous improvement of innovation capacity in the pharmaceutical field in China, the pharmaceutical industry in China will accelerate into the historical period of transformation and upgrading and gradually enter the development stage of innovative drugs from the generic drug stage. As a dosage form that occupies about 70% of all pharmaceutical dosage forms, the development of solid dosage forms has also been given new requirements and expectations.

3.4.1 Solid dosage forms development strategy is maturing

In the R & D link of solid dosage forms, due to the complex process and process, there are many key factors affecting the medicinal properties and quality of solid dosage forms, so the selection of R & D process is very important in the development link of solid dosage forms. The commonly used development processes for solid dosage forms include: direct powder compression, wet granulation, dry granulation, etc., of which direct powder compression is more preferred by manufacturers due to the simplest process. Figure 3 shows three main process methods for solid dosage forms mainstream.

In the R & D stage of solid dosage forms, R & D personnel will purposefully select different preparation processes: in the earliest preparations study design stage, the simplest preparation process (such as powder straight compression process) will generally be used as far as possible for preparatory stability and preliminary investigation, so as to facilitate R & D personnel to carry out rapid conceptual verification; in the late clinical stage or commercial production stage, R & D personnel need to consider the stability of solid dosage form drugs and reduce the risk of commercial batch amplification, when R & D personnel will consider which process to use according to specific circumstances, minimize the changes in the late process and select the preparation process most suitable for such drugs. It can be seen that the selection of processes in the R & D link is particularly important, so it is necessary to understand the advantages and disadvantages of the

main processes, and Figure 4 compares the three mainstream processes. Powder direct compression is mainly suitable for the early stage of R & D, and dry granulation and wet granulation are more suitable for the middle and late stage of R & D, in which the dry granulation process is more suitable for the continuous manufacturing mode of the production line that is now developing.

At present, the trend of pharmaceutical R & D in China has changed from "imitation first" to "innovation first", and the solid dosage form industry is also undertaking this trend and challenge. Although there are still many shortcomings to be made up, challenges and opportunities coexist. In this period of unprecedented favorable policy environment, solid dosage form pharmaceutical companies need to fully

Figure 3

Main three process methods for solid dosage forms

Name	Wet granulation	Dry granulation	Powder direct compression
Process	Mixed	Mixed	Mixed
	Granulation (Wet)	Granulation (dry)	/
	Drying	/	/
	Crushing	Crushing	/
	Mixed	Mixed	/
	Compression	Compression	Compression

Source: Public data collation, Research and Analysis of M2 Consulting

Figure 4

Process comparison in solid dosage development

	Dry granulation	Wet granulation	Powder direct compression
Principle	Crushing material into small particles by rolling press, crusher	(fluidized bed or high-speed shear granulation) sticking material to small particles and drying	Direct selection of excipients with good fluidity and compressibility
Drug load	Up to 70%-80%	Less than or equal to 50%	70%-80% or higher
Advantage	No introduction of damp heat Can be manufactured continuously	Easy to enlarge Pre-mix can be done in pot	Streamlined process Powder straight press suitable for use with drugs expected to be sensitive to ambient humidity, temperature
Disadvantages	Poor compressibility of the APIs may cause it to adhere to the drum	Higher energy consumption due to additional drying process	Mainly applicable for initial development

Source: Public data collation, Research and Analysis of M2 Consulting

arm in the software, hardware and other aspects of the R & D link, based in China, and look overseas, so that the innovation force can be more lasting, can meet more unmet clinical needs, and enterprises can get longer-term development.

3.4.2 Specialization and outsourcing of R & D link

Pharmaceutical R & D, especially new drug R & D, is a high-tech, high-risk, high-investment and long-cycle complex system engineering, of which R & D outsourcing has run through the whole process of new drug discovery, R & D and development. Studies have shown that cooperation with R & D outsourcing enterprises can shorten the R & D time of new drugs by 1/4 ～ 1/3, and save 30% ～ 70% of R & D costs. R & D outsourcing companies use rich project experience to modularize the pharmaceutical R & D process and simultaneously carry out multi-part work to improve synergistic effect and efficiency. In the clinical application and clinical stage, R & D outsourcing companies can simplify the process, directly connect with testing institutions and evaluation institutions and shorten the R & D time. At present, pharmaceutical R & D service outsourcing has become the main form of global pharmaceutical R & D. The important role of pharmaceutical R & D outsourcing in the chain of new drug R & D in China is increasingly prominent.

3.5 Development analysis of solid dosage form production link

The production process of solid dosage forms is relatively complex and requires a series of processes such as pretreatment, mixing, granulation, drying, total mixing, compression, and coating, and solid dosage forms are basically completed. For the production of solid dosage forms, it is very important to ensure the mixing uniformity, fluidity, filling and compressibility of materials. Almost all the development and production of solid dosage forms first have to go through crushing, sieving and mixing operations, which are the main unit operations to ensure the mixing uniformity of raw materials and excipients [4]. However, there are three main methods for the production process of solid dosage forms: wet granulation, dry granulation, and direct powder compression.

3.5.1 Continuous manufacturing of solid dosage forms will become a new mode of future production

With the introduction of national series policies, the pharmaceutical industry is facing profound changes, and pharmaceutical companies are facing unprecedented pressure in product quality, compliance of production processes, and production costs. Therefore, optimizing the production technology and process has become the general trend, solid dosage form manufacturers are facing fierce market competition, how to build a "new kinetic energy"? According to a survey by Pharmaceutical Engineering Technology Network, 85% of respondents are optimistic about continuous manufacturing processes, especially the application of automatic continuous manufacturing processes will gradually climb.

Advanced continuous manufacturing process can significantly improve production efficiency and reduce production costs. Continuous manufacturing of solid dosage forms has the following advantages: faster development speed, smaller equipment footprint, more flexible manufacturing scale, stricter process control, and potential for real-time release [5]. However, continuous manufacturing process requires a lot of early investment, and the current continuous manufacturing process has just

started, domestic and foreign experience is not rich. If Chinese enterprises can seize the opportunity to promote and use continuous manufacturing processes, they will improve the production efficiency of solid dosage forms in China and reduce production costs.

Pharmaceutical outsourcing refers to that pharmaceutical companies deliver drug R & D, production, sales and other links to professional enterprises for operation through outsourcing. Pharmaceutical outsourcing enterprises can be broadly divided into pharmaceutical R & D outsourcing organization (CRO), pharmaceutical production outsourcing organization (CMO) or pharmaceutical customized R & D and production outsourcing organization (CDMO) and pharmaceutical sales outsourcing organization (CSO) according to their respective operation links.

3.6 Analysis of outsourcing market development of solid dosage forms

3.6.1 Solid drug product outsourcing market is developing rapidly and will be golden period in the next 5-10 years

In recent years, China 's pharmaceutical innovation R & D policy has been continuously launched and improved, the drug marketing authorization holder (MAH) system has been implemented, and multiple favorable factors such as cost advantages and demographic dividends under the premise of ensuring quality have been concentrated, China' s pharmaceutical outsourcing (CXO) enterprises have shown a trend of rapid development, and a number of pharmaceutical outsourcing (CXO) enterprises have been listed and marketed successively. In the context of the booming development of new drug R & D, the market of China 's pharmaceutical R & D outsourcing industry will also develop rapidly.

Before the implementation of the volume-based procurement policy with quantity in 2018, the consistency evaluation of solid dosage forms and the rapid development of innovative drugs led to a rapid increase in the demand of the domestic pharmaceutical R & D

outsourcing industry. After the introduction of the volume-based procurement policy in 2018, the price of generic drugs has been significantly reduced and profits have been significantly compressed, and pharmaceutical companies have to substantially cut off the items for consistency evaluation and transform into innovative drugs. Since 2019, the demand for domestic pharmaceutical outsourcing services has increased rapidly and continuously. Driven by policies, China is beginning to enter the era of innovative drugs, and the development of innovative drugs will promote the rapid development of pharmaceutical R & D and production outsourcing services, which is expected to be a golden development period in the next 5-10 years.

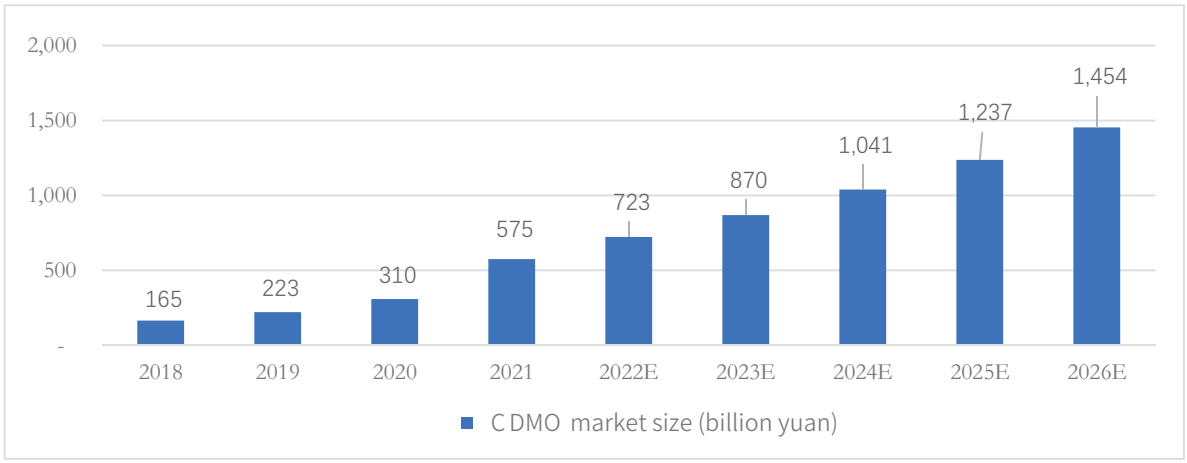
The Chinese CDMO market has achieved overall rapid growth since 2015. From 2018 to 2021, the market size of CDMO in China increased from 16.5 billion yuan to 57.5billion yuan, with an average annual compound growth rate (CAGR) of 51.6%, as shown in Figure 5. Among them, the market size of CDMO for chemical medicines increased from 11 billion yuan to 39.9 billion yuan, and the market size of CDMO for biological medicines increased from 5.5 billion yuan to 17.6 billion yuan, with an average annual compound growth rate of 53.6% and 47.4%, respectively. From 2021 to 2026, the market size of CDMO in China is expected to maintain growth at an average annual compound growth rate of 20.4%, and the market size is expected to climb to 145.4 billion yuan. The CDMO market of chemical medicines and biological medicines will continue the current rapid growth momentum, and the average annual compound growth rate will reach 16.8% and 27.3%, respectively. By 2026, the market size of biopharmaceutical CDMO is expected to increase to 58.8 billion yuan, and the market size of chemical CDMO is expected to reach 86.6 billion RMB.

3.6.2 Solid drug product outsourcing market will be further concentrated and developed towards intensification and regionalization

At present, the pharmaceutical R & D outsourcing (CRO) industry is the largest in the packaging market at home and abroad. These pharmaceutical R & D outsourcing (CRO) enterprises are mainly distributed in Beijing, Shanghai, Jiangsu and other places. The common characteristics of these three regions include: relatively mature development of industrial parks,

Figure 5

2018–2026E China CDMO market size



Source: Research and Analysis of M2 Consulting

relatively concentrated pharmaceutical enterprises, active development of innovative and entrepreneurial industries, and relatively rich talents and educational resources. At the same time, with the global industrial division of labor and the gradual stripping of the production link by large pharmaceutical companies, the pharmaceutical production outsourcing (CMO/CDMO) industry has ushered in the blue sea era and is expected to burst a new vitality.

From consistency evaluation to innovative drug research and development, the technical capacity requirements for pharmaceutical outsourcing enterprises of solid dosage forms have also been gradually improved. In this transition, leading companies with higher service levels and better quality systems will benefit first and gradually occupy more markets. Judging from the current distribution of pharmaceutical R & D outsourcing (CRO) and pharmaceutical production outsourcing (CMO/CDMO) companies in China, the drug clearance system occupies the leader in the industry, and the industry is expected to have a pattern of "more than one strong". The entire outsourcing market will be further concentrated in the future and have a regional direction development trend.

4 Application Analysis of Innovative Technology in Solid dosage form Industry

The introduction of emerging technologies into traditional industries to change the industrial structure is inevitable, such as the subversion of Internet streaming media on the film and television industry, the impact of taxi-hailing software on the traditional taxi industry, and the transformation of Internet e-commerce on traditional commerce and retail. Meanwhile, the solid dosage form industry is gradually optimizing its model under the influence of emerging technologies.

4.1 Application analysis of continuous manufacturing mode

4.1.1 Introduction of continuous manufacturing

Continuous manufacturing (or continuous production) of solid dosage forms is an "end-to-end" production mode, in which the unit of each step in the production is integrated through a control system, raw materials are continuously added into the production line, and end products are continuously obtained at the same speed, the raw materials and the end products enter and exit the production line at the same speed, and the time of the whole production process can be shortened to several minutes to several hours [6]. At the same time, the process analysis technology (PAT) is applied for real-time monitoring of intermediates and end products in the continuous manufacturing process to achieve real-time control of the production process and ensure the quality of the product.

4.1.2 Advantages of continuous manufacturing

(1)Improve production efficiency

Continuous pharmaceutical production can greatly improve production efficiency and reduce production cost by up to 50% [7]. Continuous manufacturing is suitable for long-term uninterrupted production of scaled single product variety. It can realize efficient production in an extremely small workshop, greatly reduces energy consumption, requires no intermediate transfer, occupies small space and saves

materials. As only a few kilograms of materials are being processed in certain production equipment or a certain working procedure at any given time, in the process, if unexpected events affecting the product quality occur, the production can be forced to suspend to reduce the loss to the greatest extent and improve the production efficiency.

(2)Save production cost

Continuous pharmaceutical production can greatly reduce production time, reduce logistics turnover, and shorten the production cycle. Especially when in urgent clinical need, it can quickly meet clinical needs, more easily cope with drug shortages and epidemic outbreaks, and shorten the time for marketing of new products for enterprises.

It is worth mentioning that Golden Team, a famous domestic manufacturing enterprise, provided a "smart, green and continuous manufacturing system for granules" using the "automatic horizontal continuous drying fluidized bed for medicinal use" initiated in China for a famous Chinese patent medicine manufacturing enterprise. The system consists of 8 production lines in total, and the single-line production capacity is 1,200 kg/h, which includes the whole process from unpacking and feeding, dust-free crushing, automatic preparing, wet mixing granulating, continuous drying, and particle classification to general mixing. The whole line has realized the overall production cycle reduction by 50%, production cost reduction by 50%, labor saving by 50%, rejection rate reduction by 50%, and pollutant reduction by 20%, and for material yield achieved the indexes of total feeding amount (including humidity) of 93% and equivalent dry material of 99.5%, and the return on investment cycle is less than 50%. This fully reflects the core values of intelligent manufacturing and green manufacturing engineering.

(3)Guarantee product quality

The continuous manufacturing process greatly reduces the operational personnel and greatly reduces the risks of environmental pollution, operation error and the like brought by human factors. The continuous manufacturing process implements the whole process control of quality, and the production intermediates and final products are controlled and guaranteed based on the process data. The process traces product quality on-line, and in accordance with U.S. Food and Drug Administration (FDA) and International Conference on Harmonization

of Registration Technologies for Human Use (ICH) guidelines, the final product is ready for marketing immediately after production. Continuous manufacturing avoids the arbitrary changes that affect quality operations, such as data fraud, data modification, and SOP changes, which is conducive to the supervision of the regulatory authorities, and can significantly reduce the number of flight inspections, which more conforms to the principle that quality originates from design.

4.1.3 Future trend of continuous manufacturing in China

At present, there are few pharmaceuticals that conduct continuous manufacturing research in China. The domestic development of continuous medicine manufacturing is facing the constraints of equipment, capital, talent, technology and policy. There are over 4,800 pharmaceuticals in China, with most varieties repeatedly produced, a single solid dosage form production line needs to alternate varieties often, making it not suitable for continuous manufacturing, and the existing pharmaceutical equipment is not suitable for continuous manufacturing too [5]. For domestic enterprises to implement continuous medicine manufacturing, they need to invest a lot of time and money, for low-cost profit-making enterprises in China, the development of continuous manufacturing power is insufficient. In addition, continuous medicine manufacturing requires establishing a special central control system to intelligently control the equipment at the same time, which is also very challenging. Continuous medicine manufacturing requires multi-disciplinary joint research to achieve, involving mechanical and electrical, equipment, electrical, automatic control, pharmaceutical engineering, software, mathematical statistics and other disciplines. The definition of "batch" and "shelf-life" in continuous medicine manufacturing, as well as the control of critical parameters in the production unit, the perfection of the material traceability system, the sampling and release inspection methods, and so on, all need to be agreed upon by the regulatory department and the enterprise to formulate implementable guiding principles.

Article 10 of the Guiding Opinions on Promoting the Healthy Development of the Pharmaceutical Industry (promulgated and implemented on March 11, 2016) clearly points out that: New formats

should be fostered to promote the intelligent development of the industry. The implementation of the Guiding Opinions will accelerate the development of continuous medicine manufacturing in China. Specifically, this is reflected in three aspects: First, the government and National Medical Products Administration encourage 1–2 varieties with high production volume and marketed in both China and abroad to be the pilot product of continuous medicine manufacturing and establishing 1–2 prototype models for small-scale continuous manufacturing to explore experience; Second, domestic enterprises transform the existing production equipment smaet as the starting point, explore each unit transformation, such as tablet press, coating machine, mixer and other manufacturing equipment transformation, to create domestic intelligent pharmaceutical equipment; Third, domestic enterprises actively explore the use of PAT to conduct on-line control on critical parameters, processes, intermediates and finished products in production, such as the application or modification of on-line detection equipment such as data acquisition, storage and transmission, and conduct real-time testing, regulation, data transmission and feedback tests to ensure the quality of final products.

In addition, the country has issued policies on the continuous manufacturing of solid dosage forms for specific areas, and the instructions and regulations are provided. Among them, the Guiding Principles for Continuous Manufacturing Technology of Chemical Oral Solid Dosage Forms (Draft for Consultation) issued in September 2022 elaborates the general considerations, relevant concepts, control strategies, process validation, stability research, batch changes, drug quality system, reporting data requirements and other contents for the continuous manufacturing technology of chemical oral solid dosage forms, aiming to provide guidance for the research and evaluation of the continuous manufacturing technology of chemical oral solid dosage forms.

4.1.4 Case Analysis of continuous manufacturing

As the international market leader in tablet press industry (FETTE China holds the absolute advantage in the tablet compacting market with the single machine sales volume of more than RMB 1 million in China and occupies more than 80% of the high-end market in China), it

demonstrated the cutting-edge technology foretelling the future of pharmaceutical production-the continuous manufacturing line based on FE series tablet press at the 59th (Fall 2020) National Pharmaceutical Machinery Expo and the 2020 (Fall) China International Pharmaceutical Machinery Expo, which provides a continuous manufacturing solution relying on compacting devices for direct powder compression.

The solution is to use the FE series efficient tablet press as the main body of the powder direct compacting continuous manufacturing line, equipped with horizontal mixing system and high precision feeding device, combined with the more advanced mixing technology, formed a set of safe and efficient continuous manufacturing solutions suitable for a variety of output. Compared with other continuous processes, one of the characteristics of the production line is that it can mix a variety of materials on-line, and the yield is flexible. Moreover, the production line requires less equipment to be connected, which can meet the requirement of lower space occupation, thus saving the cost for customers and increasing the production efficiency and income. In addition, the compact and efficient direct tablet compacting is more prominent in its simple and reliable operation advantages in continuous manufacturing. The production line emphasizes the continuity of the whole process from the starting to the finishing, and reduces the conversion between batches, so that numerous intermediate processes are not needed, the risks of shutdown and standby are reduced, and the intermediate losses are reduced. The technology has driven the industry from more intermittent batch production to continuous manufacturing.

FETTE's tablet presses are also equipped with state-of-the-art PAT (Process Analysis Technology) sensors based on near-infrared spectroscopy (NIR), ensuring stable product quality. The NIR in the tablet press allow real-time analysis of the strength of each tablet, making it possible to analyze data from the manufacturing process and optimize the manufacturing process, while ensuring the quality of the finished tablets. In addition, FETTE is equipped with a special competence center, where users can conduct product testing and product production optimization, and meanwhile it can also provide supporting solutions according to customers' production needs.

4.2 Industrial digital transformation and application analysis

4.2.1 Digital transformation process

Smart manufacturing can enable the whole life cycle management of drug research and development, production, quality, and logistics, and on this basis, support the continuous optimization of the operation and management of pharmaceuticals. In order to achieve this goal, pharmaceuticals need to first establish a digital system, make it possible to integrate systems, equipment, and links with each other, and establish an organization system and project management mechanism directly led by the senior management of the enterprise.

(1)Creating a digital foundation

Most Chinese traditional pharmaceuticals, especially SMEs (small and medium-sized enterprises), are still at the stage of building a "digital foundation". At this stage, the focus of adapting to smart manufacturing should be on core needs and key business areas. The company needs to determine its current performance in these areas, deploy the necessary software and hardware components, carry out small-scale digital pilots, and achieve interconnection and integration in one or more business sectors. Companies with innovative R&D as their strategic core, for instance, should focus on laboratory information management systems (LIMS), clinical trial management systems (CTMS), and corresponding applications at the control and equipment layers. Companies whose main business is in mature products need to concentrate on reducing price pressure through lean production and cost control. Their priorities should therefore be manufacturing execution systems (MES) and warehouse management systems (WMS). Pharmaceuticals of all kinds can gradually adapt to smart operations through clear management decisions, including external support where necessary, and successive pilot projects. Figure 6 shows an example of a three-tier architecture for an smart factory.

(2)Achieving empowerment through interconnection

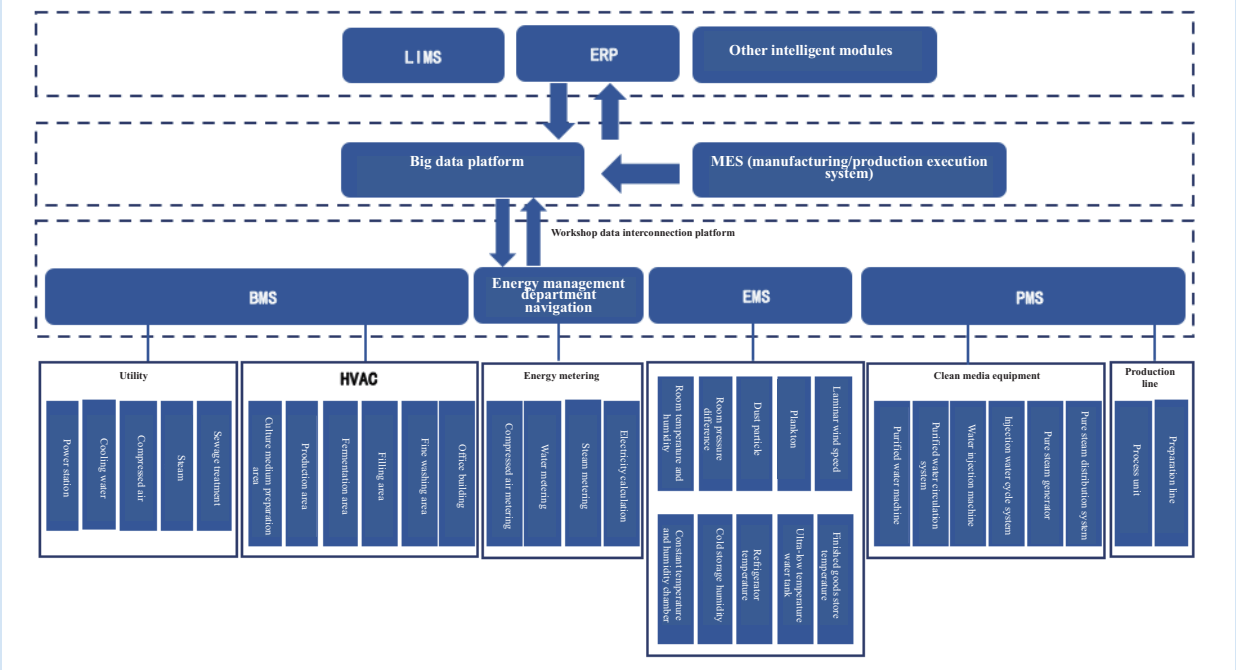
"Interconnection empowerment" requires pharmaceutical companies to complete a number of digital projects, establish software and hardware foundations in some business areas, and accumulate a degree of experience in organizational transformation. Over time this will expand to cover a wider range of business areas,

achieve deeper integration, and extend to higher management levels. With advancing technology, the complexity of smart manufacturing revolutions empowered by interconnection has greatly increased, requiring more management participation, clearer visions and more specific goals.

In terms of breadth, companies can upgrade business processes throughout the plant, move more operations online, and finally achieve digital coverage of the entire process. In terms of depth, companies can dig deeper into the functions of existing systems and achieve cluster-level automated control in some business areas. In terms of vertical integration, they can start to bring together business systems such as R&D, production, quality, and logistics. Many people attempting to bring smart manufacturing to the pharmaceutical industry are confused: "Our systems are all online," they say, "but it still feels as if we are a long way from smart manufacturing." An important reason for this is a lack of communication between systems at different levels. It is common to see a gap between "brain"

Figure 6

Three–tier architecture example of the smart factory



Source: National Bureau of Statistics, Research and Analysis from M2 Consulting

and "hand" – either between a higher-level management system and a lower-level system, or between the lower-level system and an individual device. Such gaps mean that managers' judgments are often not supported by accurate and timely information from the factory floor. To fix these information gaps, companies should aim for an integrated management culture, viewing and solving business problems through the perspective of interconnected digital systems.

(3)Implement the vision of intelligence

Such transformations are the key to smart manufacturing. In addition to further improving the integration of systems at all levels, companies need to actively explore digital governance models that shift gradually from traditional process-oriented systems to digital-oriented systems, while respecting the particular characteristics of each business.

4.2.2 Industrial digitalization case analysis

With the continuous promotion of supporting health care reform policies, the increasing emphasis on scientific and technological innovation in the industrial market, and the continuous impact of public health emergencies such as the COVID-19 epidemic in 2020, pharmaceutical enterprises are unable to maintain the traditional mode of development. The industry reshuffle is accelerating. Digital transformation has become the direction for pharmaceutical enterprises to compete for development. Effectively transforming the current high-cost and low-efficiency R&D and production links of enterprises, realizing the smart of pharmaceutical equipment and drug production process, and building an intelligent unmanned factory through data and tools will become the core competitiveness of pharmaceutical enterprises in the future.

Compared with other industries, the digitalization foundation of the pharmaceutical industry is relatively weak, and the digitalization level of the industry is still in the initial stage. It is an urgent problem to be solved in pharmaceutical industry to integrate core systems such as MES, QMS, WMS, PCS, EMS and EAM from workshop production execution system to the upper information management system of the enterprise. Domestic enterprises have begun to try digital transformation, or find outsourcing companies to complete the digital empowerment, or set up a subsidiary

to carry out digital business to help the parent company digital transformation. It is through the latter that the domestic famous pharmaceutical enterprise Tasly has carried out the digital transformation attempt.

(1)PHARM-TECH-company profile

PHARM-TECH (Tianjin) Technology Co., Ltd., a wholly-owned subsidiary of Tasly Group, a leader in modern Chinese medicine, has continuously explored and practiced in the field of intelligent manufacturing, independently developed and innovated equipment, which provides powerful equipment support for the modernization and internationalization of Chinese medicine of Tasly Group and helps Tasly achieve a high degree of automation, serving as a model for modern Chinese medicine smart manufacturing in China. In addition to providing internal services to Tasly Group, PHARM-TECH also provides external services to the industry such as automatic packaging production lines and industrial automation and software development, providing equipment and overall automation solutions for a number of well-known enterprises in the industry, such as Taiji Group, Guangzhou Pharm. PGS, Jumpcan, Hengrui, Beijing Staidson, Xiamen Chinese Medicine and Taifung Group.

(2)PHARM-TECH-Automatic stick package production line

PHARM-TECH multi-row stick package production line is developed and manufactured according to EU standards, with exquisite mechanism, small floor space and high productivity, which is at the leading level in the industry. It is suitable for filling pills, granules, powders, liquids, pastes, tablets and other dosage forms. With the imported weighing module, online single bag weighing of each lane can be completed, and online feedback can be used to adjust the loading capacity, which can realize the separation of qualified products and unqualified products or automatic bag filling of qualified products.

Its production lines are flexible, with one-on-one, two-on-one, and three-on-one production line form. It has the function of secondary counting and can realize boxing of any bag. A single production line can meet a variety of boxing form specifications and realize co-line of boxing and large bags. PHARM-TECH stick production line has provided high-quality, fast and efficient customized services to many listed companies and well-known pharmaceutical enterprises, enjoying a high reputation in the industry.

(3)PHARM-TECH —— MES project of sterile preparation workshop of tasly

The MES system project of Tasly Group developed by the help of PHARM-TECH has been put into production. It can realize batch process data management, and can query and archive data according to time and batch. It can carry out inter-batch data analysis and single variable analysis. The system monitors all production equipment in real time and calculates the OEE of the equipment in real time. The weighing part is controlled by the MES system, and the system receives the work order containing the product name, weight, batch number and other information issued by the process personnel, thus reducing the risks and errors caused by human intervention. Figure 7 shows the production process data acquisition and OEE of the system, and Figure 8 shows the MESeBR client of the system.

The application of smart manufacturing in the production of Chinese medicine solid dosage forms is of great significance. On one hand, it can continuously improve

Figure 7

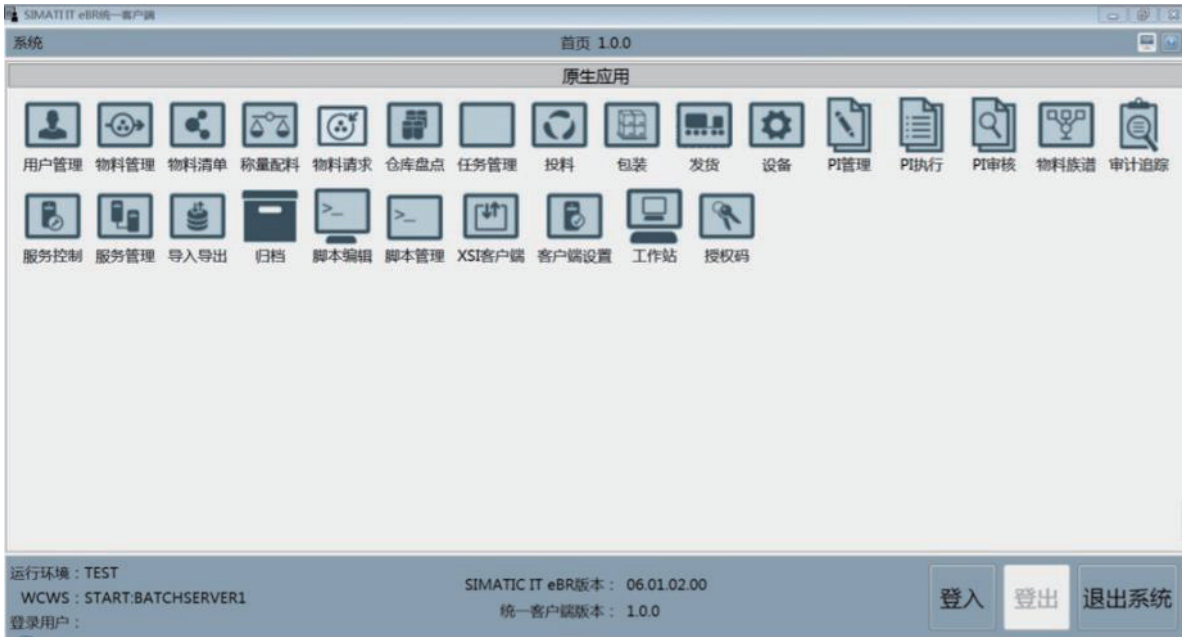
Production process data acquisition and OEE



Source: Research and Analysis of M2 Consulting

Figure 8

MESeBR client end



Source: Research and Analysis of M2 Consulting

production efficiency and effectively reduce production cost; On the other hand, the method effectively ensures the stability and uniformity of the drug quality, and ensures the authenticity and traceability of data and samples in the whole process of drug production.

The project has realized batch process data management, and can query and archive data according to time and batch. It can carry out inter-batch data analysis and single variable analysis. The system monitors all production equipment in real time and calculates the OEE of the equipment in real time. The weighing part is controlled by the MES system, and the system receives the work order containing the product name, weight, batch number and other information issued by the process personnel, thus reducing the risks and errors caused by human intervention.

4.3 Application of smart manufacturing in the production of Chinese medicine solid dosage forms

The application of smart manufacturing in the production of Chinese medicine solid dosage forms is of great significance. On one hand, it can continuously improve production efficiency and effectively reduce production cost; On the other hand, the method effectively ensures the stability and uniformity of the drug quality, and ensures the authenticity and traceability of data and samples in the whole process of drug production.

4.3.1 Application of APS advanced planning and scheduling system

The solid comprehensive preparation workshop included four dosage forms such as granules, hard capsules, soft capsules and tablets, and there were many varieties and quantities as well as many sub-packaging specifications and types. In this regard, the manual scheduling can no longer meet the needs of the overall balanced scheduling. The purchased materials cannot be in place in time, the inspection results cannot be shown in time, and the equipment and production status cannot be learned in time. In case of extra order addition and production abnormalities (person, machine and material), the related links cannot be fully considered in the production plan adjustment. The main production plan is subjected to high-frequency adjustment, which is inefficient in purely manual adjustment. The equipment production capacity cannot be used to its maximum effect.

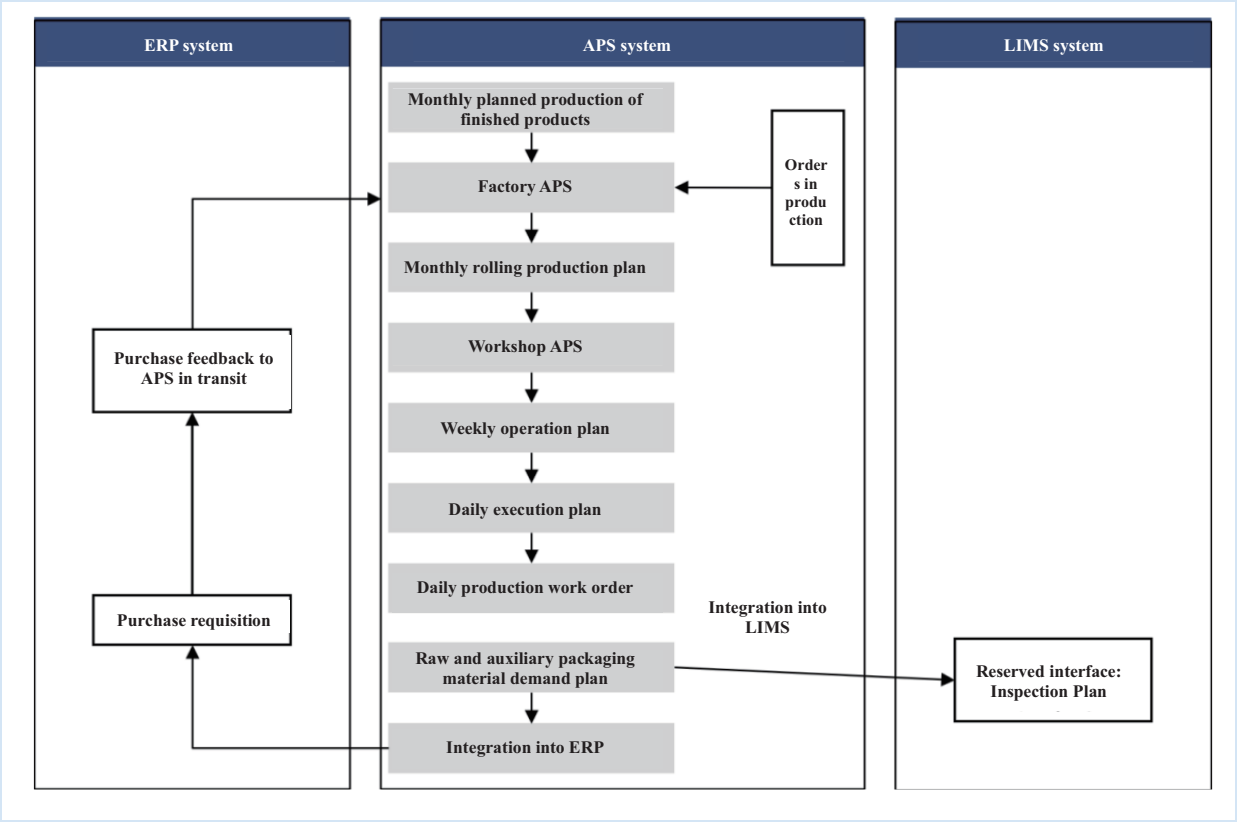
As shown in figure 9, by constructing the APS system to connect ERP, attendance, MES and other systems, and promoting flexible manufacturing, we can strengthen our rapid response to the market, improve the production scheduling efficiency, production efficiency and the utilization rate of equipment, and realize flexible production, transparent management and systematic platform to adapt to the changing needs of customers [6]. At the same time, the construction of production process cost management system to meet the needs of cost management, extended support through the APS system, strengthen the material input/output management, and the implementation

of fine cost accounting have effectively reduced the cost of the production process.

Through calculation, the production scheduling efficiency of workshop unit can be improved 200% by using APS system. The inventory turnover rate can be increased by 30% due to the shortened production scheduling time and enhanced adaptability, which also reduces the inventory cost of materials. In addition, the construction of APS system also realizes the interconnection between sales and APS system, the interconnection between APS system and production system, and the interconnection between APS system and ERP system. The interconnection rate of smart factory can reach 70%.

Figure 9

APS business process



Source: Research and Analysis of M2 Consulting

4.3.2 Application of (SCADA) production supervisory control and data acquisition

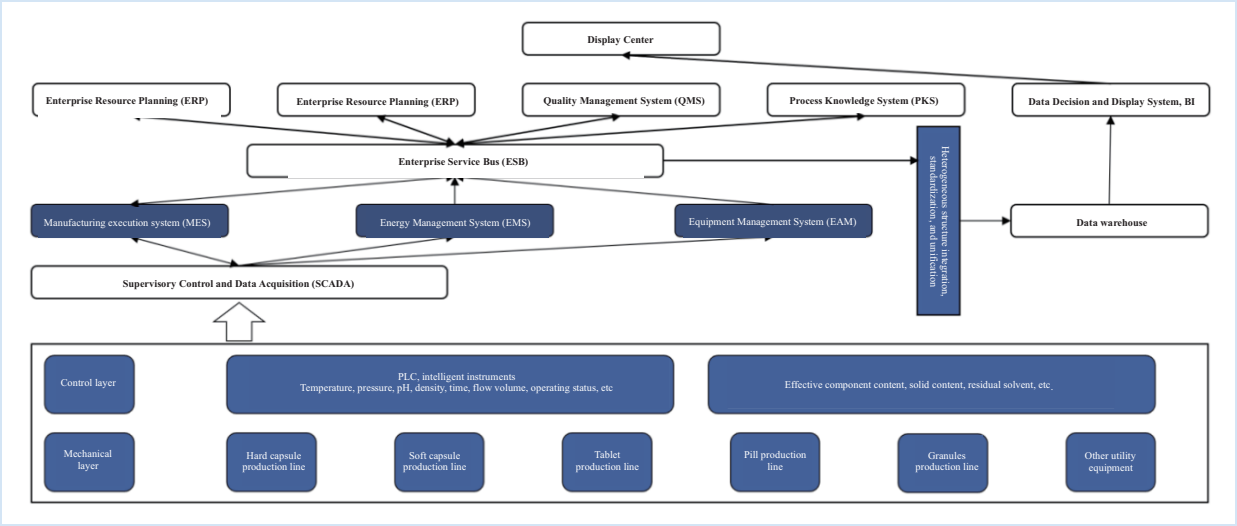
Traditional data collection method often uses manual recording, which is not only time-consuming and labor-intensive, but also prone to data loss, making it even more difficult to monitor on-site operational processes in real-time. Therefore, by establishing a SCADA system and applying a GMP-compliant computer management system and automatic control system, fully automatic collection and monitoring of production data can be achieved in a planned and step-by-step manner; efficient, accurate, and uninterrupted data aggregation can be achieved through the computer system, gradually avoiding the problems of production data lag, missing, and errors that traditional manual recording methods are prone to; real-time monitoring of drug production data, access to real-time production process monitoring screens at all stages of enterprise production at any time, ensuring comprehensive coverage of data monitoring for all key steps in accordance with GMP regulations; based on the SCADA system, each workshop is interconnected through high-speed network channels to monitor product production process data, form a production data pool, accumulate production related data, and provide basic data for other information systems; and based on data collection and statistics, conduct trend alarm analysis on key monitoring points to ensure real-time monitoring of production process trends and stable product quality. The main interface and production line of the SCADA system adopt animated display and provide advanced production process display, as shown in Figure 10. Its interface is user-friendly and easy to monitor.

4.3.3 Application of a fully automatic raw material weighing and feeding system

The main raw materials and excipients for the production of solid dosage forms are mostly extracts, dextrins, and starch with large batches and manual weighing is time-consuming and labor-intensive, resulting in low production efficiency. Introduction of a fully automatic raw material weighing and compounding system can not only improve production efficiency but also reduce production costs. The design route of the entire system is that the raw materials and excipients are transferred by the conveyor belt to the automatic unpacking machine and enter

Figure 10

Diagrammatic structure of SCADA system



Source: Research and Analysis of M2 Consulting

the receiving bin, and then transported by the automatically guided vehicle (AGV) to the unloading station, and transferred to the wet mixer of the next process through vacuum feeding. The entire system is tightly sealed and pollution-free, meeting GMP requirements, and accessories are easy to clean and disassemble. It can achieve refined, flexible, and information-based operations, shorten manual weighing and material transfer time, and greatly reduce production costs.

4.3.4 Application of near-infrared analysis technology

The main control indicator for the intermediate particles of the solid dosage form is moisture. The traditional detection method is manual sampling for off-line detection. During the drying process of the particles in a fluidized bed dryer, samples are taken every 30 min and moisture is measured using a rapid moisture analyzer. This method not only consumes manpower, but also results in delayed detection.

The near-infrared analysis technology, as a monitoring method that establishes mathematical models by collecting samples to predict detection targets, can accurately monitor particle moisture in a real-time manner during the granulation process. The near-infrared moisture measurement and analysis technology

consists of two synergistic parts: the hardware and software. The hardware part of the system includes boiling granulation dryer, near-infrared monitoring probe, online near-infrared spectrometer subsystem, and the main control system. The software part of the system includes automatic control software, chemometrics software, and the main control system software.

The near-infrared moisture monitoring and analysis technology provides a real-time monitoring tool for controlling the moisture of the solid formulation particles, which not only saves manual testing costs, but also effectively ensures the stability and uniformity of drug quality.

4.3.5 Application of automatic guided vehicle (AGV)

The traditional transfer of raw materials and excipients and packaging materials is manually carried to the production line by forklifts. This method not only involves heavy physical labor for workers, but also slows down the transfer speed, limiting the production. Using AGV carts to transfer materials can efficiently and accurately complete point-to-point material handling, achieving refined, flexible, and information-based operations, shortening logistics time, greatly reducing labor costs, and achieving local unmanned smart production levels.

4.3.6 Application of smart sample retaining warehouse

The traditional sample retention method of raw materials and excipients, intermediates, and finished products are manually stored in the sample retention room according to different product names, batch numbers, and specifications. Due to the large annual output of the solid comprehensive preparation workshop, multiple product batches, and packaging specifications, storage and requesting samples not only consumes a lot of labor, but also has strict requirements for the storage environment. The use of smart sample-retaining warehouse directly replaces manual operation. It consists of five parts: a handling system, a storage system, a robot grasping system, a drug exit and entry system, and a control system.

The smart sample retaining warehouse can automatically control and monitor the temperature and humidity in real-time, effectively ensuring the storage environment of samples. In conjunction with the remote control software, images of the warehouse and sample data can be retrieved to achieve remote monitoring. During daily sample storage

and requesting, it only requires the entry of sample name and batch number to realize the one-click automatic storage and requesting through a fully automatic robotic arm.

The smart sample-retaining warehouse adopts information-based management and smart sample tracking. In addition to storage functions, it can also perform operations such as statistics, queries, and reminder of the expiry period of the product. The use of smart sample-retaining warehouse ensures the authenticity and traceability of the data and samples during the entire process of drug production.

4.3.7 Application of WMS stereoscopic warehouse management system

The WMS system is used to meet the needs of three-dimensional warehouses for material inventory, including three functions: warehouse-in, warehouse-out, and in-warehouse operations. The function of the warehousing-in operation includes order management warehouse-in products, receiving, organizing, and querying of warehouse-in information. The function of the warehouse-out operation includes order positioning and distribution, warehouse-out of the whole inventory, goods gathering, releasing AGV position, and query of warehousing out information. The function of the in-warehouse operation includes inventory query and inventory counting, which can be completed through a handheld terminal.

After the raw materials and excipients and packaging materials are received in the solid comprehensive preparation workshop, they are automatically stored by the WMS system, and automatically warehouse out from the WMS system according to production instructions. Then, they are transported by AGV to the logistics channels of each production line. The finished products are transported by the logistics tracks of each production line to the automatic palletizing machine, screened for product names and batch numbers, and stacked and stored in sequence. The application of the WMS’s stereoscopic warehouse management system has achieved automated operation control throughout the entire process.

4.3.8 Application of visual inspection system

The visual inspection system is mainly used for the aluminum plastic packaging linkage line in the solid comprehensive preparation workshop. This equipment

consists of the image visual inspection equipment, waste removal device and a connection device, etc., which can detect the presence of bubbles in the aluminum plastic plate and whether the capsule particles are deformed. The application of this visual inspection system not only ensures the quality of drug appearance, avoids customer complaints, but also makes the production process of aluminum plastic packaging smoother and improves production efficiency.

In summary, the innovative application of smart manufacturing in the production of Traditional Chinese Medicine solid dosage forms not only improves production and management efficiency, but also reduces production costs, enabling the solid comprehensive preparation workshop to achieve the goal of halving human resources and doubling production capacity. According to M2's actual visit, it was found that after a pharmaceutical factory adopted the solution of smart manufacturing, the production capacity of Guizhi Fuling Capsules increased from 2 million capsules per shift to 4 million capsules per shift. In addition, the data of process parameters and quality parameters during the drug production process can be recorded and stored in a timely and standardized manner, ultimately achieving local unmanned control, and continuously improving the comprehensive strength of drug production enterprises.

5 Analysis of Investment Opportunities and Prospects for China's Solid dosage form Industry

Overall, the IPO of pharmaceutical companies continues to maintain a fast pace. The scale of investment and financing in the primary market in the pharmaceutical field increased substantially. The investment opportunities in the Chinese solid dosage forms market will present three major trends:

(1)In the future, enterprises that plan the R&D of innovative biologics will have greater investment potential.

With the update of the National Reimbursement Drug List, the introduction of major policies such as volume-based procurement, and the continuous reforms conducted by the CDE, the time difference between the launch of new drugs at home and abroad has been increasingly shortened. The systemic dividend in the field of biopharmaceuticals is gradually disappearing, and solid research and development of biopharmaceuticals with independent intellectual property rights has become an inevitable choice for large traditional pharmaceutical companies and small and medium-sized biotech companies to cope with the global competition. Therefore, traditional pharmaceutical leading enterprises that are actively aiming at developing innovative drugs and emerging biopharmaceutical enterprises have good development prospects.

Some traditional leading enterprises specializing in chemical medicines were established early and had been focusing on producing generic drugs and chemical raw materials. But during the past decade, they have actively transformed to innovative pharmaceutical enterprises. Such pharmaceutical enterprises have rich reserves of products under development, stronger active ability in selecting pipelines and varieties, more mainstream layout, mature commercializing ability and outstanding anti-risk ability, and will gradually develop into the backbone of China's innovative drug ,manufacturing industry by virtue of their tremendous capital and R&D strength. It is recommended to pay attention to the high-quality leading enterprises and actively provide them with comprehensive financial services.

At present, a number of innovative pharmaceutical enterprises have emerged in China that actively specializing in

developing innovative drugs such as monoclonal antibodies, recombinant proteins, and biosimilars.

The advantage of such pharmaceutical companies lies in their focus on innovative drug development, allowing them to avoid the pressure of performance growth brought about by the existing generic drug business. The disadvantage lies in the fact that some products under development have not yet been launched or fully launched, and the expenses related to the research and development exceed operating revenue, which cannot bring profits at the time. There is a shortage of innovative drugs in China, and the market space for newly developed drugs is large. Drugs that are launched earlier can easily seize the market opportunity, but they also face tremendous risks in the research and development of new drugs. It is recommended to focus on the development of leading biopharmaceutical enterprises and high-quality emerging innovative pharmaceutical enterprises.

(2)Enterprises engaged in research and development and manufacturing of medical equipment in the future will have more investment opportunities.

In order to modernize the pharmaceutical process, improve the stability of the manufacturing process, reduce product failures, and improve product quality, foreign regulatory authorities, including FDA, EMA, and PMDA have issued relevant documents in the early years to encourage and support continuous manufacturing. On September 2022, the CDE also issued a public announcement soliciting opinions on the "Guidelines for the Continuous Manufacturing Technology of Oral Solid Dosage Forms of Chemical medicines (Exposure Draft)" (hereinafter referred to as the "Exposure Draft").

In terms of equipment design and system integration, this "Exposure Draft" proposes that equipment design and its integration have an impact on process dynamics, material transportation and transformation, as well as the quality of output materials. The applicant should reasonably design or select unit operation equipment and system components to mitigate the impact of disturbances on the quality of the final products. For example, the compatibility and integrity of reasonably designed equipment components, the geometric shape of components, the spatial layout of equipment, the connection between equipment, the location of material diversion and sampling points. The industry insiders point out that equipment is actually a major challenge for

continuous manufacturing technology, as most of the existing conventional equipment is suitable for semi-continuous manufacturing processes, support from equipment suitable for continuous manufacturing is needed in the future. Currently, there is a lack of pilot-scale equipment, especially for continuous manufacturing, which urgently needs to be broken through.

Meanwhile, in the past, the integration of standalone machine equipment had the problem of inconsistent interfaces between devices, which may lead to unstable conditions during the use of the equipment and also have a certain impact on the quality of output materials. The overall solution for pharmaceutical equipment can improve the continuity and data reliability of drug production, meeting the high requirements of pharmaceutical production. The transformation from standalone equipment to overall solutions for pharmaceutical equipment will become a major trend.

At present, leading pharmaceutical equipment enterprises in China that have built a platform based and smart system, such as Fette Compacting (China) and Goldenteam, can provide comprehensive solutions in multiple fields. In the future, the production of solid oral preparations in China may accelerate the transition from semi-continuous batch production to continuous manufacturing. In this context, the upstream equipment industry may also face new opportunities.

(3)Talent investment in China's solid pharmaceutical market will grow rapidly.

A large influx of investment in the solid dosage form market and supply chain equipment and consumables market is expected to increase the industry's demand for R&D and service personnel in the field of solid dosage forms. Due to the fact that most R&D and service projects require R&D personnel with rich professional knowledge and experience for non-standard observations, production, and analysis, the commercial application of smart manufacturing in the solid dosage form market is not yet mature, and the substitutability of market R&D and service talents is low. The cultivation of professional talents in the field of pharmaceutical R&D and service requires a considerable long period of time, and the development speed of China's solid dosage form market far exceeds the cultivation speed of local talents. This is expected to accelerate the introduction of global biopharmaceutical R&D talents and the increase in labor costs in the local solid dosage form market.

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