WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 5, 123-143. Review Article ISSN 2277– 7105

# ANALYSIS ON RECENT ECONOMIC POLICIES OF PHARMACEUTICALS IN CHINA AND THE PROSPECT OF PHARMACEUTICAL MARKET OF CHINA IN THE NEXT FIVE YEARS

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Article Received on
08 Jan. 2018,

Revised on 29 Jan. 2018,
Accepted on 19 Feb. 2018,

DOI: 10.20959/wjpr20185-11321

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## ABSTRACT

On October 8, 2017, China Food and Drug Administration (CFDA) promulgated the Opinions on Deepening the Reform of Review and Approval System and Encouraging the Innovation of Drugs and Medical Devices. The Opinions were promulgated jointly by the State Council and the The Central Committee of the Communist Party of China (CPC Central Committee), which shows the authority of the policy and also the guiding significance for the policy reform roadmap in the field of pharmaceutical supervision in China in the future. Based on the working experience of more than ten years in the Chinese pharmaceutical supervision system, in combination with the perspective of macroeconomics, this article analyzed the two reforms involved in the document and their possible influence on the application strategy of the domestic and foreign applicants (that is, pharmaceutical companies) while analyzing the challenge of this policy on the CFDA itself and predicting the self-changes of CFDA that may possibly occur; it is expected to help deepen the understanding of this policy by the people all over the world who pay close attention to the Chinese pharmaceutical market and policy trend and the implementation at the practice level, and also help the people engaged in policy research and financial market to analyze and prejudge the influence of the changes and

policy restructuring in the field of Chinese pharmaceutical market in the next five years on the pharmaceutical economy of Chinese mainland.

**KEYWORDS**: Health policy; drug policy analysis; pharmaceutical market.

## I. BACKGROUND FOR THE ISSUANCE OF THE DOCUMENT

Since its official establishment in 1998, CFDA has been facing the main problem of how to reconstruct the original pharmaceutical management system of planned economics in a transitional economy in accordance with western criteria and gradually ascend and transit to a pharmaceutical supervision system meeting the western criteria and requirements. From this perspective, the twenty years from 1998 to 2017 can be regarded as a period to gradually approach, imitate and study the mature pharmaceutical supervision of the western world. It can be said that the Chinese government strives to achieve the international average and even the world advanced level in the governance capacity of pharmaceutical field, a subdivided social management field highly specialized.

As a new ministry in the Central Government of China, in terms of initial intention at the beginning of the establishment and the naming, the CFDA broke away from the framework of the economic management for special industrial areas set up by the previous planned economy government and directly imitated the name of the U.S. FDA (U.S. Food and Drug Administration), which was quite different from other ministries in the Central Government of China. It also means that the vice-ministerial-level unit starting from the era of Zhu Rongji is to shoulder some of the tasks of governmental system reform from the beginning of its establishment in addition to its own responsibilities. From the perspective of the overall situation of the reform and opening up of China in the past 40 years, it's easy to find that CFDA has been shouldering the mission with different significance. Her evolution of 20 years also demonstrated how she transformed from an industrial management authority under the planned economy to a regulatory authority under the market economy responsible for the medication safety of the public. The several twists and turns experienced during this period are exactly the defects and corrections of the understanding and actions resulted from the evolution in the mission transition. In May 2017, CFDA formally joined into the International Council for Harmonization (ICH), which indicated the completion of the transformation from an industrial management authority under the planned economic system to a professional regulatory authority meeting international standard and confirmed the achievements of the

Chinese government in the transformation and reform of management mode to gear to international conventions on the other side.

In the past 20 years, the total economic gross of mainland China has changed from ranking behind Italy, a small country in southern Europe, to firmly ranking the second in the world, and the pharmaceutical field has also changed from totally following others' footsteps and imitation to innovation in the field of biological medicine, etc.; from serious shortage of investment to the risk investment constantly looking for new projects and growth points; in the 1990s, the Research and Development (R&D) was mainly invested by state-owned enterprises, but now mainly invested by profit-oriented private enterprises. In recent years, large amounts of money from other industries including finance and real estate has been brought into R&D, and nearly every international giant has set up an R&D center in China. The pharmaceutical market environment of China has undergone great changes, which accordingly urged the CFDA to constantly adapt to new situations, constantly adjust the policies and actions as well as regulations, and take measures in time to respond to the hot spots of the society including the fabrication of application dossier and backlog of the applications to be reviewed.

Since taking the office in 2012, through the operation at the State Council level, the new CFDA leadership has successively launched a series of tough means including solving the backlog and clinical trial verification to solve the huge domestic challenges currently facing the CFDA, which swept away the disadvantages of the system and mechanisms accumulated in the delay in the transition for years, made the drug supervision back to the correct way that is scientific and efficient and played a key role in purging the industry atmosphere, boosting industry confidence and accumulating the kinetic energy for development. While taking such measures to tackle the previous backlog, CFDA has been continuously exploring the ways and methods to improve the overall level of drug supervision, for example, the release of the encouraging news of joining ICH accompanied by the near completion of solving the backlog in recent years, and the issuance of the announcement of the State Council on comprehensively deepening the reform of drug supervision, indicated that the drug regulatory system shall continue to deepen the reform in the next few years and march towards a world-class drug regulatory agency. The correction and alleviation over the past two years is only a stepping stone for future major reform while the next reform of the governance capacity of high-level and comprehensively internationalized drug regulatory system is the main event,

aiming at improving the social governance level of drug regulatory system to be not lower than the social average level accompanied by many reforms in other fields of China, even slightly higher than that of other government sectors.

Hereunder, this article will analyze and explain the key content involved in the document so as to help the readers at home and abroad master its essentials and help them make the correct judgment on their investment and industrial development in Chinese mainland market.

## II. KEY CONTENT OF THE ANNOUNCEMENT AND THE ANALYSIS

The Opinions issued this time aimed at the prominent problems currently facing the drug and medical device innovation and focused on the long-term system construction. It is an important programmatic document. After a thorough reading of the full text, the author summarized six main topics of the document (Table1), then extracted the following major reform directions (Table 2) and made the analysis to share with the readers.

### 1. Consistency evaluation

Consistency evaluation is one of the main tasks of the CFDA currently. Its purpose is to mandatorily require that, for the generic drugs marketed in China, their safety and effectiveness shall be evaluated through the Bioequivalence Test (BE evaluation) with the originators of ICH member countries.[1-5] At the same time, supplemented by such means as price control, CFDA offers the preferential policy in terms of hospital tender, pricing and packaging identification to the manufacturers taking the lead in passing the consistency evaluation. Such action now enters the implementation phase, and some pharmaceutical manufacturers have completed the consistency evaluation study and submitted the application to the CDE for review. Therefore, the next focus shall shift from how to conduct consistency evaluation and how to do it faster to the review and approval.

The biggest challenge for Center for Drug Evaluation (CDE), which is responsible for the review of consistency evaluation, is to strengthen the review forces of BE. Due to the limited remuneration and career prospect available for the staff of the CDE, it is difficult to recruit more high-level staff and form a professional operation team to conduct high flux of consistency evaluation. At the same time, the eligibility criteria set in the guidelines for consistency evaluation is very strict and the specialization and reproducibility requirements for statistical analysis are relatively high, which requires a highly professional team to undertake the work so as to withstand the subsequent re-review conducted by the expert team

of individual enterprise. Such situation is quite rare in previous review, and the transparent review will inevitably lead to the comparison of professional ability between the CDE and social forces. As for whether the CDE can win its professional authority in the society in a large number of appeals two years later, CDE still needs to intensify the organization and coordination, adjust the work process and strengthen the selection and appointment of professionals so as to maintain the authority and reliability of consistency evaluation.

From an economic point of view, the social risk of consistency evaluation is mainly that, the varieties involved in the consistency evaluation are those that have been marketed with certain sales. Especially for the hot varieties subject to consistency evaluation, their sales are quite considerable, and some can reach several billion RMB. As the policy of consistency evaluation offers a concession only for the first three enterprises that pass the consistency evaluation, the products later passing the consistency evaluation will no longer enjoy the tender, pricing and other concessions, which means a pronouncement of the deadline of such products in the Chinese sales market. Because such hot varieties involve huge interests, which is not only like the distribution of future market in the field of specific therapy by new drugs, but more like the redistribution of "existing cakes", it may bring huge social contradictions, which may go beyond the pure technical evaluation, but also involve the social stability of local government, factory bankruptcy, unemployment and other social problems. The originally specified deadline for consistency evaluation is 2018, and it is the toughest task currently facing the CFDA.

**2. Re-evaluation of injections**

If the consistency evaluation is mainly for solid oral preparations, then, the concept of injection re-evaluation as proposed in the Announcement pushes the injections with the most stable profit status in current Chinese pharmaceutical market to the front line. From the point of view of market, because injections are generally strictly controlled to be used in the hospital and patients cannot use the injections by themselves, injections depend more on the sales channels of pharmaceuticals, or in other words, it is easier for the pharmaceutical distributors to control the sales and profit trend of injections, so injections have been the most profitable in Chinese pharmaceutical market.

From a technical point of view, because the medicine of injection solution directly enters human body as molecules, it is generally considered that there is no traditional process of D-dissolution, A-absorption, M-metabolism and E-excretion, thus there is no such problem as

equivalence evaluation.[6-8] It is believed that the injection re-evaluation shall cover the following categories:

1. Special injections. For example, liposome injections, lipid microsphere injections and the freeze-dried products thereof, due to the use of special excipients such as cyclodextrin camplexation technique, they may cause the drug delivery behavior in the human body to be modified or changed, resulting in the change of the enrichment site of drugs in the body.[9-13] therefore the toxicity and effectiveness of the drugs may be substantially changed. For example, the alprostadil lipid microspheres injections have been subject to a large number of applications for imitation in China a few years ago. The range of the particle size of lipid microspheres is limited in the originator so as to enrich the drug-loaded microspheres at the inflammatory site, reducing the dose and improving the efficacy, and the targeted therapy has been achieved.[14-16] However, for a large number of generic drugs under application in those years, the lipid microsphere technique was either not adopted or not authorized by the plant of originator, so the manufacturers failed to obtain the core techniques, especially the trial data of drug distribution and enrichment in the body, and only imitated the drug by using the reverse engineering method. The particle size of preparations of each manufacturer differs from each other, so it is hard to say whether the generic drugs can achieve the same therapeutic effect as the originator. Therefore, for such drugs with a special drug delivery system (DDS), injection re-evaluation shall be carried out so as to rectify the market and clear the varieties with poor efficacy but high safety risks.

Another example is the injections using cyclodextrin camplexation technique. Because the category and specification of the cyclodextrin used in such injections can hardly be exactly the same as those in the originators due to the influence of patents and other factors, it may cause the non-standardized drug release after the drug is injected into the body, which may lead to a gap between the generic drugs and the originator. Because such products are of reservoir type, if the drug has a large amount of uncontrollable release, it will cause huge risk for the patients. Therefore, it is very necessary to carry out re-evaluation on such drugs.

2. Traditional Chinese medicine injections. Barefoot doctors were once advocated in China in the 1960s-1970s under the historical background, it was encouraged to develop drugs at the grassroots level, and some traditional Chinese medicine injections were approved to be sold by the provincial government agencies. Such approved injections were locally

developed, taking the traditional Chinese medicine decoction as the chief source, adding or subtracting the formula and undergoing a simple small-scale trial. Such injections satisfied the medical need of some people then, but from the scientific point of view, most varieties lacked sufficient pharmacological and toxicological trials and sufficient safety evaluation, many safety items in the package inserts were "unclear". In case of the drug-induced safety events, such products cannot be traced. This situation leads to huge potential risks, and is also the huge loophole in current drug supervision in China. Although the CFDA has basically quitted the review and approval of the new varieties of traditional Chinese medicine injections in recent ten years, some traditional Chinese medicine injections previously approved are still on sale in the domestic market. Moreover, due to the lack of international reference pricing and the wide range of application, their annual sales are very high, even higher than that of some blockbuster varieties of chemicals. Therefore, the rectification of such traditional Chinese medicine injections has been a gambling involving scientificity, economic interests and other aspects. Coupled with the protection of many local governments, the reform is facing a difficult circumstance.

Now, the CFDA has made a determined effort to include the re-evaluation of traditional Chinese medicine injections in the name of injection re-evaluation and the resulting rectification, which reduces the control valve for rectification to some extent and is a very pragmatic action. It aims at gradually cancelling and "discouraging" some traditional Chinese medicine injections and other high-risk varieties through raising technical requirements. Fifteen years ago, the SFDA once carried out the "Rectification of Health Products" activity, which eradicated a large number of paradoxical health products, purified the market and guaranteed the supply of the standard drugs with definite efficacy. It was such a wise behavior. This rectification for traditional Chinese medicine injections, if achieving substantial results, will well correct some abnormal sales strategies and purify Chinese pharmaceutical market and also have an epoch-making significance.

3. Rectification of the varieties of injections with interchanged dosage form: in the late 1990s, the newly established State Food and Drug Administration (SFDA) proposed the policy of converting the dosage form among the vial injection, freeze-drying agent and infusion solution to be exempt from clinical trials. Because it can save a lot of time for development and reduce the clinical investment, and allow distributors effectively control the hospital market via special dosage form, it caused a large number of disorderly

repeated applications at one time, resulting in that the SFDA had to take measures to clean up the varieties of excessive applications several years later. However, because there is no effective exit mechanism in Chinese pharmaceutical market, some varieties approved in those years are still on sale in the market, and has been prospering and enviable by virtue of the exclusive dosage form and strength and other separate pricing measures.

4. In fact, from a scientific point of view, the dosage form is not suitable for unauthorized change for some injections due to the nature of the drug itself.[17,18] For example, an originator drug in freeze-dried dosage form, it is because the main drug is not stable enough in the presence of water. But, vial injections and transfusion appear in domestic market. Due to the significantly increased degradation speed of the main drug in the water, the increase in impurity content was significantly greater than that of the freeze-drying dosage form, so such dosage forms shall be unreasonable. Another example is, a drug is incompatible with glucose, but glucose infusion was developed in China, which unnecessarily introduced the impurities of drug and glucose and resulted in increased risks for the patients, so the dosage form shall be unreasonable. Similar cases are numerous. This time, the CFDA decides to clear and rectify the varieties presented due to historical reasons through injection re-evaluation, which is in line with the scientific cognitive laws.

**3. Speed up the review and approval process, expand the CDE's scale and adopt the mode of Government Purchase of Services to ensure the talents with high quality**

Since 2010, the drug review and approval speed of the CFDA has become the focus of attention of domestic and foreign parties. For the domestic applicants, the slow review and approval results in the delayed drug marketing, objectively increasing the time difference of receiving the international advanced treatment for the patients and therefore resulting in that the news that some patients go to India to purchase the drugs can be seen in the press from time to time. On the other hand, for multinational pharmaceutical companies, due to the expected review and approval time of up to 5-8 years, they can hardly develop the simultaneous marketing plan in China and abandon the Chinese market in clinical development strategy for several drugs, which also results in a loss of the chance to receive advanced therapeutic means and diversified treatment for Chinese people. Therefore, it is very practical that the State Council approved the CFDA to expand the size of the CDE staff

by means of the mode of Government Purchase of Services to increase the review speed in the context of the efforts of the central state organs to control the scale. Of course, this decision is not from the point of view of the CDE individually, but an overall strategy considered from the perspective of promoting the development of domestic pharmaceutical economy and increasing the ways and means of Chinese people to obtain the pharmaceuticals.

It is determined in the document issued by the General Office of the State Council and the General Office of the CPC Central Committee to ensure the high-quality talents with the mode of Government Purchase of Services, avoiding the past dilemma of high-quality CDE experts with low income, opening a normal pattern of market-oriented talent flow and also reducing the extent of isolation of the CDE due to the institutional mechanism. It is conductive to the transparency of the technical principles for the review and approval, also helps to develop more talents for advanced drug evaluation and R&D for the society in the long run and is beneficial both for the country and for the pharmaceutical industry, providing human and technical basis for China to march to the highlands in the international pharmaceutical industry and occupy the high-profit section in the future.

However, rapid expansion will also bring the corresponding challenges in quality management and training. According to statistics, the newly recruited reviewers are mainly masters. Some practitioners with experience have been employed in the earlier stage while campus recruitment has been carried out later. Among the newly employed staff, the doctors and overseas returnees accounted for a low proportion. Compared with the requirements of facing the world and improving the level proposed by the CFDA, it is necessary to continuously improve the quality of recruitment and introduce more people with high quality, international vision and communication skills through competitive remuneration and career development prospect under the mode of Government Purchase of Services so as to avoid the risks in review quality assurance caused by the decrease of overall quality of the CDE due to the leave of a large number of senior staff in recent years. At the same time, it is necessary to strengthen the training, enhance the communication within and beyond the drug regulatory system and strive to maintain the evaluation of the industry on the professional level of the CFDA at a constant level and even improve it to a higher level in 3-5 years.

**4. Carry out mutual recognition of international multi-center clinical trials and reduce the time lag for drug marketing**

When foreign drugs enter Chinese market, clinical trials shall be conducted again in China, and the data of part of the international multicenter clinical study carried out in China are not recognized for New Drug Application (NDA), which has been the practice in China for the past decade. This method emphasizes the sovereignty of China in the review and approval of new drugs, overemphasizes the racial difference between the Chinese and foreigners and constructs a barrier to prevent the new drugs abroad from rapidly entering China in the name of protecting the clinical subjects. It can be said that this policy has its historical considerations. At that time, China has been very weak in the field of research and development of new drugs and it was prevalent to imitate the international new drugs in China. The policy originally intended to protect the new drug R&D forces that were relatively weak in China and provided space for their survival and development.

After the development for more than ten years, China's GDP has long been ranking the second in the world, and the investment and technology in the field of new drug research and development is no longer a problem. Therefore, it is objectively beneficial both for the local R&D enterprises to blend in the global research and development competition more quickly and for Chinese patients to access to the resources of overseas clinical trials in a more timely manner if the policy to lift the control over the admittance of overseas clinical trials to accelerate the global new drugs to enter China is proposed in time. Of course, the new policy also brings the “test to enter adulthood” and certain impact to the domestic new drug research and development field that is still immature. It is believed that the domestic trials will soon adapt to the new situation and learn from it.

Only the open market and fully flowing information can bring the real progress. It is hard to grow into towering trees under the condition of being protected. It is believed that such a prediction that has been practiced in the field of white household appliances and automobiles will also bring the upgrade and evolution to new drug research and development, and thereby bring the world's first-class new drug research and development capabilities and market promotion and marketing capabilities to the world's largest pharmaceutical market in the future ten years or even 20 years later, and thus firmly keep the high added-value in China and also improve the well-being of the people through the global synchronization and update of new drugs.

It shall be noted that the above supervision actions conducted by the CFDA seemly formed a contrast with the "invisible hand" said by Admiral Smith, the economic scientist. However, for the sake of protecting the health of citizens, the supervision on the drugs all over the world has been continuously strengthened. As the Chinese economy in transition, some system and mechanisms and varieties under the planned economy still remain in the transition from the planned economy to the market economy. For example, the management of the approval number of the raw materials and excipients as well as the traditional Chinese medicine injections never presented in the market economy countries. This time, strengthening the supervision on the matters that are unreasonable (such as mutual exemption of clinical trial among three injectable dosage forms), fail to comply with market behaviors (such as management of the approval number of raw materials and excipients) and deviate from scientific laws (traditional Chinese medicine injections without modern safety and pharmacology evaluation basis) and taking the governmental means based on modern science to eliminate such matters through consistency evaluation and re-evaluation of injections are beneficial to comprehensively improve the overall quality of the drugs in Chinese market, help the public get a better drug treatment and help the government improve the efficacy and reduce the cost of the medical insurance, instead of wasting money on drugs that are less effective or ineffective, which is a good thing to benefit the country and people from the economic point of view.

In addition, in terms of the system and mechanism, the strong introduction and the effective implementation of these regulatory measures also lays a solid foundation for the drug regulatory system of China to march to the international stage and thus conduct synchronous drug supervision with other developed market economies at the same level, which is beneficial to guarantee the timely acquisition of drugs by the public and their health right. For ICH, it is also a huge supplement and more beneficial for ICH to give a play to its benchmarking and guiding role in global drug supervision and cover a wider range of global population.

**Table 1. Six main contents in policies of pharmaceuticals in China.**

| Six topics | The reform of the management of clinical trials. | Acceleration of the examination and approval of the listing | Promotion of drug innovation and generic drug development | Reinforcement whole life cycle management of medical devices | Improvement of technical support ability | Intensifications for organization and implementation |
|---|---|---|---|---|---|---|
| **Main Contens** | The qualification of clinical trial institutions shall be subject to record administration; the support for related organizations and personnel to carry out clinical trials; the improvement of mechanism of ethics committee and the efficiency of ethical review; identification of data of overseas clinical trials et al. | The examination and approval of medical device; R&D support of medical devices for rare diseases treatment; examination and approval of drug injection; related examination and approval for drug and pharmaceutical raw materials and packaging materials; the approval of inheritance and innovation of traditional Chinese medicine; the examination and approval system for the priority of patent compulsory licensing drug; | The establishment of a catalogue of listed medicines; the exploration of a link system for drug patents; the conducting of a pilot program for compensate the drug patent period; the improvement and implement of data protection system for drug trials; the promotion for enterprise innovation and drug imitation production; the approval of new drugs' clinical application. | The promotion of related license holder system; the implement on the legal responsibility for related license holder; the establishment for direct reporting system of adverse reactions and events; re-evaluation of injections and medical devices; the standard for drug academic promotion behavior. | The improvement of technical appraisal system; the responsibility for the confidentiality of the staff; the enhancement of review and appraisal ability; the implement of inspection responsibility in whole process; the construction of a professional inspectors team; the intensification of international cooperation. | Strengthen the organization and leadership; strengthen the cooperation and coordination; conduction for work of publicity and interpretation. |

**Table 2. Four major reform directions and key points.**

| Reform Directions | Genetic drugs | Injections | Talent strategy | Consummation of the system |
|---|---|---|---|---|
| **Key Points** | Consistency evaluation for drugs shall shift from how to conduct consistency evaluation to how to review and approval it faster. | Re-evaluation of injections shall cover special injections, traditional Chinese medicine injections and rectification of the varieties of injections with interchanged dosage form. | Speed up the review and approval process, expand the CDE's scale and adopt the mode of Government Purchase of Services to ensure the talents with high quality. | Carry out mutual recognition of international multi-center clinical trials and reduce the time lag for drug marketing. |

## III. EFFECT OF THE ANNOUNCEMENT ON THE PHARMACEUTICAL ECONOMY OF CHINA IN THE FUTURE

From the perspective of economics, the pharmaceuticals are top products fusing the modern chemical industry and basic medical research and have the characteristics of high value-added, high profits and low environmental load with the same Gross Domestic Product (GDP), therefore the pharmaceutical field is regarded as the priority development field by developed industrialized countries. With the extension of the population life-span of developed economies and increase of the social welfare spending, the competition in the pharmaceutical field, especially in the innovative therapeutic means and drugs will have a meaning beyond simple treatment and save life, and have the property to take over the commanding height of global economic competition and seize the high-profit market, so the United States has been reinforcing the basis for new drug research and development through increasing the investment in the basic medical research by National Institutes of Health (NIH), colleges and universities and other research institutions over the years so as to support its predominant position in the global pharmaceutical competition. Other advanced industrialized countries including the UK, Germany and Japan also fund the in-depth study in the field of pharmaceutical research and development in multiple forms including government research funds so as to seize the excess profit in the innovative therapeutic means and advanced drugs, nurture the domestic market and meet the high-level health needs of the public.

Throughout the reform and opening up process of China of 40 years, China has experienced a transition from labor-intensive industries to technology-intensive and capital-intensive

industries, and the pharmaceutical industry is also experiencing a transition from low-quality imitation to high-quality imitation and large-scale global supply to the exploration of the global commanding height. For the moment, the current Chinese pharmaceutical economy still has the basic task to meet the basic medical needs of more than one billion people, but the intensive capital and mature technology have saved a part of the energy of Chinese pharmaceutical industry for the global competition to seize the high-end market and obtain high value-added profits. The era that the overseas returnees bring individual key technology continues, but the world's largest innovation fund between China and the United States is integrating the rich human resources of R&D and clinical trials and other advantages in China, which will certainly push the new drug research and development in China to the forefront of the world.

Under this situation, how to manage the new drug research and development and how to have the courage and confidence to approve the global innovative drugs is a major challenge to the capacity of the CFDA. To obtain such capacities, the CFDA shall not only learn from the previous domestic management experiences, and what's more, proactively open up global vision to face the original ICH founding members with rich experience, such as the United States, Japan and the European Union, continuously obtain more experience and scientific courage and insight through learning and continuous communication and even through the joint review on the same project, keep the pace of updating the experience and knowledge and culture the capacities and mechanism of the CFDA in continuous innovation and continuous review of new drugs.

## IV. MAIN CHALLENGES FACING THE CFDA REVEALED BY THE ANNOUNCEMENT

### 1. Challenges in the field of innovative drugs

As mentioned above, innovative drugs are characterized by occupying the commanding height of the industry, seizing the high profits and leading the industrial orientation. The field of drugs, especially innovative drugs, is a high-tech and experience-intensive industry. The quality of the practitioners directly affects the level of the product. From a certain point of view, the drug review staff is the further extension of the R&D chain, and also an important factor to maintain the high quality of the marketed drugs, so that is why people think highly of the quality of the new drugs approved by the U.S. FDA, the European Medicines AGENCY (EMA) and the Japan Pharmaceuticals and Medical Devices Agency (PMDA) all

over the world. It does not mean that other countries have no right to approve new drugs, but it is the natural judgment on the reputation of the new drugs approved by the sovereign institution that really matters all over the world. To achieve the recognition at global level, the CFDA and CDE need to work really hard and make a solid reform and adjustment in terms of the staff quality and evaluation mechanism. Such perennial hard work is the key for the CFDA and CDE to win the global praises and recognition.

In order to cope with the situation to solve the backlog, the CDE, a technical agency subordinate to the CFDA that is responsible for drug review has taken the strategy of rapid expansion of the scale in recent two years to take a full advantage of the policy support provided by the State Council. At the actual operation level, due to funding constraints, it is difficult to recruit the first-line talents with R&D and production experience from Shanghai, Guangzhou and other developed areas of medicine. For such a problem, the State Council proposed in the document that Government Purchase of Services may be used to improve the review quality and efficiency.[19]

Based on the pre-judgment on the market scale, the density of talents and the improvement of technical support level in China, the well-known international mainstream pharmaceutical companies have set up R&D centers in China in the past decade, mainly in Zhangjiang, Shanghai and Suzhou area.[20, 21] In mid-2017, leading by the Glaxosmithkline (GSK), there has been a wave to close the R&D centers in China, and the well-known large enterprises including Eli Lilly also successively closed the R&D centers in China.[22] In this regard, I believe that the international well-known large enterprises were not wrong in terms of their pre-judgment on the R&D capacities in the past decade, and the improvement in the R&D capacities of China is also significant. However, the operation capacities of the enterprises differs, and it is understandable that some large enterprises closed the R&D centers in China due to their global strategy and low output.

In the long run, it was the wave to establish R&D centers in China ten years ago. Currently, it is at a low ebb and adjustment period. With the foreign companies mastering the operating laws in China and placing more advanced projects in China and accompanied with the policy of the CFDA to relax the restrictions for international multicenter clinical study and patent and other intellectual property protection measures, the second round that the foreign companies carry out drug R&D in China will soon come again. It can be said that the previous wave is the decision-making based on the judgment on the large-scale situation. At

the implementation level of specific R&D, there have been such problems that there was insufficient understanding of the actual situation in China, foreign companies were unwilling to place the key and core projects in China and there was a blind following of the investment trend. With the gradual improvement to such problems, in the second wave, more important varieties and more resource integration projects with global advanced level will be settled in China, which will also bring the in-depth combination guided by the R&D resources of China and world advanced level and shall ignite more important results. The second wave is the real integration under the condition of market economy. The author is optimistic about the wave.

## 2. Challenges in the field of generic drugs

The main economic significance of generic drugs is to expand the supply, reduce the overall medical expenditure of the community, and provide mature, effective and reliable medical support for medical insurance. Therefore, the developed countries including Japan and the United States, are trying every means to encourage the development of generic drug manufacturers, thereby reducing the social welfare spending that is increasingly heavy. China will face the severe situation of rapid aging in the next two to three decades, and medical insurance burden will increase rapidly year after year. There has been the imbalance between income and expenses in some provinces and cities such as Liaoning, and especially the endless emerging of the new drugs with high price will increase the burden of health insurance cost. The management of generic drugs is bound to become the highest priority of health competent authorities.

From a certain point of view, it is also a macroeconomic regulation and control for the state to control the total amount and varieties of the new products to be put in the pharmaceutical market through review and approval, just like the central bank indirectly controls the financial market through adjusting the reserve rate. As a huge market dominated by generic drugs, the quantity and scale of the generic drugs to be put into the market may be controlled by the control over the objective standards of generic drugs. According to the existing pharmaceutical economic research in the United States, if the similar generic drugs of about 20 manufacturers are put into the market, the high profit of the new drug manufacturer will become flat, which can effectively decrease the supply price of pharmaceuticals and reduce the overall medical insurance cost of the state. In fact, generic drugs have been marketed at home and abroad for many years, and there has been an in-depth understanding of their safety and effectiveness, so it is feasible to control the scale of their entry into the market through

the review and approval standard.

To achieve the best control over the overall health expenditure of the society, the CFDA needs to strengthen its capacity in terms of the development of the National Drug Reimbursement List and management of pharmaceutical price, reserve corresponding expert management personnel equipped with both economic and pharmaceutical knowledge, seek the further authorization by the central government from the perspective of national overall fiscal expenditure, expand its management capacity for the whole industry chain of pharmaceutical industry and form the whole chain management capacity covering the R&D, market and medical insurance. Currently, the CFDA is mainly authorized in the pre-market review and approval and market admittance. By referring to the drug collection system of Japan PMDA and drug price negotiation system of the insurance industry of the United States, the CFDA shall also seek the right to control over the drug price in certain form so as to obtain the comprehensive management capacity for drug project approval, production and its terminal consumption market under the market economy. Otherwise, the current upstream management capacity is not enough to control the whole pharmaceutical market and the management capacity and effect will be greatly reduced.

**3. Challenges in the field of traditional medicine**

As an ancient civilization with a history of five thousand years, about one or two hundred years before the modern pharmaceuticals appeared, the Chinese people has accumulated large amounts of rich experience in using the natural herbs, animal medicine, mineral medicine and their rich combination and the ways of processing and administration to treat conventional diseases during its history of thousands of years.[18, 23-25], and formed a set of theoretical system for the diagnosis and treatment based on the Yin-Yang and Five Elements. However, due to the unclear safety evaluation and action mechanism, since there still exist many studies on traditional Chinese medicine in process to clarify the pharmacological mechanism.[26, 27], although traditional drugs have a good reputation of low side effect among the ordinary consumers[28], there has been an evaluation among the research community that the side effects of traditional drugs are hard to be accurately defined[29], and some trials and clinical statistics even showed that the side effect of traditional Chinese medicine was relatively high[30] For the injection re-evaluation, most attention will focus on a branch of traditional Chinese medicine–traditional Chinese medicine injections.

It is said that there is no such a dosage form as injection for the traditional Chinese medicine (the dosage form of traditional Chinese medicine with the fastest effect is the decoction).[18]

Traditional Chinese medicine injections mainly developed in a special period of 1940s to 1970s. Because there was no reference preparation of western medicine to develop a comparable price and there is lots of clinical abuse, it resulted in that the plants of traditional Chinese medicine injections were very profitable, and there were many varieties with an annual sales of tens of billions RMB. However, their pharmacology and drug efficacy remain unclear. Only because they have obtained the approval number a few decades ago, they have been sold in the domestic market. With the voice of publicity driving by sales profit, the rational expert opinions and the adverse reaction information mastered by the CFDA have not been given enough attention, not to mention being fed back to the supervision on the traditional Chinese medicine injections. The State Council issued the document to carry out the re-evaluation on traditional Chinese medicine injections, which is to initiate a complete scientific system evaluation chain of the traditional Chinese medicine injections from the mechanism to the safety, to the control over pharmaceutical purity. It is estimated that few varieties of the traditional Chinese medicine injections can pass the complete system evaluation according to contemporary medical standards. Investors are recommended to be cautious for a certain period in the future for investing the pharmaceutical companies with their main varieties as the traditional Chinese medicine injections.

As the rapid toxic and side effect of the adverse reactions of traditional Chinese medicine injections happen quickly, and it is difficult to make a timely rescue but easy to cause severe damages[31-35], therefore, the CFDA laid restraints on the traditional Chinese medicine injections at the first stage. As for other traditional prescriptions of Chinese medicine that have existed since ancient times, the regulatory strategy may be quite different. They shall mainly be maintained, consolidated and promoted. The CFDA shall take advantage of their characteristics of low cost, controllable domestic resources and wide acceptance among the people to play their indispensable role in reducing the medical insurance cost. It will also be the beneficial extension of the strategy of limited control that have been taken by the CFDA for traditional Chinese medicine in the past decade, which can not only play their unique role, but also control the risks of adverse reactions.

## V. SUMMARY AND PROSPECT

Relying on the booming domestic pharmaceutical market and large amounts of medical talents and supplemented by good mechanism operation, CFDA will eventually obtain the top abilities to approve the innovative drugs globally recognized at a certain time in the future, obtain wide recognition of its high level in the field of pharmaceutical study all over the world through years of efforts and completely solve the current deep-seated problems. However, it may take more than a decade. The issuance of the official document by the State Council is an official call to declare the comprehensive transformation and reform of drug regulatory system. The next five years is the key period for specific implementation. Let's wait and see.

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