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Review Article

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Analysis of emergency Drug Approval System in China and the United States under Public Health emergencies and its enlightenment to China

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Abstract

Objective: Public health emergencies, such as COVID-19, put forward a severe test to the response system of countries all over the world, including China. Especially under such conditions, the establishment and operation of the emergency drug approval system is particularly important. The purpose of this paper is to compare and analyze the emergency drug approval system between China and the United States, and learn from the experience of developed countries to improve China's drug review capability in response to public health emergencies.

This paper mainly analyzes the emergency drug approval system of China and the United States under public health emergencies through literature research and comparative analysis theory. Although there are four channels to accelerate the approval of drugs for listing in China, none of them can solve the problem of emergency drug use in the face of public health emergencies, and cannot become the policy basis for the use of unlisted drugs or drugs beyond the instructions.

Conclusion: On the basis of maintaining China's own institutional advantages and drawing on foreign experience, this paper puts forward relevant policy recommendations to improve China's emergency drug approval system in the event of public health emergencies.

Keywords: Public health emergencies; Emergency drugs; COVID-19, National Medical Products Administration (NMPA), Emergency Use Authorization (EUA), Department of Health and Human Services(HHS), Priority Review Voucher (PRV), FDA

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1. Introduction

The definition of public health emergencies in China refers to the sudden occurrence of major infectious diseases, diseases of unknown causes, major food and occupational poisoning and other events that seriously affect public health, causing or may cause serious damage to public health. (1) It is highly unpredictable, involves a wide range of people, and has great public hazards, which will have a great impact on people's life and health, social and economic development and order stability. (2) The outbreak of COVID-19 in 2019, as a public health emergency, had a huge impact on more than 200 countries and regions around the world, and also brought severe challenges to their response system. In the face of this epidemic, the China's national and provincial drug supervision and administration departments urgently started the emergency approval procedures for medical products, opened up green channels, and rapidly expanded the production capacity of epidemic prevention materials, which played an important role in fighting against the new coronavirus pneumonia epidemic, but there is still a certain gap with the developed countries in some aspects. Based on this, in order to further improve the relevant policies of emergency drug approval in China, and improve the level of emergency management in public health emergencies in China. This paper takes the United States as a representative to sort out and analyze the drug approval policies it urgently needs, so as to provide reference for improving China's emergency drug approval system.

2. China's emergency drug approval system under public health emergencies

China has established a series of emergency plans for public health emergencies, including *the National Overall Emergency Plan for Public Health Emergencies*, *the National Emergency Plan for Public Health*

Emergencies, and *the Law of the People's Republic of China on the Prevention and Control of Infectious Diseases*, which clearly define the classification, monitoring and early warning, information reporting, and handling of emergency plans for public health emergencies. At the same time, the formulation of relevant systems in the emergency management of public health emergencies in China has also profoundly affected the proposal of the construction of the emergency drug approval system in the field of drug supervision. At present, there are mainly four channels to accelerate the listing of drug approval in China, including special approval procedures, conditional approval procedures, breakthrough therapeutic drug procedures, and priority review and approval procedure.

2.1 Special approval procedure

The special approval procedure for drugs is the main basis for emergency approval of drugs under public health emergencies in China. Non public health emergencies cannot go through this approval channel. (3) The special approval procedure can be traced back to the special approval procedure for drugs issued in 2005, which aims to accelerate the review and approval of emergency drugs under public health emergencies. It clearly points out that when the drug reserve department under the State Council and the health administration department put forward a proposal to implement special approval for existing national standard drugs, drugs can be reviewed and approved according to the special approval procedure, and clinical trials are not required according to law. On the one hand, the inclusion of this category can reduce the risk of authorization and ensure the safety and effectiveness of the product; on the other hand, because clinical trials and related review and approval are no longer necessary, the approval process is reduced, which saves the approval time to a certain extent and ensures the rapid supply of emergency drugs. In addition, the *Provisions of the People's Republic of China for the Administration of Drug Registration* issued in 2020 also explained the special approval procedures for drugs (4) , which clearly stipulates that the National Medical Products Administration(NMPA) can decide to implement special approval for prevention and treatment drugs needed for public health emergencies in accordance with the law when the threat of public health emergencies occurs and after the occurrence of public health emergencies; With respect to drug registration applications subject to special approval, the NMPA shall, in accordance with the principles of unified command, early intervention, rapid and efficient approval and scientific approval, organize to accelerate and simultaneously carry out drug registration acceptance, review, validation and inspection; The circumstances, procedures, time limit, requirements, etc. of the special approval shall be implemented in accordance with the provisions of the special drug approval procedures; The drugs that have been specially approved shall be used within a certain time limit and scope according to the needs of disease prevention and control; The drugs included in the special approval procedure can be used within a certain period and scope according to the specific needs of disease prevention and control. If it is found that the drugs no longer meet the requirements for inclusion, the special approval procedure for the drugs shall be terminated and the applicant shall be notified.

Finally, in terms of the approval process, the NMPA is mainly responsible for accepting the drugs applying for the special approval procedure. The applicant submits the drug related materials according to the administrative regulations. The applicant can also apply for the feasibility evaluation of the drugs before the formal submission of the application. The NMPA only needs to evaluate the scientificity and feasibility of the drugs, and reply within 24 hours to decide whether to accept the application and start the technical evaluation, After that, the drug regulatory department and drug inspection institution of the province, autonomous region and municipality directly under the Central Government where the applicant is located shall be notified to conduct on-site inspection and test of the drug, and report the inspection results and opinions to the NMPA within 5 days and 2 days respectively. In addition, the first technical review needs to be completed within 15 days, and the administrative review time limit is 3 days. The final approval decision is made by the NMPA.

2.2 Other approval procedure

Conditional approval procedure: Conditional approval procedure is also a mechanism to accelerate drug approval in China. Applicants can apply for conditional approval during drug clinical trials. The drugs approved by this procedure are mainly used for diseases that seriously threaten the lives of patients and have no effective treatment methods at present, or for public health emergencies to quickly alleviate the crisis situation. In addition, conditional approval procedures will be initiated to approve relevant vaccines for public health emergencies. (5) For the drugs that are conditionally approved for marketing, the holder of the drug marketing license shall take corresponding risk management measures after the drugs are marketed, complete the clinical trials of drugs and other relevant studies as required within the specified time limit, and apply in the form of supplementary application. (6) On November 19, 2020, the Center for Drug Evaluation issued *the Technical Guidelines for Conditional Approval of Drugs for Marketing (Trial)*, (7) in which specific technical requirements were put forward for drugs to be marketed. In addition, the conditions attached to the drugs to be marketed are described in detail. By formulating implementation rules, the operability of the approval procedure can be ensured, and the relevant responsible subjects can better respond.

Breakthrough therapeutic drug procedure: The establishment of breakthrough therapeutic drug procedure aims to encourage research and innovative development of drugs with obvious clinical advantages. The applicant may apply for the application of breakthrough therapeutic drug procedures for innovative drugs or improved new drugs, which are mainly used to prevent and treat diseases that seriously endanger life or seriously affect the quality of life during the clinical trial

of drugs, and which have no effective means of prevention and treatment or have sufficient evidence to show obvious clinical advantages compared with existing treatment methods. Applicants can apply for breakthrough therapeutic drug procedures in Phase I and Phase II clinical trials, usually no later than before the implementation of Phase III clinical trials. For drugs included in breakthrough therapeutic drug procedures, the Center for Drug Evaluation will give priority to allocating resources for communication and exchange, strengthen guidance and promote drug research and development.

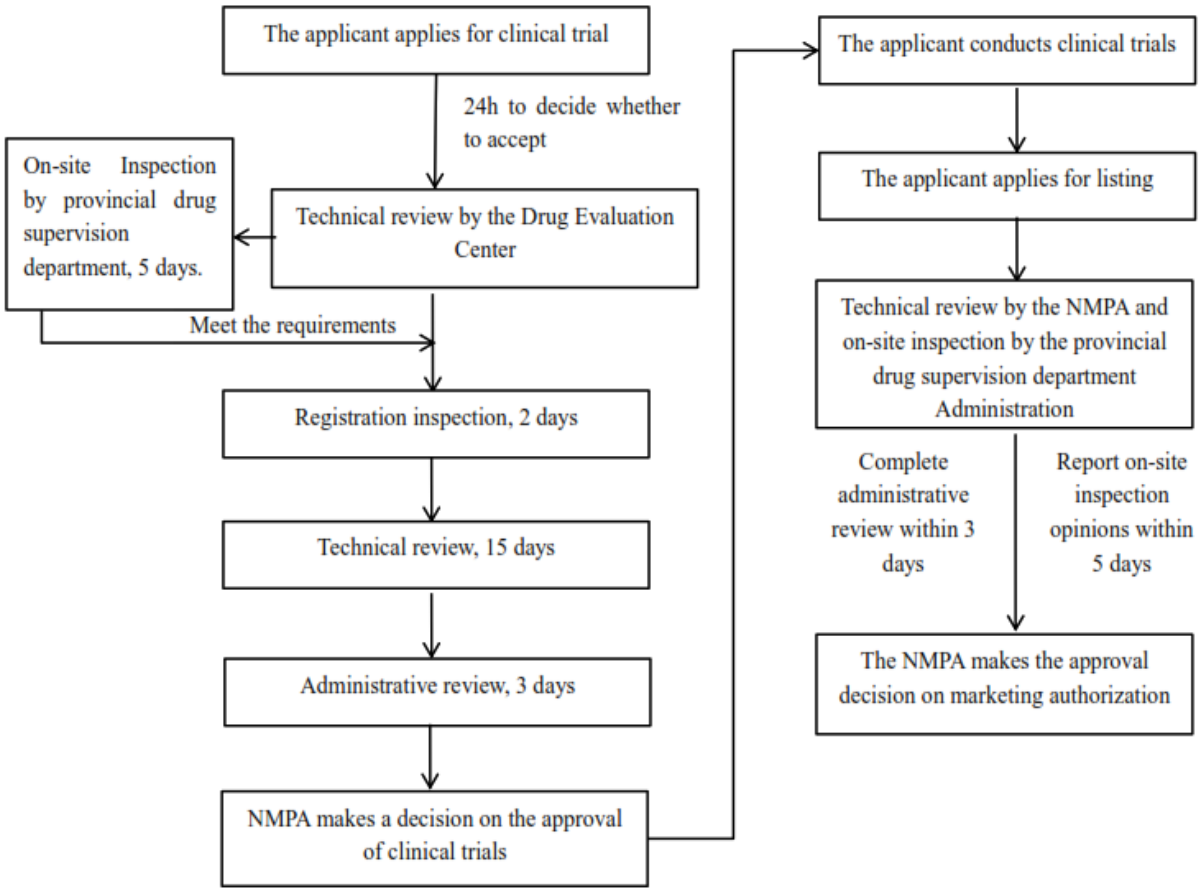

Figure 1. The specific approval process by NMPA

Priority review and approval procedure: priority review and approval procedure is applicable to innovative drugs and improved new drugs for the prevention and treatment of major infectious diseases, as well as vaccines urgently needed for disease prevention and control. Its purpose is to speed up the drug evaluation process and encourage innovative drug research and development. When applying for drug marketing license, the applicant can apply for priority review and approval, but it needs to have the following obvious clinical values:

- Shortage drugs urgently needed clinically, innovative drugs and improved new drugs for the prevention and treatment of major infectious diseases and rare diseases;
- New varieties, dosage forms and specifications of medicines for children that meet the physiological characteristics of children;
- Vaccines and innovative vaccines urgently needed for disease prevention and control;
- Drugs included in breakthrough therapeutic drug procedures;
- Drugs that meet the conditional approval procedure;
- Other situations where the NMPA stipulates that the review and approval shall be given priority.

3. Emergency Drug Approval System in the US under Public Health Emergencies

3.1 Emergency use authorization system

The Emergency Use Authorization (EUA) mechanism is the core of America's response to public health emergencies. It allows FDA to quickly respond to new threats by approving new drugs, devices or diagnostic procedures or by accelerating the approval process to expand the off label use of existing drugs, that is, in actual or potential public health emergencies, FDA can urgently use unapproved pharmaceutical products or unapproved uses of approved pharmaceutical products. (8) EUA plays a vital role in the emergency system of the United States, and is most widely used. Therefore,

the following will mainly start from the system elements of emergency authorization to study the US EUA.

3.1.1 Legal basis

The EUA in the United States is mainly based on Article 564 of the *Federal Food, Drug and Cosmetic Act (FD&Act)* and the *Bioterrorism Epidemic Prevention Plan Act* of 2004. In actual or potential public health emergencies, when there is a shortage of approved treatment products, FDA can use specific medical products for emergency diagnosis, treatment and prevention. Later, the United States introduced the *Prevalence and Disaster Prevention Reauthorization Act* in 2013, the *21st Century Cure Act* in 2016 and the *Public Law 115-92* in 2017 to supplement and improve the EUA. In addition, FDA also released the *Guidelines for Emergency Use Authorization of Pharmaceutical Products* in January 2017, establishing the EUA operating procedures, which have been used up to now.

3.1.2 Approval process

Before FDA issues the EUA, the Minister of Department of Health and Human Services (HHS) must state the reasons for the existence of the approval authorization, and at the same time publish it on the FDA official website in the form of announcement. This form enables the public to clearly understand the actual situation and status, and also makes the approval process more formal, laying a foundation for the following applicants and regulatory authorities to strictly comply with and implement the approval process. Secondly, the products shall be reviewed. The permanent Emergency Authorization Group established by the HHS is mainly responsible for identifying, reviewing and providing expert advice on potential candidate products before or during the declaration of the state of emergency. The establishment of the emergency authorization team can support the rapid review of products. The team covers experts and representatives in the field of public health and federal agencies, and can effectively coordinate the work of various departments to improve the efficiency of the review. In addition, FDA will consult with the Assistant Secretary for Preparedness and Response, the Director of the Centers for Disease Control and Prevention, and the Director of the National Institutes of Research, as applicable. Finally, after the review, the Director of FDA decides whether to authorize the product urgently.

3.1.3 Approval conditions

The United States has described in more detail the approval conditions for emergency authorized products. FDA can issue EUA only when the products applied for meet the following four statutory standards, including:

a) CBRN (Chemical, Biological, Radiological and Nuclear) substances mentioned in the EUA statement issued by the HHS Secretary must be able to cause serious or life-threatening diseases or conditions.

b) Evidence of validity. It refers to the product's "possibly effective" prevention, diagnosis or treatment of serious or life-threatening diseases or conditions caused by CBRN (Chemical, Biological, Radiological and Nuclear). It can be seen that the level of EUA's "possibly valid" standard is significantly lower than the FDA's "validity" standard for routine product approval. FDA will evaluate the potential effectiveness of the product and analyze its use risks and benefits. If, based on all available scientific evidence, it can be reasonably inferred that the product may be effective for a specific use, FDA may authorize its EUA, provided that it also complies with other statutory standards for issuing EUAs.

c) Risk benefit analysis. If the known and potential benefits of the product exceed the known and potential risks of the product when it is used to diagnose, prevent or treat the identified disease or condition, the product's EUA application can be approved. FDA will determine the overall risk benefit based on multiple sources, such as the results of domestic and foreign clinical trials, and the efficacy data of animal models in vivo and in vitro. Given the current level of scientific knowledge, FDA will also assess the quality and quantity of available evidence.

d) There is no substitute. At the time the EUA was issued, there were not enough approved alternatives in the market to diagnose, prevent or treat the disease.

3.1.4 Termination conditions

The termination conditions for emergency authorized products in the United States are divided into two situations:

a). The emergency use authorization is terminated with the end of the emergency state. After discussion by the Department of Health and Human Services (HHS), the Ministry of Homeland Security and other relevant departments, it is decided to announce the lifting of the state of emergency, and the emergency authorized products will be automatically terminated;

b). The validity period is 1 year. If the emergency state has not been lifted, but the EUA has been published for one year, the Minister of HHS or the FDA Administrator will decide whether to continue the product state. If the product cannot meet the needs of protecting public health or safety, the authorization will be canceled. The termination mechanism adopted by the United States for emergency authorized products is very flexible. Because the validity period of the authorization is short, it can be adjusted according to the actual state to avoid occupying resources. In addition, the 1-year validity period is also set with more caution. Compared with other licensed drugs that are routinely marketed, the safety of emergency authorized drugs inevitably has greater risks, Setting a shorter period of validity can ensure that the product can be quickly terminated when it has safety problems or does not meet the conditions, reducing government and enterprise costs and adverse effects.

3.1.5 Risk control measures

Because the risk of approving products for public health emergencies is greatly increased, the risk control measures after the products are launched are crucial. The United States has made detailed provisions on risk measures after the products are launched.

- Information about the product. The contents that need to be explained to health care professionals or authorized dispensing personnel include: known or potential benefits and risks related to the use of the drug in an emergency; Provide the product information manual of relevant personnel, including the basic information, indications, usage and dosage, precautions, etc. of the product. Explanations to patients include: known or potential benefits and risks related to the use of the drug in an emergency; Have the right to choose to accept or reject the use of the product and the consequences after rejection; the fact sheet of the product provided to the patient. In view of the nature and authorization conditions of the emergency, FDA recommends that more information about the product be provided as much as possible and expressed in plain language.
- Monitoring and reporting of adverse events. During the effective period of the authorization, FDA will take appropriate mechanisms to collect and analyze information about the safety and effectiveness of EUA products. The safety information and adverse event reporting system or vaccine adverse event reporting system are used to timely monitor adverse events.
- Relevant records. The manufacturer is required to keep product records and allow FDA to access records and inspections related to EUA products. For example, according to the dose delivered or sold by EUA, the number of devices or other units (including batch identification); Name and address of the facility from which the EUA products are shipped.
- Additional conditions for authorization. For example, it describes the distribution and management of products, and specifies which products can be distributed and who is responsible for the management. In addition, there will be restrictions on the advertising of EUA products.

3.2 Medical Counter-Measure and Priority Review Voucher

In addition to emergency use authorization system, in order to ensure the effective supply of urgently needed drugs when public health emergencies occur, the United States has also developed relevant drug approval systems from other perspectives. Medical Counter-Measure (MCM) product is a medical product regulated by FDA, including biological products, drugs and medical devices, which are used to deal with biological, chemical, nuclear threats caused by terrorist attacks or public health threats caused by new naturally occurring diseases. This type of product is mainly used to diagnose, prevent, protect or treat diseases caused by the above threats. (9) In 2007, HHS established the Public Health Emergency Medical Countermeasures Agency, which mainly includes three HHS subordinate institutions: FDA, Centers for Disease Control and Prevention and the National Institutes of Health. In addition, HHS also cooperates with the U.S. Department of Defense, Department of Veterans Affairs and other government institutions, non-governmental organizations, universities and research centers, and the industry. In 2010, FDA launched the Medical Countermeasure Initiative (MCMi) on the basis of the original MCM work. FDA mainly supported the MCMi work in three aspects, including: strengthening the MCM product review and approval process; Establish an effective regulatory policy and legal framework; Improve MCM monitoring and evaluation level.

The Priority Review Voucher (PRV) program was first proposed in 2007. (10) When the drugs developed by the sponsor are used for the diseases covered by the PRV, they can also apply for the PRV at the same time of submitting the new drug application, which will be granted by FDA. The sponsor who obtains the certificate can cash the PRV in the future new drug application, or sell or transfer the PRV to another sponsor. In addition, according to relevant regulations, the holder of PRV must pay the FDA the PRV usage fee in addition to other fees required by PDUFA. It can be concluded from the relevant regulations of *Material Threat Medical Countermeasure Priority Review Vouchers* that not all MCM meet the PRV approval requirements, and the conditions for obtaining medical countermeasure vouchers are as follows (11) :

(1) The purpose is to prevent or treat the injury caused by CBRN that is identified as a major threat; Or reduce, prevent or treat diseases that may lead to adverse health consequences and death.

(2) It shall be a drug for human use, and the active ingredient (including ester and salt) contained in the drug has not been approved in other applications. For combined drugs, it shall include at least one active ingredient that has not been approved.

4. Comparative analysis of emergency drug approval system between China and the US

The current drug special approval procedure and other accelerated approval channels in China cannot become the policy basis for the use of unlisted drugs or drugs beyond the instructions under the emergency state of public health, and cannot solve the problem of emergency drug use under the emergency state of public health. Therefore, a comparative analysis is made between China's emergency drug approval system and the United States' emergency drug approval system from the following aspects to provide a theoretical basis for improving China's emergency drug review and approval.

4.1 Comparison of legal basis and background

The United States has stipulated emergency use authorization through a number of laws, and has also issued more targeted use guidelines, fully taking into account the feasibility and operability of the system. It is a relatively mature, complete and valuable emergency use authorization system. The legislation of China's drug emergency approval system for public health emergencies mainly includes the *Drug Special Approval Procedures of the NMPA* and the *Provisions of the People's Republic of China for the Administration of Drug Registration*. See Table 1 for details. In addition, the United States has taken full account of various

situations that may occur in public health emergencies, including chemical, biological, radiological or nuclear threats, as well as natural disasters and military struggles. The relevant drug approval system is also based on the background of these major security events. Therefore, the United States can take targeted measures in the face of CBRN attacks, and carry out follow-up emergency response according to the policy provisions. However, from the perspective of relevant laws and regulations in China, there is no specific explanation of public health emergencies, and the legislative background is not prominent.

Table 1. Comparison of Legal Basis between China and the US

Parameters	China	US
Legal basis	Drug Special Approval Procedures of the NMPA, Provisions of the People's Republic of China for the Administration of Drug Registration	Federal Food, Drug and Cosmetic Act (FD&Act), Bioterrorism Epidemic Prevention Plan Act, Epidemic and Disaster Prevention Reauthorization Act, Cure Act of the 21st Century, Public Law 115-92, and Guidelines for Emergency Use Authorization of Pharmaceutical Products

4.2 Comparison of approval process

Before the approval process, the United States will make a statement on the reasons for approving the emergency use authorization, and publish it on the FDA official website in the form of announcement. A permanent emergency authorization team has been established to be responsible for the review of drugs. However, China does not make a statement, nor has it set up a special working group for emergency authorization, but has set up an approval mechanism different from the normal listing license. See Table 2 for specific comparison.

Table 2. Comparison of approval process between China and the US

Parameters	China	US
Statement	Nothing	Statement by HHS Minister
Review department	NMPA	Emergency Authorization Team
Approval department	NMPA	FDA

4.3 Comparison of approval conditions and termination conditions

In China, there is no clear provision on approval conditions, but the termination conditions are added to the *Provisions of the People's Republic of China for the Administration of Drug Registration*, namely, Articles 74 and 75 of Chapter 4. Drugs that have been specially approved are required to be used within a certain time limit and scope according to the needs of disease prevention and control; When the drugs no longer meet the inclusion conditions, the special approval procedure shall be terminated and the applicant shall be informed. These two provisions are institutional breakthroughs in response to public health emergencies, but they are only principled statements, lacking operability. The United States has made more detailed provisions on approval conditions and termination conditions, as shown in Table 3.

Table 3. Comparison of Approval Conditions and Termination Conditions between China and the US

	China	US
Approval conditions	No specific provisions	1.CBRN substances meet the conditions 2. Evidence of validity 3. Risk benefit analysis 4. Irreplaceable
Termination conditions	No specific provisions	1. The emergency use authorization is terminated when the emergency state ends 2. Valid for 1 year

4.4 Comparison of risk control measures

China has clearly stipulated that drug production and distributing enterprises and medical and health institutions should report the adverse reactions related to the drugs that have been specially approved to the corresponding regulatory authorities in a timely manner. At the same time, the drug adverse reaction monitoring authorities are required to focus on the drugs that have been specially approved for public health emergencies. In addition, it has also clarified that the NMPA should strengthen the re-evaluation of drugs after marketing that have been specially approved. Although China has clarified the main responsibilities of the relevant regulatory authorities in the procedures, compared with the risk control measures in the United States, they are not comprehensive enough, and there are no more specific requirements for the production and distributing enterprises, which may lead to problems such as confusion in drug use management and unclear responsibility subject. In addition, because of the risks of emergency drugs, medical institutions and patients should be cautious in using them, and the drug instructions should be strictly managed. However, from the perspective of China's drug emergency approval procedures, there are no relevant provisions, and drugs cannot be effectively controlled, which is not conducive to the life safety of patients. See Table 4 for specific

comparison.

Table 4. Comparison of risk control measures between China and the US

	China	US
Risk control measures	1. Monitoring and reporting of adverse reaction events 2. Re-evaluation after listing	1. Provide product information 2. Monitoring and reporting of adverse reaction events 3. Maintain and access relevant records of EUA products 4.Additional conditions for authorization

4.5 Comparison of coordination mechanisms

For MCM products, under the leadership of HHS, the United States has set up a public health emergency medical response agency, which not only includes its FDA, Centers for Disease Control and Prevention and National Institutes of Health, but also includes government agencies other than HHS departments, such as the Department of National Defense and the Department of Veterans Affairs, and also cooperates with non-governmental organizations and universities. The high-level work coordination mechanism can enable close cooperation within and between departments, and at the same time cover the support of non-governmental organizations and university research centers, which can better promote the development of MCM. At the same time, in the 21st Century Cure Act of 2016, a priority review voucher plan for medical countermeasures against material threats was established, and the review time can be shortened from 10 months to 6 months. The establishment of the priority review voucher system will have a positive effect on all parties. In addition, as a drug regulatory authority, FDA provides MCM with professional and scientific knowledge and information related to policies and regulations in R&D, procurement and storage, which plays a vital role in ensuring the safety and effectiveness of MCM.

From the perspective of the departments and working mechanisms involved in the current drug approval system in China, the competent department is only related to health and drug supervision departments, with less departments, and also lacks a coordination working mechanism and group that can effectively coordinate cross departments, superior decision-making departments and specific implementation departments, with fewer coordination levels. When public health emergencies occur, problems such as delayed information and slow efficiency will occur, which will affect the approval and use of urgently needed drugs.

5. Enlightenment and Suggestions

5.1 Adapt to the special needs of public health emergencies

The COVID-19 has made the Chinese government pay more attention to the prevention and control of biosafety. It is not only necessary to reflect biosafety in the national governance system and strategic deployment, but also to highlight the environmental background of public health emergencies in the corresponding procedures for emergency drug approval, and to formulate the process, approval conditions and relevant requirements of drug review and approval procedures in line with public health emergencies. In addition, we should give full play to the important role of the national biosafety department and include it in the drug R&D approval and other links and mechanisms. In the case of public health emergencies, from the perspective of overall safety prevention, professionals can be selected from relevant departments such as biosafety and disaster response as review members of urgently needed drugs to ensure that the drug approval mechanism can better adapt to the special needs of public health emergencies.

5.2 Establish emergency use authorization system

5.2.1 Strengthen the upper law support of emergency use authorization system

The emergency authorized use of pharmaceutical products is a special path for the marketing license of pharmaceutical products under special circumstances, which needs a complete legal basis to be effectively and rapidly implemented. With the gradual implementation of national measures to promote the standardization of the pharmaceutical industry, the gradual introduction of macro policies, and the frequent occurrence of major public health events, the laws on pharmaceutical products should also keep pace with the pace of development. Therefore, from the national strategic level, we should start from two aspects: 1. improve relevant laws, introduce emergency use authorization clauses, and define their legal status: relevant national laws need to be supplemented with relevant provisions on the emergency authorized use of drugs, vaccines, and medical devices, and promote the research, development, production, and storage of related products to deal with major public health emergencies of different natures. 2. Formulate administrative rules and provide scientific guidance: through the formulation of administrative rules that specifically provide for emergency use authorization, such as the Provisions for the Administration of Drug Emergency Authorization, make clear provisions on emergency authorization, provide scientific guidance for relevant operations, and clarify the management path. (12)

5.2.2 Establish approval conditions for emergency use authorization

When public health emergencies occur, a large number of special approval applications will be generated in a short time to meet the urgent need for drug research and development and supply, and these applications are often uneven. The original special approval procedure did not specify the approval conditions for drug approval. To distinguish these

applications would lead to a waste of human and material resources, and approval resources could not be used centrally. Therefore, we can learn from the approval conditions of the United States for applying for emergency use of authorized drugs, and define the indicators and requirements that need to be met in the emergency drug approval process. In addition, we can also classify various applications according to different fields, and submit them to experts in different fields for research and judgment. We can bring the really needed qualified applications into the queue of the review and approval process, so as to effectively centralize review resources and improve the approval efficiency, Promote the rapid launch of emergency drugs in the event of public health emergencies.

5.2.3 Establish termination conditions for emergency use authorization

Although China has mentioned the termination of drugs with special approval procedures in the *Provisions of the People's Republic of China for the Administration of Drug Registration*, it is only a brief statement of principle. Specific implementation rules need to be issued in the future to specify the validity period of authorization for emergency drug approval, the conditions and procedures for revocation and termination. Since the emergency use of authorized drugs is mainly aimed at public health emergencies, compared with conventional marketing licensed drugs, it is inevitable that there are greater risks in safety. Therefore, a more cautious approach can be considered in the design of specific approval procedures. For example, the approach of the United States can be used for reference. When the public health emergencies are terminated, the corresponding special approval product license will be automatically terminated or after evaluation, it is found that the data submitted subsequently no longer meet the authorization conditions, it shall also be terminated.

5.2.4 Strengthen risk control measures

Because the risk of approving products for public health emergencies is greatly increased, risk control measures after marketing are particularly important. In the design of risk control measures, China should emphasize the difference between emergency approval products and general approval products after they are launched on the market, reflecting the particularity and urgency of emergency approval products. In terms of documents, the applicant shall be required to submit a risk management plan on product safety, including safety characteristics, pharmacovigilance plan, effective research plan after listing, risk minimization measures, etc., and shall submit a safety update report at least every 6 months after drug approval or re-registration. In terms of product information, the United States can be used for reference. The applicant is required to mark a proprietary label on the product package, and provide a detailed drug description to medical institutions and patients, clearly informing them of possible risks and benefits. In terms of legal liability, the subject liability shall be specified in writing. Under specific circumstances, such as the distribution and management of emergency authorized products, the legal liability of relevant subjects such as manufacturers and medical institutions can be reduced or exempted to protect their rights and interests. In addition, in case of physical damage caused by using emergency authorized products, corresponding compensation mechanisms should be established to provide compensation and assistance to individuals or family members.

5.3 Establish cross department linkage and coordination mechanism

Before the COVID-19 epidemic, there was a lack of departmental coordination mechanism for drug approval in China, which restricted the implementation of the approval procedure. However, from the perspective of the overall organizational structure and coordination mechanism for responding to the epidemic, the policies of speeding up the review and approval issued by the NMPA are in essence part of the joint prevention and control mechanism, an emergency mechanism that requires joint efforts by different departments, and also serve the epidemic prevention and control policies formulated by the country as a whole. Compared with the organizational model of the United States, the cross sectoral coordination mechanism adopted by China for emergency drugs fully demonstrates China's institutional advantages, and has greater flexibility and practical operability. It is not easy to support such a large and complex organizational structure, which also reflects from the side that our government has a strong overall planning ability, and all departments can implement policies efficiently. Therefore, we should maintain the advantages of this system, but we should also establish a cross sectoral linkage coordination mechanism in the drug approval system, and include more functional departments through working groups. For example, for China's drug emergency approval procedures, we can refer to the model of the United States, establish a standing working group under the NMPA, accept the leadership of the Emergency Response Office of the State Council, and review and provide expert advice on candidate drugs for emergency authorization. In addition, China needs to give priority to legalizing and sequencing the coordination response mechanism at the level of relevant superior laws to provide a legal basis for the implementation of the drug approval system, so as to achieve the effect of long-term operation.

5.4 Formulate the integrated layout of R&D, approval, production and reserve

In the emergency response system for public health emergencies, the review and approval of emergency drugs is only one link, and the overall layout of the whole chain of medical supply under public health emergencies needs to be further strengthened. Therefore, the following suggestions are put forward: First, define the value orientation of new drug supply, fully consider the demand under emergency state of public health emergencies in the layout planning, and carry out the overall layout with the basic concept of combining prevention and emergency. The second is to establish a directory of medical reserves for public health emergencies. We can learn from the practice of the

United States, use technical means to screen and identify drugs with potential value, and arrange R&D projects in advance to ensure rapid supply in case of public health emergencies. Third, formulate policies to encourage research institutions and enterprises to carry out research and development. On the one hand, the state should continue to invest in therapeutic drugs for public health emergencies, and provide financial support for R&D and innovation carried out by scientific research institutions and production enterprises; On the other hand, we will set up major special projects to support scientific research institutions and enterprises to carry out clinical research on antiviral drugs, vaccines, etc., so that they can quickly enter clinical trials in the face of public health emergencies and accelerate the process of research and development.

6. Conclusion

On the basis of maintaining its own institutional advantages, China should fully learn from foreign experience, further optimize the approval system of emergency drugs in China, and strengthen the overall chain layout of medical emergency products under public health emergencies, so as to improve China's response and implementation capacity in public health emergencies.

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Author Contribution

Wei Chen has made substantial contributions to the conception and design of this work. Yi Liang has revised work and approved the final version to be published.

References

1. Emergency Regulations on Public Health Emergencies [Internet]. China: The Central People's Government of the People's Republic of China; 2003 May 09 [cited 2022 Nov 10]. Available from: http://www.gov.cn/zhengce/2020-12/26/content_5574586.htm
2. Yanan Wang, Rong Jiang, Rong Shao. Research on Emergency Approval System of Pharmaceutical Products in China under Public Health Emergencies. Chinese Journal of Pharmaceuticals. 2022; 53(1):140-147.
3. Juan Chen, Yan Lu, Dongzi Xu, et al. System Problems and Recommendations for the Emergency Use of Drugs in China. China Pharmaceuticals. 2021; 30(14):6-10.
4. Provisions of the People's Republic of China for the Administration of Drug Registration [Internet]. China: State Administration for Market Regulation; 2020 Mar 30 [cited 2022 Nov 10]. Available from: https://gkml.samr.gov.cn/nsjg/fgs/202003/t20200330_313670.html
5. Vaccine Administration Law of the People's Republic of China [Internet]. China: Center for Drug Evaluation, NMPA; 2019 Jul 2 [cited 2022 Nov 10]. Available from: https://www.cde.org.cn/main/policy/view/4568289019d49f2f7d2a7daf35c5371e
6. Xue Wang, Shuning Zuo, Qi Zhang, et al. Analysis on emergency authorization policies of medical products. Chinese Journal of New Drugs. 2021; 30(7):596-600
7. Technical Guidelines for Conditional Approval of Drugs for Marketing (Trial) [Internet]. China: Center for Drug Evaluation, NMPA; 2020 Nov 19 [cited 2022 Nov 10]. Available from: https://www.cde.org.cn/main/news/viewInfoCommon/d1716db06f90c3adf134de337373b22c
8. Emergency Use Authorization of Medical Products and Related Authorities [Internet]. US: FDA; 2017 Jan 17 [cited 2022 Nov 10]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities
9. What are Medical Countermeasures? [Internet]. US: FDA; 2022 Mar 16 [cited 2022 Nov 10]. Available from: https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/what-are-medical-countermeasures
10. GAO. DRUG DEVELOPMENT FDA's Priority Review Voucher Programs [Internet]. US: United States Government Accountability Office; 2020 Jan 20 [cited 2022 Nov 10]. Available from: https://www.gao.gov/assets/gao-20-251.pdf
11. Material Threat Medical Countermeasure Priority Review Vouchers [Internet].US: FDA; 2018 Jan 17 [cited 2022 Nov 10]. Available from: https://www.fda.gov/media/110193/download
12. Xuanwei Zhong, Ruosi Han, Bo Li. The Analysis and Consideration for Emergency Policies of Medical Products Used for Dealing with Public Health Emergency in China and US. Chinese Pharmaceutical Journal. 2020;55(23):1979-1984.