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The Implementation of Parametric Release Policies for Pharmaceutical Products in China: A stakeholders' Approach

LIU Ying

Doctor of Management

Supervisors:

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ISCTE University Institute of Lisbon

PhD Gu Lihong, Professor,
Southern Medical University

September, 2023



BUSINESS
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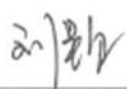
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Abstract

This study investigates the feasibility of implementing the parametric release of moist heat sterilization products in China from a stakeholder approach. Semi-structured interviews were conducted with 33 participants to gain an in-depth understanding of their common interests and respective concerns regarding the implementation of parametric release. Through the grounded theory method, the interest demands, conflicts of interest, and influencing factors of various stakeholders in the process of promoting the parametric release policy were analyzed in depth, and the coordination path of key stakeholders to promote the policy was discussed. Based on theoretical and applied research, analysis and summary are conducted using multiple-streams framework, then strategies and suggestions for promoting policy coordination are proposed from the perspective of policy entrepreneurs. The study concluded that the macro environment, institutional system, technical capabilities, and interactive communication are the key objective factors to affect the implementation of the parametric release policy. The above objective factors have an impact to the subjective factors including the risk perception of regulatory authorities and the market, the trust relationship between government and enterprises, and the regulatory and industry acceptance of policy implementation, thus affecting parametric release policy adoption. Policy entrepreneurs can drive the implementation of parametric release in China by promoting the influencing factors. Some suggestions are proposed as: to establish a supporting regulatory system for parametric release policy; to build an implementation path; to conduct a series of training; to restart pilot work, and to pay attention to the development opportunities of policy windows.

Keywords: parametric release; grounded theory; stakeholder theory; multiple-streams framework; policy entrepreneurs

JEL classification: L65; L50

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Resumo

Esta tese estuda a possibilidade da implementação da libertação paramétrica de produtos farmacêuticos na China, através de uma abordagem de *stakeholders* (partes interessadas). Realizaram-se entrevistas estruturadas a 33 participantes para se compreender os interesses comuns e preocupações das partes interessadas na implementação da libertação paramétrica. Com base no método da teoria fundamentada em dados, analisaram-se em profundidade os interesses em presença, potenciais conflitos e os fatores que influenciam as diferentes partes interessadas no processo de promoção da política de libertação paramétrica, e discutiu-se o caminho coordenado de partes interessadas chave para promover a política. Com base em pesquisas teóricas e aplicadas, análises e resumos são conduzidos usando uma estrutura de múltiplos fluxos e, em seguida, estratégias e sugestões para promover a coordenação de políticas são propostas a partir da perspectiva dos empreendedores de políticas. O estudo conclui que os principais fatores que influenciam a implementação da política de libertação paramétrica dos produtos farmacêuticos estudados são a envolvente macroeconómica e social, o sistema institucional, as competências técnicas e a necessidade de uma comunicação interativa. Estes fatores objetivos influenciam por sua vez fatores subjetivos tais como a percepção de risco por parte das autoridades reguladoras e do mercado, a relação de confiança entre o governo e as empresas, e a aceitação das políticas pela indústria, afetando assim a adoção da política de libertação paramétrica. Os promotores das políticas podem impulsionar a implementação da libertação paramétrica de produtos farmacêuticos na China através da promoção dos fatores influenciadores. Algumas sugestões propostas incluem: estabelecer um quadro regulamentar para a política de libertação paramétrica; conceber um caminho para a implementação; realizar formação adequada; reiniciar ações piloto, e estar atento ao aparecimento de janelas de oportunidade para a introdução das políticas necessárias.

Palavras-chave: libertação paramétrica; teoria fundamentada em dados; teoria das partes interessadas; estrutura de múltiplos fluxos; empreendedores de políticas

Classificação JEL: L65; L50

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摘 要

研究从利益相关方视角探讨湿热灭菌产品在中国实施参数放行的可行性。通过对行业内 33 名不同的利益相关方进行半结构化访谈，深入了解各利益相关方对推行参数放行的共同利益点以及各自的顾虑。通过扎根研究方法，深入分析了参数放行政策推进过程中各利益相关方的利益诉求、利益冲突和影响因素，探讨促进参数放行政策推进的关键利益相关方的协调路径。在理论与应用研究的基础上，基于多源流分析框架进行分析总结，从政策企业家角度提出推进政策协调的对策建议。研究得出，参数放行政策实施受到宏观环境、制度体系、技术能力、互动沟通等客观因素的影响。而上述客观因素会对监管及行业对政策推行的风险感知，政企之间的信任关系，以及监管及行业对政策推行的接纳度等主观因素产生影响，从而影响参数放行政策的采纳。政策企业家可通过推动这些影响因素，来推动参数放行在中国的实施。提出的建议包括，建立适合我国国情的参数放行配套监管体系、建立实施参数放行的路径、开展参数放行系列培训、重新开启相关的试点工作，以及关注政策窗口的开发契机。

关键词：参数放行；扎根理论；利益相关者理论；多源流理论；政策企业家

JEL 分类：L65；L50

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List of Acronyms

Description	Acronym
Center for Drug Evaluation	CDE
Center for Drug Evaluation and Research	CDER
China Food and Drug Administration	CFDA
Committee for Medicinal Products for Human Use	CHMP
China Pharmaceutical Association of Plant Engineering	CPAPE
China Quality Association for Pharmaceuticals	CQAP
China Society of Drug Regulation	CSDR
United State Pharmacopeia	USP
European Medicines Agency	EMA
Failure Model & Effects Analysis	FMEA
Good Manufacturing Practice	GMP
Institutional Analysis and Development Framework	IAD
International Conference on Harmonization	ICH
Institutional Analysis and Development Framework	LAD
Japanese Pharmacopoeia	JP
Large Volume Parenterals	LVPs
Marketing Authorization older	MAH
National Health and Clinical Excellence	NICE
National Medical Products Administration	NMPA (China)
Process analytical techniques	PAT
Parenteral Drug Association	PDA
Pharmaceutical Inspection Convention / Co-operation Scheme	PIC/S
Quality by Design	QbD
State Drug Administration	SDA
State Food and Drug Administration	SFDA(China)
World Health Organization	WHO

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Chapter 1: Introduction

1.1 Research background

The quality of drugs is the primary guarantee for the safety of patients. In 1961, the thalidomide incident that spread around the world caused a thousand of teratogenic cases, leading to a drastic revision of the U.S. drug act in 1962 and the enactment of the world's first Good Manufacturing Practice (GMP) in 1963 (Gao, 2011). In 1969, the World Health Organization (WHO) made a recommendation at its 22nd session, recommending all member states to implement the GMP system for pharmaceutical production. During the 1970s and 1980s, the European Community, United Kingdom, Japan and other countries and regions accepted the GMP system and entered the peak period of development, and then was gradually accepted by all countries. In 1982, China issued its first pilot version of GMP, which was officially released in 1988 and has undergone several revisions till now.

In 1963, the first GMP in the United States required final products to pass a batch release test. A batch release test is necessary to ensure high-quality pharmaceuticals and biopharmaceuticals prior to release for sale, supply, or export. For sterile products, traditional testing method is through sampling inspection for finished products to prove the sterility level. However, during the ten years following the implementation of GMP, sterile large volume parenteral in the United States were found to be qualified in the sterility test at delivery. However, there are many serious adverse events occurred in clinical practice.

The practice of the following years has increasingly demonstrated that the statistical sampling methods, no matter how sophisticated, could carry risks especially for sterile large-volume parenteral. This risk increases as the degree of microbial contamination of the sterilized products decreases, thus there are often cases where products pass the sterility test when they leave the factory, however severe adverse events still occur in clinical use. Therefore, judging whether a batch of products is sterile based on the results of sterility test cannot guarantee the sterile condition of drugs. The FDA set up a special investigation team composed of drug regulators, microbiologists, and equipment engineers. The investigation results showed that the defects in sterilization equipment and process were the main cause of product contamination, that is, out-of-control production process. Sterility testing by culturing finished units drawn

from the batch is limited in its ability to detect contamination due to a) the small number of samples required for testing, which restricts the ability to capture those microorganisms dispersed in a large volume, and b) the limited ability of the prescribed culture media to stimulate growth of all potential microorganisms. Typically, these tests will detect only major errors in the manufacturing process that result in contamination of many product units. However, data derived from in-process controls of a validated terminal sterilization process can provide more accurate information regarding product sterility because the probability of product bioburden surviving the sterilization process in any single unit of a product can be calculated to be less than one in a million.

The parametric release means to evaluate the sterility assurance of the product according to the data of effective control, monitoring, and validation of the sterilization process, to replace the release system based on the sterility test results of the finished product. Consequently, parametric release used as an operational alternative to routine release testing of certain, specific parameters. The development of quality management theory makes people more and more deeply realize that it is difficult to guarantee and improve the quality of drug products by quality inspection alone, it depends on all aspects of product manufacturing, including design, development, production control and logistics management. In other words, quality comes from the process. Every process of drug production will inevitably affect the quality of drugs. To ensure and improve the quality of drugs, it is necessary to consider all processes of drug production. Parametric release reflects the basic idea that drug quality control focuses on production process control and changes the quality control of sterile drugs from afterward control to pre-control and in-process control. To carry out parametric release without sterility inspection is not simply to cancel sterility inspection, but to strengthen the production process control (GBW, 2015). The implementation of parametric release needs to be demonstrated from the following three elements (see Figure 1.1):

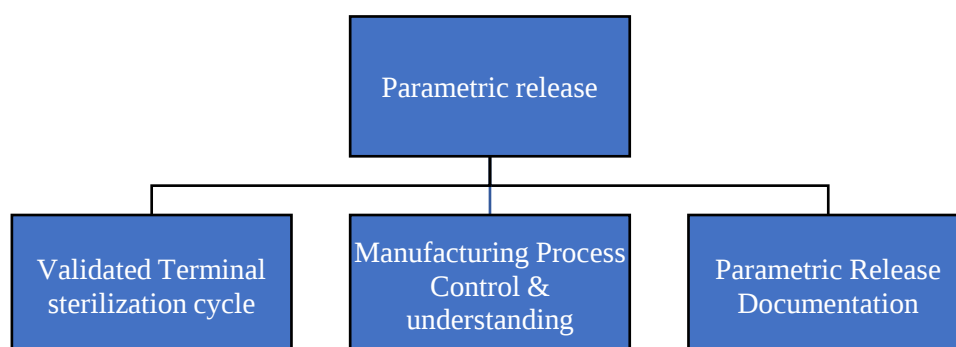


Figure 1.1 Deconstructing parametric release recommendations

Source: Marla (2015)

The following examples explain the fundamental difference between parametric release and sterility test release. For a product released using the United States Pharmacopeia (USP) <71> Sterility Tests, once the drug product is terminally sterilized, there is an incubation period of a minimum of 14 days to allow for possible microbial growth in samples before obtaining results from this test. During this waiting period, the drug product is placed on hold (not released for sale), potentially occupying valuable space, but more importantly delaying patient access to critical drug products. For a product released using parametric release, once the drug product is terminally sterilized and the acceptance criteria for the critical process parameters are documented as being met, the product can be released for commercial sale (provided that all other release test criteria have been met). A sterility test is not performed on any units, so there is no waiting period associated with the sterility test and/or subsequent investigations (Marla, 2015).

One of the most apparent benefits of parametric release is the savings of time and resources. There is no performance of a sterility test, so no waiting for results and no additional delays due to investigations of common false sterility test positive results. Another benefit may be financial savings from the absence of expenses related to sterility testing and product holding. Moving products to commercial sale quickly could also lead to saving space. Additionally, other less obvious benefits include manufacturing flexibility (moving products to market quickly in cases of drug shortage) and possibly better process understanding and manufacturing control. Given the small sampling size of test lots required for sterility testing, the USP <71> Sterility Tests methodology has limited capability to detect small numbers of contaminated units. Based on the understanding, development, and implementation of process controls for parametric release, it was concluded that parametric release can lead to better sterility assurance (Marla, 2015).

In the U.S., FDA approved the first firm to use parametric release in 1985. In 1987, FDA issued the guidance document for parametric release (7132a. 13). Start from then, parametric release formally listed in US GMP. In 1996, another firm applied for parametric release and received approval. In 2009, parametric release has been listed in USP as appendix (USP 1222). Until 2015, 12 pharmaceutical firms have received approval from Center for Drug Evaluation and Research (CDER) for parametric release of one or more drug products, resulting in a significant number of drug products currently released by this program. These firms demonstrated Quality by Design (QbD) approaches, process knowledge, and manufacturing history and have benefited from a parametric release program for almost three decades (Marla, 2015).

European Medicines Agency (EMA) developed parametric release guidelines in 2001 and

Pharmaceutical Inspection Convention/Pharmaceutical Inspection Co-operation Scheme (PICS, 2007). EMA issued real-time release guidelines (original parametric release guidelines) in 2012.

In addition, the International Conference on Harmonization (ICH) accepted the parametric release method in 1999. It is defined in ICH Q6A 2.6 as “parametric release can be used as an operational alternative to routine release testing for the drug product in certain cases when approved by the regulatory authority. Sterility testing for terminally sterilized drug products is one example. In this case, the release of each batch is based on satisfactory results from monitoring specific parameters, e.g., temperature, pressure, and time during the terminal sterilization phase(s) of drug product manufacturing. These parameters can generally be more accurately controlled and measured, so that they are more reliable in predicting sterility assurance than end-product sterility testing.

At present, drug regulatory authorities in developed countries have generally accepted the concept of parametric release and put it into practice. In fact, the concept of parametric release is now accepted not only in the field of pharmaceuticals, but also in the field of medical devices and diagnostic reagents.

Pre-approval is required for the parametric release of large volume injections. The content and form of the approval and daily supervision of parametric release in the United States, Canada, Australia, and other countries as well as the European Union are the same. Based on the current GMP management, guidelines and declaration methods for parametric release are promulgated, and the enterprises apply voluntarily according to the drug varieties. The drug regulatory department shall decide whether to approve the enterprise's application after conducting a strict data review and on-site inspection. For approved drugs, if there is a change of important factors, such as change of manufacturing address, a new application is required. The daily supervision after approval shall require the relevant drugs to comply with GMP management, and particular parametric release guidelines (Q. Q. Hu et al., 2007). Pre-approval ensures the aseptic safety of products entering the market.

1.2 Research problem

Chinese GMP was developed in 1988 and experienced several revisions. Since then, the awareness of drug quality control was continuously improved. In 2002, after referring to the parametric release guidelines and investigating the specific implementation practice of the U.S., the EU and other developed countries, China State Food and Drug Administration (SFDA) (currently National Medical Products Administration, NMPA) kicked off the feasibility

research for parametric release in China. On March 1, 2005, SFDA issued the notice about drug parametric release pilot project, approving Wuxi HuaRui Pharmaceutical Co., LTD., and Guangzhou Baxter Healthcare Co., LTD as pilot enterprises to implement parametric release. The pilot products are mainly produced by moist heat sterilization of large volume parenteral. The pilot program lasted for 2 years. This two-year pilot project marks the formal introduction of parametric release into China's GMP management of drug production and quality. During the pilot period, enterprises should implement drug parametric release in strict accordance with relevant requirements. During the pilot period, parametric release and traditional sterility test release of relevant drugs should be carried out simultaneously. Products with unqualified sterility test results and those that do not conform to the provisions on parametric release of drugs shall not release from the factory. Pilot enterprises should constantly summarize experience and accumulate data to provide basis for improving relevant regulations and requirements. At the end of the trial project, to further accumulate data and obtain more solid experience, SFDA issued the 2nd Notice to extend parametric release pilot project in next three years for from 2007. In 2012, The SFDA announced to clarify that parametric release is of great significance for strengthening production process control and ensuring product quality. Since the pilot project implementation of parametric release in 2005, pilot enterprises have been continuously exploring, accumulating data and improving the quality management system, which is worthy of support and encouragement.

In 2013, Shanghai General Pharmaceutical Co., Ltd. submitted a drug registration application to U.S. FDA, in which the full set of parametric release method was adopted to control the quality of the products. By implementing the strict parametric release method and providing the completed validation data, FDA approved the product registration and even waived the regular on-site inspection. Nevertheless, to meet the requirements of Chinese regulations, Shanghai General must maintain a production line with traditional sterility testing in accordance with Chinese GMP requirements while adopting the parametric release method for U.S. exports.

So far, these are the only examples of parametric release practice in China.

There is strong consensus that parametric release embodies the essence of GMP and is more advanced method compared with traditional sterility test release for terminally sterilized drug products.

However, the problem is that such a suitable method and best practice, which has been 18 years since pilot project in China, is still stagnating, as the Chinese health authorities and industry can't adopt this approach.

This research aims to investigate the possibility to adopting and implementing a parametric release policy in China from the perspective of stakeholders, and through the analysis of stakeholders, understand the common interests of stakeholders and their respective concerns about the implementation of the innovation policy, as well as understand the obstacles in the implementation process in China. Based on the stakeholder analysis result, to explore the coordination path to promote effective partnership from the perspective of policy entrepreneurs.

1.3 Research questions

This study aims to promote the coordination of various stakeholders in promoting this project. Based on the analysis of the conflicts and coordination among stakeholders in this case, this study deeply observes the cooperation between various stakeholders in the promotion of this project, the interests in the process, behavior patterns and the mechanism behind the action, to focus on answering the following questions:

Who are the key stakeholders? What are the interests of the key stakeholders?

How do their interests conflict? And how do they play the game?

What are the factors that influence stakeholder cooperation?

How to explore ways to facilitate stakeholder coordination in implementing the parametric release policy?

1.4 Research method

This research project will be conducted in China. The research will use a combination of several research methods. Firstly, the project and the theory to be adopted are summarized from the literature collection and analysis perspective. According to the design of research objectives and research questions, qualitative research methods are adopted in this study.

This study mainly adopts the interview method in qualitative research and uses grounded theory to analyze interview texts.

The interview method refers to the research method that the researcher and the subject contact and talk directly to achieve the purpose of data collection. Since the parametric release policy is a specialized topic, with the help of in-depth interviews, researchers can directly understand the interviewee's personal experience, thoughts, emotions, and other deep content, establish contact with the interviewee, and obtain more information through follow-up. In this work, semi-structured interviews control the content and direction of interviews and provide

interviewees with space for active participation. The combination of online and offline methods in the study can maximize the impact of the novel coronavirus epidemic, expand the selection of interviewees, and improve the efficiency of interviews.

Grounded theory is a qualitative research method that advocates the researchers obtain data from social phenomena and daily experience, condense concepts and construct theories after systematic analysis. It is a bottom-up research method. By sorting, coding, and summarizing the interview data. This study aims to investigate the stakeholders' understanding of the implementation of the parametric release policy in China, their concerns and obstacles, and their attitudes towards the implementation of the policy, and then analyze the main factors that promote the implementation of the parametric release policy, therefore to explore the coordination path of the stakeholders who promote the implementation of the parametric release policy. In this process, we strive to integrate, condense, and generate a whole from many different concepts and viewpoints, to summarize and generate a theoretical framework that affects the policy process from the original data.

1.5 Research route and research content

This thesis focuses on the research question and conducts the research work according to the research method. The research route is as follows:

a) Raise questions

Firstly, the research background is described based on the challenges faced in promoting the implementation of the parametric release policy in China, and the related concepts and research objects are defined.

b) Literature review

By referring to the literature, we first summarized the status of policy research and implementation. Then, the stakeholder research method and policy entrepreneur theory adopted in this study are thoroughly researched, and the theories involved in this study are reviewed according to the questions raised in the first step.

c) Develop an interview guide

The semi-structured interview guide was designed and determined based on the literature review. The interview guide quality was tested through pre-interview and adjusted according to feedback to form the final guide.

d) Data collection

Data is collected through interviews with selected stakeholders, and the interview text is

formed.

e) Data analysis

Data analysis was carried out on all the interview results. Firstly, a saturation test was carried out. Secondly, correlation analysis was carried out on the data through grounded theory, and theoretical construction was obtained through coding to form the theory.

f) Conclusions and prospects

The results are discussed, the academic and practical significance of the research is summarized, and the research limitations and future research directions are proposed.

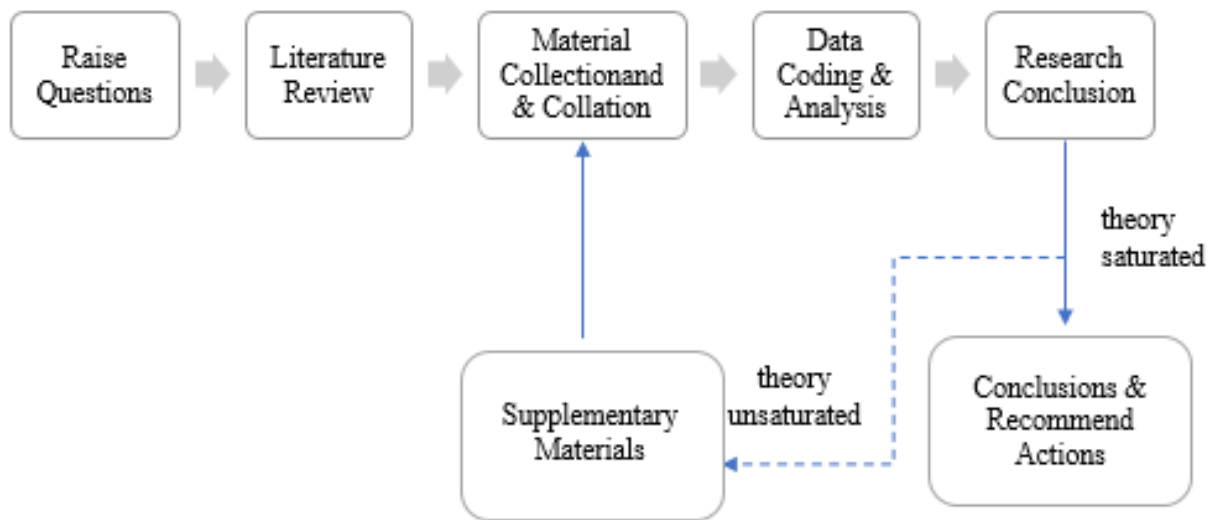


Figure 1.2 Research route and content

1.6 Research contribution

Starting from the practice and problems faced by the promotion of parametric release policy in China, the study introduces the perspective and methods of stakeholders in the research field of innovation policy setting and diffusion in public policy. From the perspective of policy entrepreneurs, it explores the coordination and conflict factors of policy promotion based on the perspective of stakeholders, to propose a theoretical framework for policy entrepreneurs to drive policy innovation.

Existing studies have focused on the role of entrepreneurs in promoting policy innovation, summarized, and classified how entrepreneurs influence policy innovation, however few studies have observed the conflicts and value trade-offs that entrepreneurs may face when promoting policy from the perspective of multi-subject interest interaction, as well as their influencing factors. There are two innovations in this study: First, innovation in cross-field research: introducing stakeholder theory into the field of policy innovation research, exploring

the views of multi-subject stakeholders, including regulators, industry experts and scholars on the implementation of parametric release through in-depth interviews, and comprehensively analyzing the influencing factors of parametric release implementation in China from multiple perspectives, breaking the limitations of traditional policy innovation research ideas and methods; The second is the perspective innovation of policy research: by introducing the theory of multiple stream policy agenda setting model, the problem stream, political stream and policy stream are analyzed, and the driving path of parametric release policy promotion is constructed from the perspective of policy entrepreneurs.

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Chapter 2: Literature Review

Based on the research content, this study first summarizes the current status of policy research and implementation. Then, it chooses to summarize the stakeholder theory and the policy entrepreneur theory. Regarding stakeholder theory, it discusses the basic concept of stakeholders, their identification and classification, their application in the field of medicine and health, their application in public policy/health policy, and the development of stakeholder theory in China. The policy entrepreneur theory, it reviews the policy science, policy process, policy innovation related to public policy, and the development and application of the multiple streams theory of policy entrepreneur. The literature review includes relevant literature from both China and abroad.

2.1 Current status of policy research and implementation

From SFDA (2003), we know that from the 1960s to 1970s, in the U.K and USA, contamination of large volume parenterals (LVPs) caused many serious adverse events, resulting in patient injury and even death. For instance, a severe adverse drug event occurred in 1972 in Devonport, England, where the contaminated glucose infusion caused the death of six people due to Sepsis. In 1976, according to the U.S. General Accounting Office, between 1965 and 1975, there were more than 600 recalls of LVPs due to quality problems, reported 410 injuries and 54 deaths. FDA had set up a special team to investigate these incidents. The results show that the sterility test before production release is qualified for all the relevant products batched. However, the actual cause for that is the sterilization equipment and sterilization process imperfection. Therefore, the uncontrolled production process is the main cause of contamination. After the investigation, the FDA concluded that products need sterility tests, however the testing results cannot 100% ensure product quality. After that, the FDA and industry realized that process control of production is more important than the final sterility test result. Process control began to be emphasized then.

In 1978, FDA published the “Current Good Manufacturing Practice in the Manufacture, Processing, Packing, or Holding of Large Volume Parenterals for Human Use”. Putting forward the idea that verifying the production process, especially the sterilization process, is more critical in the case of ensuring injection products meet sterility requirements. From this point

of view, drug regulators began to focus on the limitations of sterility tests.

At the same time, the quality management system of the pharmaceutical industry has gradually developed and improved. In the 1980s, scholars in the USA found the sterility test's limitations. When choosing twenty samples to test (twenty is the routine sample size prescribed by pharmacopoeia), if the product has a bacterial contamination rate of 1%, there is an 82% chance that the sterility test will fail to detect 1% of the contaminated products, which could mistakenly release to market. If the proportion of infected bacteria is lower, it is more challenging to see by sterility test (Shang et al., 2022). Therefore, the sterility test result can only partially prove the sterility of the whole batch of products and the probability of non-sterile units of 1 in 10^6 units. It should rely on rigorous sterilization verification and process control. In January of 1985, the FDA approved about 40 products of Baxter's parenteral injection and peritoneal dialysate for the first time for parametric release, and it has been 38 years since then.

2.1.1 The concept of parametric release

The U.S. Food and Drug Administration Compliance Regulatory Guide "CPG Sec. 490.200 Parametric Release of Parenteral Drug Products Terminally Sterilized by Moist Heat" defined parametric release as a "sterility assurance release program which demonstrated control of the sterilization process enables a firm to use defined critical process control data, in lieu of the sterility test, to fulfill the intent of 21 CFR 211.167(a)".

USP <1222> Terminally Sterilized Pharmaceutical Products-Parametric Release defines parametric release as the "release of terminally sterilized batches or lots of sterile products based upon compliance with the defined critical parameters of sterilization without having to perform the requirements under Sterility Tests<71>. Parametric release is a possibility when the mode of sterilization is very well understood, the physical parameters of processing are well defined, predictable, and measurable, and the lethality of the cycle has been microbiologically validated using appropriate biological indicators or, in the case of ionizing radiation, the appropriate microbiological and dosimetric tests". Adopting parametric release needs prior FDA approval. Pharmaceutical companies need to prepare a list of documents, including the sterilization process and validation data, that could ensure the sterile of marketed products will meet the sterility requirements. Pharmacopoeia sterility tests methods have limitations in statistics and sensitivity. At the same time, parametric release uses process control methods to pre-empt risk control measures for such products, ensuring the sterile quality of products to the greatest extent (Shang, 2021).

2.1.2 Overview of parametric release implementation in the USA

In 1987, the FDA promulgated CPG 7132a.13, a regulatory compliance guideline to guide FDA reviewers and inspectors to conduct data review and on-site inspection of parametric release applications.

In 1999, the Parenteral Drug Association (PDA) took the lead in formulating the TR-30 technical report to guide the implementation of parametric release. TR-30 has an updated version in 2012. Afterwards, global pharmaceutical companies began to carry out parametric release work regarding TR-30.

In 2010, FDA promulgated “Guidance for Industry for the Submission of Documentation in Applications for Parametric Release of Human and Veterinary Drug Products Terminally Sterilized by Moist Heat Processes”. Companies use this document guide to prepare application materials for parametric release.

In 2012, the FDA revised the CPG 7132a.13 promulgated in 1987, and the update number is CPG 490.200 Parametric Release of Parenteral Drug Products Terminally Sterilized by Moist Heat.

USP <1222> clarifies that sterility tests have sensitivity and statistical limitations and are not suitable for terminal sterilization of products subject to low contamination levels. The basis of parametric release is to prove that the process conditions related to the product's critical quality attributes can be achieved and maintained during the production process, and the sterility tests of the final product can be replaced by process control for sterile quality.

PDA TR-30 technical report “Parametric Release of Pharmaceutical and Medical Device Products Terminally Sterilized by Moist Heat” defines parametric release in detail and provides an Enterprise Application Guide. The main content includes a) Elements of parametric release procedures: quality risk management, personnel, product design, production process design (product bioburden monitoring, product isolation, sterilization system design and sterilization process considerations), and biological indicator test. b) Process development: definition of loading, determination of operating parameters. c) Equipment confirmation and process verification. d) Continuous process monitoring: loading release, change control, reconfirmation, and revalidation, and planned preventive maintenance. e) Submitted documents: risk assessment summary, sterilization process description, manufacturing process description, sterilization process validation summary, sterile product release procedures, and previous manufacturing experience for risk assessment.

2.1.3 Overview of parametric release implementation in the EU

European Pharmacopoeia <1.1> specifies that testing of final products may be replaced by Process Analytical Techniques (PAT) and/or real-time release testing, including parametric release.

In 2002, the EU Committee for Medicinal Products for Human Use (CHMP) began implementing GMP Annex 17 “Parametric Release for terminally sterilized sterile pharmaceutical products”. In 2009, the European Union hoped to extend the scope of parametric release to other drug dosage forms. It released the “Guideline on Real Time Testing Release”, which came into effect on October 1, 2012. On September 15, 2015, the European Commission intended to replace the 2002 GMP Appendix 17 Parametric Release and released the Good Manufacturing Practices for Medicinal Products for Human and Veterinary Use. GMP Appendix 17 “Real-time Release Test (Draft for Comment)”. The revision was finally officially released in 2018 under the name Real Time Release Testing and Parametric Release based on PAT, QbD, and Quality Risk Management principles in drug development and manufacturing have shown that combining process control with timely monitoring and verification of pre-established material properties can provide greater assurance of product quality than testing of finished products alone, thus the scope of application of GMP Appendix 17 was expanded to include other pharmaceutical preparations such as solid oral preparations.

2.1.4 Overview of parametric release implementation in Japan

In 1997, Japan began to use parametric release instead of sterility testing for sterile medical devices using moist heat sterilization, electric radiation sterilization and other sterilization methods.

In 1999, to study the application of parametric release in sterile drugs, Japan began to implement the ICH Q6A guidelines. In 2001, the Japanese Pharmacopoeia (JP) clarified that when a high level of sterility assurance is continuously maintained, the sterility tests usually required for product release can be omitted based on the research on the validation of the production process and the records of process control. The JP chapter “Sterility Assurance of Terminally Sterilized Drug Products” defines parametric release as a release procedures based on production records of validation results and evaluation of key parameters of the sterilization process, rather than release based on finished product sterility tests results (Sasaki, 2002).

In 2016, parametric release of terminally sterilized drug was officially included in the JP as guiding principles for implementing the parametric release of sterile drugs that adopt moist heat

sterilization and irradiation sterilization processes in the industry. In 2019, Japan joined the PIC/S. PIC/S already has relevant parametric release guidelines. Thus, the parametric release of terminally sterilized drugs was deleted from the Supplement (II) of the JP. Afterwards, the general requirements of real-time release and parametric release were introduced in the chapter G10 Other Changes: Basic Concepts of Quality Assurance of APIs and Preparations. It indicates that parametric release is the release of the finished product based on the parameters of the sterilization process rather than the sterility test results. The use of parametric release of the product is more reliable regarding sterility assurance than release using limited samples for sterility tests. When the process parameters of parametric release do not meet the set requirements, the product cannot be released based on the result of the sterility tests of the finished product. In addition, even if parametric release is adopted, the stability study and post-market random inspection still require the sterility test of the product.

2.1.5 Overview of parametric release implemented by other international organizations

On October 6, 1999, ICH released Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, indicated in Section 2.6 that, subject to approval by the regulatory body, parametric release may replace routine release sterility test. The release of each batch depends on satisfactory monitoring of specific parameters such as temperature, pressure, and time of the terminal sterilization phase. These parameters can be more precisely controlled and determined. Thus, they are more reliable in judging sterility assurance than the results of the sterility test of the final product.

In September 2007, PIC/S released the Guidance on Parametric Release, focusing on training GMP inspectors to conduct facility inspections on those companies using parametric release. The guideline emphasizes the use of risk assessment tools, such as Failure Model & Effects Analysis (FMEA) and other methods for risk assessment and control.

2.1.6 Introduction of research and pilot work of parametric release in China

China began to research parametric release in 2002. On March 1, 2005, the former SFDA issued the “Notice on Carrying out the Pilot Work of Parametric release”, approving Wuxi HuaRui, and Guangzhou Baxter to conduct pilot work. The approval period is from March 1, 2005, to February 28, 2007, and the products are mainly LPVs that are terminally sterilized by moist heat. In July 2007, the former SFDA issued another “Notice on Continuing the Parametric Release Pilot Work”, agreeing that the two companies mentioned above continue to carry out

the pilot work of parametric release from July 1, 2007, to June 28, 2010.

After the pilot work, the two companies submitted the summary report to the former SFDA via the provincial Food and Drug Administration. On December 11, 2012, the former State FDA pointed out that parametric release is essential for strengthening production process control and ensuring product quality. In addition, General Electric Pharmaceuticals (Shanghai) Co., Ltd. applied for the parametric release of two varieties to the U.S. FDA in 2011 and got approval in March 2013. Three companies have accumulated a wealth of pilot data and experience.

Since 2013, with the experience of pilot work, industry associations and some experts have conducted the comprehensive study on all aspects of parametric release in different stages and reached a conclusion on the feasibility of implementing parametric release in China.

Since 2013, with pilot work experience, industry associations and some experts have conducted a comprehensive study on all aspects of parametric release in different stages.

From 2013 to 2017, the China Pharmaceutical Association of Plant Engineering (CPAPE) gathered experts to work together, translating the parametric release related technical documents and the publication of monographs. It lays a theoretical foundation for parametric release policy research.

In 2018~2020, the China Quality Association for Pharmaceuticals (CQAP) organized experts to suggest amendments to the regulations and provisions of the 2019 Drug Administration Law. Before that, products must have a tests result when released from the factory. On July 1, 2020, they issued and implemented the first group standard of Parameters Release Requirements for Moist Heat Sterilization Sterile Products in China and that implemented on October 1, 2020, to guide manufacturers to use parametric release of final moist heat sterilization products.

2020~2021, the China Society of Drug Regulation (CSDR) has done a feasibility study on the implementation of parametric release, elaborated on the feasibility of implementing parametric release from the aspects of regulatory feasibility, technical feasibility, and industry-level feasibility, and put forward policy recommendations to the State Drug Administration.

2020~2022, the CQAP and the China National Pharmacopoeia Committee conducted relevant research to explore the inclusion of the content related to parametric release in the form of guiding principles in the 2025 version of the Chinese Pharmacopoeia.

China's research and pilot work on parametric release began in 2002, which has been 21 years till now. 2023 is the 25th anniversary of the reform of the modern drug regulatory system. The research period on parametric release has coincided with the regulatory system change. In the past 25 years, the drug regulatory system of China has had four iterations. In 1998, an

independent State Drug Administration (SDA) was established, and drug regulation in China is under province-vertical management. In 2003, the SFDA was established and supervised by the State Ministry of Health. China Food and Drug Administration (CFDA) was founded at the ministerial level in 2013, and the central government stressed the perfection of a unified and authoritative drug safety regulatory organization. In 2018, the Party and State institutions thoroughly considered the uniqueness of drug regulation and established NMPA based on drug safety. Overall, the structure of drug regulatory system of China has changed along with its functions. When a specific goal becomes the theme of that era, the drug regulatory system will adjust accordingly (Y. L. Hu, 2023). Frequent institutional reform and personnel turnover are one of the reasons why the parametric release has yet to be formally adopted.

2.2 Stakeholder theory

2.2.1 Basic concepts and characteristics of stakeholder theory

Stakeholder theory can be traced back to Barnard (1938), who articulated value creation and trading issues, capitalist ethics, and management thinking patterns in his writings. His ideas have provided a solid foundation for the development of modern stakeholder theory. This theory developed gradually since the 1960s, and its influence expanded rapidly after the 1980s. It began to influence the choice of corporate governance model in the United States, Britain, and other countries, and promoted the transformation of enterprise management mode.

Penrose (1959) made a point that an enterprise is the collection of human capital and interpersonal relationship, and that would lay the foundation for stakeholder theory. Till 1963, Stanford Research Institute clearly raised their definition of stakeholder theory, stating that Stakeholders are groups without which the organization cannot survive. This definition is not comprehensive today, it only considers the single impact from stakeholder to enterprise. And the scope of stakeholders is limited. But it pointed out that there were other communities that will impact the firm in addition to shareholders (Freeman et al., 2013). Later, Rhenman (1968) put forward a comprehensive definition in his research on industrial democracy, which is that the stakeholders rely on enterprises to realize their personal goals, and enterprises also rely on them to maintain their survival. This definition makes the stakeholder theory become an independent theoretical branch.

Ansoff (1965) first introduced the term into the management and economics circles, arguing that when developing an ideal enterprise goal, conflicting claims must be balanced among many

enterprise stakeholders, including managers, workers, shareholders, suppliers, and distributors.

In the following 30 years, there were more than 30 definitions of stakeholders, and scholars defined stakeholders from different perspectives. Edward Freeman, probably the most representative of the scholars, put forward a general definition of stakeholder, which is that stakeholders are the ability to influence to achieve the goals of an organization, or is affected by an organization to achieve its goal of all individuals and groups (Freeman, 1984). For the first time, Freeman included the individuals or groups affected by actions taken in the process of achieving corporate goals in the stakeholder system and officially put the community, government, environmental groups and other entities into the research category of stakeholder management, greatly expanded the connotation of stakeholders, and therefore becomes the highest frequency definition as the researchers used (Lin, 2010).

Freeman and Mcvea (2001) summarized the distinguishing characteristics of stakeholder approach, he believes that the interests of key stakeholders must be integrated into the firm's purpose, and stakeholder relationships must be managed in a coherent and strategic manner. The stakeholder approach developed from this work has several distinct characteristics. First, the stakeholder approach aims to provide a single strategic framework that can respond flexibly to environmental changes without requiring managers to often adopt new strategic paradigms because of environmental changes. Second, the stakeholder approach is a strategic management process, not a strategic planning process. The focus of strategic planning is to try to anticipate the future environment and then develop plans independently so that the company can play to its strengths. In contrast, strategic management actively charts a new direction for the company, considering how the company affects the environment and how the environment affects the company. Third, the central concern of the stakeholder approach is the survival of the company, which, in Freeman's words, is "achieving an organization's goals". To survive in a volatile environment, management must give direction to the company, not just optimize existing outputs. To successfully change direction, management must have the buy-in of those who can influence the company and understand how the company will influence others. Therefore, understanding stakeholder relationships is at least a matter of achieving organizational goals, which in turn is a matter of survival. Fourth, the stakeholder approach encourages management to strategize by looking outward from the company's perspective, identifying, and investing in all relationships that will ensure the company's long-term success. From this perspective, there is a key value and "value-based management" in the business strategy. As the business world becomes more volatile and interconnected, the lines between businesses and industries, public and private life are blurred, and the stakeholder approach is increasingly telling us about value

and value creation. Fifth, the stakeholder approach is both normative and descriptive, rather than purely empirical and descriptive. It requires a strategic approach to the management that integrates economic, political, and ethical analysis. Sixth, the stakeholder approach is about specific “names and faces” of stakeholders, rather than just analyzing specific stakeholder roles.

Therefore, it is important to understand the real, specific stakeholders for the company, as well as the environment in which it operates. According to this approach, good strategic management should emerge from the details, not from the general and theoretical. Finally, stakeholder management requires an integrated approach to strategic decision-making. Managers must find ways to satisfy multiple stakeholders at the same time, rather than strategizing for each stakeholder on a stakeholder basis.

Clarkson (1995) introduces the concept of specific investment to make the definition of stakeholders more specific. The following Table 2.1 summarizes the representative stakeholder definitions.

Table 2.1 The definition of stakeholder

Authors	Definition of stakeholder
Stanford University (1963)	Stakeholders are groups without whose support an organization cannot survive
Rhenman (1964)	Stakeholders depend on the business to achieve their personal goals, and the business depends on them to survive
Ahlstedt & Jahnukainen (1971)	Stakeholders are the participants of an enterprise. They are driven by their own interests and goals, so they must rely on enterprise. In order to survive, enterprises must also rely on stakeholders
Freeman (1983)	Broader definition: Stakeholders can influence an organization's goals by thinking about it, or they themselves are influenced by an organization's process of achieving its goals Narrower definition: Stakeholders are those on whom an organization must rely in order to achieve its goals
Freeman (1984)	A stakeholder is a person who can influence the realization of an organization's goals or is influenced by the process by which an organization achieves its goals
Freeman & Gilbert (1987)	A stakeholder is a person who can influence or be influenced by an enterprise
Cornell & Shapiro (1987)	Stakeholders are the claimants who have contractual relations with the enterprise
Evan & Freeman (1988)	A stakeholder is a person who “makes a bet” or has a claim on the business
Evan & Freeman (1988)	Stakeholders are those who benefit or suffer from the activities of the company; They are violated or respected for their company's activities
Bowie (1988)	Without their support, the organization could not survive
Alkhafaji (1989)	Stakeholders are those for whom the business is responsible
Carroll (1989)	A stakeholder is a person who makes one or more bets in a business and who can exercise earnings and (legal or moral) rights in the name of ownership or law over the assets or property of the business
Freeman & Evan (1990)	Stakeholders are those who have contractual relationships with the business

Authors	Definition of stakeholder
Stanford University (1963)	Stakeholders are groups without whose support an organization cannot survive
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Thompson etc. (1991)	A stakeholder is a person associated with an organization
Savage etc. (1991)	The interests of stakeholders are affected by the activities of the organization... And they also have the ability to influence the organization's activities
Hill & Jones (1992)	A stakeholder is a group that has a legitimate claim to a business and establishes its relationship through an exchange in which they provide critical resources to the business in exchange for the satisfaction of a personal interest goal
Brenner (1993)	Stakeholders have some legitimate and unusual relationships with an organization, such as transactional relationships, behavioral impact, and moral responsibility
Carroll (1993)	Stakeholders put in one or more forms of "bets" and they may influence or be influenced by the activities of the business
Freeman (1994)	Stakeholders are participants in the process of joint value creation
Wicks etc. (1994)	Stakeholders are associated with the enterprise and give the enterprise a certain meaning
Langtry (1994)	Stakeholders have moral or legal claims on the enterprise, and the enterprise bears obvious responsibility for the welfare of stakeholders
Starik (1994)	Stakeholders may or are placing a real "bet" on the business, and they can be significantly or potentially affected by the business's activities
Clarkson (1994)	Stakeholders have invested some physical capital, human capital, financial capital or something valuable in the enterprise, and thus take some forms of risk, or they take risks because of the enterprise's activities
Nasi (1995)	Stakeholders are the people connected to the business who make it possible to run the business
Brenner (1995)	Stakeholders can influence the enterprise and are affected by its activities
Donaldson & Preston (1995)	Stakeholders are individuals and groups that have a legitimate interest in the process and activities of the company

Source: Mitchell et al. (1997); Sheng (2009)

2.2.2 Stakeholder identification and classification

Stakeholder should be prioritized since the influence of different types of stakeholders on the management decisions of enterprises and the degree to which they are affected by enterprise activities are different (H. Chen, 2004).

Freeman (1984) believed stakeholders influence enterprises different due to different resources. He classified stakeholders into three aspects: 1) ownership stakeholders, such as board members and managers, are those who hold company shares. 2) relevant groups that have

economic contact with the company, such as employees, creditors, internal service organizations, consumers, suppliers, competitors, local communities, and management structure, are called economically dependent stakeholders; 3) stakeholders related to the social interests of the company, such as government agencies, media, and special groups, are called social stakeholders.

Frederick (1988) divided stakeholders into direct and indirect ones according to how they influence the enterprise. Charkham (1992) divided stakeholders into contractual and public stakeholders according to whether relevant groups had contractual relationships with enterprises.

Donaldson and Preston (1995) provide a systematic analytical framework for stakeholder research. They divide stakeholder theory into three aspects: descriptive, instrumental, and normative. Among them, a) descriptive stakeholder theory explains how organizations actually consider stakeholder interests, or describes, and sometimes to explain, specific corporate characteristics and behaviors. b) The instrumental stakeholder theory considers whether it is beneficial for an organization to engage with its stakeholders. c) Normative stakeholder theory focuses on why organizations should consider stakeholder interests. In this branch of theory, companies focus on stakeholders not because of what the outcome will be, but because the act of focusing on stakeholders is itself ethically necessary. Mitchell grading method was proposed by Mitchell et al. (1997). It combines the definition and classification of stakeholders. Firstly, all stakeholders of an enterprise must possess at least one of the following three attributes: legitimacy, power, and urgency. According to their ratings of stakeholders from these three aspects, stakeholders of enterprises are divided into three types according to their scores. a) fit for the three attributes is the definitive stakeholders; b) fit for two attributes is the expectant stakeholders; c) fit for one attribute is the latent stakeholders, as presented in Figure 2.1. The Mitchell score-based approach, which can be used to judge and define the stakeholders of enterprises, is relatively simple to operate, which is a great progress of stakeholder theory (Mitchell et al., 1997). The composition of stakeholders is dynamic. Different stakeholders can transform with the change of condition (Chu, 2004).

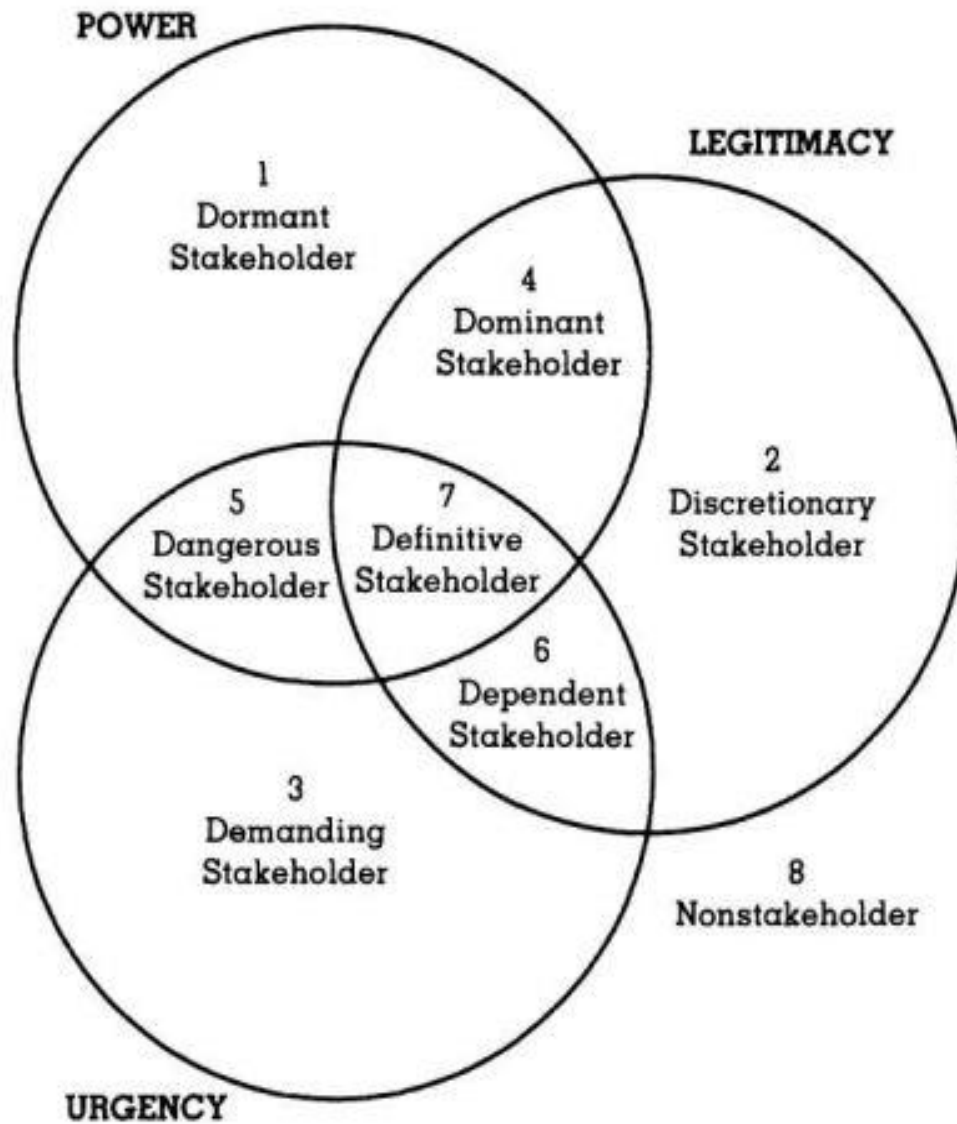


Figure 2.1 Stakeholder salience model

Source: Mitchell et al. (1997)

The stakeholder salience model research has been ongoing and continuously developed. Best et al. (2019) studied stakeholder salience in public sector value co-creation by studying the key determinants of stakeholder salience and the impact of stakeholder salience on public sector value co-creation at different stages and different service scenarios. This work adopts the definition of stakeholder salience as the degree to which managers prioritize competing stakeholder claims (Mitchell et al., 1997). He raised twofold research questions about what are the key determinants of stakeholder salience in public service networks? And how does stakeholder salience affect value-co-creation within the public service network at different stages and levels of service contexts (Best et al., 2019).

Jensen (2002) says that many managers are caught in a dilemma: between a desire to

maximize the value of their companies and the demands of “stakeholder theory” to consider the interests of all the stakeholders in a firm. If a firm ignores the interests of its stakeholders, it cannot achieve value maximization. But because the advocate stakeholder theory refuses to specify how to make the necessary trade-offs between these competing interests, it prevents managers from making purposeful decisions. He argues that the way out of conflict lies in a new way of measuring value. Based on this, Jensen proposed the enlightened stakeholder theory, and he believed that it was necessary to integrate a new interpretation of value maximization and stakeholder theory and specify long-term value maximization or value pursuit as the goal of the company, to solve the problem caused by multiple goals in traditional stakeholder theory.

Chen (2004) put forward the concept of core stakeholders based on stakeholder research, that is in any enterprise, it is inseparable from the three types of personnel, shareholders, managers and employees, and as direct participants in the operation of the enterprise, their interests must be closely related to the enterprise. In any case, they should be considered as core stakeholders of the business. Through empirical research, he applied the Michelle scoring method to define the core stakeholders as shareholders, managers, and employees, which are closely related to the enterprise and deeply affected by the development of the enterprise, from the three dimensions of stakeholder initiative, stakeholder importance and stakeholder interest requirement. This view is based on the need to find a balance between maximizing shareholder value and balancing all stakeholders.

Rowley (1997) analyzes enterprise stakeholder management from a network perspective. The network perspective does not focus on the attributes of the actors themselves, nor does it focus on the relationship between actors in isolation, but emphasizes that the basic focus of enterprise stakeholder management is the relationship between the enterprise and its stakeholders, and restores this relationship to the stakeholder network it is embedded, and pays attention to the impact of the structure of the network on the behavior of the enterprise and its stakeholders.

Stakeholders are embedded in the relationship network, and according to the size of stakeholders' interests and needs and the level of influence power, by building an interest impact matrix, determining the position of stakeholders in organizational activities or management decisions, to determine the participation of various stakeholders (Guan, 2021).

2.2.3 Application of stakeholder theory in public policy/health policy

Although the stakeholder theory is most widely used in business, it has been gradually discovered the value in the research of other disciplines, and it is especially important for the study of organizations. For example, it has been widely used in law, public administration, health care, health policy, and broader public policy.

The core of public policy is the issue of interests (Jin, 2016). Vedung (1997) from Sweden was the first to introduce the concept of stakeholders into the Policy field. In his book “Public Policy and Program Evaluation”, he discussed the Policy Evaluation Model from the perspective of stakeholders for the first time.

Dunn (1981) defines policy stakeholders as individuals or groups of individuals who have a stake in policy and who influence or are affected by government decisions. Examples include citizens, policymakers, dissidents, officials, intermediaries, users, academics, and stakeholders in the wider environment (Vedung, 1997). The traditional government management model is government-centered, policies are made by the government, and citizens can only passively accept it. With the advancement of science and technology and the development of the economy, people pay more attention to civil rights, and the stakeholder theory provides a good framework for the government to balance the interests of multiple subjects in public management (Y. Li et al., 2006).

In a review article, Brugha and Varvasovszky (2000) tracked the impact of stakeholder theory in the health policy and broader public policy literature. The author has found some of the roots of stakeholder theory in his public policy work, describing it as a method for policy analysis, which makes this article a good turning point for reviewing the public policy literature. In terms of how the term is used in the health care and health policy literature, they emphasize the precise use of the term stakeholder analysis and distinguish it from other forms of analysis. In their view, much of the literature on health policy emphasizes on the retrospective or synchronous analysis of health policy formulation in different contexts. In contrast, stakeholder analysis is more forward-looking, systematic, and structured than other tools used by researchers in this area. For them, stakeholder analysis should only be used for the systematic analysis of the roles, relationships, interests, and influences of stakeholders (Brugha & Varvasovszky, 2000).

Brugha and Varvasovszky (2000) identified the historical and conceptual basis of stakeholder analysis in the public policy literature. For them, policy analysts have long been aware of the importance of interest groups in the policy process, as well as the delineation and

classification of interest levels and powers that are needed to impact a particular policy. In the context of this literature, stakeholder analysis becomes one of a series of potential tools for thinking about the groups that make up, power, and management for achieving goals.

Bryson (2004) provides a continuing discussion of stakeholder theory, particularly the detailed progress of specific stakeholder analysis techniques. He mentioned the importance of defining stakeholders and how they can be considered stakeholders. In his opinion, stakeholder theory should not only focus on those stakeholders who have power or are easy to identify but also urge to consider a broader range of people, groups, or organizations, including those who are nominally powerless. Bryson also provided a set of thinking methods for stakeholder analysis and relevance, as well as specific methods that can contribute to the process of public sector management.

Friedman and Mason (2005) discussed stakeholder analysis and stakeholder management and their utility and think thoroughly about important public policy decisions from this perspective. Friedman and Mason (2004) followed the four-step process outlined earlier by. a) drawing a preliminary schematic of the core stakeholders; b) modify its schematic diagram to adapt to the background environment of specific events and the particularity of stakeholders involved; c) conduct event analysis to understand how focus stakeholders manage to gain support and reduce dissent; d) reassess important events and stakeholders over time to reflect changing circumstances. The case study emphasizes the importance of stakeholder analysis systems for more efficient and effective factor management (Friedman & Mason, 2005).

Frederick (1988) divides public policy making into four phases, including changing stakeholder expectations, political action, legislative/regulatory action, and legal implementation (see Figure 2.2).

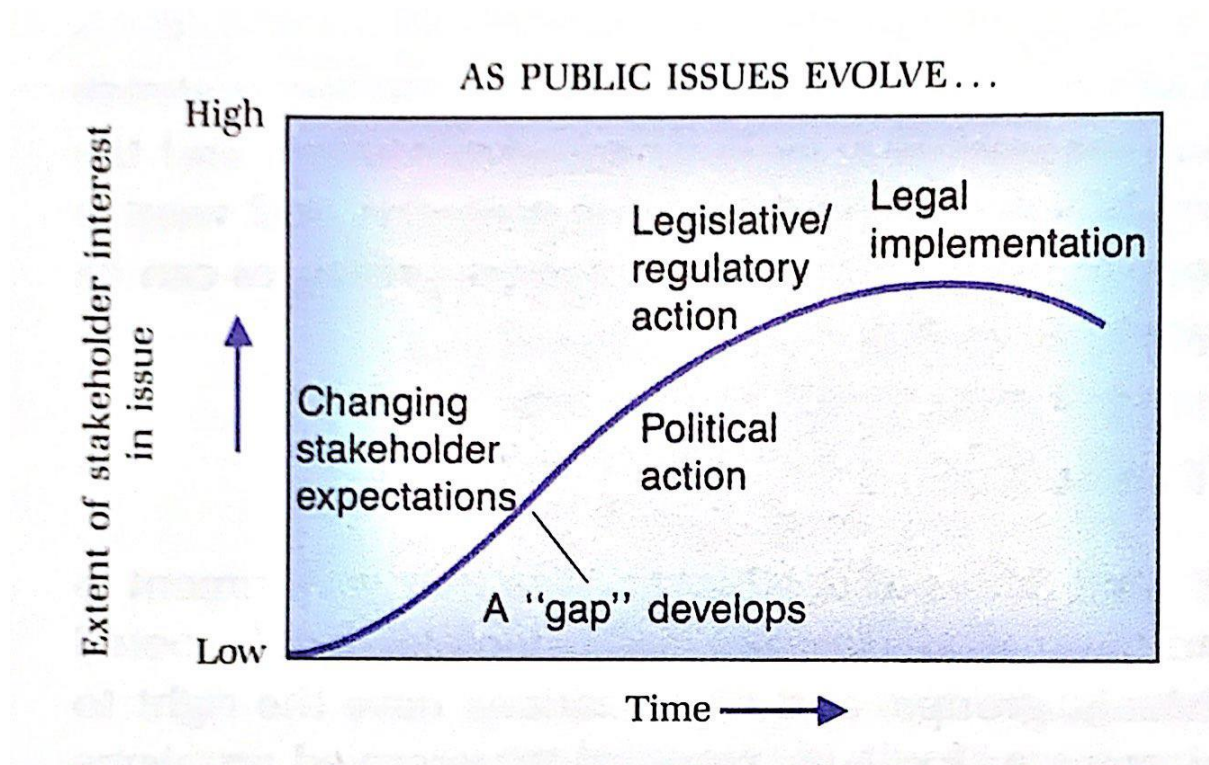


Figure 2.2 Phases of the public issues life cycle

Source: Frederick (1988)

Provan and Milward (2001) uses stakeholder theory to analyze organizational networks in the public sector. They point out that how to think about organizational networks, and the multi-level analysis involved, presents a significant challenge for researchers. At the same time, they believe that such intra-network cooperation in the public sector is an important development that deserves the attention of scholars.

2.2.4 The application of stakeholder theory in the field of medicine and health

Although Freeman's book was widely cited in 1984, most of the healthcare literature rarely cites the stakeholder literature on business ethics. Blair and his team devoted themselves to the study of stakeholder theory, which was marked by an instrumental article written by (Blair et al., 1996). They argue that healthcare has evolved and that executives within healthcare organizations need to pay attention to who the key stakeholders are, especially since key stakeholders are changing at an unprecedented rate and are likely to continue to change. Blair et al. mentioned in their article that the degree and speed of structural changes in the industry have been unprecedented in post-industrial society. Given this background, they focus on properly classifying stakeholders and adopting appropriate management strategies to treat these stakeholders. They claim executives should classify stakeholders in one of the four kinds of populations, which are supporters, a mixed blessing, non-supporters, and peripheral individuals.

In addition, they should take generic strategy to manage them in participation, collaboration, defense, and monitoring.

Taking the stakeholder theory as the context of an analysis tool, Blair and Fottler (1990) defined the process of stakeholder management as the development process of a strategic analysis tool. They identified six discontinuous phases: a) stakeholder identification, b) stakeholder assessment, c) stakeholder diagnosis and classification, d) stakeholder strategy formulation, e) stakeholder strategy implementation, and f) stakeholder management effectiveness evaluation. Dymond et al. (1995) based on the above work, emphasized stakeholder assessment in empirical research (Stage 2). In subsequent research, Blair and Buesseler (1998) investigated a range of issues regarding the opportunities and threats faced by management stakeholders in a changing environment, with the focus on providing accuracy in the analysis of forces in the industry. They used Porter's five Forces model and applied it to stakeholder analysis. Porter emphasizes the role of power, while they claim that cooperation is as important as power in determining how stakeholders will behave.

Savage et al. (1997) emphasized the importance of network and systems theory as a way of thinking about healthcare. They take a stakeholder theory perspective to understand the dynamics of complex operations in healthcare. The deeper assumption of this study is that the existence of stakeholders is both an opportunity and a threat, and that managers need to shift from emphasizing the management of individual stakeholders to considering multiple relationships, and that managers manage stakeholders for the benefit of the organization.

As one of the world's most authoritative drug and medical technology evaluation agencies, the National Institute for Health and Clinical Excellence (NICE) not only draws on the opinions of a large number of medical experts, pharmaco-economics experts, health care practitioners and other relevant professionals in the process of formulating health care standards, but also actively attracts the participation of government officials, academics, patients, other stakeholders and other groups. NICE sets out the conditions and procedures for becoming a stakeholder so that relevant stakeholders can be effectively involved in the development of the guidelines. The participation of a large number of participants has increased the transparency of NICE, facilitated the development of more reasonable guidelines that meet the needs of all parties, and facilitated the implementation of the guidelines. This is a classic success story of stakeholder engagement in the field of health policy (Lu, 2010).

Q. B. Wang et al. (2016) said in their analysis of the dynamics and resistance of China's graded diagnosis and treatment system that stakeholders' attitudes and behaviors towards a policy are mainly affected by the degree of interest correlation and policy influence. Those with

a strong degree of interest correlation and strong policy influence not only have strong interest demands, but also have considerable power and enforcement power, so they are active implementers of policies. Those who have a weak degree of interest correlation but strong policy influence, although their interests are average, but their power is large, and they are the key force for the effective implementation of policies, so they need to win their support and try to satisfy them in the process of policy implementation, or at least ensure that their interests will not be damaged in the implementation process, otherwise there may be games and competition between departments. Those with a strong degree of interest correlation but not strong policy influence, although the interest appeal is very strong, but the influence is relatively limited, so they are in a relatively weak position, and generally adjust their behavior according to the policy orientation to maximize their own utility as much as possible. For those who do not have a strong degree of interest correlation and policy influence, they do not have huge interest demands to force them to participate in the policy process, nor will they have a decisive impact on the policy process, but only selectively participate in certain links in the process of interaction with other stakeholders according to their own development strategies. Similarly, the promotion and obstruction of a policy by stakeholders are mainly reflected in the degree of interest correlation and the willingness to implement the policy. When both are strong, it shows that the policy objectives are generally in line with the interests of various stakeholders and show that there is a motivation to promote the realization of the policy objectives; Conversely, stating that the policy objectives are not in the interests of the various stakeholders may be an impediment to the implementation process. Whether policy objectives can be achieved, and expectations will be met depends largely on the dynamic balance between drivers and obstacles.

2.2.5 Evaluation of stakeholder theory

Stakeholder theory has been vigorously developed since the Freeman period, and in the past 40 years, stakeholder theory has been widely used in corporate governance, politics, economics, law, and other fields.

Integrating stakeholders into corporate governance allows companies to focus more on long-term goals and sustainable development, rather than focusing only on short-term benefits because of the goal of maximizing shareholder value. At the same time, because the interests of stakeholders are maintained, they in turn will pay more attention to the development of enterprises, thereby reducing supervision incentive costs and opportunistic behaviors, and they form a long-term stable cooperative relationship based on trust with enterprises, which will

greatly reduce transaction costs and costs due to information asymmetry. Finally, good reputation, unique organizational culture and long-term and stable cooperative relations with customers and suppliers form intangible, valuable, difficult for competitors to imitate or directly obtain assets, and these assets enable enterprises to create advantages over competitors and form the core competitiveness of enterprises.

But at the same time, there are different voices on stakeholder theory. Friedman (1982) believes that a business has only one social responsibility, it uses its resources, according to the rules of the game, to engage in activities that increase profits. The goal of maximizing the interests of multiple stakeholders can confuse the enterprise, and the cost incurred by the enterprise due to social responsibility may be passed on to consumers by increasing the price of the product. To meet the needs of consumers, enterprises increase R&D investment and reduce product prices, which may also cause short-term damage to the interests of shareholders. The interests of stakeholders are difficult to balance. American scholars Josephine Matterby and Louis Wilkinson have commented that the corporate stakeholder theory is only a “flashy” theory that cannot be operated (H. Wang & Jiang, 2007).

Although it may seem different in perspective, Freeman and his team argue that Friedman’s view of maximizing shareholder value is compatible with stakeholder theory. Because after all, the only way to support the maximization of shareholder value is to meet the interests of stakeholders.

2.2.6 Development of stakeholder theory in China and its application in health policy making

In China, until the 1990s, many scholars still regarded capital hired labor as the mainstream enterprise theory, but the stakeholder theory has not aroused the general attention of Chinese scholars. Professor Yang Ruilong of the Renmin University of China judged that, this may be related to the fact that many Chinese scholars have been attracted to the study of mainstream enterprise theory after 1995, or it may be the result of the lack of literature (S. H. Jia & Chen, 2003). With the introduction of stakeholder theory, there are more and more research on this theory. At the same time, the application of the theory in public policy process tends to be extensive. The thinking of stakeholders is also introduced to the formulation of medical and health policies.

2.3 Policy entrepreneur theory

2.3.1 Public policy and policy science

Lasswell and Kaplan (2014), the founders of policy science, believe that public policy is a designed plan that contains goals, values, and strategies. This definition emphasizes the constituent elements of public policy, including goals, values, and strategies for action.

Dye (2013) proposed that public policy is whatever the government chooses to do, or whatever it chooses not to do. This definition emphasizes the behavioral choice of the government, indicating that the government's non-action is also a policy and has policy significance.

According to Wright and Jenkins (1978), public policy is a set of interrelated decisions made by political actors in a specific situation, including the choice of goals, the means to achieve goals, and these policies are in principle within the reach of actors. This definition emphasizes that public policy consists of a series of decisions.

According to Eston (1993), public policy is the authoritative assignment of value to a society. This definition emphasizes the value distribution function of public policy. Social interest can replace Easton's social value. That is, the essence of public policy is the authoritative distribution of social benefits. The formation of public policy is a dynamic process. Various interest groups input their own interest demands into the policy-making system, and decision makers synthesize various interest demands and distribute them authoritatively in the form of public policies (H. S. Yang, 2020).

Chen (1996) concluded that the authoritative distribution of social interests through public policy means includes four links: interest selection, interest integration, interest distribution, and interest implementation.

Lindblom (1959) pointed out that in policy making, decision makers usually do not consider all possible solutions, but make gradual and marginal public policies on existing behaviors. It is continuous revision in practice, each revision is a partial and marginal small adjustment to the current policy, and public policy is always constantly formulated and revised.

A public policy consists of three elements: policy goal, policy objective and policy tool that are shown in Figure 2.3.

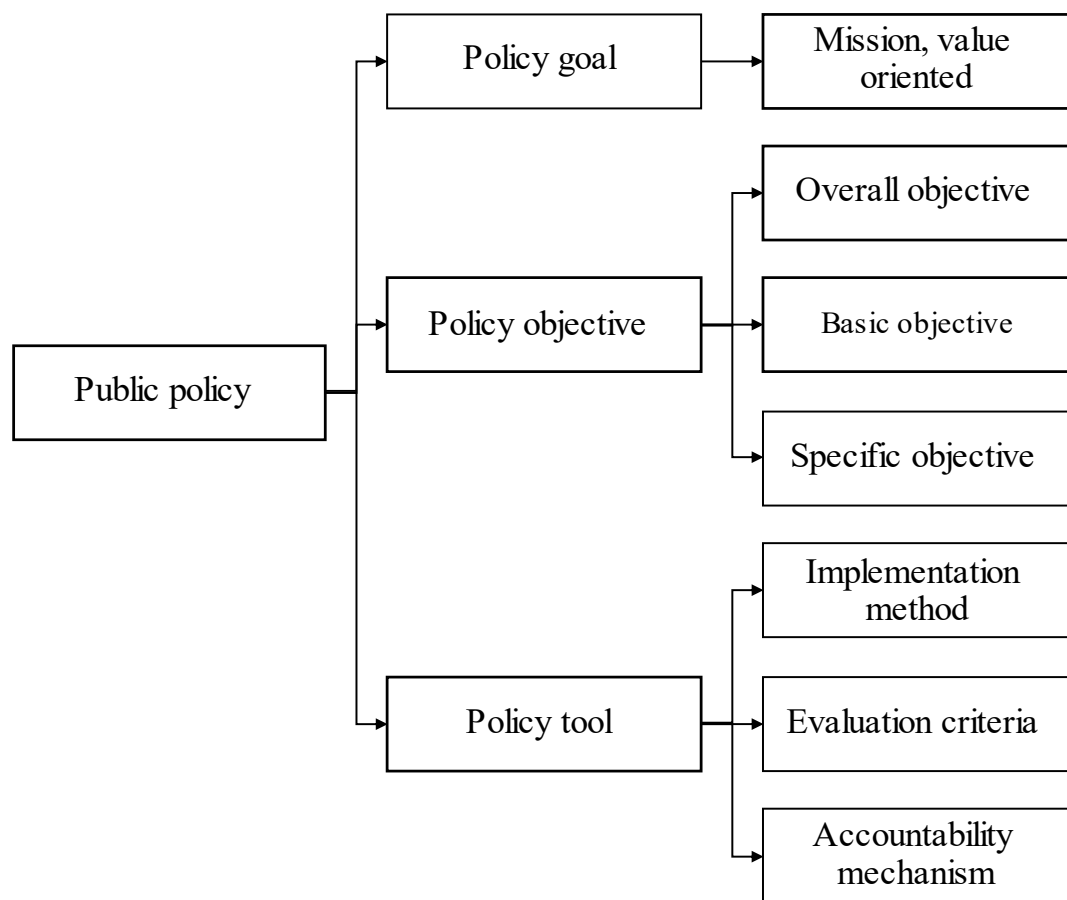


Figure 2.3 Elements of public policy

Source: H. S. Yang (2020)

The policy goal is value orientation, which expresses the macro vision. The policy objective can be regarded as the specific vision, which is the expected result, index, or effect to solve the specific policy problem. Policy objectives can be further decomposed into three levels: general objective, basic objective, and specific objective. Policy tools are the means to achieve policy objectives, including means of implementation, evaluation criteria, and accountability mechanisms.

Due to the limited cognition of decision makers, not all public policies have clear policy objectives and policy instruments. Matland (1995) pointed out that in political decision-making, policy ambiguity may also be a strategy to reduce conflicts and contradictions. For the innovation policy, a commonly used method is to carry out pilot projects in local areas to accumulate experience and reduce decision-making bias before full implementation. With the advancement of policy pilots, the central government can summarize replicable local pilot experience and further improve policy content (H. S. Yang, 2020).

The so-called policy science is a discipline that uses multidisciplinary knowledge to explore the general knowledge of public policy processes and policy analysis methods. Based on its own core concerns, policy science integrates the knowledge of many disciplines to deepen the understanding of complex policy processes and is committed to solving real social problems (H. S. Yang, 2020). Gu (2004) believes that policy science refers to academic evaluation research on the effect of public policy intervention in general, and its core content is the general process of public policy formulation and its specific policy issues, including policy ideas in a narrow sense, policy research and policy evaluation. Liu et al. (2007) states that policy science should build a logically unified framework that considers multiple value theories, behavioral assumptions, and environmental assumptions.

Lerner and Lasswell first proposed the concept of policy science, marking the birth of modern policy science theory (Gray, 1973).

Lasswell and Delors were the most prominent in the early research on policy science, and a policy science tradition represented by Lasswell-Delors was formed in the 1950s (C. K. Zhu, 2016).

Lasswell advocates breaking the status of only partial use of knowledge and establishing a problem-solving-oriented policy discipline to coordinate different research paths and knowledge systems. He emphasized the use of policy to integrate the existing division of discipline, put forward the idea of constructing a discipline based on policy research, defined this discipline as the scientific study of policy, and used policy science to refer to this discipline. In the 1950s and 1970s, he published *Decision-Making Process*, *The Future of Political Science*, and *Policy Science Prospects*, which analyzed the main stages of the policy process, and analyzed the knowledge application and knowledge development of policy science (H. S. Yang, 2020). Therefore, many scholars believe that “problem orientation” is the essence and core of Lasswell’s “policy science”.

Delors inherited and developed Lasswell’s tradition of policy science, further demonstrated the object, nature, theory, and method of policy science, and believed that policy science is a new way of social science that tends to be perfect. Bridges the gap between research and applied research.

Early policy science research mainly focused on policy formulation, but since the 1970s, policy research has gradually expanded to focus on policy implementation, policy evaluation, and policy termination.

2.3.2 Policy process

Since the 1980s, policy science has further expanded its research horizon and proposed new research topics such as policy agenda, policy tools, and policy networks. Kingdon (2017) put forward the Multiple Streams Theory which is also known as Policy Streams Theory, Bryan Jones and others put forward the break-balance theory (Baumgartner, 2011), the initiative coalition frame work proposed by (Sabatier & Jenkins, 2011), the Institutional Analysis and Development Framework (IAD) proposed by Elinor Ostrom (Sabatier, 2004), and research on policy instruments and policy network governance models research has a greater impact on the development of policy science (H. S. Yang, 2020).

In the 1970s, Gary Brewer, a student of Lasswell, divided the policy process into six stages, namely Initiation, Estimation, Selection, Implementation, Evaluation, Termination (Brewer, 1974). Since then, many scholars have discussed the policy process stages. According to Dunn (2011), the policy process consists of a series of interdependent activities, which are arranged in time to form Agenda Setting, Policy Formulation, Policy Adaptation, Policy Implementation, Policy Evaluation, Policy Adjustment, Policy Succession, Policy Termination which are listed in Figure 2.4.

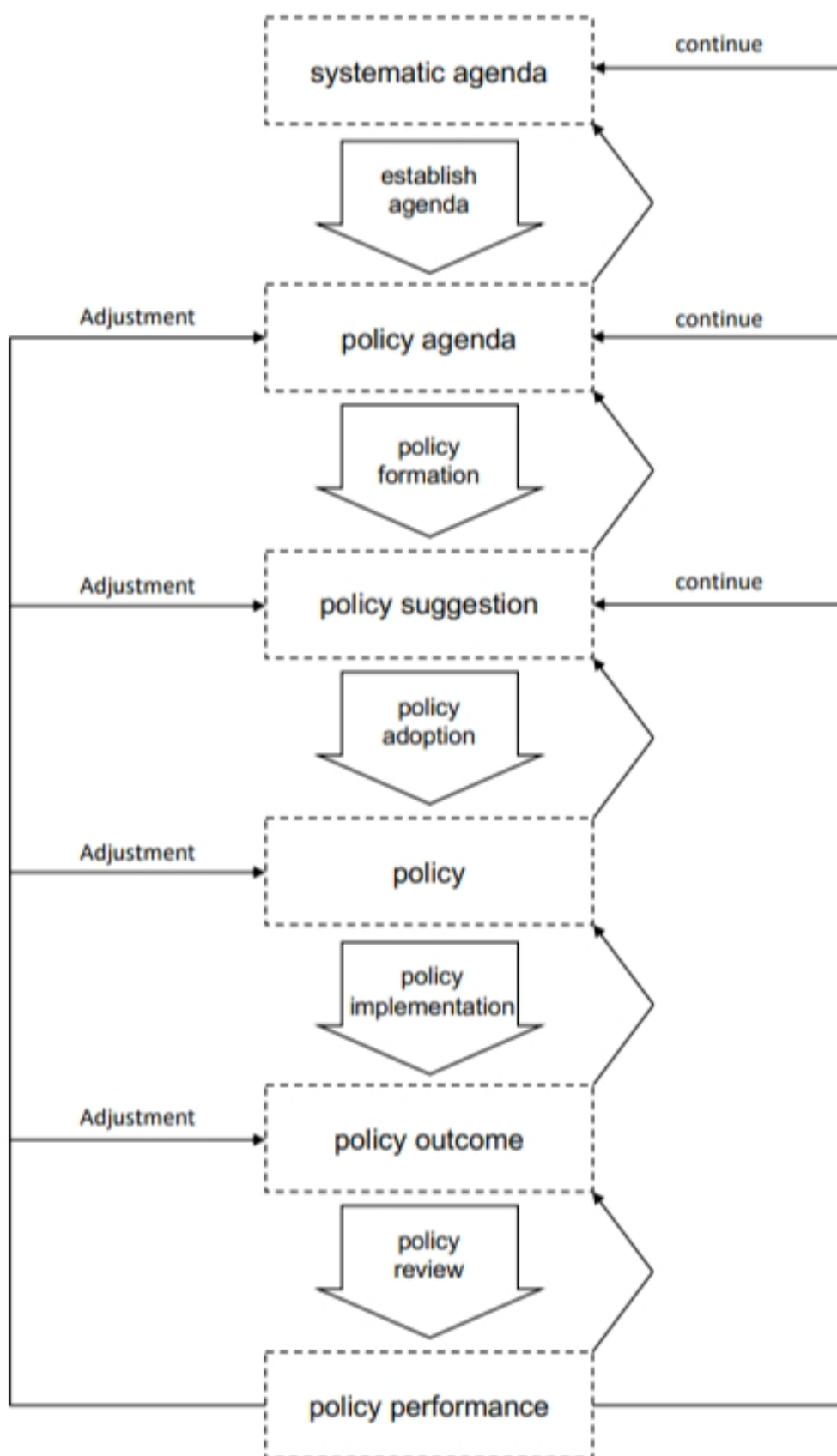


Figure 2.4 The main stage of the policy process

Source: Dunn (2011)

As shown in the Figure 2.4, there will be feedback in each stage of the above-mentioned process, so that the policy process returns from the next stage to the previous stage, and at the same time, some stages of the policy process may also be skipped.

In policy science research, scholars use political science, management science, economics, and other multidisciplinary knowledge to study the policy process and policy system. The decision-making process is at the core of the policy process, scholars have studied the policy decision-making process and put forward many influential theoretical explanations. Lejano (2006) divides the classical theories of policy analysis into decision theory and game theory.

H. S. Yang (2020) concludes that from the perspective of theoretical construction, there are two different logical dimensions. One dimension is from the perspective of political game theory, focusing on the game and its results between actors; The other dimension focuses on the rational status of decision-makers and the choice of goals from the perspective of knowledge and information application. The decision-making theory of the political game dimension focuses on the interaction, game, and outcome between actors in policymaking, and focuses on the dominant actors. The representative decision theories of the game dimension include elitism theory, pluralism theory, nationalism theory, corporatism theory and professionalism theory. The more classic models in decision-making theory models include rational decision-making model, bounded rationality model, progressive decision-making model, hybrid scanning model, and garbage can decision-making model (H. S. Yang, 2020).

Rational choice model is once the most popular decision-making theory in the field of public policy theory, which emphasizes the main role of people in the process of policy decision-making, and believes that policy is “a choice based on rational calculation”, and the so-called decision-making is the process of the government according to a clear public policy goal, conducting a cost-benefit analysis of the various options it faces, weighing the pros and cons, and selecting a public policy plan with the least cost in exchange for the greatest effect. The theory includes the following basic elements: a) Policymakers face an established problem that distinguishes it from other issues; b) The various goals, values, or objectives that guide decision-makers to make decisions are clear and can be ranked in order of importance; c) The various options for dealing with the problem are considered by decision makers; d) Policymakers investigated the possible outcomes of each option available; e) Decision-makers estimate the benefits or losses of each solution under different natural conditions and compare the results; f) Decision-makers will adopt the one whose outcome maximizes its purpose, value or objectives. The result of this process is a rational result, and this decision will most effectively achieve the set goal.

The rational choice model requires the collection of information related to various aspects of the problem, the possible results and impacts of each solution, and the best solution in the comparison. However, under the circumstances of complex problems, lack of information, tight time, social concerns, lobbying by all parties, and conflicting demands, it is difficult to adopt rational decision-making methods. According to Simon (1955), the rationality of decision-makers is limited due to various constraints, and most decisions, whether individual or collective, are committed to finding satisfactory solutions, rather than pursuing optimal solutions. Based on this, Simon proposed the bounded rationality model. Bounded rationality is the theory that consumers have limited rational decision making, driven by three main factors – cognitive ability, time constraint, and imperfect information that result in sub-optimal decision making. which believes that individuals are affected by knowledge, ability, energy, psychology, information, and other factors, and it is impossible to meet the requirements of the rational decision-making model. The decision-making behavior is the product of bounded rationality (Mintrom, 2016).

Lindblom (1968) also believes that due to the lack of human knowledge, political problems, human weaknesses, social values, decision-making techniques, time changes, structures and other factors make the traditional decision-making model impossible. Lindblom believes that decision analysis is not a panacea, and that there is no end to analysis for a complex decision. Because decision-making is limited by time, decision-makers often have to make decisions before the analysis is far from complete, otherwise they will lose the opportunity. Decisions are also subject to cost constraints, and for some decisions, the use of analytical tools to increase costs may not be worth it, although it is possible to conduct a definitive analysis of the decision. Lindblom also argues that decision-making is influenced by values. Because of the differences in the values of individuals within decision-making collectives, there is bound to be disagreement in the selection of policy options. Lindblom built on his critique of the traditional rational model and established the incremental decision-making model. He believes that the process of decision-making is a gradual process, that is, policy formulation is regarded as a process of interaction and bargaining between various political forces and interest groups, and policy formulation is regarded as a process of revising and supplementing past policies. The reason why policy analysis cannot be rational analysis, but rather gradual analysis is because decision-making is necessarily constrained by politics, technology, and existing plans, which determine that fixed policy must become a gradual process. The progressive decision-making model is a useful descriptive and analytical decision-making theory, which has some rationality, but cannot be extended to all decisions, because it also has its own limitations. On the one hand,

decisions made by the incremental model tend to reflect only the interests of the most powerful segments of society, while on the other hand, incremental decision-making tends to focus only on short-term goals and only change certain aspects of existing policies, while making fundamental decisions that are important and long-term appear weak.

Other scholars believe that the rational model is not useless, and that the decision-making process needs to have both a macro vision and a grounded reality to conduct in-depth and detailed observation and analysis and try to combine the rational model with the progressive model. The mixed scanning model proposed by the American scholar Etzioni is a hierarchical mode of decision-making that combines higher-order, fundamental decision-making with lower-order, incremental decisions that work out and/or prepare for the higher-order ones. It attempts to form a policy focus and better solve policy fine-tuning with the pursuit of rationalist policy vision and vision, coupled with the foothold of gradualism (Etzioni, 1967).

The garbage can model believes that the coherent and orderly decision-making depicted by the rational decision-making path is unreal, and the gradual adaptation depicted by the incremental decision-making is equally untrue, both of which mistakenly believe that there is too much certainty and rationality in decision-making. In fact, many decision-making processes have problems such as unclear goals, ambiguous cause and effect, poor concentration of key actors, and unpredictable decision-making results. There are irrational factors in the decision-making of the organization, and there is a chaotic state like the garbage can. Participants will continue to ask questions and give corresponding solutions, which are passed to the policy system, which is equivalent to being thrown into a garbage can, and only a very small number will become part of the final decision (H. S. Yang, 2020). This model was first proposed by organization theorists (M. Cohen et al., 1972), they believed that there was an organized state of chaos. They argue that policymakers often lack enthusiasm for highly complex policy issues, procrastinate or pass the buck as much as possible, and consider solutions only when faced with an urgent situation that cannot be avoided. The choice of alternatives by decision makers is not the result of rational analysis, however, has their own preferences.

According to the garbage can decision-making model, the organized chaos in decision-making is reflected in, a) Problematic preference. In the policy agenda, the understanding of the problem and the preferences of the actors are not consistent, and even conflict with each other, personal preferences will also change, and the organizational goals themselves are vague. b) Unclear technology. The means and methods of how to achieve the goal are not clear. c) Fluid participation. In the process of policy formation, many participants are trying to exert

influence, the participants have considerable mobility, and the preferences of different participants are also different (H. S. Yang, 2020).

James March and others proposed that the outcome of the decision is unknown and random. The final decision depends on the interaction of four forces: problem, solution, participant, and opportunity. These four forces are like four streams of water. Sometimes they flow separately and are independent of each other, and sometimes they merge. Each participant has his own preference. They all tend to choose problem-solving methods that are close to their own preferences. The policy agenda provides a garbage can, and when the four forces converge, the policy window opens and decisions are made (Cohen et al., 1972).

According to the garbage can decision-model, the policy agenda is like a garbage can. When faced with a policy problem, all participants will give solutions, and the final decision is the product of multi-party preferences and games. The garbage can decision model introduces irrational factors into decision analysis, which is very effective in explaining many policy phenomena and provides a new policy perspective for understanding policy agendas (H. S. Yang, 2020).

China's policy research runs through China's long history of civilization, but this kind of policy research on specific fields and specific problems is different from policy science that explores the general laws of public policy. Modern policy science began in the West, and with China's reform and opening, policy science began to rise and develop in China in the 80s of the 20th centuries. While accepting foreign policy science theories, we also see that most of the Western policy theory models are based on the Western political system, and its political system, culture and environment are very different from China. Therefore, China's policy science has certain uniqueness.

Since the 50s of the 20th centuries, foreign policy scientists have begun to study China's policy system and policy process out of the needs of foreign policy-making such as diplomacy and foreign trade. The theoretical explanations of China's policy process include elite decision-making and bureaucratic organization decision-making, as well as the policy planning model and policy experiment model for China's medium- and long-term planning process.

German scholar Sebastian Heilmann and American policy researcher Oliver Melton have studied China's medium-term and long-term planning process and proposed a policy planning model. This model believes that planning is the core mechanism of China's policy process, which goes beyond a policy text or a closed policy process, and is a cyclical process of continuous consultation, drafting, experimentation, evaluation, and adjustment of policies between the central and local governments through various interaction modes (Heilmann et al.,

2013).

Heilmann explained the miracle of China's economic take-off since China's reform and opening and proposed a policy experiment model. He believed that the Chinese government often used the pilot method in the policy process. That is, allowing local governments to explore various solutions to problems according to local actual conditions. The successful local experience will be absorbed into the policies formulated by the central government, and then promoted throughout the country, forming a point-to-surface policy change. He believes that the large-scale experimentation under hierarchy is a unique feature in China's policy process. It provides an incentive mechanism to support local governments to carry out policy experiments and improves the Chinese government's policy innovation and adaptability (Heilmann, 2010).

In recent years, Chinese domestic policy scholars have taken root in China, observed the policy process in China's institutional environment, and constructed some theoretical models of local dialects. It includes consensus decision-making model, "learning-adaptation" analysis model, "path-incentive" analysis model, and so on.

L. Chen et al. (2010) conducted research on China's public policy formulation process, analyzed the actions and roles of policy communities, think tanks, and stakeholders, and proposed a consensus decision-making model. The model believes that under the Chinese political system, the goal of policy participants is to reach a consensus. Consensus decision-making includes bounded rational decision-making and gradual decision-making. Learning from each other's strengths is also characterized by compromise, negotiation, and gradual progress. In the decision-making discussion, the actors involved in policy formulation negotiate disputes, compromise with each other if they can compromise, and adjust language expressions if they cannot compromise. This means that the content of the policy tends to be blurred and it is necessary to find an expression acceptable to all parties. But at the same time, the consensus decision-making model also has limitations. For example, consensus decision-making lacks an institutionalized mechanism for resolving differences of opinion. In fact, high-level political authorities always play the role of the final arbiter; in addition, the consensus decision-making process is difficult to guarantee Participants have equal channels for expressing their opinions. Consensus is mainly manifested as consensus among limited participants.

In real life, society faces many problems. Not all social problems will attract the attention of policy actors, and often only some of them will receive real attention and enter the government's policy agenda. As the starting point of the policy process, agenda setting is a key step in transforming social issues into policy issues.

Social issues need to go through a certain stage of development before they enter the formal official agenda. Davies (1974) divides the policy agenda process into three stages: presentation phase, diffusion phase and processing phase. Nelson (1984) proposed a new stage division method. The author divided the policy agenda into four independent stages which are problem issue recognition, issue adoption, issue prioritization, and issue maintenance. She pointed out that after an issue is included in the official agenda, the government needs to rearrange the agenda and determine the order of processing, and the priority items will be given priority. Items that are not prioritized may not be scheduled or discussed only symbolically.

The latest and most influential theoretical construction in the field of policy agenda research is Kingdon's multiple streams agenda setting model. In the book "Agenda, Alternatives and Public Policy", Kingdon (2017) inherited the irrational analysis method of the garbage can model, and further refined the four sources that affect the policy agenda proposed by the model into three sources. That is, problem stream, policy stream and political stream. In his view, policy agenda-setting is the result of the interaction of these three sources. The occurrence, development, and operation of the three streams of multiple streams theory are independent of each other. When the streams converge at a critical point in time, the policy window will open. When the policy window is opened, multiple streams are integrated, policy agendas are established, alternatives are created, and public policies are introduced. The analytical framework of the multiple stream's framework theory is shown in the Figure 2.5.

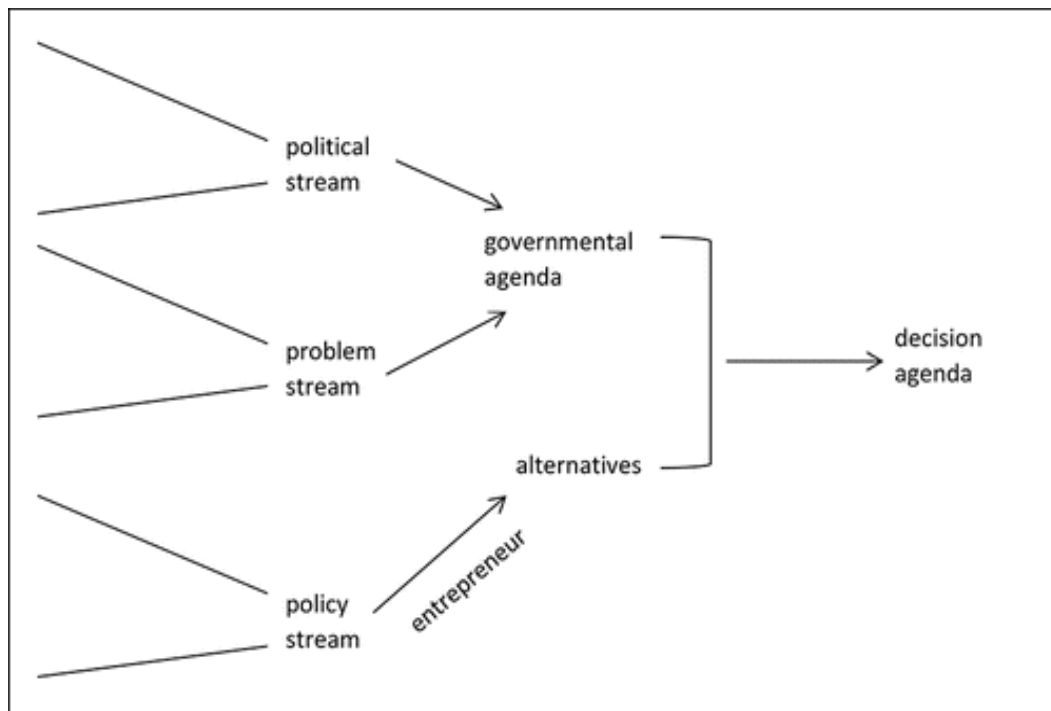


Figure 2.5 Multiple streams policy setting model

Source: Kingdon (2017)

Among the three streams, the problem stream involves the definition of the problems to be dealt with. It includes how the problem is perceived and how the objective situation is defined. Policy stream involves the technical feasibility of solving problems, the budgetary feasibility of solutions, the acceptance of the public and the coordination of dominant values. Political stream refers to political factors that affect problem solving, including national sentiment, competition among interest groups, government changes, major changes in congressional seats, major personnel adjustments, changes in the focus of public opinion and others. Changes in various forces in the political stream will also affect the setting of the policy agenda. From a political perspective, agenda setting is not driven by scientific analysis and rational persuasion but is achieved through compromise and bargaining (Kingdon, 2017).

Kingdon believes that the policy window is a rare opportunity to promote policy formulation, which is fleeting. If the opportunity cannot be grasped in time, participants will have to wait for the next opportunity to open. Gerston pointed out that one of the trigger mechanisms of the policy window is the occurrence of major events through which everyday problems are transformed into a general concern (Geston, 2001). A series of events in the problem stream and political stream often play a catalytic role and become the trigger mechanism to open the policy window. The opening of some policy windows is predictable, while others are not. To seize the opportunity, participants also need to be prepared in the policy stream. Policy issues that lack policy analysis and program design are often difficult to put on the formal official resolution agenda (Kingdon, 2017).

The multiple streams analysis model believes that the three streams are independent of each other, in policy making, these three streams often influence each other. Sabatier believes that in Kingdon's analytical model, the attitude of policy analysts is too apathy. Indeed, policy analysts are also biased and work to build advocacy coalitions across political streams. Both government agencies and non-governmental actors attempt to control the definition of policy issues and to have clear orientation by organizing policy learning to build a policy community brings together groups and organizations with the same policy beliefs to form a coalition of initiatives that support a certain policy goal (Sabatier, 1991).

Policy agenda setting is the first and most critical part in policy formulation. It is impossible for any government to solve all social problems, only a limited number of problems will be included in the policy agenda, discussed in a specific time, and proposed possible solutions.

2.3.3 Policy innovation and diffusion

Policy innovation and diffusion is a hot field of policy process research in recent years. Rogers has long been committed to the study of the diffusion law of innovation. Rogers (2016) pointed out that innovation does not mean creating something completely different from the past, when an idea, method or object is considered new by an individual or group. At that time, it is an innovation.

Policy innovation research emerged in the 1960s, the government policy innovation theory has developed rapidly and has become an important topic in policy process research (Y. P. Zhu, 2010). Walker (1969) pointed out that policy innovation refers to the first time that a new idea or program is put into practice by a certain government, regardless of whether it is adopted by other governments. Policy innovation does not focus on the originality of policy ideas, but on whether the policy was admitted for the first time. Any policy that is new to a government is policy innovation (Boehmke & Witmer, 2004).

The process of policy innovation can be divided into five stages: cognition, persuasion, decision-making, implementation, and confirmation (Rogers, 2016). After a lot of empirical research, policy scholars believe that there are two main reasons for policy innovation, namely, internal determinants and external diffusion and influence (Berry & Berry, 1990). The internal decision model mainly seeks the causes and motivations of policy innovation by focusing on the internal factors that determine policy adoption. To a certain extent, the situation in this aspect determines the preference, intensity, and possibility of innovation of the government. The model of external diffusion explores the driving force of policy innovation more from the perspective of external factors (Y. P. Zhu, 2010). From the perspective of the diffusion model, the reasons and motivations for policy innovation mainly come from the external world, and the key factors of innovation are successful learning, competitive imitation, and information communication network among officials (Gray, 1973). In the late 1990s, scholars gradually tended to believe that the motivation for policy innovation should not be internal or external factors alone, but a combination of the two factors to form an integrated model.

Policy innovation is often not smooth sailing. Rogers (2016) believes that the key factors affecting the adoption rate of innovation come from five aspects: First, the government's understanding of the characteristics of innovation. For instance, the government's understanding of the relative advantages, complexity, and feasibility of innovation projects will affect the adoption of policy innovation projects. Second, type of innovation decision. Different decision types tend to affect the adoption rate of policy innovation projects. Third, the channel

of exchange and communication. The diversity and smoothness of communication channels often affect the adoption rate of policy innovations. Fourth, the nature of the social system, such as the basic norms in a certain social system, the degree of internal connection and openness of the policy network, will all affect the adoption of policy innovation projects. Fifth, the extent to which an agent's efforts can also affect the adoption of policy innovation programs.

With the continuous advancement of China's reform and opening, policy innovation theory has important reference value for China's policy practice. In fact, the entire reform process in China can be described and explained by the continuous process of policy innovation. A typical manifestation is the policy experiment (pilot), forming a reform process of crossing the river by feeling the stones (Y. P. Zhu, 2010).

H. S. Yang (2020) summarized the model of China's policy pilot projects and diffusion, which is shown in Figure 2.6. Usually, if a policy innovation is implemented successfully in a pilot area, the pilot will attract widespread attention and policy learning will follow. The superior governments will also acknowledge the pilot as a typical policy experiment and organize broader regional exchanges for learning. The policy innovation will then spread from point to area and be promoted on a larger scale. For mature policy proposals, central decision-makers can transform the pilot into formal laws and regulations for nationwide implementation.

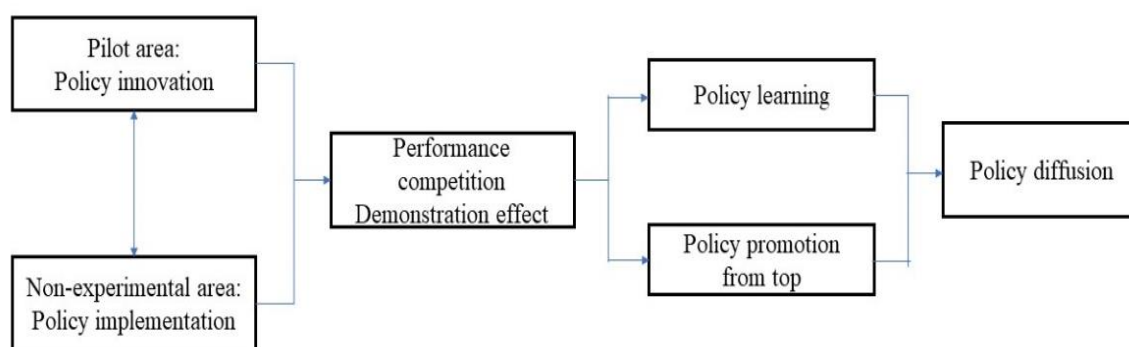


Figure 2.6 The diffusion of policy pilot

Source: H. S. Yang (2020)

2.3.4 Policy entrepreneur

Policy entrepreneur is an important concept in policy agenda research, developed through the accumulation of research by policy scholars, forming the theory of policy entrepreneurship. The concepts of entrepreneur and entrepreneurial spirit originate from the study of economics and business organizations. Policy science researchers have incorporated them into the study of

public policy, emphasizing how individual policy participants influence the process of public policy (Y. P. Zhu, 2012).

The study of policy entrepreneurs originated in the 1970s. In the early stages, the research focused on describing the key individuals involved in the policy process and their role in driving policy change. In the 1980s, Kingdon introduced the concept of policy entrepreneurs into the multiple streams model and conducted a detailed and systematic analysis. This emphasized the important role of key individuals or organizations in policy change. As a result, policy entrepreneurs have gradually received attention and recognition from public policy researchers. Subsequently, numerous studies have been conducted by policy scholars, resulting in a significant body of literature. Policy entrepreneurs are considered as key variables in explaining public policy change and innovation (Weissert, 1991).

The term policy entrepreneur typically refers to those individuals who seek to change the existing allocation of public resources through organizing and mobilizing collective forces (Woll & Lewis, 1981). Policy entrepreneurs are enthusiastic about identifying the forces driving organizational change and actively providing solutions to policy challenges for organizations (Crow, 2010). Specifically, in the risky policy process, policy entrepreneurs are more willing than other policy participants to invest their own resources, such as time, energy, and sometimes even money and reputation, in order to disrupt the existing policy equilibrium and promote policy transformation by selling their policy ideas for future material gains or shared interests (Kingdon, 2017).

Kingdon believes that policy entrepreneurs are individuals and groups who advocate, implement, and accomplish policy innovation. Their basic traits include: a) having some form of hearing power, being well-informed, and having broad knowledge; b) being well-known for their political connections or negotiation skills; c) having persistence and strong determination (Kingdon, 2017). Mintrom and Norman (2009) define policy entrepreneurs as advocates for policy change. A key element of policy entrepreneurs is their ability to seize the timing of policy change, and their actions require creativity, enthusiasm, and political skills. Brian Jones suggests that policy entrepreneurs are individuals who introduce new ideas into the government (Jones, 2010). They can be elected politicians, government officials, or professionals from specific policy interest groups or research institutions (Spill et al., 2001). Regardless of the type of policy entrepreneur, they all possess the inherent qualities of entrepreneurship and play a role in policy formation, agenda setting, policy making, and policy implementation processes. Successful policy entrepreneurs tend to have the core elements of social acumen, problem definition, team building, and leading by example (Mintrom & Norman, 2009).

Roberts and King (1996) divided policy entrepreneurs into four types according to specific criteria. According to the three conditions of whether policy entrepreneurs have formal positions in the government, whether they have played a leadership role, and whether they have been elected, policy entrepreneurs subdivided into: political entrepreneur (all three conditions are met), executive entrepreneur (the first two conditions are met), bureaucratic entrepreneur (who does not meet the last two conditions) and policy entrepreneur (none of the three). Roberts and King (1996) also argued that different types of the impact of policy entrepreneurs on policy changes is not the same, and careful classification can help researchers identify which type of researchers has had a decisive impact on policy changes.

Maor (2017) divides policy entrepreneurs in the policy evaluation process into four categories based on specific strategies employed by policy entrepreneurs: Norm entrepreneurs, they seek to influence international and national rules, specifically conflict of rules, rule-takers and rule-makers; Reputation entrepreneurs, they seek to influence the international reputation of policy-related individuals, institutions, national and global policy actors; Meaning entrepreneurs, they seek to influence the process of policy change by giving it a specific meaning; Standards and performance metrics entrepreneurs, they seek to influence the implementation standards and performance indicators of state or non-state-driven programs. In their view, policy entrepreneurs playing different roles have different dimensions and degrees of influence on policy change, researchers should focus on “whether policy entrepreneurs are more active and successful as change-seeking actors than those who defend the status quo”.

Policy Entrepreneurs and the Policy Process

Western scholars started research on policy entrepreneurs earlier, and mainstream policy process analysis frameworks such as multiple streams theory, advocacy alliance theory, punctuated equilibrium theory, and policy innovation diffusion theory have all paid attention to the key role of policy entrepreneurs in promoting policy change.

Policy entrepreneurs are key factors influencing policy agenda setting, and they are often discussed by researchers as important influencing factors (Baumgartner & Jones, 1993). Policy entrepreneurs outside the government will actively advocate and promote certain social issues they care about to attract the attention of the public and use various methods that can attract the government’s attention to force officials within the system to form pressure to solve the problem. On the other hand, policy entrepreneurs within the government system will use the resources and power at their disposal to mobilize all social forces and patiently wait for the right time to come. Policy entrepreneurs outside the system, in particular, may not have the ability to influence the final decisions of policymakers, according to the multi-stream model, but they

can focus their efforts more effectively on influencing the policy agenda-setting stage, so that governments realize that a policy issue must be addressed immediately, and they can start to think about it, which is a great contribution.

Kingdon's multiple streams framework, which is adapted by G. W. Chen and Lin (2021) that is shown in Figure 2.7. Kingdon believes that the opening of the policy window is sometimes predictable and sometimes unpredictable. The policy window does not last long, and participants need to seize the opportunity quickly or they will have to wait for the next opportunity (Kingdon, 2017). Kingdon states that policy entrepreneurs often play a key role in this process. Successful policy entrepreneurs not only have extraordinary political skills and tenacity, but also have a keen sense of touch, able to perceive the policy window with great accuracy and act at the right time to promote the three streams. The policy window will open, and social and political events are the factors to promote the opening of the policy window. At this time, policy entrepreneurs must act quickly to promote the realization of policy innovation.

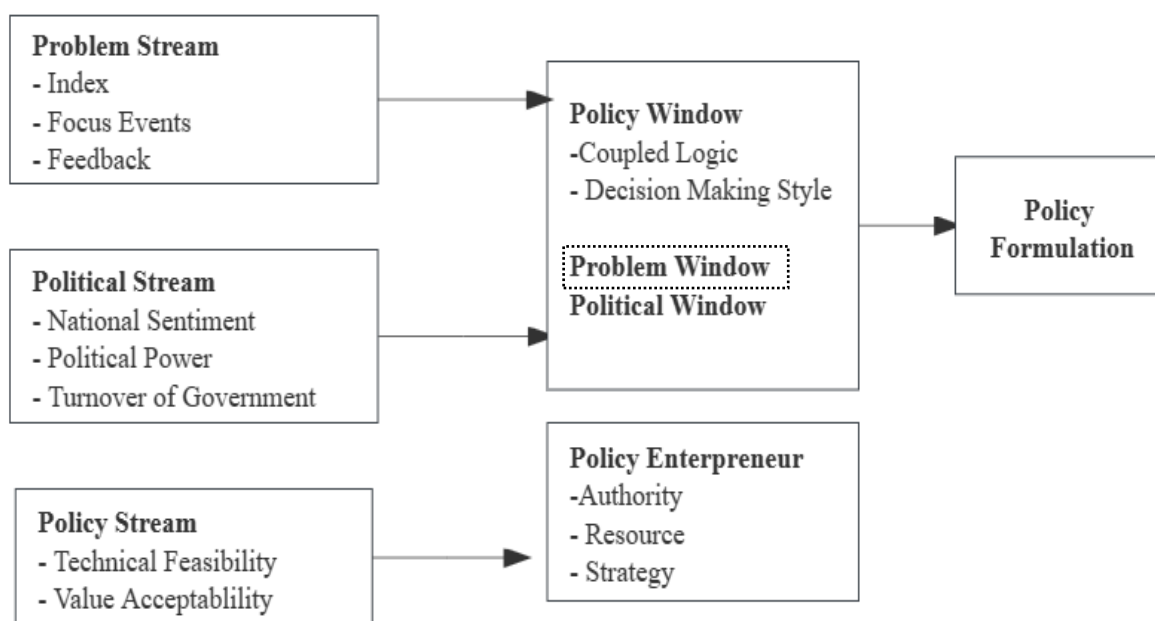


Figure 2.7 Multiple streams framework

Source: G. W. Chen and Lin (2021)

In a multiple streams framework, each active participant may be involved in issues, politics, and policy processes. However, different participants have varying levels of influence on agenda-setting and alternative solutions, and no participant can control or influence all processes. For example, the influence of the news media on the agenda is much lower than expected. It mostly plays a role in reporting and communication, or indirectly affects the agenda setting through influencing public opinion within a limited range. Public opinion has only a

moderate level of influence on the agenda, but it is stronger than its influence on alternative solutions. Only policy entrepreneurs are the core driving force behind problem entry into the agenda. They not only engage in policy streams but also persuade and sell their preferred solutions, as well as drive issue definition and raise the status of their concerned issues on the agenda. This is especially true when the policy window opens, and it promotes the coupling of issues, politics, and policies. Without the mediation of policy entrepreneurs, these three streams will not be coupled, and the agenda cannot be set. Although policy entrepreneurs are involved in problems, politics, and policy streams, conceptually, they are independent of these three processes, and they can come from any community. In fact, the reason why policy entrepreneurs play such an important role in agenda setting is because of the separation of politics and administration, the separation of legislative, judicial, and executive powers, and the competition between elected officials, career bureaucrats, and interest groups. In this context, government organizations exhibit the characteristics of organized anarchy, and policy communities are fragmented. Authority and decision-making are also fragmented, and no participant can completely dominate or control all processes of information systems and decision-making. In this sense, compared to rational choice theory and gradualism theory, the multiple streams framework more accurately depicts the process of agenda setting in government under the above conditions (Kingdon, 2017; Sabatier, 2004; Zahariadis, 2007).

Possible reasons why the policy transition did not occur: The first is unfavorable conditions in one or more streams, so that coupling between streams is impossible. The second is that even if conditions in the stream itself were favorable, no window of opportunity presented itself. The third is that even when a potential policy window is open, there are no suitable policy entrepreneurs to exploit the existing window and achieve coupling.

Based on the identity of the policy agenda proposer and the degree of public participation in the agenda setting process, S. G. Wang (2006) divided the setting of the public policy agenda into six modes (Table 2.2): closing the door, mobilizing, internal reference, borrowing power, proposal submission and external pressure. The external pressure mode frequently appears in the current policy agenda setting, which provides a large space for policy entrepreneurs.

Table 2.2 The modes of public policy

		Policy agenda proposer		
		Decision-maker	Think-tanker	Public
The degree of public participation	Low	I Closing the door	III Internal reference	V Submitting proposal
	High	II Mobilizing	IV Borrowing power	VI External pressure

Source: S. G. Wang (2006)

The introduction of a new policy will have an impact on the original interest structure and management mechanism. Unpredictable risks will affect the adoption of new policies by policy makers. Policy entrepreneurs should try to dispel the concerns of policy makers (Mintrom & Norman, 2009). A feasible way is to provide the successful experience of other places or the timing effect of local policy pilots, so that policymakers can firmly implement the new policy. policy determination.

Policy Entrepreneurs and the Policy Innovation

Policy entrepreneurship focuses on the role of personal concepts, abilities, and political skills in promoting policy change, and literature focusing on policy entrepreneurship theory usually regards commitment to policy innovation as the core element of policy entrepreneurship.

Michael Mintrom is a representative of the perspective of policy innovation. He believes that policy entrepreneurs are the advocates of policy ideas, and they are the political subjects who promote policy innovation into the government agenda and promote the diffusion of policy innovation. He raised the question of how policy innovation ideas are salient in policy agenda setting and what is willing to cause their diffusion, and believes that policy entrepreneurs can achieve their goal of promoting policy change by striving to win the support of policy innovation ideas (Mintrom, 1997).

In the process of influencing policy innovation, policy entrepreneurs mainly interact with policy actors included in the policy system. Specifically, policy actors include three categories: first, organizations or individuals that directly exercise or influence decision-making power, including political parties, governments, legislatures, courts, politicians, bureaucrats, among others; second, organizations or individuals that indirectly affect decision-making power , including interest groups, public media, think tanks, people's representatives, citizens, among others; the third is the object of policy action, including target groups, social groups or individuals (Tao & Cui, 2008).

Roberts and King (1991) described the interaction between policy entrepreneurs and policy participants inside and outside the government in detail, extracted the common and typical behaviors, and conceptualized the mechanism of their influence on policy innovation as: creating new ideas — designing policy scheme — implement policy program — institutionalization. Subsequent studies on the actions of policy entrepreneurs in policy innovation mostly follow this analytical framework. Y. P. Zhu and Xiao (2015) formed a theoretical model to explain policy innovation based on three questions, that are who plays the role of policy entrepreneur, what factors will affect policy entrepreneur's participation in

innovation, and how policy entrepreneur realizes policy innovation.

Mintrom et al. (2014) believes that teamwork and alliance building are the core elements of the policy entrepreneur action process. It further explores how policy entrepreneurs can take cooperative actions to carry out broad social changes and promote the process of change to achieve sustainable development goals (Mintrom & Thomas, 2018). N. Cohen and Naor, (2013) focuses on the process of how policy entrepreneurs cooperate with government officials and lobby groups to promote policy innovation, and emphasizes that building a strong alliance and government support play an important role in the successful promotion of policy innovation by policy entrepreneurs.

The application of policy entrepreneur theory in China

In China, more and more scholars have also begun to pay attention to the theory of policy entrepreneurship. On the one hand, it is used for analysis of China public policy setting, on the other hand, influenced by China's political system, the adoption of this policy has its uniqueness. These policy entrepreneurs include both administrative bureaucrats inside the government and experts outside the government, which is what we usually call concepts inside and outside the "system" (Y. P. Zhu, 2012). In different institutional environments, policy entrepreneurs face different institutional constraints, which in turn affect their success in promoting policy innovation (Zhou & Li, 2016). Although some studies have shown that policy subjects, especially the decision makers among them, dominate the operation of the public policy system, enjoy the final decision-making power on the layout of policy plans, and occupy a dominant position in the process of policy innovation (Kong, 2004). However, through their own efforts, policy entrepreneurs inside and outside the system also played a key role in promoting the realization of policy innovation.

Current research on policy entrepreneurs focuses on the characteristics of policy entrepreneurs, strategies in the reform process, and their role in policy diffusion. In addition to the basic characteristics of policy entrepreneurs, due to the differences in institutional environments, the behavior, and strategic choices of policy entrepreneurs in the Chinese contexts have special performance. In specific situations, policy entrepreneurs can use "technology not feasible" strategies to drive policy change (Y. P. Zhu, 2008). Administrative bureaucrats within the government can gain support from their superiors by constructing policy issues and proposing innovative ideas, so as to promote policy innovation (Y. P. Zhu & Xiao, 2015). The mobility of policy entrepreneurs also has an impact on promoting policy innovation and diffusion (K. Zhang, 2015)

In China, for the innovation policy, a commonly used method is to carry out pilot projects

in local areas to accumulate experience and reduce decision-making bias before policy full implementation. With the advancement of policy pilots, the central government can summarize replicable local pilot experience, further improve policy content (H. S. Yang, 2020). Policy entrepreneurs often influence the implementation of policy innovation by promoting policy pilots.

Chapter 3: Research Method

This study is designed as qualitative research. Using qualitative methods enables researchers to dissect the environment of each interviewee from a global perspective (Khan & Puthussery, 2019). This research project will be conducted in China.

The research method is to adopt a combination of several research methods, including a preliminary sorting out of the project and the theory to be adopted from the perspective of literature through literature collection and analysis. In the research phase, semi-structured interviews were conducted with different stakeholders to understand their thoughts on the implementation of parametric release regulations for large-volume injections in China, to explore the influencing factors of different stakeholders on policy formulation, and how to promote policy adoption and implementation. Through the grounded analysis of the interview data and the coding method of constructive grounded theory to analyze the data, finally construct the policy-driven path of stakeholders in the process of promoting policy innovation based on the multiple streams theory of policy entrepreneurs.

3.1 Semi-structured interview: sources of data collection

The qualitative part of the empirical research of this study mainly plans to conduct semi-structured in-depth interviews with key stakeholders to obtain the results of different stakeholders' understanding and knowledge of parametric release, views on the implementation of the policy in China, and the results of core issues such as the obstacles in the implementation process of the policy. Based on the data obtained by the interview method, the data obtained by the interview are coded and summarized according to the constructive grounded theory in the grounded theory, so that it is gradually transformed from abstract to concrete, condensed concepts are formed after categorization, theory are constructed, and finally the analytical framework of this thesis is formed.

Semi-structured interview is the main source of data in this work.

The data collection process lasted from 2020 to May 2023, and the interviews were conducted between June 2022 and March 2023. According to the influence of stakeholders on policy making and the degree of relevance, 33 stakeholders were selected based on the research purpose for semi-structured in-depth interviews. The respondents included 13 regulators, 10

industry personnel, 4 end users, and 6 experts and scholars from industry associations and research institutes. These interviewees include policy makers in various government departments, including regulators from multi departments of National Medical Product Administration, such as the Department of Drug Registration, Department of Drug Regulation, Center of Food and Drug Inspection, Center of Drug Evaluation, China Pharmacopoeia Committee, as well as several local Drug Administration regulators, pharmaceutical Industry representatives including industry senior relevant quality and regulatory personnel, they can come from foreign enterprises that have adopted parametric release already globally, domestic large injection manufacturers with advanced levels, representatives from enterprises with China's average quality management level, among others and also include the voice of the industry as trading enterprise. At the same time, the interviews also included hospital administrators, medical staff and patients representing the users, as well as relevant pharmaceutical Industry Associations and senior experts and scholars in the industry.

All interviews were conducted either in person or online. All interviews were arranged according to the time and convenience of the interviewees. Interviewees were selected with a small sample size based on questions set, data saturation, and practical factors such as resources and availability. Inclusion criteria are at least 20 years of working experience in the relevant central or local drug regulatory authorities, or the pharmaceutical industry, Academia and clinical users related to the implementation of the parametric release policy. The work is directly or indirectly related to the content of this study. The characteristics of the interviewees and the work related to the implementation of the parametric release policy are presented in the Table 3.1.

Table 3.1 Interviewee profile

Interviewee Code	Occupation / Organization	Main responsibility	Position
A1	Regulator	China Pharmacopoeia Committee	Former head
A2	Regulator	Beijing Drug inspection and supervision Department, MPA	Former head
A3	Regulator	National Institute for Food & Drug Control	Former head of Generic Drug development
A4	Regulator	Center of Drug Evaluation, NMPA	Former Director of Chemical drugs
A5	Regulator	Department of Drug Regulation, NMPA	Former Head
A6	Regulator	Center of Drug Re-evaluation, NMPA	Former Director
A7	Regulator	Center of Drug Evaluation & Authentication, Guangdong MPA	Senior reviewer
A8	Regulator	Center of Drug Evaluation, NMPA	Former Deputy Director
A9	Regulator	Sichuan Medical Product Administration	Former head

Interviewee Code	Occupation / Organization	Main responsibility	Position
A10	Regulator	Shanghai Drug Evaluation & Inspection Center, Shanghai FDA	Deputy Director of chemical drug
A11	Regulator	Shanghai Drug Evaluation & Inspection Center, Shanghai FDA	International Auditor
A12	Regulator	Shanghai FDA	Former head
A13	Regulator		Director of Microbiology Department
		National Institute for Food & Drug Control	President
B1	Industry Association	China National Pharmaceutical Packaging Association	
B2	Industry Association	China Quality Association for Pharmaceuticals	Director
B3	Industry Association	Zhongguancun Modern medicine productivity promotion center	Secretary-General
B4	Industry Association	Beijing Pharmaceutical Shield (PSM) Foundation	President
B5	Industry Association		President
		China Health Culture Association	
B6	Industry Association	School of Public Policy & Management, Tsing Hua University	Professor
C1	Industry	Baxter (China) Investment Co., Ltd.	VP, Government Affairs
C2	Industry	Baxter Healthcare	Head, Sterility Assurance
C3	Industry	Fresenius Kabi SSPC	Director, Quality
C4	Industry	Shanghai GE Healthcare	Director, Quality
C5	Industry		VP, Regulatory Affairs
C6	Industry	Johnson & Johnson Medical Suzhou Medtron Pharmaceutical Technology Co., Ltd.	General Manager
C7	Industry	Gene Science Pharmaceutical Co., Ltd.	Director, Quality
C8	Industry	Wuxi AppTec	Director, Quality
C9	Industry	Xi'an-Janssen Pharmaceutical Co., Ltd.; Beijing Shuanghe Pharmaceutical Co., Ltd.	Director, Regulatory Affairs
C10	Industry	Sichuan Kelun Pharmaceutical Co., Ltd.	Director, Quality
D1	Hospital	Ningbo Private Hospital	Hospital president
D2	Hospital		Chief nursing officer
		Shangdong University Qilu Hospital	
D3	Hospital		Chief nursing officer
		Beijing University No. 1 Hospital	
D4	Hospital	Beijing Xuanwu Hospital Pharmacy	Chief of Pharmacy

The informed consent of the interviewees will be obtained before starting each interview.

A qualitative approach enables interviewees to dissect each interviewee's environment in a global context (Al-Busaidi, 2008). All interviews are conducted in a conversational format, in which questions are asked naturally and smoothly in conversation with the interviewee, rather

than in a formal question-and-answer format.

The development of semi-structured interview guidelines focused on exploring stakeholders' views on the parametric release policy in earlier studies (Khan & Puthussery, 2019). Flexible interview guidelines involve, a) the interviewees' understanding and recognition of parametric release; b) the interviewees' views on the reasons for implementing the parametric release policy in China; c) what obstacles they perceive to the implementation of the policy; d) how to promote the implementation of parametric release regulations. The interviews were conducted in Chinese and the average length of each interview was about one hour. All interviews were recorded with the permission of the interviewees, and all recordings were subsequently transcribed into text manuscripts, which were collated and proofread by the pair to check the correctness of transcription and translation.

In the interview process, the researcher will explain the technical terms that the interviewees cannot understand, and timely adjust the content and focus of the questions according to the interviewees' background and expression style. To confirm that the interview questions can be fully understood by the interviewees and control the effect of the interview, after the interview outline is confirmed, two interviewees from enterprises are first interviewed, and the questions are revised according to the actual situation of the interview so that the questions of the interview questionnaire are more simplified and clearer. The revised interview outline is in Annex 1. Subsequent interviews were conducted using the revised and confirmed interview outline. All interviews include face-to-face interviews, as well as video and teleconferencing. Most of the interviews were conducted online due to the COVID-19 pandemic and geographical constraints. With the consent of the interviewees, the researchers recorded the whole process. (Two respondents also provided written responses and conducted online interviews.) After the interview, professional voice software transcribes the recording (iFLYTEK), sorted out related documents and chat records, and finally obtained about 450,000 words of interview materials.

Due to the semi-structured interview method, the specific questions of the interview and the order and focus of the questions were adjusted according to the actual situation. Therefore, during the interview, the author, based on referring to the interview outline, combined the personal experience and answers of the interviewees to dig deeper. After each interview, the author organizes the interview materials in time, writes a memo, and records the inspiration obtained in the interview and the reflection on the interview content. As an important link in grounded theory, the memorandum runs through the whole research.

3.2 Grounded theory--a framework for analyzing interview data

This study uses the research method of grounded theory coding to encode and classify the content obtained through semi-structured interviews, aiming to extract categories from many qualitative data and build a conceptual model of conflict-coordination relationships from the perspective of stakeholders.

Grounded theory originated from sociologists Glaser and Strauss. In 1965, in the process of writing *Dying Consciousness*, these two scholars used grounded theory for the first time to carry out empirical research on how hospital nurses deal with dying patients. Charmaz (2006) put forward the constructive grounded theory, heralded the birth of grounded theory. It is clear from this work that grounded theory is proposed to answer how in social research, data can be systematically obtained and analyzed to discover theories, ensure that they fit the actual situation, and provide relevant predictions, explanations, Interpretation, and application. Simply put, grounded theory is a method for discovering theory from data (Glaser & Strauss, 1967). Therefore, Grounded Theory has made its mission clear from the day of its creation, that is to establish theory through qualitative methods (Strauss & Corbin, 1997). Since then, Glaser and his collaborators have continued to develop and improve Grounded Theory, making Grounded Theory gradually become a complete method system.

Among many qualitative research methodologies, grounded theory overcomes the lack of standardized methodological support in general qualitative research, difficulty in tracing and testing the research process, and its weak convincing conclusions. It is a more scientific method in qualitative research. It is more suitable for theoretical construction among the five traditional research methods of sociology (Denzin & Lincoln, 2011). Xu and Zhang (2005) pointed out that scholars should use inductive methods or the construction of grounded theory to study the actual problems in their situations. Eisenhardt (1989) and Lee (1999) also put forward that compared with direct application of theories produced in different social and cultural backgrounds, local theory proposed by the research method may have higher internal validity and external validity. When the phenomenon is not clear and the existing theory cannot explain the research object reasonably, people generally accept the research method of grounded theory.

After grounded theory was first proposed in 1967, it has been widely used in the fields of nursing, education, religion and management, and three schools have emerged in the long-term development, a) Take the study of Glaser and Strauss (1967) as the representative of the classical grounded theory school; b) In 1990, Strauss and Corbin co-authored the “Foundations of Qualitative Research: Grounded Theory Procedures and Technique”, which introduced new

concepts and methods on the basis of classical grounded theory, established a three-level coding procedure, and used the canonical matrix analyzing the relationship between categories, program grounded theory, and become a programmed grounded theory (Strauss & Corbin, 1997); c) In 1995, in constructivism under the influence of thought, Charmaz (2006) put forward the constructive grounded theory, thinking that the theory is not discovered, but interpreted, analyzed and constructed by researchers. There have been disputes between the factions.

Classical grounded theory is the original version of grounded theory. Its core methodological principle is to avoid any preconceived assumptions of researchers but to allow research questions to emerge naturally from social processes and research on them (Charmaz, 2006; Glaser & Strauss, 1967). By the principle of continuous comparison, follow the standardized data processing steps to complete the theoretical construction. Compared with classical grounded theory, programmatic grounded theory also emphasizes that the theory is loyal to the data, but it focuses more on exploring the laws in the data with the help of presupposition and other techniques. The classical grounded theory school believes that the programmed grounded theory school deviates from the purpose and essence of grounded theory to discover the theory from the data, and makes the research have a preconceived conception and oppose it. The constructive grounded theory took shape (Charmaz, 2006). This school not only inherits and develops the ideas of the previous two schools, but also has different views. For example, it believes that although the laws in the data exist objectively, they can be understood by others. Construction and cognition, but the classical grounded theory school does not agree with this.

Different from quantitative research, the biggest methodological feature of grounded theory is that it emphasizes that research questions arise in context, and the three grounded theory schools hold the same view on this. In the beginning, researchers just entered the situation with interest, allowing the research questions and subsequent theoretical construction to emerge naturally from the obtained data, while the reading and comparison of existing theoretical literature was put behind the theoretical coding. This is the embodiment of the core concept of grounded theory, that is, researchers must let go of preconceived assumptions when entering a situation, avoid preconceived subjective influences, and truly improve the theory from social reality and practice, which is also the essence of the grounded theory research method (X. D. Jia & Tan, 2010). The core of the grounded theory is based on coding, usually including three levels of Coding, that is, open type, associated type, and core type (X. M. Chen, 2015), which has been gradually summarized and refined to realize the evolution from concept to category

and then to the relationship between categories. Its purpose is to Multiple refinements and abstractions of the obtained information to discover the relationship between things, which is often used to construct the causal mechanism of complex logical relationships (R. R. Li et al., 2023).

The grounded theory research process of this study is as follows in Figure 3.1.

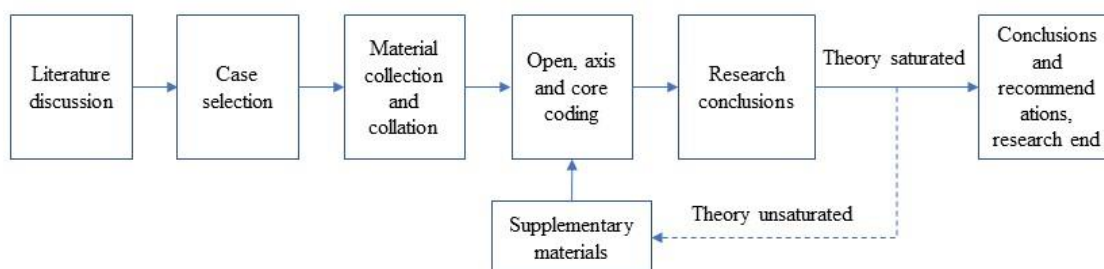


Figure 3.1 Study process of grounded theory

The grounded theory follows the sampling principle of theory saturation, emphasizes the close relationship between interviews and analysis, and advocates analyzing the content of interviews, clarifying concepts, determining categories, constructing theoretical hypotheses, and further conducting sampling interviews based on theoretical hypotheses to verify and improve the theory. It is assumed that until no new information emerges from the interview content, at this point the theory can be deemed saturated and there is no need to continue the interview. On this basis, this research uses NVivo12 software to organize and analyze the interview data, and through open coding, axial coding, and selective coding, it summarizes the influencing factors that affect the implementation of the parametric release policy in China and explains its influencing mechanism.

Research reliability and validity control is an important part of research design. According to the design of the research content and research methods, the main reliability and validity control methods of this link include pre-interview, theoretical sampling, interviewee test, theoretical saturation test, and other series of methods, which effectively ensure the validity level of the research conclusions. The specific application of these reliability and validity control measures will be specified in the research implementation link.

Questions to be addressed in the research include:

Define stakeholders and their demands.

In-depth understanding of the different interest considerations of stakeholders and clarifying the game relationship of stakeholders.

It is hoped to find out the key factors to promote cooperation, and to propose the feasibility

study conclusions of parametric release policy for moist heat sterilization drugs from the perspective of stakeholders.

See Annex A for a semi-structured question outline for the interview.

3.3 Research paradigm: analytical framework

The research roadmap is showed in Figure 3.2. Based on the literature review and the determination of the research roadmap, the fourth chapter conducts data analysis, codes the interview content layer by layer, through the theoretical saturation test, determines the influencing factors of the implementation of the parametric release policy in China, and draws the driving path for policy entrepreneurs to promote the parametric release policy. Based on that, the fifth chapter leads to conclusions.

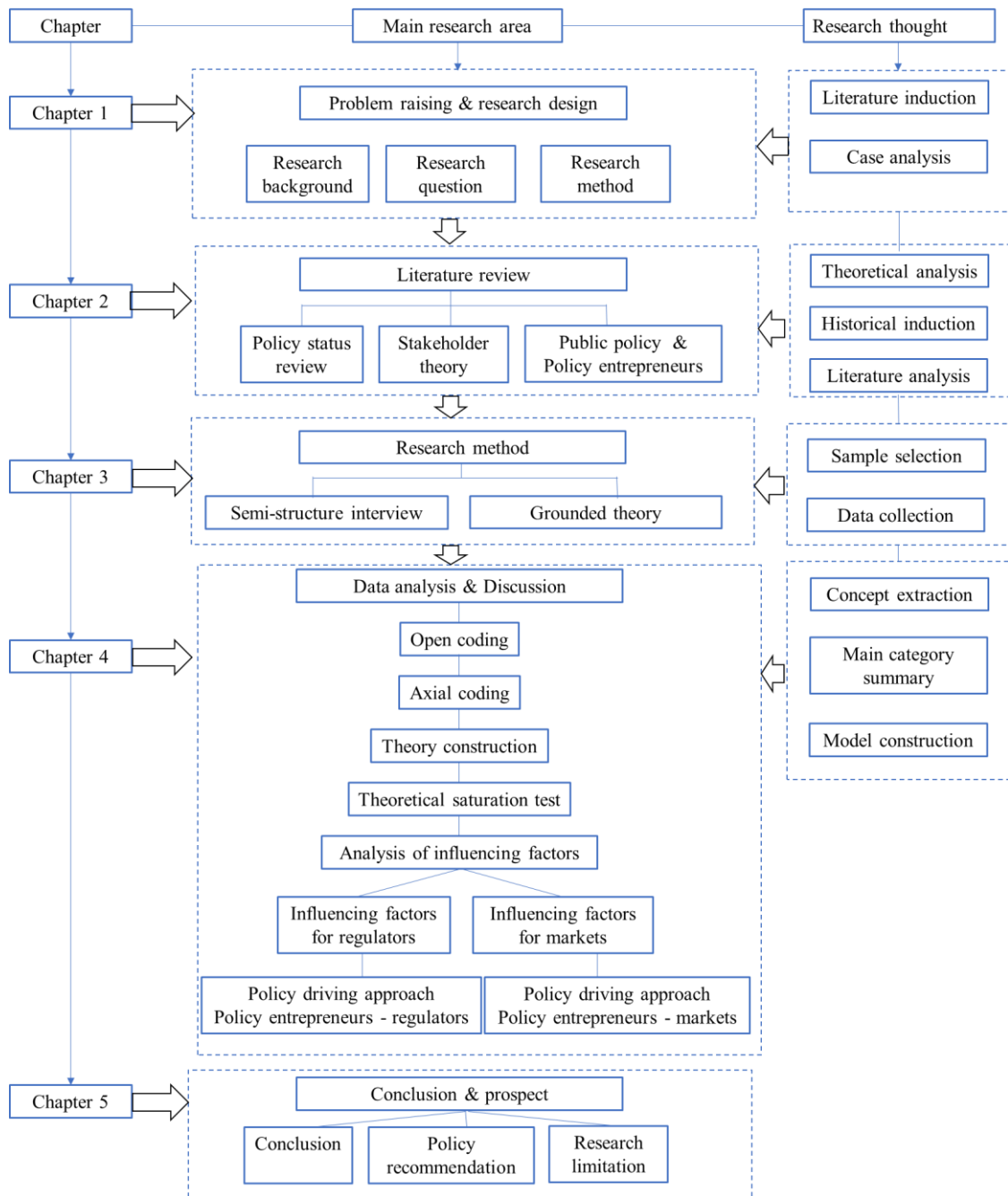


Figure 3.2 The research roadmap

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Chapter 4: Results, Analysis and Discussion

4.1 The current implementation status of parametric release policy from a stakeholder perspective

This study takes first-hand interview data as the core and adopts NVivo 12 qualitative research data analysis software to run the coding.

Based on interviews with 33 stakeholders from health authorities, pharmaceutical companies, industry associations and medical institutions, the study sorted out the role of each stakeholder in the process of parametric release policy promotion. In the pilot of promoting parametric release policy, pilot enterprises become policy entrepreneurs actively promoting parametric release policy based on their accumulated pilot experience and competitive interests. In the process of pilot promotion, as an administrative organization, the China FDA and its subordinate technical centers are the main communication objects of the pilot enterprises to promote the parametric release policy.

Figure 4.1 shows the relationship of interests in the process of implementing the parametric release policy with the pilot enterprises as the core.

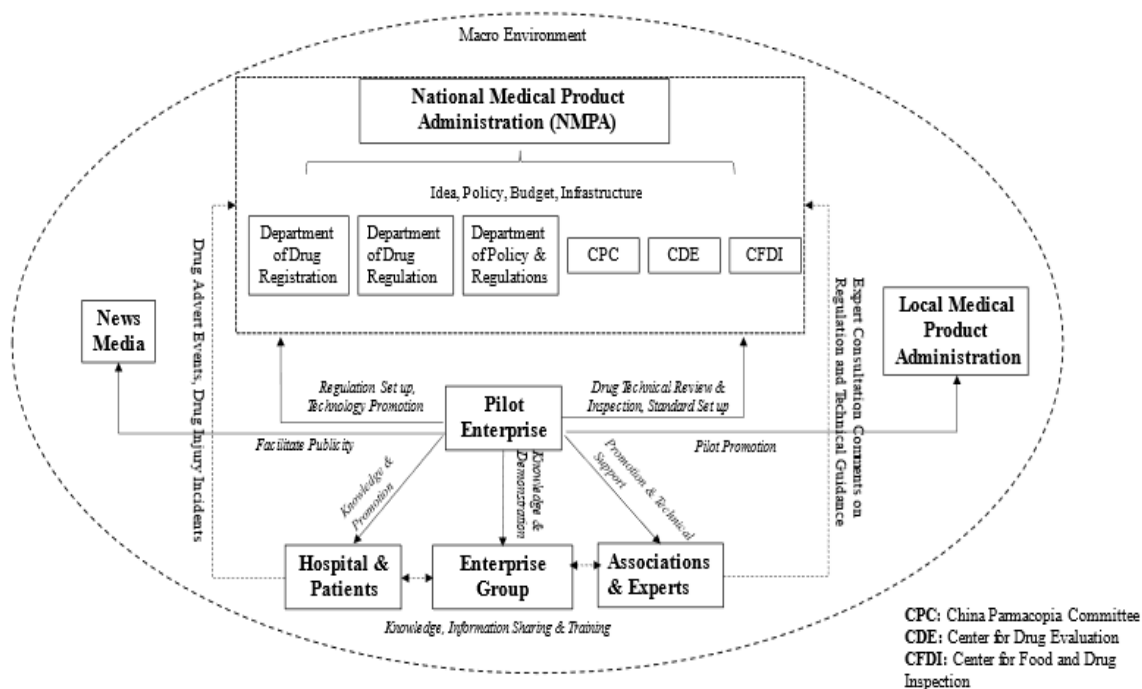


Figure 4.1 Interest correlation in the process of the parametric release policy promotion

China's drug regulatory system is highly centralized. The Department of Drug Regulation under the State Drug Administration is responsible for organizing the formulation and supervising the implementation of Good Manufacturing Practice (GMP) according to its duties, organizing the formulation and guiding the implementation of business, use quality management practices. It is also responsible for organizing and guiding production site inspections and organizing the investigation and punishment of major violations. The Department of Drug Supervision is also responsible for the implementation of the parametric release pilot program released in 2005.

The Department of Drug Registration is responsible for organizing the formulation and supervision of the implementation of drug standards and technical guidelines such as the National Pharmacopoeia, and the formulation and implementation of the drug registration management system. The registration path for enterprises to apply for parametric release must be approved by the Drug Registration Department and technically reviewed by CDE. The Department of Policies and Regulations is responsible for studying major policies on the supervision and management of drugs, medical devices, and cosmetics, and organizing the drafting of laws, regulations and departmental rules. For example, the Drug Administration Law released in 2019 was led by the Department of Policy and Regulations to organize research and submit it to the Legal Work Committee of the National People's Congress. Through the link of soliciting opinions from the society in the Drug Administration Law, policy entrepreneurs have solved the problem of establishing a superior law, which allow the product release method different from the traditional inspection and release.

In addition, CDE and the National Pharmacopoeia Commission (CPC) are affiliated institutions directly under the State Drug Administration. Comparing with the FDA, CDER is responsible for the technical review of parametric release, and CDE is also mainly responsible for the technical review after the establishment of a routine registration path for parametric release. The National Pharmacopoeia Commission is responsible for organizing the compilation, revision and compilation of the Pharmacopoeia of the People's Republic of China and supporting standards. Because the United States Pharmacopoeia, the European Pharmacopoeia and the Japanese Pharmacopoeia all include content related to parametric release, policy entrepreneurs are also interested in including relevant content in the Chinese Pharmacopoeia in the form of guiding principles in the process of promoting the implementation of the parametric release policy. Willing enterprises are offered options for implementation.

The China Food and Drug Inspection Center is an institution responsible for organizing the formulation and revision of drug inspection system specifications and technical documents and

is also responsible for on-site inspection of drug production. When a manufacturer declares a product for parametric release, the inspection center is responsible for inspecting the production site by relevant requirements. In the relevant inspection requirements of GMP and PIC/S, there are relevant chapters on parametric release. The local Food and Drug Administration is mainly responsible for safety supervision and management including drug production and distribution, but at the same time, the local Food and Drug Administration can draft and supervise the implementation of local laws and regulations. Therefore, local pilots are also an option to promote the implementation of regulations related to parametric release. In addition to pilot enterprises and drug authorities, industry associations and medical institutions are also important stakeholders in the promotion of parametric release policies. As a bridge connecting enterprise groups and drug regulatory departments, the association participates in the technical guidance and promotion process of parametric release policy as a third party. On the one hand, it can help enterprises to carry out research and publicity training and help the development of the industry. On the other hand, it can help the regulatory authorities to formulate technical implementation rules and establish a government-enterprise communication platform. As the final recipients of parametric release products, medical institutions and patients' acceptance and satisfaction with the technology will also affect the promotion of parametric release policies in China. We believe that information on some adverse reactions and drug quality incidents that occurred in hospitals can also promote the State Food and Drug Administration's emphasis on changing the regulatory concept. The enterprises group here refers to the relevant large-volume injection production units, and their capabilities and attitudes are also an important basis for regulators to consider whether to promote the implementation of parametric release. At the same time, the policy entrepreneurs from the associations and the pilot enterprises also hope that through the transfer of some knowledge and the role of demonstration, these pilot enterprises can drive the willing enterprises to jointly improve industry standards and improve the quality of medicines. The role of the news media can also play an important role in coordinating public awareness and conveying positive information about parametric release.

4.2 The emotional attitude of stakeholders toward the promotion of parametric release

During the interview with stakeholders, a survey was conducted on the emotional attitude and promotion intention towards the parametric release policy. The results are shown in Table 4.1.

Table 4.1 The evaluation of emotional attitude and belief in promoting parametric release policy

		The Emotional Attitude					Belief	
		Strongly agree	Agree	Neutral	Disagree	Strongly disagree	Can be promoted	Difficult to promote
Health authority	A1	1					1	
	A2	1					1	
	A3	1					1	
	A4				1			1
	A5		1					1
	A6				1			1
	A7	1					1	
	A8		1				1	
	A9	1					1	
	A10	1						1
	A11	1					1	
	A12	1					1	
	A13	1					1	
Industry Associations	B1	1						1
	B2	1						1
	B3		1					1
	B4		1					1
	B5	1						1
	B6		1					1
Enterprises	C1	1					1	
	C2	1					1	
	C3	1					1	
	C4	1					1	
	C5	1					1	
	C6		1					1
	C7			1				1
	C8		1					1
	C9		1				1	
	C10	1					1	
Health institutions	D1				1			1
	D2	1					1	
	D3		1				1	
	D4		1				1	

The data in the table is further analyzed and summarized as follows in Table 4.2.

Table 4.2 The interviewee's emotional attitude in the implementation of parametric release

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
A	9	2	0	2	0
B	3	3	0	0	0
C	6	3	1	0	0
D	1	2	0	1	0
Total	19	10	1	3	0

More than 88% of interviewees have a positive attitude towards the implementation of parametric release in China. More than 65% of these respondents were very positive. This shows that in general, the interviewees generally recognize the scientific nature of parametric

release policy and the significance of improving the quality of pharmaceutical products and believe that it should be implemented in China. 12% of interviewees are cautious about the implementation of parametric release and do not care about or disapprove of the implementation in China.

The interviewee's belief in the implementation of parametric release indicated in Table 4.3. About 36% of the interviewees are more confident in the implementation of parametric release in China, believing that parametric release can be promoted in China. About 45% of interviewees believe that there is hope for promotion in the future, and more preparations need to be done at present. However, 18% of interviewees still believe that parametric release is difficult to promote in China.

Table 4.3 The interviewee's belief in the implementation of parametric release

	Can be promoted	Can be promoted in the future	Difficult to promote
A	6	5	2
B	0	6	0
C	6	1	3
D	0	3	1
Total	12	15	6

4.3 Grounded theory analysis and theoretical model construction

In the implementation process of the parametric release policy, it is important to understand what factors affect the implementation of the policy, and the mechanism of the influence of these factors. This study adopts the three-level coding of grounded theory, presents the influencing factors and logic of policy promotion through open login, relational login, and the core login. In this study, 652 original sentences and corresponding concepts are preliminarily extracted through the process of coding and frequency statistics. 530 are related to the influencing factors. After further classification and integration of the influencing factors, a total of 35 initial concepts and 12 initial categories were obtained, and finally classified into 5 categories.

4.3.1 Stakeholder subject category coding

This study first screens the stakeholders contained in the interview data. During the coding process, the researchers found that the respondents had a consistent perception of the regulator as a stakeholder, among which the Food and Drug Administration was generally considered to be a direct stakeholder with decision-making power over the policy. During the interview, the

interviewees mentioned that regulators of different departments within the Food and Drug Administration have different roles in implementing the policy, “our supervision is divided into many departments, so you may have to treat different departments as separate stakeholders, because they may perform different responsibilities. For example, they are combined to represent the regulator” (C2). In addition, regulatory agencies are also divided into different levels, “there are national bureaus, provincial bureaus, municipalities, and the industry park where the enterprise is located has their local bureau...” (C5). But there is no doubt that the entire drug regulatory agency, the drug regulatory department plays a decisive role in whether to implement the parametric release policy. At the same time, some interviewees pointed out that in addition to the Food and Drug Administration, the Health Security Bureau is also one of the stakeholders as decision-makers, but they have different opinions on the role that the Health Security Bureau can play. Some people think that “Health Security Institutions will adopt the method of value procurement in the future, in the method of value procurement, they should still care about safety and effectiveness, not just a matter of cost, price control problem. So from the perspective of longer-term strategic procurement in the future, he should also be a very important party” (B6). However, some people think that “from the perspective of medical insurance payment, I just got this product. As for how this product is produced, medical insurance is not very concerned” (C7). In addition, some interviewees pointed out that the local government is also one of the stakeholders. “On the one hand, he has regulatory and security requirements and considerations, and on the other hand, he also has such considerations for industrial development, so he also needs to strike a proper balance between the two” (B6).

Respondents generally agree that pharmaceutical manufacturers are key stakeholders. However, different types of enterprises have different attitudes towards the implementation of the parametric release policy. “Enterprises are divided into domestic enterprises and foreign-funded enterprises” (C2). “Those low-level companies in the industry who have not reached this average level are also key stakeholders” (C5). “Some good companies, they want to advocate the implementation of this parametric release, it is an advocate” (A10).

In the interview, some interviewees also mentioned drug distribution companies, they are between manufacturers and users, as a link in the drug supply chain, they are also stakeholders of the parametric release policy. “The current regulations in our country, as long as you operate, no matter whether you know the situation or not, as long as there is an accident, you must bear the responsibility” (D1).

From the perspective of users, hospital managers, such as the dean, the chief of the pharmacy department, doctors and nurses, and the patients as final users, the safety of drugs is

a matter of great concern to users. Most of the interviewees think that they are also the stakeholders involved in the policy. Respondents all agree that patients, as the end users of medicines, are direct stakeholders, but because of the particularity of the industry, they hardly have any influence on policies. “Patients are related, but patients have unequal knowledge. He doesn't understand these things, or how medicines are produced. He just needs to give him the safest medicines” (A6). For hospital managers and clinical users, the interviewees believe that the most important thing is to provide clinically safe and qualified products. “The clinic should also be a stakeholder, because in this way, if the resulting products are more reliable, their use will be safer” (B1). “From a doctor’s point of view, I think this policy can be promoted. You must give me qualified products. I do not have this safety problem during use” (C6). But regardless of patients and medical institutions, the overall feeling is that they are a bit far away. “The end users do not understand the front-end, so they do not have this demand” (A1). Therefore, the degree of impact on policy is limited.

Experts from industry associations and scholars in the health field appear as third parties, but they play a key role in the development of the industry. From the interview results, this group of people, as a third party who influences policy formulation, is also a stakeholder in the implementation of the parametric release policy. “They have influence on the regulatory agencies, and they can also communicate with enterprises” (C5).

Individual interviewees also mentioned the public and the media. “Because the infusion itself is relatively risky, especially in China, we generally use it more commonly, including at the grassroots level. So, when there are some serious quality problems in the infusion, it will still cause a lot public attention. So, their reactions among others should also be considered” (B6).

4.3.2 Open coding

Open coding is essentially a word-for-word encoding of raw interview material. To reduce the personal bias of the researcher as much as possible, in principle, the original expression of the interviewees is used to refine the initial concept (J. M. Wang & Wang, 2011). In this study, 652 original sentences and corresponding concepts are preliminarily extracted through the process of coding and frequency statistics. 122 are related to Stakeholder identification and the emotional attitude of stakeholder. 530 are related to the influencing factors. After further classification and integration of the influencing factors, a total of 35 initial concepts and 12 initial categories were obtained. To save space, this article only presents the frequency of

occurrence and corresponding categories of initial concepts. See Table 4.4 for details.

Table 4.4 The initial coding categorization of effectiveness factors regarding parametric release policy implementation

No.	Categorization	Initial Concept
1	turnover of regulators 12	leadership change of Health Authority (HA) 4, human resource change of HA 5, professional mobility 3
2	segmentation of regulatory powers 17	multi-headed supervision and nobody to lead 12, institutional reform 2, lack of regulatory Top-level design 1, stagnant of pilot 1, multiple and frequent changes of regulatory system 1
3	size of regulatory organization 2	understaffed 1, too busy 1
4	Covid-19 Pandemic 5	Conflict of priority due to R&D and evaluation for COVID prevention & treatment drugs 5
5	drug injury incidents and quality incidents 2	vaccine incident 1, QiErYao event (counterfeit drug) 1
6	disconnection of international market 5	the difference in finished goods release procedure 4, changes in international situation 1
7	International standard harmonization 4	products and regulations are in line with international standards 4
8	good foundation of quality supervision 28	the good foundation of Chinese GMP 9, awareness of the limitations of sterility testing 9, cognition of the concept of parametric release 5, relevant knowledge reserve 3, concept of quality control 1, group standards 1
9	ability of regulators 4	reviewers and inspectors lack of experiences 3, unfamiliar with front-line work in industry 1
10	regulatory philosophy 19	culture of quality management 11, regulatory environment tends to be conservative 2, public consensus on drug supervision 1, Chinese atheism culture 3, integrity of society 2
11	legal basis for technology 33	regulatory environment of parametric release 23, regulatory compliance 10
12	technical accountability system 8	the enterprise/MAH is the first responsible person 2, responsibility subject 5, authority have unlimited liability 1
13	the communication skill with regulators 4	enhanced communication 4
14	the communication channel with regulators 11	association facilitates communication / information asymmetry 11
15	social reputation of enterprise 15	low levels of government trust with enterprise 13, low levels of public trust with enterprise 2
16	basics of production technology and quality management 12	weak implementation of GMP in China 10, backward production technology 2
17	clinical demand-oriented policy trends 8	patients benefit 6, the policy development trend centered on clinical needs 2
18	bacterial infection events 1	bacterial infection events in China 1
19	technical advantage of parametric release 41	traceable digitized regulatory process 9, enhanced process control 7, more reliable product quality improvement technology 11, risk control moved forward & supervision efficiency improvement 9, drive the total quality management 5

No.	Categorization	Initial Concept
20	enterprise production advantage 21	14-day production turnaround savings & reduced testing and storage costs 10, cost reduction 7, gain economic benefit 3, increased production capacity 1
21	promotion and education status 3	parametric release education 2, promotion in industry 1
22	VBP policy 10	centralized procurement prices are lowered 6, policies supporting centralized procurement 3, increased medical insurance expenditure 1
23	technology optimization cost 12	high up-front optimization cost 10, difficult to articulate the benefit 2
24	capability level of domestic pharmaceutical companies 29	unbalanced levels of development 16, technical talent is not available 2, cognitive bias towards parametric release 8, accumulation of professional knowledge 3
25	advantages of product differentiation 5	parametric release promotes product differentiation 5
26	leading companies promote 5	leading companies have strong belief in implementing parametric release 4, favorable for financing activities of listed company 1
27	promoted by industry associations 22	help companies and regulators develop implementation rules 10, conduct training 3, conduct research studies 3, promote industry development 4, profit driven 2
28	insufficient market demand 7	scattered enterprise needs 7
29	enterprise innovation momentum 17	little motivation for a business without profit 3, Manufacturers have little incentive to raise standards 14
30	regulatory risks 58	liability risk 42, Technical risk/product qualification conclusion lacks direct inspection proof data 10, product risk 3, public opinion risk 2, integrity risk 1,
31	regulatory trust 18	concerns about the ability of the enterprise 13, regulators believe that firms are profit-oriented 5
32	regulatory priorities 59	leadership acceptance of parametric release technology 35, many more important things than implementing parametric release 7, Not the focus of regulatory work 17
33	Market Risks 8	risk management 3, product qualification conclusion lacks direct inspection proof data 5
34	opportunities for reform and some policy release 12	need of the Great Power of Pharmaceutical Industry 1, need of the Great Power of Quality 2, hot issues of regulatory 5, younger leadership team promoted 1, Green & Environment Protection 3
35	pilot experience 13	Demonstration Effect/Experience Accumulation 13

4.3.3 Axial coding

By further analyzing and concluding the initial concept and category, axial coding attempts to retrieve the logical relationship between categories and summarize the main category. This work further classifies the categories obtained by initial coding and obtains 12 main categories and 5 core categories which is shown in Table 4.5.

Table 4.5 Axial coding of influence factor for parametric release implementation

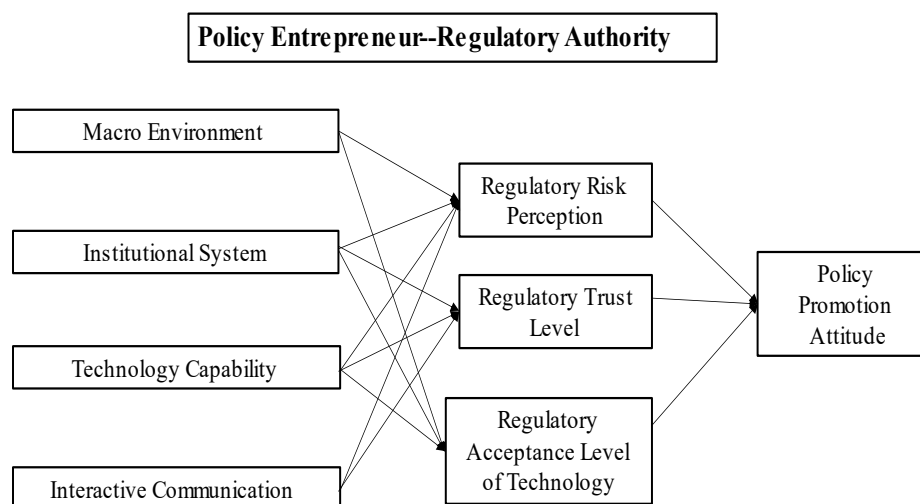
Core categories	Main Categories		Related Category
Macro environment	The conflict of regulatory macro environment	Regulatory Macro environment	Regulatory reform direction Drug injury incident COVID-19 pandemic
	The conflict of market macro environment	Market macro environment	Disconnect from international market Insufficient promotion and education VBP Policy
Institutional system	The promotion of regulatory macro environment	Regulatory macro environment	The good basis of quality management supervision The trend of clinical oriented policy Virus infection events
		Organization construction	Turnover of regulatory officials Segmentation of organizational power Size of FDA organization
	The conflict of regulatory supervision system	Policy & regulation	Technology legal basis Technology implementation standard Technology accountability system
		Internationalization of regulation	The acceptance of international standard Unification of standard in local & global
Technical capability	The conflict of regulatory capability	Regulatory capability	Personnel literacy of HA official Regulatory cultural concepts Regulatory experience accumulation
	Catalyst of technical capability	Production efficiency Pilot experience	Technical advantage of parametric release Process demonstration Expert pool
	Conflict of industry capability	Manufacturing cost Industry average technical level	Cost for technology optimization Quality test level of average local players
Interactive communication	The conflict of interaction between gov. and enterprise	The interaction between Gov. and enterprise	The communication skill with HA The communication channel with HA Corporate social reputation
	The conflict of market information exchange The motivation of interests group	Market information transmission Interests group	Question from NHSA Question from patients Driving by leading enterprises Driven by Industry

Core categories	Main Categories		Related Category
Subjective factor	Subjective factors of regulator	Regulatory risk perception	Associations
		Regulatory trust level	Public opinion risk
		Technology acceptance level of regulator	Enterprise fraud risk
	Subjective factors of Market	Market enthusiasm	Regulatory trust
		The acceptance level of technology by market	Regulatory priority
		Market risk perception	Enterprise innovation dynamic
			Insufficient market demand
			The risk of lack of product release testing report
			The risk of quality management and analysis

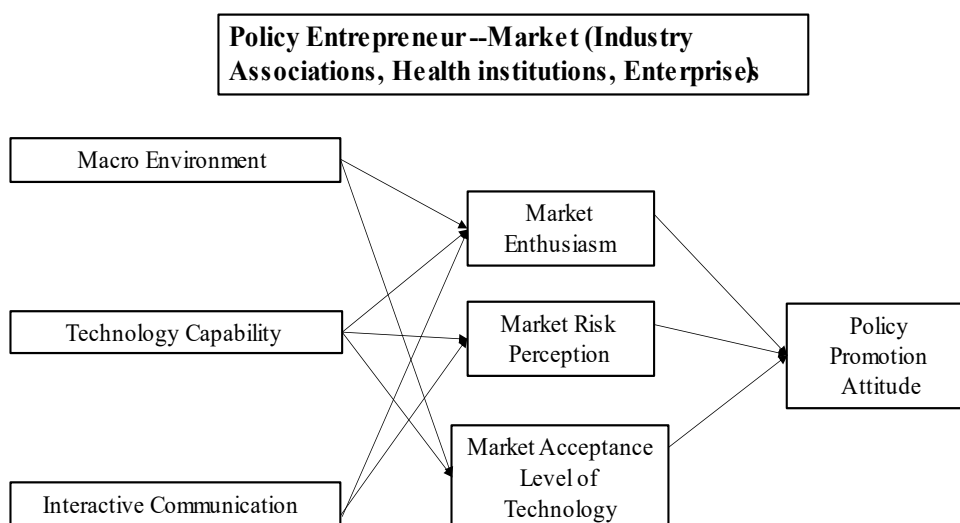
4.3.4 Interpretation of the relational structure of core category

Core logging is to further analyze the relations between the main categories and refine the core categories and connect the logical relations between the categories. From the perspective of policy entrepreneurs, this study believes that the promotion and hindering factors existing in the promotion process of parametric release policy can be understood from the logical relationship between policy entrepreneurs and regulatory authorities/policy entrepreneurs and market entities (enterprises, patients, and industry associations), and the confusion of why a good policy cannot be implemented into a good execution can be explained in Figure 4.2.

Policy Driven Approach



Policy Driven Approach



A → B The presence of A has an impact on B

Figure 4.2 Policy driven approach

4.4 Theoretical saturation test

Theory saturates when new interview material emerges and does not generate new categories. The last three interview manuscripts were selected, the categories and axes were coded separately, and the coding results were compared with the total coding results to test the theoretical saturation of the research results.

Overall, the comparison between the coding results of the three samples in the control group and the coding results of the total sample shows that the coding content of the samples in the control group still conforms to the context and relationship summarized based on the coding of the total sample, and no new categories and relationships are found. As a result, this study considers the theoretical model shown in Figure 4.2 to be saturated.

To further test the reliability and validity of the theory, two senior scholars who focus on public policy management are sought to verify the relationship results obtained through grounded theory coding. From the perspective of two senior scholars, the theoretical model has a logical rationality.

4.5 Analysis of influencing factors

When policy entrepreneurs promote a policy, they may be associated with many interest groups. Taking the implementation of parametric release policy for large-volume injections as an example, these interest groups include regulatory agencies, production and distribution companies, medical institutions as users, patients, industry associations, experts and scholars, among others. These stakeholders consider the pros and cons of policy advancement based on their interests.

However, due to differences in positions, environments, regulatory and technical capabilities, among others, there are cooperation and conflicts in the promotion of existing policies. After using the grounded theory to complete the coding of the interview data, it is necessary to further explore the impact of the interviewees on the policy entrepreneurs to promote the parametric release policy, because in the process of the parametric release policy, the policy entrepreneurs will promote the regulators and the market separately,

Therefore, the analysis is also divided into two parts: regulation and market, respectively exploring the influence of the macro environment, institutional system, technical capabilities, and communication when policy entrepreneurs promote regulation, and the macro environment, technical capabilities, and communication of policy entrepreneurs when promoting the market.

impact of communication. This chapter analyzes the influencing factors of the promotion of the parametric release policy obtained through coding analysis. After, we will further analyze the driving path of policy entrepreneurs to promote the parametric release policy.

4.5.1 Influencing factors in the process of policy entrepreneurs promoting regulators

4.5.1.1 Regulatory macro environment

The macro environment is a powerful force in the construction of policy entrepreneurs to drive policy agenda setting. Through the analysis of the macro-environment of supervision, we can see that the macro-environment of both conflict and promotion will have an impact on policy implementation. The regulatory macro-environmental conflicts mentioned in the interview include opportunities for reform and policy release, drug injury and drug quality incidents, and the impact of the new crown pneumonia epidemic. Factors promoting the regulatory macro-environment include the current relatively sound quality regulatory foundation, clinically oriented policy trends, and the occurrence of bacterial infection incidents leading to awareness of the limitations of traditional sterility testing.

According to the theory of multiple streams of policy entrepreneurs, the political stream is an important part of the three streams. The opportunities for reform and policy release mentioned in the interviews reflect the general environmental trend. On the one hand, China's pharmaceutical industry is moving from a big pharmaceutical country to a powerful pharmaceutical country. A very important factor of pharmaceutical power is the quality of medicines. A9 believes that "whether or not our country does this is a sign of whether we can become a pharmaceutical power"; A13 "a quality power is fundamentally to ensure the risk of product going to market. Relying on inspection, our quality will never improve. We must to take this step". Therefore, to realize the transformation of China's pharmaceutical industry from a big pharmaceutical country to a powerful pharmaceutical country, the government should increase its efforts and formulate more powerful measures. A younger leadership team was mentioned by interviewers as a favorable factor for promoting reform. The leadership of the younger generation has a more scientific and innovative concept of supervision, and is willing to introduce advanced international concepts and technologies into China, which will be a favorable factor for the introduction of new technologies and concepts.

From the perspective of the public policy process, the occurrence of an event is often the fuse that triggers the formation of policies. On the one hand, if there is no such major incident, the relevant agenda may be easily put on hold, such as what A7 said, "there is no key drug

injury incident now. Then they have no such enthusiasm”. On the other hand, some interviewees pointed out that due to the occurrence of individual drug injury incidents, regulatory agencies and personnel are cautious about the risks that may be brought about by the introduction of any new policies. As A2 said, “Because there have been many so-called drug-injury incidents, including from QiEr Pharmaceutical AE issue to the Changsheng vaccine incident, who will take care of it now”?

The COVID-19 pandemic is another very critical timing issue. In the more than three years since the outbreak of the new crown epidemic in early 2020, the authority's work has focused more on matters related to the new crown epidemic. For the Drug Administration, the biggest problem is how to quickly review and approve products related to the new crown epidemic, such as nucleic acid detection related reagents, preventive and therapeutic drugs, establish an emergency approval mechanism, and control the quality of epidemic prevention products. In this general environment, the Drug Administration is bound to give priority to this part of the work and put other seemingly less urgent agendas on hold. (A9: After the epidemic in 2019, no one has the energy to take care of such a very specific project with relatively high technical requirements.)

On the other hand, in terms of the regulatory macro environment, we also see some catalysts that help set the policy agenda. For example, most of the interviewees still believe that the foundation of my country's quality supervision is relatively perfect. It has been 25 years since China started to establish GMP regulations in 1998. After so many years of accumulation and improvement, our GMP quality management system has a good foundation, which is a necessary condition for the implementation of parametric release. An interviewer mentioned, “China's 2010 version of GMP has been implemented for more than 12 years, and a good GMP quality management foundation is a necessary condition for the implementation of parametric release” (C1). From this point of view, our current GMP drug quality management foundation is completely different from the domestic GMP situation in 2005 when the pilot program was launched. A11 believes that after the implementation of the new version of GMP in 2011, whether it is the “General Principles” or the “Appendix for Sterile Drugs”, it is basically in line with the EU GMP. Therefore, from the perspective of GMP regulations, it should have a basis to support parametric release. A2: In all aspects, these domestic companies have indeed improved rapidly in recent years, including many companies that have passed EU certification and FDA certification, so they all have such capabilities. So, we feel that this (policy) should be no problem when it is rolled out.

Most interviewees agree with the limitations of sterility testing, and believe that the results

of sterility testing may not necessarily represent the sterility level of the entire batch, and believe that the industry has a consensus on this aspect. C4 believes that the sterility guarantee of the product is guaranteed through a process, not through a confirmation of the final inspection that the product is sterile. A8 believes that to solve the limitations of aseptic release, more effective methods and methods are needed, that is, parametric release. Some interviewers believe that parametric release is not a new thing, it has a history of 30 years and is a mature technology.

4.5.1.2 Regulatory system

The regulatory system is an important influencing factor in setting the regulatory policy agenda. We can also see this very clearly from the interviews. The institutional system involved in the interview can be roughly divided into several aspects, such as organizational construction, institutional regulations, and international standards.

Organizational construction

Organizational construction involves the division of organizational powers, the flow of supervisory personnel, and the scale of supervisory organizations.

First of all, most of the interviewees talked about the situation caused by the division of powers in the regulatory system. Parametric release is a technical regulation, and the agenda setting, and implementation of the policy are supervised by multiple parties and no one takes the lead. As shown in the previous stakeholder map, the implementation of the parametric release policy requires the participation of multiple departments of the Drug Administration. The Registration Department of the Food and Drug Administration and the Drug Evaluation Center are involved in the pre-approval of parametric release; the Supervision and Management Department of the Food and Drug Administration and the Drug Inspection Center under the Food and Drug Administration are involved in the review and daily supervision of the actual implementation process; The China Pharmacopoeia Committee is involved in the formulation of specific standards; and the Policy and Regulation Department of the Food and Drug Administration is involved in how to solve the obstacles in the regulations, to formally include the parametric release in the regulatory system of Chinese drug administration. The attitudes of these departments towards parametric release, and how to coordinate the interests and contradictions among these six departments to form a complete working model have become the key issues to be resolved in the policy formulation stage.

C1: In the drug supervision system, there are many departments related to it, such as the Department of Drug Supervision & management, Registration Department, Policy & Regulations Department, and some of its implementation departments of these regulations, such

as Center of Drug Evaluation, Drug Inspection Center, the Pharmacopoeia Commission, and many institutions are related to this subject. The question is who is taking the lead? Everyone is willing to follow, but no one is willing to lead.

A13: We feel that the scope is getting wider and wider. Some policies specifically involve a unilateral policy, which is easy to implement. This one involves such a reversal and some subversive things. It is very difficult now.

Lack of coordinated supervision and absence of leadership are the main reasons why there is a lack of effective top-level supervision. Without a clear overarching framework, individuals tend to act on their own accord. Usually, a policy agenda that involves multiple departments also lacks proper top-level regulations, resulting in various issues arising chaotically. People often pass the blame to one another, making it difficult to reach agreements and compromises.

A4: Perhaps the biggest obstacle is that the top-level design does not have... From the whole framework path, you have to implement it, how many steps you need to take, and what each department should do, all of which are not available now.

In addition, China's institutional reforms and system changes in the past 20 years, as well as the government's deliberate frequent adjustments and changes in leaders have also made the implementation of this work inconsistent. In addition to the frequent change of leaders, the frequency of change of staff and technical personnel related to policy formulation is also very large. This leads to a discontinuous state in the discussion and promotion of policy agenda setting.

Some interviewers talked about the problems in the previous pilot process. He believed that the failure of the pilot was mainly due to changes in the regulatory authorities. As A4 mentioned, "Parametric release is a task assigned to Department of Drug Supervision by Food and Drug Administration at the beginning. At that time, the task was to let them try out what to do. The final problem was that the pilot project couldn't be closed, and you didn't know who to turn to for the problem... No one cared about it".

A9: Due to the repeated adjustments and changes of our country's drug regulatory system and the corresponding adjustments of regulatory personnel, the administrative advancement of this work has been affected many times.

C1: Some leaders who are familiar with and accept such a regulatory concept, because these leaders are often changed, and some new leaders do not understand, or accept, or completely understand such a concept. Such a system has not been well developed and implemented.

B2: We have too many job rotations, which makes us technical officials feel uneasy. I am doing it, but I do not know where I am going next year, there is no continuity.

The size of the regulatory organization can also lead to sidelining parts of the policy agenda. During the interview, some interviewees mentioned that the drug administration is severely understaffed and overwhelmed. In this case, even though they realize that some policy agendas should be put forward, due to the lack of organizational scale, he can only selectively implement the most urgent and important things to him. In many cases, their agenda is often pushed.

Institutions and regulations

Institutions and regulations include the legal basis of technology and the meaning of the technical accountability system.

Parametric release refers to the evaluation of product sterility assurance based on effective control, monitoring, and sterilization process validation data, instead of release system based on finished product sterility test results. From a technical point of view, does the so-called "direct release without inspection" violate the current legal system? Is it feasible at the legal level? This question concerns the legal basis of technology.

The promulgation of regulation requires the support of the regulatory system. Many people pointed out in the interviews that the implementation of parametric release lacks a superordinate method. China's version of the "Drug Administration Law" before 2019 stipulates that products need to be inspected before release. While one of the main purposes of parametric release is to replace the inspection and release of final products through process control. This has been an obstacle in the regulatory system since the pilot project of parametric release in 2005. In the process of formulating and revising the 2019 version of the "Drug Administration Law", policy entrepreneurs inside and outside the system have made unremitting efforts to change this part of the content from the original "Drug manufacturers must conduct quality inspections of the drugs they produce; Or..., shall not leave the factory" (Drug Administration Law 2007 Edition, Article 12), amended to "drug manufacturers shall conduct quality inspection of drugs, and those that do not meet the national drug standards shall not leave the factory" (Drug Administration Law 2019 Edition, Article 47) changed from "must" to "should", leaving room for the adoption of parametric release. However, during the interview process, some interviewees still think that this statement is not clear, and the regulatory compliance is still in doubt.

A7: From the point of view of the leaders of the health authority, what they worry about is still a kind of violation of the higher-level law. The Drug Administration Law stipulates that products must be tested before they can be released to the market. Is it illegal to cancel the inspection? This is a relatively large obstacle.

Another problem in the legal system is that there are no comprehensive supporting

regulations, which is very important to the implementation of policies. For example, for the relevant regulatory authorities, how to manage and evaluate? For the enterprises, what standards should refer to, and through what path to apply for approval? For the Center for Drug Evaluation, what is the criteria and pathway to evaluate? When the Inspection Center inspects the site, what standards should they refer to? After the product release to the market, how to show the benefit of the products that implement parametric release compared with those that do not implement parametric release? These are supporting policies that need to be introduced before the implementation of the parametric release policy.

The 2019 version of the “Drug Administration Law” implements the marketing authorization system and the corresponding responsibilities and obligations of the marketing authorization. This is a very big change in the evolution of China’s legal system. For policy innovation, it will give the government more confidence. But from a practical point of view, the Chinese government has always been big, and the government often must cover the responsibility of enterprises.

From the description of the accountability system, with the advancement of the marketing authorizer system, everyone realizes that the enterprise, as a marketing authorizer, should assume the main responsibility and take full responsibility for the quality of the product. But at the same time, we also see that this concept is still in a process of gradual advancement, and it will take time to fully accept it. In the process, regulators will still assume certain responsibilities for enterprises. In addition, from the perspective of regulatory agencies, because policies are formulated by regulatory agencies, they will also worry about the rationality of policy formulation and whether the technical indicator requirements will not bring new risks. If there is a quality problem under the new policy system and is not discovered by timely supervision, the regulatory agency should also bear corresponding responsibilities. In such a big environment, regulators will be more hesitant to introduce innovative policies.

B6: Regulators are accountable for life, although it is stated in the document that there is due diligence and exemption, there are still difficulties in the process of implementation.

C9: Once this policy is formulated, in fact, under the method of parametric release, he is worried that if something goes wrong, they will be held accountable, and everyone will point the finger at them first, without blaming that company first.

A8: Once you have a problem, although the company is the first responsibility, it still must bear the responsibility from the perspective of supervision.

Internationalization of regulation

In terms of globalization, Chinese regulators have been working to promote international harmonization of regulations. The landmark event is that in 2017, the China Drug Administration officially joined the ICH and became the Management Committee in 2018. Member. China's drug registration management system is speeding up to be in line with international standards. However, in the actual operation, considering the complex situation of China's pharmaceutical industry and local characteristics, regulatory agencies do not unconditionally accept international standards. Some internationally accepted regulations and the guidelines are still not implemented in China. Parametric release is officially like this. In fact, in 2021, ICH Q6A, that is, parametric release, has also been transformed by the Food and Drug Administration and officially approved by the Food and Drug Administration. But it is still seen that in the actual operation environment, parametric release It has not yet been officially adopted. So, from this perspective, the advancement of globalization still needs to be worked hard.

4.5.1.3 Regulatory technical capacities

The technical capabilities of regulatory agencies are mainly manifested in regulatory capabilities, including regulatory cultural concepts, the quality of regulatory personnel, and the management basis of production quality from a regulatory perspective.

An important element of the concept of regulatory culture is the culture of quality management. Firstly, the concept of QbD was proposed 20 years ago. Its core is to move the control point of drug quality supervision forward, from relying solely on final product inspection in the past to the control of the production process, and then to Product design and control of the research phase. Simply put, it is to ensure the quality and safety of drugs from the source. This concept has been recognized and adopted by the industry in China for more than ten years. The essence of parametric release is based on the concept of quality by design, which moves the control of product quality to the design and production stage. However, in China's actual GMP implementation, our traditional thinking, the concept of "drug quality is controlled through inspection", "inspection and quality control" to judge product quality still exists in the industry, resulting in parametric release certain concerns.

A3: Everyone will say that (quality) comes from design and process control, but in fact, the Chinese have said it for more than 10 years, and foreign countries have written it for more than 20 years, but they still all stay in their mouths (in China). There is no deep understanding, deep sentiment.

D4: My idea is that the implementation of this in China is actually a change in concept or culture, and then what kind of process or technology should we adopt on the specific technical level, or other monitoring methods.

The quality of supervisory personnel is another aspect that reflects supervisory capabilities. From the perspective of review and verification, most reviewers have no industry background, and they have no practical experience in front-line R&D, production, and quality control, especially in microbial control and sterilization processes. The review of parametric release is based on a comprehensive understanding of the product in terms of design and development, process verification, quality control, and risk assessment. Therefore, there are certain concerns from the interviews regarding the introduction of technical regulations such as parametric release.

C2: In many times, one of their concerns may also be whether the reviewers and inspectors have the level to grasp the limits.

Supervision capabilities are also reflected in the production and quality management foundations of my country's current pharmaceutical industry. Although China's GMP has been implemented for more than 20 years, compared with the period when GMP was first implemented, our overall level has been greatly improved. However, the GMP foundation of the entire industry is still relatively backward compared with developed countries and regions such as the United States and Europe. The level varies among industries. During the interview, some experts expressed concern about the actual situation of domestic GMP: “B4: I think there are differences compared with domestic ones. The domestic equipment has been upgraded, but there are still gaps in the quality of personnel, the concept of GMP, and the execution of the system. I even think that this gap is not very small, nor can it be changed in a short period” (B4).

Some interviewers also mentioned that the product process and prescription reviewed in the past are problematic according to the current GMP requirements, and do not fully meet some requirements of terminal sterilization. Therefore, he cannot implement parametric release in this state. This restricts the promotion of parametric release in China (A11).

4.5.1.4 Interaction with regulatory authorities

The communication channels between industry and regulators in China are not very smooth. The government is unwilling to communicate more with enterprises for multiple reasons. Some policy suggestions from policy entrepreneurs outside the system, from the perspective of regulatory agencies, he will think that these policy entrepreneurs are making profits for their interest groups.

Under the current situation of poor communication, policy entrepreneurs have to rely on industry associations to communicate with drug supervision. On the one hand, as a neutral institution, the association has no conflict of interest with industry companies and regulatory agencies. They stand in the position of a third party. When they think this matter is beneficial to the industry and regulation, they will be willing to build a platform for communication and exchange in the middle. Compared with enterprises, it is easier for associations to create opportunities, so that supervision, industry, and associations can sit together and communicate through meetings and other forms.

On the other hand, when companies and regulatory agencies discuss parametric release policies, they are often unable to accurately interpret parametric release, and sometimes cannot clearly explain its technical characteristics and advantages from a regulatory perspective, which makes the communication effect less effective. As proposed in D3, “communicate more, understand the considerations and problems during supervision of health authority, and clarify the problems in a targeted manner (D3)”.

4.5.1.5 Subjective factors of regulators

The subjective factors of regulators mainly involved in the interviews are regulatory risk perception, regulatory trust, and regulatory technology acceptance.

Regulatory risk perception

Regulatory risk was the most frequently discussed category in the interviews. A total of 59 occurrences occurred in the subcategory.

First, from the perspective of supervision, there are still relatively big concerns about the possible responsibilities for implementing a new policy. Parametric release is mainly applicable to sterile preparations of injections, which are for intravenous use, and large infusion products are widely used in China, so they are high-risk products in China. Any product quality problem may lead to serious drug quality incidents or even drug injury incidents. However, China's current industry situation is not at a relatively high overall level. For example, the world's top 500 companies often have relatively reliable quality management systems, which are trustworthy in terms of technical capabilities and management levels. There are a large number of low-to-medium-level injection manufacturers, and it may be very difficult for their technical capabilities and quality management levels to meet the most basic requirements. If these companies implement parametric release, it is difficult to guarantee the sterility of the product. Therefore, for such products, it is very prudent for regulators to introduce an innovation related to product quality.

From the point of view of the operation of parametric release, although theoretically speaking, all the quality control points of parametric release have been moved forward and verified, which can ensure the sterility of the product to the greatest extent, but from the perspective of superficial operation, it reduces the last step of sterility inspection is equivalent to the lack of final confirmation inspection from the time of release, and it seems that the quality risk seems to be magnified.

From the perspective of approval, parametric release has very high requirements for review technicians and inspectors responsible for product review. These personnel need to have very rich experience in product development, production, sterility, and quality control, and be able to judge whether the previous control measures and control points can fully realize the sterility of the product based on the information provided by the company. If the reviewers do not have rich experience in such a new thing, they will worry that they will not be able to handle the registration and approval process well, leading to the risk that the products released by the company's parameters may not meet the standards. Even when supervisors do not have full confidence, they will worry that substandard products may be released to the market, resulting in the risk of serious adverse events due to product quality problems. In this way, the risk of supervision will be magnified.

Even if the product is listed on the market after providing complete information and passing the review of the regulatory agency, the regulatory agency still has to undertake a large number of market monitoring responsibilities after the product is distributed to the market. Because the responsibilities of post-listing supervision are scattered among the regulatory agencies in various provinces and municipalities, it means that the supervisory personnel at the grassroots level need to have a certain understanding of parametric release technology. And once relevant quality doubts arise, supervisors need to change their past habits and rely on the factory inspection report as the basis for product sterility and need to find relevant evidence from the source of production. These in-depth investigations require higher requirements on the technical capabilities of supervisors and supervisory resources.

From the perspective of technical acceptance, some interviewees feel uneasy about canceling the final sterility test. The traditional method has been used for so many years and has become the accepted norm. The product is produced, tested, and released as qualified. Whether it is a regulatory agency or the public, this is the most direct way to prove product safety. If the final inspection is eliminated and the final inspection is replaced by the control of production process parameters, it seems that there is no direct evidence to prove whether the product meets the standard. It seems that this kind of feedback is caused by ignorance of the

front end and insufficient understanding of quality control, but it does represent the mentality of some supervisors. For them, once a sterility-related problem occurs after the product is launched, at least the factory inspection report can be used as the basis for the product to be qualified, and it can also prove that the regulatory agency is in control and the regulatory measures are in place. However, if the final inspection is replaced by the control of production process parameters, supervisors may be passive because of the cancellation of the final release inspection and lack of direct evidence. Therefore, for such new technologies and new things, regulators often have a sense of “insecurity” (A5) and feel that “it is better to avoid unnecessary trouble” (A12).

Judging from China’s current general environment, ordinary people have placed more demands on regulatory agencies. Although the regulations stipulate those enterprises, as the legal owners of products, are responsible for the full life cycle management of products, but because we are owned by the big government. However, when something goes wrong, the people will still think that the state should bear the relevant responsibilities and take the responsibility for the bottom line. The vaccine incident mentioned in the interview, although the regulatory agency discovered the company’s problems during the verification process, and thus imposed corresponding penalties on the company and disposed of the product accordingly, but from the public’s point of view, the government has regulatory responsibilities. Regulators have also been punished to varying degrees. Some regulators may be inclined to stick to established practices, with a mentality of “that’s how the regulations are, not mine” (A1), rather than pushing for new approaches. On the contrary, if a new practice is actively introduced, once something goes wrong, the person who introduced it is likely to be implicated, resulting in damage to personal interests. Some people may even think that there may be compliance risks: “I do not want to start with this first, some people may think that I am suspected, and what benefits the company will give me?” (C1).

The risk of public opinion is also an issue that regulators are very worried about. Introducing new measures, new methods, the intention is good. But because medicines are closely related to people's lives and safety, we will be very cautious in this regard. Once a signal that is easy to be misinterpreted is released during the process of introducing new policies, such as “the product has not been tested, the common people will use it”, and it is amplified by the media, or once an adverse event occurs, it may cause a large public opinion. Pay attention to or public opinion events.

Therefore, many people think that from the perspective of the benefit-risk ratio, the enthusiasm for promoting the parametric release policy is not high.

A10: The main concern of regulators lies in the risk of approval itself.

B6: I feel that regulators are worried. On the one hand, they do not have the opportunity and means to fully understand, nor do they have detailed data in this regard to allow them to dare to make decisions.

C10: In the current China, he may be mainly seeking stability. He thinks that you should not make a breakthrough. If you make a breakthrough, there may be unexplainable risks.

B6: This benefit itself is not so direct, but the negative impact brought about by the change is more direct and visible in the short term.

Regulatory trust

From the interview text, it can be concluded that regulatory trust is mainly divided into two aspects. On the one hand, it is the supervision's concern about the company's ability, and on the other hand, it is the suspicion of the company's interest orientation.

From the perspective of many regulators and industry experts, they believe that although China's GMP has been implemented for more than 20 years, the overall GMP level of the pharmaceutical industry is still at an uneven level. Some interviewers believe that "foreign companies may be possible, but domestic companies cannot" (C1). It is believed that the implementation of such a policy will only allow a small number of foreign-funded enterprises to implement and benefit, and it lacks universality. An interviewer mentioned, "It is very important to consider the national conditions... If it is put in the national pharmacopoeia, 50% of the enterprises will not be able to produce, and then it may cause instability to the economy and society" (B3). Generally speaking, the Health Authority is still worried about the ability of enterprises, and believes that in the current Chinese environment, the basic conditions for large-scale promotion across the country have not been met.

From past regulatory experience and their cognitive perspective, some interviewers believe that policy entrepreneurs have different motivations for putting forward this policy demand. They believe that this demand is only available to enterprises, and "there are still many profit-seeking organizations" (B6). Especially when the parametric release policy is proposed by a few companies, the regulators may preconceive that the companies are completely considering their interests, such as meeting their own needs for product release without inspection and saving storage costs among others. In addition, some interviewers also mentioned that if parametric release is implemented, it is necessary to ensure that enterprises do not make fraudulently from a subjective perspective. Therefore, from the perspective of supervision, it is natural to consider this issue with full vigilance (A7).

Regulatory Technology Acceptance

Regulatory acceptance of parametric release technology is mainly reflected in insufficient regulatory priority. It emerged from the interview text that one reason for the lack of regulatory prioritization was an insufficient understanding of parametric release by the leadership of the regulatory agency. In the previous statement on the regulatory macro-environment, institutional system, and regulatory capacity, a detailed description has been given of the status quo of regulatory agencies' understanding of parametric release in the above aspects, as well as the obstacles and concerns they face. Leadership tendencies often play a decisive role in policy agenda setting. "In the horizontal diffusion of China's policy innovation, top-down factors will be embedded" (H. S. Yang, 2020). There may be blind spots and misunderstandings in the leadership's cognition of technical regulations, including sterility assurance, quality evaluation system, scientific basis for parametric release. As we mentioned earlier, leaders perceive greater risk. Some leaders think that companies want to implement parametric release to save costs. They only see that one inspection link has been reduced, but they have not seen the addition of multiple control steps. They think that companies are promoting it purely from the perspective of profit. These will have an impact on the attitude of the leader. Even based on a certain understanding, he may continue to worry about the ability of supervision, such as how the Drug Evaluation Center at the central level should review the data, what criteria the Drug Inspection Center should follow to conduct the inspection. Since comprehensive supervision after approval needs to be delegated to local Food and Drug Administrations, do local regulatory agencies have the resources and capabilities to conduct supervision? They even worry that once a product safety incident occurs, it may cause unnecessary troubles. Therefore, if the leaders cannot correctly and comprehensively recognize the advantages of this technical path, then the priority of supervision will be reduced, which will lead to the shelving of the policy agenda.

The promotion of policies is inseparable from the influence of political winds. China began to promulgate GMP for the first time in 1998. At that time, the industry focused on how to improve the production process, product quality, and comply with GMP. The concept of parametric release was put forward by policy entrepreneurs inside and outside the system in early 2000, and it was immediately regarded as a very advanced quality management method and an innovation of quality management. Against this background, the Food and Drug Administration launched two pilot projects for 5 years and sent a team of experts to visit abroad to understand the implementation of parametric release abroad, the legal system, and learn from the implementation experience of enterprises. However, after the pilot, due to various reasons, the Food and Drug Administration did not summarize the experience of the pilot and formally

introduce parametric release, and the relevant policy agenda has been shelved until now. After 20 years of development, China's pharmaceutical industry has continuously improved the overall quality management level of the industry through the transformation of hardware and software. GMP has also undergone several revisions in the later stage and has aligned with EU GMP. From the perspective of regulatory agencies, the current state has met the requirements of drug quality management from the framework of policies and regulations to the actual level of the industry. In recent years, with the continuous changes in the macro environment, China's pharmaceutical industry has developed rapidly, and industry hotspots have shifted more to product research and development, clinical development, marketing authorization systems, pharmaceutical licensing transactions (license in / license out), among others on the one hand, the focus of supervision has gradually shifted from production to circulation supervision, such as spot checks and information traceability. Compared with the current priorities, parametric release may appear less important. Therefore, in terms of the development of the country's general trend, it may not be so urgent.

Compared with the demands seen from the supervision, large-volume injection itself is a relatively niche professional field. The current routine aseptic release operation has been verified by the industry for many years. At present, there is a demand for parametric release. Businesses are not in the majority either. However, under the environment of macro-reform in recent years, especially the new crown epidemic in the past three years, the drug administration has invested a lot of resources in the review and approval of diagnostic reagents, vaccines, emergency medicines and medical devices, and epidemic prevention supervision. Items on the work schedule may have been backlogged and delayed. In the post-epidemic era, policies that are directly related to people's medication, such as centralized procurement of drugs and medical devices, have been brought into the front line and urgently need to be resolved. However, policy agendas that have little impact on the industry and seem to have less urgent needs, such as parametric release, do not see the general needs of the industry, and coupled with the limitation of regulatory resources, they are often not included in the current regulatory focus.

In summary, the regulatory priority reflects the regulatory acceptance of technology. Increased regulatory priority is critical to drive parametric release.

From the above analysis, the regulatory macro environment, institutional system, regulatory technical capabilities, and interactive communication all exist as objective influencing factors. These objective factors will affect regulatory subjective factors such as regulatory risks, regulatory trust, and regulatory technical capabilities. make an impact.

4.5.2 Influencing factors in the process of policy entrepreneurs promoting market

While policy entrepreneurs push regulators to set policy agendas, they are also constantly influencing all aspects of the market, hoping to create an environment suitable for agenda setting, thereby driving policy innovation. Although the decision-making power for policy agenda setting rests with the Food and Drug Administration, by promoting the market environment and providing policy makers with more sufficient reasons, it is conducive to the opening of the policy window.

As can be seen from the stakeholder review, in the market segment, the main stakeholders include the entire group of injection companies, hospital administrators, medical staff, and patients, as well as related associations and experts.

In terms of the market, the factors influencing the setting of the policy agenda from the interview information mainly include the macro environment of the market, technical capabilities, interactive communication, and market subjective factors.

4.5.2.1 Market macro environment

In the market macro-environment, technical standards are not in line and synchronized with international standards, which is a relatively important factor affecting the formulation of parametric release regulations. With the vigorous advancement of drug regulatory reform in recent years, China has done a lot of work in international coordination since it entered into the WTO and its entry into ICH and other international organizations. However, considering that the entire industry in China is still in a complex situation with uneven levels, the acceptance of international regulations and standards is not comprehensive, and there is a time lag and selective acceptance. Back to parametric release, it has been implemented in major foreign markets for more than 30 years, and already belongs to an internationally recognized quality standard, but because it has not been accepted in China, there may be two release standards for the same product. The most typical example is the case of Shanghai GM. The same products produced in the Shanghai factory are released with parameters for the US market, but for the same product supplied to the Chinese market, to meet the needs of Chinese regulations, an independent production line has to be established, and after 14 days of sterility test after the product is produced, it can be released only after passing the test. This greatly increases the complexity of enterprise operations and reduces the efficiency of its production. Similarly, some imported products of some companies generally adopt parametric release in foreign production, but if they want to sell them to China, they need to make separate arrangements for the

production, process parameters, quality control, sterility inspection and product release of this part of the product, which increases production. complexity.

Another factor affecting the acceptance of the parametric release policy agenda is the current policy of bulk procurement of medicines. China has launched a new medical reform since 2009, and gradually introduced a series of policies since 2015 which stated in the Guiding Opinions on Improving the Centralized Procurement of Drugs in Public Hospitals issued by the General Office of the State Council and a series of policies including the pilot plan for the centralized procurement and use of drug organized by the state in 2019, especially the policy of centralized drug procurement with quantity, as a major measure to deepen the reform of the medical and health system. The price is low, so that the common people can use good medicine and reduce the cost of national medical commercial insurance. To put it simply: in the past, major hospitals purchased on their own, but now the state has united with hospitals in various cities to establish a joint procurement office, agree on a unified procurement volume, let pharmaceutical companies bid, and force more drugs to achieve substantial price cuts. In other words, the profits of generic drug companies are diluted by the country's huge procurement volume. With the large-scale implementation of the centralized volume-based drug procurement policy in recent years, the price of drugs has dropped significantly, corporate profits have shrunk significantly, and drug costs are facing tremendous pressure. Under such circumstances, many companies are unwilling to increase investment in software and hardware such as equipment and facility updates and personnel training to implement parametric release. Secondly, the most critical factor in the centralized volume-based procurement is the price. At present, if they pass the “consistency evaluation” of generic drugs, they can enter the scope of centralized procurement. At present, there is no trend to further stratify the quality of these products, so that high-quality products have priority in the centralized procurement process or have certain advantages in pricing. If value-added benefits cannot be generated by investing in new technologies, it will be difficult to drive the adoption of new technologies. Therefore, there are still certain obstacles in the large market environment.

4.5.2.2 Market technical capabilities

Parametric release is a release system that evaluates the sterility assurance of products based on effective control, testing, and sterilization process validation data to replace the sterility test results of finished products. In the production and quality control of sterile drugs, parametric release is a more effective method than traditional control methods. Its role in promoting the technological capabilities of the market is significant. The interviewers have a positive attitude

towards the technical advantages of parametric release itself, especially the experts engaged in quality management. On the other hand, process control is strengthened. By controlling the key process parameters in the production process, the production process is kept stable and reliable, thereby ensuring the sterility assurance level of the product. This process strengthens monitoring and controls risks at the front end of production, rather than relying only on final sampling inspections. As stated by A7, “parametric release is a higher-level control method in process control and a higher-level stage of GMP implementation, which is more guaranteed for product quality control”.

Digitization is another technical advantage of parametric release. Parametric release needs to control the process, including the temperature, pressure, time, among others of the terminal sterilization process. These key process parameters need to be monitored in real time in a digital system, and all quality data are recorded and traceable. On the one hand, the sterility of the product is ensured to the greatest extent by monitoring the compliance in the production process, and at the same time, the authenticity and traceability of the data are effectively guaranteed. By regularly reviewing electronic data and conducting trend analysis, it is possible to see whether the product quality attributes are stable and whether there are any abnormal phenomena, and to better analyze possible deviations and causes. Therefore, for enterprises, the implementation of parametric release is a better-quality management method, which effectively guarantees the quality of products. At the same time, this digital model also provides enough convenience for regulatory agencies. Regulatory agencies can view all production records, and even directly connect enterprise data to the regulatory system to achieve real-time monitoring, thereby improving supervision’s efficiency.

The implementation of parametric release not only promotes the quality control of the product itself, but more importantly, it drives the quality management culture of all employees. Parametric release requires the participation of various departments. In addition to the quality management department, R&D, production, engineering, microbiology, IT, among others all need to participate in this part of the work. In terms of hardware, it is necessary to upgrade key facilities and equipment, and improve and strengthen production and quality management. In terms of software, product sterility needs to be considered at the R&D stage, combined with the product packaging system, sterilization process, among others to design, it is necessary to equip special aseptic and microbiological experts to participate in the design of the production process, and establish a reliable Risk assessment and management system. This is a change in the concept of the traditional product quality that is only the responsibility of the quality department in the past. Quality management is integrated into the entire life cycle of the product, realizing

the concept of quality by design, and truly embodying the quality management culture of all employees.

B1: Compared with the traditional release after sterility tests, the control point of parametric release is earlier, and it is a control of the whole process, which is more advantageous.

C1: The security of this system, through data traceability and data analysis, is not just a result, but a slight disturbance in the process, it can be displayed by the system.

B6: Because of such a parametric release, it also forms a higher mechanism internally to mobilize all people to pay attention to this quality, especially the process quality... Its incentive mechanism should be more significant.

In addition to the advantages of quality management, parametric release is freed from the aseptic sampling inspection of products before they leave the factory by moving forward the aseptic control, to increase production capacity, improve production efficiency, reduce costs, and finally achieve economic benefits for enterprises the result of. The traditional sterility test and release method not only requires a certain number of samples to be consumed for each batch of products, but also requires manpower and material resources for testing. More importantly, it takes 14 days for the sterility test to produce results. Before the results appear, all produced products must be stored in the warehouse and not released until the test results are qualified. The use of parametric release can effectively reduce the release cost and inspection cost, especially shorten the release cycle, and save storage costs.

C10: I understand that parametric release is a mode with the lowest total social cost after long-term implementation A10: The ability to implement parametric release can shorten the cycle from production to patient use of the drug for enterprises and patients, and can also save some storage, storage, and transportation costs for enterprises.

From the point of view of the technical capabilities of the entire market, the Drug Administration began to conduct pilot projects for parametric release in 2005 and conducted pilot projects for two leading multinational pharmaceutical companies in Guangdong and Jiangsu, two major pharmaceutical provinces. Through two rounds of pilot projects for a total of five years, the two companies have accumulated a large amount of data and experience, and at the same time cooperated closely with regulatory agencies, so that the central and provincial bureaus have also accumulated a large amount of regulatory experience through learning and practice and gained an in-depth understanding of parametric release in this process. At the same time, since 2005, through the pilot project, domestic large-scale injection companies have also been actively learning and exploring and spontaneously began to prepare for the pilot project. These manufacturers, including those that have implemented and are planning to implement,

account for more than half of the total production capacity of large-volume injections in China. This demonstration effect has laid the foundation for the formal implementation of parametric release in the future and accumulated rich experience.

Although the interviewers talked about the technical advantages of the above parametric release promotion, we also saw that there are still certain obstacles and challenges in terms of market capabilities. As mentioned before, the implementation of parametric release requires enterprises to invest in hardware and software such as production line facilities and equipment, computer systems, professional equipment personnel, microbiology personnel, and training. In reality, injection companies have very little profit in the macro-environment of volume-based procurement. If parametric release is implemented, a certain cost will be invested in the early stage. However, because the product enters the scope of volume-based procurement in the market, the price of the product is no profit margins, even if parametric release is implemented, it is uncertain that this quality differentiation can be converted into a premium bonus in the general environment of centralized procurement, which will lead to many companies' unwillingness and even resistance.

From the perspective of the enterprise capabilities of the entire industry, different from the relative concentration of foreign companies, the level of injection companies in China is uneven. Some leading companies, including large multinational companies and large domestic injection companies, are in the advanced level of quality management. level, for them it is feasible to implement parametric release. However, there are still a large number of injection companies that are still at the middle and lower levels in China. First of all, they do not understand the parametric release, and their knowledge and technical reserves may not be achieved. Some enterprises have never been in touch with parametric release and have no idea of what parametric release is and how to do it. Some enterprises have doubts, "Implement parametric release, how to set my parameters? If the range of parameters is set too strict, will it affect the scrapping of my product (A3)"? "Many times, in the past, our industry hoped that the regulator would tell them what to do and how to do it, and he would do it, but he was not clear about why he did so" (A11). For these companies, it is not easy to meet the current domestic GMP requirements. "For the implementation of parametric release, they may not be ready in terms of facilities, technology, personnel, and knowledge levels. This is a process that requires learning, understanding, and practice" (A5). If parametric release is implemented without the relevant capabilities, it is likely to lead to product quality incidents and even affect the drug safety of patients. From this perspective, both regulatory agencies and some companies in the industry will also hesitate to implement parametric release.

To sum up, the advantages of parametric release at the technical level are obvious. The implementation of parametric release can effectively improve production efficiency and reduce costs in the long run, so that the quality level of enterprises can meet higher requirements. And through the pilot project, some leading enterprises have already or will have the ability to implement parametric release, giving full play to their demonstration advantages and accumulating experience for large-scale implementation in the industry. But at the same time, it is also seen that although the technical capabilities of enterprises have been greatly improved compared with the pilot period of 2005~2010 when parametric release was started, the current scale of injection companies is large, and the level of enterprises is uneven. There are still technical difficulties regarding full implementation of parametric release. Furthermore, the implementation of parametric release requires enterprises to modify and invest in their software and hardware in the early stage, which increases the cost in the early stage, and in the environment of centralized drug procurement, it is difficult to benefit from profits. Therefore, there are certain obstacles and conflicts.

4.5.2.3 Market communication and interactions

It has been almost twenty years since parametric release was studied as a subject in China. During the pilot period, several leading companies have done a lot of work in this process to help the industry and regulatory agencies understand the concept and practice of parametric release, such as joining the pilot work, and simultaneously carrying out the dual process of traditional sterility inspection and parametric release in Chinese factories, to accumulate relevant data on parametric release, share the implementation experience and belief of parametric release, and help regulators understand the concept and advantages of parametric release. At the same time, assist industry associations to participate in several research topics related to parametric release.

Industry associations have played a very important role as a bridge in the publicity of parametric release by taking advantage of their third-party status. China Medical Equipment Association has been committed to promoting the implementation of parametric release in China. Since the 1990s, they have been involved in the promotion and pilot work of parametric release. they hope to promote the implementation of parametric release in China by helping the drug administration establish GMP and approval guidelines and standards, establish enterprise alliances, and carry out training. At present, with the gradual implementation of scientific supervision concepts and leading technologies in China, more and more industry associations and experts have also paid attention to the technical field of parametric release. The China

Pharmaceutical Quality Management Association and the China Pharmaceutical Quality Research Association will respectively set up projects for the implementation of the policy of parametric release in 2019 and 2020. They hope to formulate relevant standards, guidance documents, approval procedures and requirements, and strengthen official and industry through training. Measures such as improving the quality of enterprise quality management personnel and quality management capabilities can promote the construction of a legal system, introduce this advanced management system into China as soon as possible, and make China, a large injection country, reach the international advanced level in technology.

But compared with the huge number of Chinese injection manufacturers, the above work is still in limited range. Leading companies account for more than half of the supply of injections, but compared with the number of companies, this is still a very small number. Since the parametric release regulations have not yet been implemented in China, the industry has not shown great enthusiasm for the training and learning organized by the association, and the participation is insufficient. How to achieve larger-scale industry exchanges, promote, and make more companies realize the advantages of parametric release, and gradually improve their quality management level, so that most enterprises in the industry can have the ability to implement parametric release, is the next step to be solved.

In addition, it can be concluded from the interviews that end users, including medical staff and patients, do not understand parametric release at present, and there are almost no channels to understand it. However, as product users, they are most concerned about quality and safety. If they can understand the qualitative advantages of parametric release, their voices will also have an impact on the ultimate policy makers.

4.5.2.4 Subjective factors in the market

Subjective factors at the market level mainly include market enthusiasm, market technology acceptance, and market risk perception. Judging from the results of encoding, subjectively, conflicts and obstacles are still unresolved.

From what has been mentioned above, it can be found that the enthusiasm of the market is still not high at present. This can be observed from two perspectives. First, enterprises are willing to innovate and introduce new technologies, new ideas and new products. Their ultimate goal is profit driven. As for parametric release, judging from the current situation, some companies in the industry believe that a large amount of investment is required in the early stage, but they cannot see clear benefits. Second, from the perspective of improving quality management capabilities, enterprises have no strong motivation to raise their standards.

Parametric release is not a mandatory regulation in ICH and European and US regulations. Regulatory agencies recognize that it is a better-quality management measure than GMP. When an enterprise applies and provides a large amount of research materials and verification data as supporting evidence, the regulatory agency will go through procedures such as data review and on-site inspection, and the company can implement it after approval. Therefore, even if parametric release is adopted, enterprises can choose to implement it. Many enterprises believe that implementing parametric release is difficult and requires high requirements for enterprises. In that case, if there is no national policy guidance or mandatory requirements of laws and regulations, many enterprises will not be willing to implement it.

From the perspective of market demand, the demand seen so far is limited, mainly concentrated in a few pilot enterprises and some leading domestic enterprises. Pilot enterprises hope to use their own experience to drive the high-level development of the entire industry, and at the same time hope to obtain corresponding benefits through the implementation of parametric release. Some willing leading enterprises hope to improve product quality and establish leading enterprise brands, and to maximize benefits by reducing costs and increasing efficiency. Especially when enterprises need to go overseas, it is very necessary to implement parametric release; however, most enterprises still have low demand for technology improvement and implementation due to the aforementioned reasons.

Enterprises also have concerns about the related risks arising from the implementation of parametric release. If the company is not particularly confident in the technology itself and its management capabilities, he will worry about whether the quality of the product is consistent with expectations or whether substandard products will flow into the market when releasing the product directly without traditional sterility testing. On the other hand, although the traditional sterility inspection method has limitations, if the company has produced by the requirements of GMP and released it after passing the traditional sterility inspection, then even if there is a problem, at least the company has not violated the regulations. The problem is caused by the limitation of technology itself, not the problem of enterprise management.

From the above analysis on the market level, the market macro environment, technical capabilities, and interactive communication exist as objective influencing factors, and these objective factors will in turn affect market subjective factors such as market enthusiasm, market technology acceptance and market risk. Conflict or facilitate, influence, and thus ultimately influence policy agenda setting.

4.6 Policy entrepreneurs' driven approach for parametric release policy promotion

From the analysis of influencing factors in Chapter Five, we can see that there are many factors influencing the implementation of the parametric release policy in China. The macro environment, institutional system, communication, and technical capabilities are all objective factors that exist in the process of promoting parametric release. These factors will affect the subjective feelings of regulators and the market, such as regulatory (market) risk perception, regulatory trust (market enthusiasm), and regulatory (market) acceptance of technology, thereby affecting policy implementation. These objective factors constitute the policy flow that affects the policy window. Policy entrepreneurs are in the process of promoting policies, that is, by influencing objective factors in the policy flow, they promote changes in supervision and subjective perceptions and attitudes of the market. Once the policy window is open, policy entrepreneurs can seize the opportunity to set the policy agenda and drive its implementation. The existence of objective influencing factors affects the subjective influencing factors, and then affects the attitude of policy promotion. This chapter analyzes the driving path of policy entrepreneurs to the parametric release policy from two aspects of regulation and market.

4.6.1 Policy entrepreneurs' driven approach to health authority

4.6.1.1 Influencing factors of regulatory risk perception

The regulatory macro-environment, institutional system, regulatory technical capabilities, and interaction with regulation will all have an impact on regulatory risk perception.

From a regulatory point of view, for the management of high-risk products such as injections and other sterile preparations, regulatory agencies attach great importance to product quality assurance. The overall level of China's pharmaceutical industry is relatively low, and there are many difficulties in technical capabilities and quality management. Therefore, great care needs to be taken to introduce innovations related to product quality.

In terms of the regulatory macro environment, the occurrence and impact of drug hazards and drug quality events are directly related to the perception of drug regulatory risks. Drug manufacturers should control the quality of the drugs they produce and assume the main responsibility. However, the level of drug manufacturers in my country is uneven. At present, drug regulatory authorities mainly focus on random inspections and unannounced inspections of drug quality, and it is difficult to conduct full-time and full-time supervision of the drug

production of each manufacturer. As a big government, the Drug Administration bears big responsibilities, and the government must bear unshrinkable regulatory responsibilities for any related problems.

There are also promoting factors in the macro-environment of supervision. With the rapid development of the pharmaceutical industry in the past three decades, a relatively complete foundation for quality supervision has been established. my country's GMP benchmarks against EU GMP, and the adoption of various international coordination guidelines and standards also marks a significant improvement in the overall level of the industry. Clinically oriented policy trends and positive attitudes towards the introduction of new technologies and ideas. The leadership of the younger generation is more inclined to introduce advanced concepts and technologies from abroad, which will help promote the development of the regulatory macro environment.

The regulatory macro environment will affect the risk perception of regulation. On the one hand, the occurrence of major events may trigger the fuse of policy formation. On the other hand, the occurrence of individual drug injury events may lead regulators to be cautious about the risks of new policies. Overall, the regulatory macro-environment is a powerful force in policy agenda setting, with both conflicting and facilitating factors. The interaction of different factors will affect the emergence of regulatory risks and the formulation of prevention and control measures.

The influencing factors of the institutional system on regulatory risk can be summarized as follows:

Organizational construction, the institutional system involves the division of organizational powers, the flow of supervisory personnel, and the scale of supervisory organizations. The situation of multi-management regulation and no-one-leadership may lead to difficulties in policy advancement. When the policy agenda involves multiple departments, the lack of a dedicated coordinating group may lead to difficulties in coordinating relationships, pushing issues to each other, and making it difficult to reach agreement and compromise. The top-level design of supervision is lacking, individuals are self-sufficient, and there is a lack of overall planning.

The flow of supervisory personnel: China's institutional reforms and system changes in the past 20 years, as well as frequent government leadership and relevant personnel adjustments, have affected the continuity of supervisory work. Frequent changes of leaders and related personnel will create obstacles to policy continuity, which is not conducive to the promotion and implementation of policies.

The size of the regulatory organization: Regulatory agencies such as the Food and Drug Administration are understaffed, and their busy working conditions may cause some policy agendas to be put on hold. With limited resources, regulators may only be able to selectively advance the most urgent and important issues and may not be able to comprehensively advance other agendas.

If parametric release is introduced under the conditions of the above-mentioned institutional system constantly changing, multiple supervision and no one taking the lead, the supervisor may worry about the risk of quality incidents due to the lack of sufficient guidance and supervision in the policy implementation process, which will have a negative impact Promoting attitude of parametric release regulation.

The absence of a higher-level method for parametric release is a major obstacle to promote parametric release on the regulatory path. Through the efforts of policy entrepreneurs, the 2019 version of the Drug Administration Law has revised the clause that drugs must pass the inspection before they can be released from the factory, giving a certain space for the implementation of the parametric release policy, but there are still doubts that even after the revision, the statement still cannot clarify the legality of parametric release. If the promulgation of a legal article conflicts with the higher-level law, it will be difficult to break through in legislation. If the regulation pushes for parametric release under such circumstances, it needs to bear corresponding risks.

Rationality of laws and regulations and accountability system: From the perspective of supervision, a big question is the rationality of laws and regulations. The upper law Drug Administration Law has revised the clause that drugs must pass the inspection before they can be released from the factory. There is a certain space for the implementation of the parametric release policy, but there are still doubts that even the revised statement still cannot clarify the legality of the parametric release. If the promulgation of a legal article conflicts with the higher-level law, it will be difficult to break through in legislation. If the regulation pushes for parametric release under such circumstances, it needs to bear corresponding risks.

From the point of view of the accountability system of the Chinese government, the introduction of new policies by regulatory agencies may cause unknown risks due to problems in the implementation of the new deal. Even if China has officially launched the MAH system and improved the industry's responsibility system, the government still needs to bear the approval and supervision responsibilities. Therefore, regulators will think that the risk of launching a new policy is relatively high.

In summary, the institutional system has an important impact on regulatory risk.

Organizational construction, the flow of supervisory personnel, and the scale of supervisory organizations are important factors for the impact of institutional systems on supervisory risk. Based on improving the system, stabilizing personnel and rationally planning resources, it is possible to better deal with regulatory risks and advance relevant policy agendas. The setting of the higher-level law provides a clear legal basis for parametric release, and better implementation of MAH in China will help reduce the risk of regulatory agencies and help promote policy agenda setting.

Regulatory technical capabilities are also an important factor affecting regulators' risk perception. The traditional concept of inspection and control quality still exists, and a conservative attitude is taken towards the quality management change of parametric release. Parametric release has high requirements for technical personnel and inspectors in charge of product review. They need rich experience to judge whether the information provided by the company is sufficient to prove the sterility of the product. For regulators, lack of confidence may worry that a product is of substandard quality and placed on the market, leading to serious adverse events. Parametric release also puts forward higher requirements for the approval of regulatory agencies and market surveillance and requires regulators to have higher technical capabilities and resources. These factors together affect the ability of regulatory technology to assess and respond to regulatory risks.

When interactions with regulators are poorly communicated, the implications for regulatory risk are manifold. First, poor communication between the government and enterprises may lead to difficulties in policy implementation. Enterprises need to communicate with regulators to express their views, provide suggestions or solve problems, to promote the smooth implementation of policies. However, if the communication channels are not smooth, this will directly affect the degree to which the opinions of enterprises are understood and considered.

On the other hand, due to the consideration of clean government, the government may be reluctant to communicate frequently with enterprises, so as not to arouse accusations of profit-making by interest groups. This has also led to some barriers and concerns between the government and enterprises, making it difficult for enterprises to get in touch with government departments. Enterprises may not even be able to enter the door of the Food and Drug Administration. In this case, industry associations have become important.

As a neutral institution, the industry association has the advantage of a communication platform between different interested parties. It can build an opportunity for policy entrepreneurs to communicate and exchange, bring together regulators, industry practitioners and associations, and use meetings and other forms to promote communication. Associations

can play the role of building a neutral platform, giving voice to and connecting all parties, helping the industry understand the considerations and issues of regulators, and explaining the views of enterprises in a targeted manner.

Therefore, poor communication with regulatory agencies may lead to risks such as policy difficulties, damage to corporate social reputation, and decreased trust in the industry by regulatory agencies. Therefore, it is very important to strengthen the communication channels between the government, regulators, and enterprises, and enhance dialogue and understanding, which will help reduce potential regulatory risks and promote the sustainable development of the industry.

4.6.1.2 Influencing factors of regulatory trust

Trust is the willingness of one party to form a bond with another party in the belief that the mutual behavior of the other party will benefit rather than harm the first party (Gambetta, 2000). Cooperation between organizations requires mutual trust to be successful. Regulatory trust in the market is one of the important factors for regulators in considering the establishment and implementation of innovative policies. The regulatory system, regulatory technical capabilities, and interaction with regulatory agencies will all affect the degree of trust in regulation.

Regulatory institutional systems have a significant impact on regulatory trust.

In terms of organizational construction, my country's institutional reforms and system changes in recent years have had an impact on the continuity of authority management. In the process of institutional reform changes, as well as the frequent flow of personnel, the adjustment of supervisory personnel has resulted in a lack of continuity in policy implementation. In this process, it is difficult for regulators and the market to establish a good relationship of trust in a short period. Regulators do not have enough time and energy to understand the capabilities and demands of enterprises, as well as the background, policy content, and benefits of policies that policy entrepreneurs hope to implement, and they often only focus on short-term goals. Even if some officials are willing to invest energy and are willing to promote the establishment of an innovation policy agenda, they are often transferred away during the work, and the trust relationship generated in the early cooperation process is interrupted. After the new officials joined, because they did not understand the previous work, it was difficult to continue this trust relationship in a short period, and thus conflicted with the policy-driven process.

In terms of institutions and regulations, the technical accountability system will also have an impact on regulatory trust. China's accountability system is still in the development stage. At present, China's laws and regulations stipulate that leading cadres are lifelong accountability

system. In recent years, the accountability system has been continuously strengthened, and sometimes it may face the risk of going too far. The layer-by-layer transmission of accountability pressure complicates and generalizes accountability. Under this strict accountability system, officials tend to take a conservative attitude towards the introduction of new things, fearing that the adoption of new technologies and new measures will lead to unknown risks, which will lead to accountability. For the pharmaceutical industry, in recent years, with the revision of the new Drug Administration Law, strengthening the responsibility of market players is the core of the MAH system. But even so, officials often need to bear responsibilities from supervision and the market because of the strict accountability system. Under the general environment, the public's distrust of the government triggers public events and public opinion, which in turn will increase the government's conservative attitude. Therefore, from the current environment, the conservative attitude of the technical accountability system is not conducive to the establishment of regulatory trust, which will negatively affect the attitude of policy advancement.

Regulatory technical capabilities also have implications for regulatory trust. The quality of the regulator itself and the traditional concept of supervision will affect the establishment of a trust relationship. The regulator's limited understanding of new technologies and new things will cause regulators to be skeptical of the motions of policy entrepreneurs from the industry when considering the introduction of new technologies and new things. Sometimes even if they understand the scientific nature and advanced nature of motions in theory, However, regulators hesitated to implement the new policy due to their distrust of the industry's capabilities and their regulatory capabilities. Parametric release is based on the concept of quality by design, moving the entire quality control point forward, and does not depend on the final factory inspection of the product. This concept is essentially different from the traditional release concept of products can only be released from the factory if they pass the inspection. If the supervision adheres to the traditional concept of factory inspection, it will be difficult to resonate with the so-called product release without sterility testing for parametric release. Even if some officials agree with the concept of parametric release, however, due to concern of their regulatory capabilities, they still worry about the corresponding regulatory technical challenges in the process of policy implementation, such as whether the reviewers have enough ability to review the company's technical data and the grassroots supervisors can judge and identify possible risks in the process of production and quality control properly.

Regulators' concerns about the capabilities of enterprises and doubts about the orientation of enterprises' interests have also affected the trust relationship between government and

enterprises. Regulators believe that the GMP level of the domestic pharmaceutical industry is uneven. Some people think that only a few multi-national companies can meet the requirements, which lacks universality. Some people worry that the demand for parametric release policies only comes from companies, and they think that companies mainly consider their interests rather than the whole industry development. At the same time, due to concerns about the overall technical level of the industry, we are still worried about implementing parametric release nationwide. In terms of the general regulatory environment, the government is often skeptical about the integrity of companies. The government may have doubts about the compliance and authenticity of the data that companies have in the process of implementing parametric release, and they are worried that product quality will be out of control, thus increasing the defensive of the Health Authority. At the same time, since the public often has a paternalistic perception of drug regulatory agencies, they believe that any incidents with drugs should first be investigated for the regulatory responsibility of the regulatory agency, causing regulators to be cautious about the implementation of the new deal.

Establishing good communication with regulators will strengthen the trust between regulators and companies. The analysis results show that both regulators and the industry are the core stakeholders of parametric release, and there are differences and conflicts in interest demands. Based on factors such as interest distribution, risk taking, and information asymmetry, the two are likely to be caused by lack of communication. Conflict, a crisis of confidence due to ignorance of industry needs or misunderstandings. The main root of the conflict is the lack of cooperation motivation among stakeholders and the lack of good communication and information sharing among stakeholders. Improving the interaction and communication between government and enterprises can effectively strengthen the trust relationship between the two.

To sum up, the regulatory system, regulatory technical capabilities, and interaction with regulation all have an important impact on regulatory trust. Establish a coordinated top-level design, improve regulations and supporting regulations, strengthen international coordination, and enhance trust between regulation and enterprises. are the key to solving these problems.

4.6.1.3 Influencing factors of regulatory technology acceptance

The technology acceptance of regulatory is also affected by the above-mentioned regulatory macro environment, institutional system, and regulatory technical capabilities.

Regulatory priorities play an important role in technology acceptance. The regulatory macro-environment has an impact on regulatory priorities. In the past two decades, China's

pharmaceutical industry has continuously improved its quality management level. At present, the requirements for drug quality from the legal level are the same as those of foreign countries. With the passage of time and changes in the macro environment, the focus of the industry and the focus of supervision have gradually shifted to the fields of product innovation, clinical development, and biological drugs, while the urgency of parametric release has become less important.

From the perspective of the institutional system, the frequent turnover of personnel in regulatory agencies and the regular rotation of leaders lead to ignorance of technology by leaders and relevant regulators, resulting in insufficient understanding of parametric release technology, resulting in lower regulatory priorities. Leadership attitudes often play a decisive role in policy agendas. If leadership does not fully embrace the benefits of the technology, regulatory priorities will be lowered, leading to policy shelving. The fragmentation of organizational authority led to a lack of collaboration across departments, with each department reluctant to make this work a priority for itself, waiting for others to act first. It is hard to prioritize this work in this situation. In addition, the resource constraints of regulators may also delay the advancement of agendas such as parametric release. In recent years, regulatory agencies have invested a lot of resources in diagnostic reagents, vaccines, emergency drugs and medical device reviews, and epidemic prevention supervision. As such, issues like parametric release may be relegated to the back burner for an agenda that has less impact on the industry and is not urgently needed.

In brief, the low priority of supervision makes the technical acceptance of parametric release by the regulators not high, which hurts the attitude of policy promotion. Raising regulatory priorities can help advance policy agenda setting.

A very important aspect of the institutional system is the basis for technical legitimacy. The concept of parametric release has a certain conflict with the concept of product release in the upper law Drug Administration Law. Although the drug control law changed the release clause from drugs must be inspected and released before leaving the factory to drugs should be inspected and released when they leave the factory, which created a certain regulatory space for the implementation of parametric release from the perspective of higher-level laws, but there are voices that the legitimacy of this technical regulation is still questionable. The accountability system in the institutional system is also a potential factor restricting new technologies and regulations. The Chinese government's unlimited responsibility for supervision, as well as rules such as the lifelong responsibility system of Chinese supervisors, have made it more costly for regulators to try new policies.

The impact of regulatory technical capabilities on the acceptance of parametric release policies by regulatory agencies is multifaceted.

First, factors such as traditional quality management culture, current conservative regulatory environment, public consensus on regulation, Chinese atheism culture, and the concept of an honest society will all have an impact on the acceptance of parametric release policies. Even in terms of quality management culture, many people verbally support that quality comes from design and process control, but there are still certain gaps and difficulties in actual implementation.

Secondly, the quality of supervisors is also an aspect that affects supervisory capabilities. It was mentioned in the interview that most of the reviewers lack industry background and practical experience, especially in microbial control and sterilization process. These aspects are very important for the review of parametric release. Therefore, it is necessary to train and improve the technical level of supervisory personnel to ensure that they can correctly judge the feasibility of parametric release.

Finally, the production and quality management foundation of China's current pharmaceutical industry is relatively lacking. Although China's GMP has been implemented for more than 20 years, there is still a gap compared with developed countries. The level in the industry is uneven, and the experts in the interview also expressed concerns about the actual situation of domestic GMP. This lack of foundation will also restrict the promotion of the parametric release policy in China.

In general, there are certain challenges in the acceptance of the parametric release policy by regulatory technical capabilities. It is necessary to strengthen the transformation of the concept of regulatory culture, improve the professional quality of regulatory personnel, and strengthen the production and quality management foundation of the pharmaceutical industry. These efforts will help promote the implementation and development of parametric release policies in China.

4.6.1.4 Policy driven approach

From the above analysis of the factors affecting the supervisory side, it is shown that the macro-environment of regulation, the regulatory system, the interaction with regulation, and the technical capabilities of regulation are important factors that affect the acceptance of policy innovation by regulatory agencies. These factors determine the risk perception of regulatory bodies in terms of policy adoption, trust in regulation, and technical acceptance of regulation affect their attitude towards policy advancement. Increase the risk-taking coefficient within a

reasonable range, improve the trust between supervision and the market, and strengthen the acceptance of technology by supervision, which will increase the willingness and enforceability of supervision to promote the new policy. Once the policy window is opened, the adoption of policies will become possible.

4.6.2 Policy entrepreneur's driven approach to market

4.6.2.1 Influencing factors of market risk perception

Market risk perception is affected by the macro environment, market technical capabilities, and interaction and communication factors between markets.

The impact of the macro environment on market risk perception is also significant. The recent domestic drug injury incidents and drug quality incidents will intensify the vigilance of the regulatory authorities on the risks of new technologies. As a result, manufacturers, distribution companies, and hospitals should first consider the possible risks when considering the introduction of new technologies, rather than benefit. Manufacturers are worried that the products produced by the parametric release will be circulated on the market. Once quality problems occur, no factory inspection report can prove their innocence. Distribution companies and hospitals also need to be able to protect to the greatest extent due to the indirect responsibilities they may have to bear. For their interests, it is hoped that a specific test report can prove that it can effectively check the quality of the product in the circulation and use link, thereby reducing possible medical disputes. In this case, the macro environment increases the perception of market risk, which in turn negatively affects the attitude towards policy advancement.

As the technical capabilities of the market increase, the market's perception of risks will decrease, which will play a positive role in promoting policies. As the technical capabilities of the industry increase, the adoption of new technologies will have a positive attitude. When the advantages brought by new technologies are recognized, the willingness to adopt new technologies will often increase. When the technical ability does not reach the corresponding level, they often adopt a conservative attitude towards technological innovation and quality improvement, and often take the minimum level required by the regulatory agency as the standard, rather than consider continuous improvement and product quality. The risks arising from the technical capabilities of the market are mainly concentrated in two aspects. One is the confidence in its ability to implement parametric release. When the quality management level of the enterprise fails to meet certain requirements, it is difficult to implement parametric release.

Enterprises with strong technical capabilities will take the initiative to improve manufacturing and quality control technology, enhance the hardware and software among others to achieve parametric release. As a result, manufacturers can achieve better quality product with lower cost, and increase productivity. For these enterprises, the purpose of adopting parametric release is precisely to break through the limitations of traditional sterility test release and effectively reduce the risk of unqualified product sterility assurance level. However, enterprises with insufficient technical capabilities often have insufficient understanding of the requirements for parametric release. If the parametric release is copied, it may cause the product to fail to achieve the expected sterilization effect and affect product quality. Another worry that manufacturers have about implementing parametric release is that products that adopt parametric release are circulated in the market, once a problem related to drug safety occurs during product use, the manufacturer does not have a first-hand test report to prove its innocence. Based on concerns about market risks, the enthusiasm for implementing parametric release is not high. By enhancing the technical capabilities of the market, including production companies, distribution companies, and hospital users, they will have a better understanding of the control methods of parametric release, thereby effectively reducing the risk perception of the market.

Strengthening the interaction and communication between markets will help reduce the market's perception of the risk of parametric release, play a positive role in policy promotion. Leading companies in the industry have called on industry and government to accept parametric release two decades ago. When through technical exchanges, most enterprises in the industry, not just a few enterprises, realize the advantages of parametric release in terms of product quality improvement and enterprise production efficiency, the number of enterprises willing to join in the industry will increase. Through association training, publicity and communication, more enterprises and users will understand the positive effect of this technology on product sterility assurance and recognize the limitations of traditional sterility testing on the risk of product sterility assurance, then their concerns about technology will be reduced, and their willingness to implement parametric release will be enhanced.

4.6.2.2 Influencing factors of market enthusiasm

From the perspective of the macro environment, the attitude of domestic regulatory agencies on the coordination of international standards will affect the enthusiasm of the market for policy acceptance. At present, the implementation of parametric release is not in line in China and global. Internationally ICH, PIC/s, and other coordination organizations have incorporated parametric release into the legal system. However, due to Chinese regulations not accepting

parametric release, most industry companies do not have the motivation to initiate the implementation of parametric release. This has a negative impact on the implementation of parametric release. In addition, the volume-based procurement measures currently implemented in China have minimized the profit margin of the product, and when the parametric release itself cannot be reflected in the centralized procurement price as a product advantage in the centralized volume-based procurement policy, the company's willingness to further invest resources, transform facilities and equipment, improving the quality of personnel, and thus improve product quality. In brief, the market macro-environment has a conflicting relationship with market enthusiasm, which in turn negatively affects policy promotion attitudes.

The higher the technical capabilities of the market, the stronger the enthusiasm of the market, which plays a positive role in the attitude of policy promotion. When the industry has a deeper understanding of parametric release, it will help the industry to understand the advantages of implementing this technology. On the one hand, at the quality level, moving the quality control step forward, will break the limitation of the final sampling inspection of the product, so that the sterility level of the product can be better, which will guarantee and improve product quality; on the other hand, in terms of production efficiency, although there is some investment in software and hardware in the early stage, 14 days of storage costs can be saved after implementation, the speed of product circulation will be accelerated, and the production cost will be reduced in the end. In addition, at the market level, the quality differentiation of existing products can be achieved through parametric release, making the product more competitive in the market. Therefore, improving the technical capabilities of the market will increase the enthusiasm of the market, thereby positively affecting the attitude of promoting parametric release.

Through interactive communication in the market, leading companies, with the help of the association, bring the concept of parametric release to more companies in the industry, and even extend it to distribution companies and hospital users, so that more relevant parties can understand parametric release, thereby enhancing the enthusiasm of the market, thus positively affecting the policy promotion attitude.

4.6.2.3 Influencing factors of market technology acceptance

The analysis shows that market technology acceptance is affected by the macro environment and technical capabilities.

The current macro environment of the market makes it difficult for enterprises to implement parametric release even if they think that the input-output ratio of implementing parametric

release is not high, and they have greater concerns about the risks brought about by it. Only a few leading companies want to implement parametric release, which cannot form a favorable environment for promoting regulations and has a negative impact on the attitude of promoting parametric release.

Through the previous analysis of technical capabilities, it is found that the increase in technical capabilities will increase the willingness to promote parametric release, which will positively affect the market's acceptance of technology.

4.6.2.4 Policy driven approach

The analysis of market influencing factors shows that the macro environment, market technical capabilities, and the interaction between markets are important factors that affect the market's acceptance of policy innovation. These factors determine the risk perception, market enthusiasm, and market acceptance, thus affecting its attitude toward policy advancement. Policy entrepreneurs can cooperate with leading companies and associations to drive industry learning through experience exchanges, training, among others, so that more companies can recognize the advantages of parametric release, and by improving industry capabilities, increase market trust and technology ability. This can enable most enterprises in the industry to have the conditions to implement parametric release, laying the foundation for the implementation of parametric release.

4.7 MAH case study –successful factors for policy promotion

The factors affecting the promotion of the parametric release policy are summarized and logically deduced, but it is not yet possible to explain what factors the necessary conditions for the failure of the parametric release pilot policy window are to open. To further explore the necessary conditions for the lagging promotion of the policy of influencing parametric release, the successful policy promotion case of the China Drug Marketing Authorization Holder (MAH) System was selected for the study, and the case studies were compared from the aspects of macro environment, technical capabilities, institutional system, and interactive communication.

4.7.1 Background of MAH system in China

Before the comprehensive revision of the Drug Administration Law in 2019, China's drug approval system adopted a management model that bundled drug marketing authorization and production license (Y. Yang et al., 2015), and only allowed pharmaceutical manufacturers to

produce drugs after obtaining a new drug registration license and GMP certification. If R&D institutions obtain new drug registration licenses, they have to transfer this new drug research and development technology and license to pharmaceutical manufacturers with drug production qualifications since they cannot obtain production licenses due to a lack drug production capacity. This bundling system design has been the only marketing authorization model since the 80s of last century. Under the circumstance that the market economic order has not yet been established, the overall R&D innovation ability is limited, and the enterprises are mainly focused on generic drug production, it is reasonable that drug registration and supervision is based on drug production, which meets the development needs of our country's economy at that time and has its historical significance and value. However, with the gradual improvement of China's market economy system, the continuous development of the innovation and R&D capabilities of the pharmaceutical industry, and the growing demand of the people for safe, effective and accessible drugs, the drawbacks of this bundle system registration management have become increasingly prominent, and have become one of the factors restricting the further development of China's pharmaceutical industry (C. G. Wang, 2016).

First of all, the motivation for drug research and development is insufficient. Due to the bundling of marketing authorization and production license, it creates a dilemma for R&D enterprises, or in order to transform their results into drugs, invest in the construction of new factories, and obtain the Drug Production License before they are eligible to apply for drug marketing authorization, which pushes up the cost of drugs from R&D to production, and makes R&D institutions must pay attention to the whole process from product development to production, rather than focusing on new drug research. If the R&D institutions do not want to establish production capacity, they must go through the technology transfer pathway, sell the ownership of the product to other manufacturers to obtain limited benefits but rather than enjoy the long-term market return. As a result of this legal role transfer, the R&D institutions will no longer participate in the post-marketing improvement and perfection of the product. No matter how which approaches been adopted, the incentives for R&D institutions is insufficient to focus on drug development.

Second, this policy is also the main reason of overcapacity. The production of new drugs must invest in the construction of new facilities, resulting in a large number of small enterprises and a high level of duplication. The number of drug registration certificates held by manufacturers is often much higher than the varieties they actually produce, resulting in empty production lines and a great waste of resources. And due to the uneven production level among the industry, the quality of the product is worrying.

Third, the legal rights and responsibilities of the relevant entities are not clear, and the safety of drugs cannot be guaranteed. The R&D institution is disconnected from the product after the technology transfer is realized, and the manufacturer is fully responsible for the quality of the product. Due to the lack of knowledge and ability of manufacturers in product design and development, they cannot ensure the systematic monitoring of drug quality throughout the life cycle, therefore cannot effectively form the post-marketing adverse events monitoring and improvement system.

Finally, government administrative resources are wasted. Regulators spend a lot of resources on low-level duplicate product approval and supervision, without enough energy to promote innovation in the pharmaceutical industry. Furthermore, it is difficult to establish a scientific and effective drug regulatory system.

The above obstructive factors have greatly affected the development of China's pharmaceutical industry, so policy entrepreneurs in the industry have begun to conduct a feasibility analysis of the adoption of the marketing authorization holder system in China since 2010, hoping to refer to the institutional systems of developed countries in the pharmaceutical industry such as Europe, the United States and Japan, establish a marketing authorization holder system, and unbundle the marketing authorization from the production license.

The so-called drug marketing authorization holder system usually refers to the system in which drug R&D institutions, scientific research personnel, drug manufacturers, and other entities with pharmaceutical technology bear the main responsibility for the quality of drugs throughout their life cycle by submitting applications for drug marketing authorization and obtaining drug marketing authorization approvals. Under this system, the marketing authorization holder and the manufacturing authorization holder can be the same entity or two independent entities. Depending on its own situation, the MAH can produce on its own or entrust it to other manufacturers. If production is commissioned, the MAH is fully responsible for the safety, efficacy, and quality controllability of the drug according to law, and the manufacturer is responsible for the quality of the drug in accordance with the provisions of the commissioned production contract (C. G. Wang, 2016).

In this context, the State Council issued "The Opinions on Reforming Review and Approval Process for Drugs and Medical Devices" (No. 44) in August 2015, which proposed for the first time the implementation of MAH system to solve problems such as insufficient innovation in China's pharmaceutical field, further improve the drug market innovation mechanism, and improve the overall research and development level of drugs. The opinions specify that drug marketing authorization holders are allowed to produce drugs on their own or entrust other

manufacturers to produce drugs (Dong, 2019).

Due to the attention of the state, the drug marketing authorization holder system has been established from top to bottom. In November 2015, in order to provide practical experience for the reform and improvement of the drug management system, the Standing Committee of the National People's Congress authorized the State Council to carry out a three-year pilot drug marketing authorization holder system in 10 provinces and cities including Beijing, Shanghai and Jiangsu, allowing drug R&D institutions and scientific researchers to obtain drug approval licenses and bear corresponding responsibilities for drug quality (State Council, 2015).

Immediately afterward, a series of documents were issued, which promoted the continuous deepening and improvement of reform exploration. In June 2016, the State Council issued the "Notice of the General Office of the State Council on Printing and Distributing the Pilot Program of the Drug Marketing Authorization Holder System", followed by the "Notice of the State Food and Drug Administration on Doing a Good Job in the Pilot Work of the Drug Marketing Authorization Holder System", which emphasized the responsibility of the MAH system as a subject of laws and regulations, marking the official launch of the pilot work of the MAH system in 2018.

Subsequently, relevant policies were issued one after another to improve the pilot system. In October 2017, the General Office of the CPC Central Committee and the General Office of the State Council jointly issued the "Opinions on Deepening the Reform of the Review and Approval System to Encourage Innovation in Drugs and Medical Devices (No. 42)", proposing to promote the full implementation of the drug marketing authorization holder system; In October 2018, the Sixth Meeting of the Standing Committee of the 13th National People's Congress deliberated and issued the "Decision on Extending the Pilot Period of the Drug Marketing Authorization Holder System Authorized by the State Council in Certain Places", proposing to extend the original three-year pilot period of the drug MAH system for another year. In August 2019, the new version of the Drug Administration Law was officially released, marking the full implementation of the MAH system in China. The MAH system took more than ten years from entering the policy horizon, to the pilot promotion, then to the official release, and finally the system was successfully implemented.

The main advantage of the MAH system is that it separates the marketing authorization of drugs from the manufacturing authorization, encouraging innovation; Its core is that MAH is fully responsible for drug quality, optimizing resource allocation and curbing low-level duplicate construction, and is responsible for the safety, efficacy, and quality controllability of drugs in the life cycle and assumes the main responsibility (Y. Wang, 2021).

4.7.2 Key influencing factors analysis to promote MAH implementation

In the process of implementing this innovation policy, we can see that the macro environment, institutional system, technical capabilities, and interactive communication have played a key role. It is precisely these rationalities that enable the policy window to be opened, and through the efforts of policy entrepreneurs, the policy can be promoted from these aspects, and finally realize the formal implementation of the marketing authorization system in China. The following elaborates on the role of these aspects.

The drug MAH system can finally be promoted in China, which is greatly affected by the macro environment. Since China issued the first version of the Drug Administration Law in 1998, the primary focus of drug management is to on production, promoting China to become a pharmaceutical power in the pharmaceutical field. Since 2015, the CPC Central Committee and the State Council have intensively issued relevant regulations and policy documents. Opinions of the State Council on Reform of the System of Evaluation, Review and Approval of Drugs and Medical Devices (No.44) in 2015 and Opinions on Deepening the Reform of the Review and Approval System and Encouraging the Innovation of Drugs and Medical Devices in 2017, which mentioned that in recent years, China's pharmaceutical industry has developed rapidly, the quality and standards of drugs and medical devices have been continuously improved, and the public's drug demand has been better guaranteed. However, at the same time, it also talks about the problems that still exist in drug and device approval and believes that these problems have profound historical, structural, and institutional reasons. Therefore, it is proposed to promote institutional reform, including the launch of the pilot MAH system, to accumulate relevant experience for the revision of the MAH system in the Drug Administration Law.

This has formed a favorable factor for the promotion of the system at the level of the regulatory macro environment. At the same time, the market also urgently needs the introduction of the MAH system, which can give full play to the advantages of the industry itself. R&D enterprises can focus on R&D without spending additional construction to maintain production capacity; while production enterprises can accept entrusted production by R&D enterprises according to their own production capacity, give full play to production advantages, and maximize the use of production capacity, thereby accelerating innovation, optimizing industrial structure, and reducing low-level duplicate construction. For users, medication safety is their primary concern, and MAH's efforts to enhance drug quality and safety are welcome.

The original Drug Administrative law has significantly limited the development of

innovation. Driven by this macro environment aimed at promoting innovation, the priority of the New Deal and the acceptance of regulations are guaranteed to the highest extent. The government and industry actively participate in policy pilots to jointly explore the problems existing in the pilot work, and the risks in the process of promoting MAH are more acceptable and the risk-taking concerns will be reduced. Therefore, the macro environment has formed a key factor driving MAH's promotion in China.

From the perspective of the institutional system, the establishment of a sound institutional system is the key to ensuring the successful implementation of the MAH system. There is a relatively large gap between the MAH system and the original bundled system. Fundamentally, the MAH system is a life-cycle management system. In order to implement the MAH system, the regulatory authorities amended the Drug Administration Law from the perspective of regulations, so that the relevant requirements of the MAH system run through product development, registration, production, listing, circulation, and other steps, and clarified the obligations and responsibilities of each stakeholder of the MAH holder. At the same time, corresponding penalties are stipulated in the Drug Administration Law and supporting regulations to effectively protect the interests of consumers. The MAH system fundamentally promotes the strengthening of the obligations and responsibilities of holders and changes the traditional supervision concept of parenting in the past, fearing that enterprises will have problems, replacing enterprises to check, and also leading to problems to bear responsibility for enterprises, resulting in increased regulatory risks and low regulatory efficiency. So as to truly achieve the goal that the enterprise is the responsible subject, and thus reduce the regulatory pressure. According to the regulatory concept of full life cycle management, the regulatory authorities will carry out corresponding reforms to their organizational structures in combination with the implementation of regulations in the pilot process to adapt to the requirements of the new system for regulatory capabilities. By forming an institutional system that matches the new MAH system, it can effectively control regulatory risks, strengthen the trust between supervision and the market, and increase the acceptance of supervision to the new policy, thereby playing a positive role in the promotion of regulations.

Regulatory capacity and industry capability are one of the key success factors in the implementation of the new deal. Regulators can improve their regulatory capabilities by learning the regulations and practices of the MAH system in Europe and the United States, as well as through the practical operation process of pilot projects, and through interaction with the industry. As regulatory capacity improves, regulators become more confident in regulating under the New Deal, and organizations become less aware of the risks that may arise from

regulation. The regulator's trust in the market has enhanced, and the acceptance of the new policy has increased, which has a positive effect on the policy impact.

Finally, active and effective interactive communication plays a key role in the promotion of the MAH system in China. In the pilot process, the government and enterprises link to establish a positive communication and feedback mechanism, and the government selects pilot enterprises to promote specifically, gain experience, and conduct in-depth research and discussions with industry experts to understand the pain points of enterprises in the implementation stage and help pilot enterprises solve problems in the implementation process. Taking Shanghai as an example, by actively cooperating with the State Drug Administration, the Shanghai authority carried out investigative inspections on the marketing authorization holders of 12 approved varieties of R&D institutions across the country. Hold a thematic forum on Post-marketing Supervision Strategy and Practice under the Drug MAH System to exchange practical experience in post-marketing supervision under the system and discuss the quality control strategies of different entity holders. From this kind of practice, Very valuable pilot experience was gained by both authority and industry (Du, 2020). At the same time, the regulators of the pilot cities share the results and experience of the pilot implementation process through exchanges and interactions, to form and amend the implementation provisions of the regulations; Through increased publicity and training, the core content of the MAH system is promoted in the industry, so that more enterprises in the industry can understand the essence of the MAH system and the benefits it can bring, so that enterprises have the motivation to implement the MAH system. Meanwhile, through proactive, positive, and multi-faceted interactions, regulatory and industry capabilities are enhanced, and their concern of risk is reduced accordingly. Active communication can also increase market enthusiasm, and increase the trust between government and enterprises, thus playing a positive role in policy promotion.

Chapter 5: Conclusion

This research completed the contents regarding the preset research route and answered all the research questions. This doctoral thesis researches the implementation of parametric release in China based on the stakeholder perspective. The subject research also obtained the answer to the preset research question. First, we identified the stakeholders involved in implementing parametric release and analyzed how these stakeholders' conflict in the policy context. This is the basis for analyzing why this policy has yet to be implemented in China and how to break through the dilemma. We then identified the factors that might influence stakeholder cooperation and conflict. Finally, we explored ways to help policy entrepreneurs carry out policy promotion.

5.1 Research conclusions

The parametric release is on the route of meeting the requirements of GMP, based on advanced concepts such as quality by design, quality risk management, and design space, using risk management tools to improve the sterility assurance system and quality management system comprehensively, establish parametric release procedures and standards, and upgrade. It is achieved by transforming critical equipment and facilities and will improve and strengthen production and quality management. The implementation of parametric release is the deep integration of scientific supervision and information technology (Shang et al., 2022). The promotion and implementation of parametric release have great practical value for the development of the industry and play a significant role in promoting the quality of drugs. Therefore, it is recommended to steadily promote the parametric release of moist heat-sterilized drugs in China as soon as possible and promote scientific, modern, legalized, and internationalized drug supervision to ensure drug safety.

By applying stakeholder theory and policy entrepreneurs theory, this study conducts in-depth research on semi-structured interviews with regulators, industry experts, medical personnel, scholars, and key opinion leaders from associations and research institutions, and deeply analyzes the interest demands, conflicts of interest, and influencing factors of various stakeholders in the process of promoting parametric release policy through grounded research methods, and discusses the coordination path of key stakeholders to promote parametric release

policy. Based on theoretical and applied research, this thesis proposes a strategy to promote policy coordination from the perspective of policy entrepreneurs.

The main research conclusions are as follows:

First, as a regulation that has been implemented abroad for many years but has not yet been implemented in China, the process of policy innovation and diffusion has been affected in many ways. Key stakeholders involved include drug regulators, the pharmaceutical industry, healthcare professionals, as well as other regulatory agencies including the health insurance sector, industry associations, and media, which are also stakeholders involved in policy promotion and implementation. However, due to the particularity of policy formulation, the main bodies that play a key role are mainly drug regulatory agencies and industries.

Second, the promotion of parametric release is mainly affected by the objective factors of the macro environment, institutional system, technical ability, and interactive communication. These objective factors, in turn, affect the subjective attitudes of key stakeholders in regulatory authority, including the risk perception of regulator and industry to policy implementation, the trust relationship between government and enterprises, and the policy acceptance level of regulator and industry.

Through interview analysis, it is found that there are both promoting factors and obstructive factors in the macro environment. On the whole, at present, China has a good GMP level of drug production and has the basis for promoting parametric release. However, due to the current trend of regulatory reform is more inclined to innovative drug development and other innovation-promoting aspects, and due to the historical drug adverse events and the impact of the new COVID pandemic in the last 3 years, the drug regulatory agency has increased its risk perception of the implementation of the new policy. Under this circumstance, the parametric release has not yet been listed as the priority policy formulation scope. Policy entrepreneurs should consider how to seize the policy reform opportunity to promote the development of regulations.

The implementation of parametric release also requires in-depth reform from the aspect of the institutional system. It can be clearly seen from the promotion process of parametric release in the past 20 years that the organization's construction of regulatory authorities is a key limiting factor for the implementation of parametric release policy. At the same time, the regulatory system also needs to be improved, and international standards need to be taken into account in the process of building the regulatory system. A sound institutional system will effectively alleviate regulators' concerns about the risks of implementing the New Deal, strengthen the trust between the authority and industry, and effectively increase the acceptance of the New Deal.

Technical competence in regulatory and industry represents a necessary condition for regulatory implementation. Strengthening supervision and the construction of the industry's technical capabilities related to regulations will play a key role in promoting regulations. From the current situation, both the regulatory agency and the market side already have a certain technical capability base, but it still needs to be further strengthened in order to effectively improve the confidence of authority and the industry of policy implementation, thus reducing concerns about risks, and enhance the acceptance of the new policy.

The establishment of a good interactive communication relationship between the health authority and the industry will also be conducive to the improvement of the technical capabilities of both sides. Establish a good relationship of trust between the government and enterprises, thereby reducing the worry about the risks of implementing the new policy and strengthening the confidence and enthusiasm of both sides in the implementation of the parametric release policy. The current interactive communication is affected by the institutional and macro environment and still needs to be improved.

From the research results, to further promote the parametric release policy, policy entrepreneurs need to continue their efforts from the above aspects, promote the coordination of key factors in the policy flow, wait for the policy window to open, seize the opportunity of policy reform, and promote policy acceptance and implementation.

5.2 Policy recommendations

Based on the research result, the following policy recommendations have been proposed:

5.2.1 Establish a supporting regulation system to fit in China's national conditions

Parametric release has been widely accepted and implemented by international regulatory bodies, with mature regulations and technical guidelines. China began to explore the parametric release policy in 2002, and after 20 years of development, it has initially met the basic regulatory conditions for implementing the policy. The Drug Administration Law, the Measures for the Supervision and Administration of Drug Production and the Measures for the Administration of Drug Registration clarify the main responsibilities of drug marketing authorization holders and require holders to establish marketing release procedures. As a member of ICH, the China Food and Drug Administration is transforming the guideline document for parametric release (ICH Q6A). Meanwhile, the first group standard for the parametric release of humid heat-sterilized drugs in China has also been released. It is

recommended to establish a scientific supervision system for parametric release suitable for China's national conditions in combination with the above-mentioned established regulations and technical guidance documents, including the establishment of China's parametric release pharmacopeia standards, technical guidelines and GMP inspection guidelines, and determine the registration pathway for drug post market variation application. At the same time, based on ICH Q6A, the PIC/s parametric release inspection and other international guidelines, establish China relevant regulations and technical requirements further in line with international standards.

5.2.2 Establish implementation path

In terms of institutional system, referring to other successful cases for policy diffusion, it is recommended to set up a task force at NMPA, to make sure the regulatory priority, lock resources and coordinate the organizational division among different departments. Through the task force, fully listen to the suggestions of industry experts and other stakeholders to establish a practical implementation path.

In view of the differences in quality management level, key technical personnel, facilities, and equipment of different production enterprises, it is recommended to implement parametric release step by step. Parametric release of terminally sterilized preparations is not a one-size-fits-all requirement. Whether a drug can implement parametric release is directly related to the enterprise's quality management system. It is recommended to allow companies to apply for parametric release through post-marketing variation registration pathway, encourage more terminally sterilized aseptic preparation companies to achieve industrial upgrading and transformation, and accelerate the industry's progress towards modern production and intelligent manufacturing.

5.2.3 Carry out a series of training program

Technical capability is one of the main influencing factors affecting the implementation of parametric release. When a sound regulatory system is built up, it is recommended that the NMPA cooperate with domestic and foreign industry experts to conduct in-depth and extensive training for central and local regulatory personnel and the practitioners from this industry. The training should cover global and local regulations, guidelines, relevant technical requirements, and practical experience sharing. Domestic enterprises are in a critical period of transformation and upgrading, and comprehensive and systematic training can help enterprises deeply study

and understand the necessary process control parameters in the production process, strengthen verification to improve drug quality and enhance risk control capabilities. At the same time, through training, industry practitioners can have a deeper understanding of the significance of parametric release to drug quality improvement actions, which is conducive to enhancing the confidence of regulators and industry and promoting the coordination of the implementation of parametric release regulations.

5.2.4 Re-start pilot work in the provincial drug administration

Pilot is the most used paradigm of policy innovation and diffusion in China's reform practice. Before a certain policy is officially implemented, several local governments try first and further determine the policy content based on the results of the pilot (typical experience), and after they move on to promotion and implementation (X. W. Zhang & Gao, 2020). This parametric release study was led by the Drug Supervision Department of the Food and Drug Administration in 2005. Two rounds of pilot work were carried out in Jiangsu and Guangdong provinces. Two typical local enterprises with conditions were selected to accumulate experience in the implementation of parametric release through the pilot. However, the legal system, regulatory level, and industry quality management system at that time did not reach the level capable to promoting parametric release. After 20 years of industry development, China's regulatory system has been relatively sound. China's current version of GMP is benchmarked against the latest EU GMP. The level of regulatory agencies has also been greatly improved, and the quality management level of the entire pharmaceutical industry has also reached a relatively good level. Therefore, now is a good time to restart the pilot. In fact, the provincial Food and Drug Administration where several leading companies are located have also expressed their willingness to restart the pilot work of parametric release. This research suggests that the provinces where these leading companies are located, such as Shanghai, Guangdong, Jiangsu, and Sichuan, can further carry out the pilot work of parametric release, accumulation of regulatory and industry experience, and lay the foundation for subsequent nationwide implementation.

5.2.5 Pay close attention to policy window opportunities

To further increase the pace of regulatory internationalization, actively promote participation in international regulatory coordination, in September 2021, the NMPA formally sent a letter to the Pharmaceutical Inspection Co-operation Scheme Program (PIC/s) to apply for the start of

the pre-accession process. PIC/s is one of the international organizations that accept parametric release, and its guidance for parametric release inspection in its GMP Annex 1: Manufacture of Sterile Medicinal Products, which focus on training GMP auditors to conduct facility inspections of enterprises involved in parametric release. If China NMPA wants to join PIC/s and promote international regulatory harmonization, it must consider transforming its relevant regulations, including parametric release. Policy entrepreneurs should seize the policy window and work with various stakeholders to promote the implementation of the parametric release in China.

5.3 Research limitations and future research

This study focuses on the conflict and coordination among stakeholders in the process of promoting the parametric release policy in China. It adopts a qualitative research method, conducts semi-structured interviews with senior practitioners, conducts grounded research on the interview results, and proposes policies for entrepreneurs' driving path for parametric release policy promotion. However, because parametric release is a relatively professional topic in the field of pharmaceutical-related policies and regulations, based on years of work experience in the pharmaceutical industry, the researchers interviewed 33 interviewers with rich industry experience from regulators, enterprises, medical institutions, industry associations, and scholars. Interviews were conducted and a large amount of interview data was obtained. However, for a policy study, the sample size is still relatively limited. The policy-driven theoretical framework of policy entrepreneurship based on the results of essential research needs to be further confirmed by larger-scale research.

Based on this study, empirical research can be considered, through quantitative methods, more influencing factors of parametric release policy implementation can be deeply explored, and the driving path relationship and influence degree of parametric release policy promotion by policy entrepreneurs can be analyzed in depth to verify the rationality of the model. It is hoped that through the empirical research, it can help to prepare for the full implementation of parametric release.

The above research limitations will be used as the focus and starting point of future research, and further analyzed and solved in future research.

Bibliography

- Al-Busaidi, Z. (2008). Qualitative research and its uses in health care. *Sultan Qaboos University Medical Journal*, 8, 11-19.
- Ansoff, H. I. (1965). *Corporate strategy: an analytic approach to business policy for growth and expansion*. McGraw-Hill.
- Barnard, C. I. (1938). *The functions of the executive*. Harvard University Press.
- Baumgartner, F. R. (2011). 美国政治中的议程与不稳定性 [Agenda and instability in American politics]. Beijing University Press.
- Baumgartner, F. R., & Jones, B. D. (1993). *Agendas and instability in American politics*. Chicago University Press.
- Berry, F. S., & Berry, W. D. (1990). State lottery adoptions as policy innovations: an event history analysis. *American Political Science Review*, 84, 395-415.
- Best, B., Moffett, S., & McAdam, R. (2019). Stakeholder salience in public sector value co-creation. *Public Management Review*, 21(11), 1707-1732.
- Blair, J. D., Rock, T. T., Rotarius, T. M., Fottler, M. D., Bosse, G. C., & Driskill, J. M. (1996). The problematic fit of diagnosis and strategy for medical group stakeholders—including IDS/Ns. *Health Care Management Review*, 21, 7-28.
- Blair, J. D., & Buesseler, J. A. (1998). Competitive forces in the medical group industry: a stakeholder perspective. *Health Care Management Review*, 23, 7-27.
- Blair, J. D., & Fottler, M. D. (1990). *Challenges in health care management: strategic perspectives for managing key stakeholders*. Jossey- Bass.
- Boehmke, F. J., & Witmer, R. (2004). Disentangling diffusion: the effects of social learning and economic competition on state policy innovation and expansion. *Political Research Quarterly*, 57(1), 39-51.
- Brewer, G. D. (1974). The policy sciences emerge: to nurture and structure a discipline. *Policy Sciences*, 5(3), 239-244.
- Brugha, R., & Varvasovszky, Z. (2000). Stakeholder analysis: a review. *Health Policy and Planning*, 15(3), 239-246.
- Bryson, J. (2004). What to do when stakeholders matter. *Public Management Review*, 6, 21-53.
- Charkham, J. (1992). Corporate governance: lessons from abroad. *European Business Journal*, 4, 8-16.
- Charmaz, K. (2006). *Constructing grounded theory*. Sage Publication.
- Chen, G. W., & Lin, X. H. (2021). 网络舆论是如何形塑公共政策的？一个“两阶段多源流”理论框架——以顺风车安全管理政策为例 [How does online public opinion shape public policy? A theoretical framework of "two-stage multi-source flow": a case study of the rideshare safety management policy]. *Journal of Public Management*, 18(02), 58-69.
- Chen, H. (2004). *Corporate stakeholder theory and empirical research* [Doctoral dissertation]. Zhejiang University.
- Chen, L., Zhao, J., & Xue, L. (2010). 择优还是折衷？——转型期中国政策过程的一个解释框架和共识决策模型 [Merit-based or compromise?—— an explanatory framework and consensus decision-making model for China's policy process in transition]. *Journal of Management World*, (8), 59-72.
- Chen, Q. Y. (1996). *公共政策分析* [Analysis on public policy]. Economic Press China.
- Chen, X. M. (2015). 扎根理论在中国教育研究中的运用探索 [Critical application of

- grounded theory in chinese education research]. *Peking University Education Review*, 13(01), 2-15.
- Chu, Y. S. (2004). 利益相关者理论最新发展理论综述[A review of the latest development for stakeholder theory]. *Journal of Liaocheng University (Social Science edition)*, (2), 33-36.
- Clarkson, M. B. E. (1995). A stakeholder framework for analyzing and evaluating corporate social performance. *The Academy of Management Review*, 20(1), 92-117.
- Cohen, M., March, J., & Olsen, J. (1972). A garbage can model of organization choice. *Administrative Science Quarterly*, 17, 1-25.
- Cohen, N., & Naor, M. (2013). Reducing dependence on oil? How policy entrepreneurs utilize the national security agenda to recruit government support: the case of electric transportation in Israel. *Energy Policy*, 56, 582-590.
- Crow, D. A. (2010). Local media and experts: sources of environmental policy initiation? *Policy Studies Journal*, 38, 143-164.
- Davies, J. C. (1974). *The governance of common property resource*. John Hopkins University Press.
- Denzin, N. K., & Lincoln, Y. S. (2011). *Handbook of qualitative research*. SAGE Publications, Inc.
- Donaldson, T., & Preston, L. E. (1995). The stakeholder theory of the corporation: concepts, evidence, and implications. *Academy of Management Review*, 20, 65-91.
- Dong, Y. (2019). 以创新激励为导向的药品注册改革——基于上海市药品上市许可持有人制度的试点经验分析 [Innovation incentive oriented drug registration reform: an analysis of pilot experience based on the Shanghai drug marketing authorization holder system]. *Chinese Pharmaceutical Affairs*, 33(08), 857-863.
- Du, B. (Ed.). (2020). 药品上市许可持有人制度试点 [Pilot of drug marketing authorization holders system]. In D. Z. Wang (Ed.), *Shanghai economy alamanac*, (pp. 65). Shanghai Economy Alamanac Editorial Department.
- Dunn, W. N. (1981). *Public policy analysis*. Pearson.
- Dunn, W. N. (2011). *An introduction on public policy analysis*. China Renmin University Press.
- Dye, T. R. (2013). *Understanding public policy*. Pearson.
- Dymond, S. B., Nix, T. W., Rotarius, T. M., & Savage, G. T. (1995). Why do key integrated delivery stakeholders really matter? Assessing control, coalitions, resources and power. *Medical Group Management Journal*, 42(6), 26-38.
- Eisenhardt, K. M. (1989). Building theories from case study research. *Academy of Management Review*, 14(4), 532-550.
- Eston, D. (1993). 政治体系—政治学状况研究 [Political system—a study of the state of political science]. The Commercial Press.
- Etzioni, A. (1967). Mixed-scanning: a 'third' approach to decision-making. *Public Administration Review*, 27(5), 385-392.
- Frederick, W. C. (1988). *Business and society: corporate strategy, public policy*. McGraw-Hill.
- Freeman, E., S. Harrison, J., Andrew C, W., & Bidhan, P. (2013). 利益相关者理论：现状与展望 [Stakeholder theory: the state of the art]. Cambridge University Press and Intellectual Property Publishing House.
- Freeman, R. E. (1984). *Strategic management: a stakeholder approach*. Pitman.
- Friedman, M. T., & Mason, D. S. (2004). A Stakeholder approach to understanding economic development decision making public Subsidies for professional sport facilities. *Economic Development Quarterly - ECON DEV Q*, 18, 236-254.
- Friedman, M. T., & Mason, D. S. (2005). Stakeholder management and the public subsidization of Nashville's coliseum. *Journal of Urban Affairs*, 27(1), 93-118.

- Friedman, M. T. (1982). *Capitalism and freedom*. University of Chicago Press.
- Gambetta, D. (2000). *Trust: making and breaking cooperative relations*. The British Journal of Sociology.
- Gao, J. (2011). *Research on the development of pharmaceutical GMP standards in China* [Master's Thesis]. Henan University.
- Geston, L. N. (2001). 公共政策的制定: 程序和原理 [Formulation of the public policy: procedures and principles]. Chongqing Press.
- Glaser, B. G., & Strauss, A. (1967). *The discovery of grounded theory: strategies for qualitative research*. Aldine.
- Gray, V. (1973). Innovation in the states: a diffusion Study. *The American Political Science Review*, 67(4), 1174-1185.
- Gu, J. G. (2004). 公共政策分析学 [Public policy analytics]. Shanghai Renmin Press.
- Guan, L. J. (2021). *Research on stakeholder conflict and coordination in PPP model of rural infrastructure* [Doctoral Thesis]. Shandong Agricultural University.
- Heilmann, S. (2010). 通过试验制定政策:中国独具特色的经验 [Policy development through experimentation: China's unique experience]. *Contemporary China History Studies*, 17(03), 103-112.
- Heilmann, S., Melton, O., & Shi, L. (2013). 规划:中国政策过程的核心机制 [Planning: a central mechanism in China's policy process]. *Open Times*, (06), 8-31.
- Hu, Q. Q., Liang, Y., & Huang, X. M. (2007). 浅析无菌药品的参数放行[Brief comments on parametric release of axenic drug products].*Shanghai Medical & Pharmaceutical Journal*, (04), 184-187.
- Hu, Y. L. (2023). 中国药品监管体制改革25年回顾 [Retrospection of drug regulatory system reform in China through 1998-2023]. *China Food & Drug Administration Magazine*, (03), 4-15.
- Jensen, M. C. (2002). Value maximization, stakeholder theory, and the corporate objective function. *Business Ethics Quarterly*, 12(2), 235-256.
- Jia, S. H., & Chen, H. H. (2003). 利益相关者管理:新经济时代的管理哲学[Stakeholder, management: management philosophy in the new economic era]. *Soft Science*, (01), 39-42.
- Jia, X. D., & Tan, X. H. (2010). 经典扎根理论及其精神对中国管理研究的现实价值 [The practical value of classical grounding theory and its spirit in Chinese management research]. *Chinese Journal of Management*, 7(05), 656-665.
- Jin, Y. R. (2016). 浅析利益相关者视角下的行政审批制度改革 [Remark on the reform of administrative approval system from stakeholder perspective]. *Administration and Law*, (12), 26-31.
- Jones, B. D. (2010). 再思民主政治中的决策制定 [Politics, rethink decision-making In democratic]. Beijing University Press.
- Khan, N. N., & Puthussery, S. (2019). Stakeholder perspectives on public-private partnership in health service delivery in Sindh province of Pakistan: a qualitative study. *Public Health*, 170, 1-9.
- Kingdon, J. (2017). 议程、备选方案与公共政策 [Agendas, alternatives and public policies]. China Renmin University Press.
- Kong, X. L. (2004). 论我国地方政府政策创新能力的提升 [On the policy innovation capability of local governments in China]. *Administrative Forum*, (3), 43-46.
- Lasswell, H., & Kaplan, A. (2014). *Power and society: a framework for political inquiry*. Routledge.
- Lee, T. W. (1999). *Using qualitative methods in organizational research*. Sage Publication.
- Lejano, R. P. (2006). *Frameworks for policy analysis--merging text and content*. Routledge.
- Li, R. R., Li, X. D., & Duan, M. Q. (2023). 重大公共卫生事件中政治态度的变化路径研究

- 基于扎根理论的分析 [A study on the change path of political attitudes in major public health events: an analysis based on grounded theory]. *China Public Administration Review*, (2), 77-98.
- Li, Y., Kang, D. Y., & Qi, E. S. (2006). 政策评估的利益相关者模式及其应用研究 [Stakeholder models for policy evaluation and their applications]. *Science Research Management*, (02), 51-56.
- Lin, X. (2010). 企业利益相关者管理：从个人、关系到网络 [Enterprise stakeholder management: from individual, relationship to network]. Dongbei University of Finance and Economic Press.
- Lindblom, C. E. (1959). The science of "muddling through". *Public Administration Review*, 19(2), 79-88.
- Lindblom, C. E. (1968). *The policymaking process*. Prentice-Hall.
- Liu Q. H., Yao, H., & Xu, S. Y. (2007). 基于技术科学视角的现代政策科学体系新架构 [A new framework of modern policy science system based on the perspective of technical science]. *Studies in Science of Science*, (01), 2-8.
- Lu, Y. (2010). 英国:利益相关者在国家卫生医疗质量标准署中的作用 [United Kingdom: the role of stakeholders in the national agency for health quality standards]. *China Health Insurance*, (09), 61-63.
- Maor, M. (2017). Policy entrepreneurs in policy valuation processes: the case of the coalition for environmentally responsible economies. *Environment and Planning C: Politics and Space*, 35(8), 1401-1417.
- Matland, R. E. (1995). Synthesizing the implementation literature: the ambiguity-conflict model of policy implementation. *Journal of Public Administration Research and Theory*, 5(2), 145-174.
- Mintrom, M. (1997). Policy entrepreneurs and the diffusion of innovation. *American Journal of Political Science*, 41(3), 738-770.
- Mintrom, M. (2016). *Herbert A. Simon, administrative behavior: a study of decision-making processes in administrative organization*. Free Press.
- Mintrom, M., Salisbury, C., & Luetjens, J. (2014). Policy entrepreneurs and promotion of Australian state knowledge economies. *Australian Journal of Political Science*, 49(3), 423-438.
- Mintrom, M., & Norman, P. (2009). Policy entrepreneurship and policy change. *Policy Studies Journal*, 37, 649-667.
- Mintrom, M., & Thomas, M. (2018). Policy entrepreneurs and collaborative action: pursuit of sustainable development goals. *International Journal of Entrepreneurial Venturing*, 10(2), 153-171.
- Mitchell, R. K., Agle, B. R., & Wood, D. J. (1997). Toward a theory of stakeholder identification and salience: defining the principle of who and what really counts. *The Academy of Management Review*, 22(4), 853-886.
- Nelson, J. B. (1984). *Making an issue of child abuse: political agenda setting for social problems*. University of Chicago Press.
- Penrose, E. (1959). *The theory of the growth of the Firm*. Oxford University Press.
- Provan, K., & Milward, H. (2001). Do networks really work? A framework for evaluating public-sector organizational networks. *Source Public Administration Review*, 61, 414-423.
- Rhenman, E. (1968). *Industrial democracy and industrial management: a critical essay on the possible meanings and implications of industrial democracy*. Van Gorcum.
- Roberts, N. C., & King, P. J. (1991). Policy entrepreneurs: their activity structure and function in the policy process. *Journal of Public Administration Research and Theory*, 1, 147-175.
- Roberts, N. C., & King, P. J. (1996). *Transforming public policy: dynamics of policy entrepreneurship and innovation*. Jossey-Bass.

- Rogers, E. M. (2016). *创新的扩散* [Diffusion of innovations]. Electronic Industry Press.
- Rowley, T. J. (1997). Moving beyond dyadic ties: a network theory of stakeholder influences. *The Academy of Management Review*, 22(4), 887-910.
- Sabatier, P. A. (1991). Toward better theories of the policy process. *Political Science & Politics*, 24(2), 147-156.
- Sabatier, P. A. (2004). *政策过程理论* [Policy process theory]. Life, Reading, Xinzhi Joint Publishing.
- Sabatier, P. A., & Jenkins, S. (2011). *政策变迁与学习：一种倡议联盟途径* [Policy change and learning: an initiative alliance approach]. Beijing University Press.
- Sasaki, T. (2002). Parametric release for moist heated pharmaceutical products in Japan. *PDA Journal of GMP and Validation in Japan*, (4), 7-10.
- Savage, G. T., Taylor, R. L., Rotarius, T. M., & Buesseler, J. A. (1997). Governance of integrated delivery systems/networks: a stakeholder approach. *Health Care Management Review*, 22(1), 7-20.
- SFDA. (2003). *药品生产验证指南* [Guidelines for pharmaceutical manufacturing validation]. Chemical Industry Press.
- Shang, Y. (2021). 无菌药品参数放行国际实施历程及我国现状浅析 [International implementation process and a brief analysis on current situation in China of parametric release of sterile drugs]. *Chinese Journal of Pharmaceuticals*, 52(09), 1248-1252.
- Shang, Y., Ma, S. H., Zhang, Q. M., & Yang, Z. P. (2022). 科学监管方法之湿热灭菌药品参数放行探索研究 [Study on parametric release of moist-heat sterilized drugs by scientific supervision methods]. *China Academic Journal Electronic Publishing House*, 36(05), 497-502.
- Sheng, Y. (2009). *Enterprise technology innovation management: stakeholder approach* [企业技术创新管理：利益相关者方法]. Guang Ming Daily Press.
- Simon, H. A. (1955). A behavioral model of rational choice. *The Quarterly Journal of Economics*, 69(1), 99-118.
- Spill, R. L., Licari, M. J., & Ray, L. (2001). Taking on tobacco: policy entrepreneurship and the tobacco litigation. *Political Research Quarterly*, 54(3), 605-622.
- Strauss, A., & Corbin, J. (1997). *Grounded theory in practice*. Sage Publications.
- Tao, X. R., & Cui, Y. W. (2008). *公共政策分析* [Public policy analysis]. Huazhong University of Science & Technology Press.
- Vedung, E. (1997). *Public policy and program evaluation*. Transaction Publisher.
- Walker, J. L. (1969). The diffusion of innovations among the American states. *The American Political Science Review*, 63(3), 880-899.
- Wang, C. G. (2016). 药品上市许可持有人制度——我国药品注册制度改革的突破口 [Drug marketing authorization holder system - a breakthrough in the reform of China's drug registration system]. *China Food & Drug Administration Magazine*, (07), 21-24.
- Wang, H., & Jiang, R. (2007). 利益相关者理论综述研究 [A review of stakeholder theory]. *Inquiry Into Economic Issues*, (4), 4.
- Wang, J. M., & Wang, J. H. (2011). 公众低碳消费模式的影响因素模型与政府管制政策——基于扎根理论的一个探索性研究 [Influencing factor models of public low-carbon consumption patterns and government regulatory policies—an exploratory study based on grounded theory Research]. *Governance World*, (04), 58-68.
- Wang, Q. B., Hu, J., & Dai, T. (2016). 建立分级诊疗制度的动力与阻力分析——基于利益相关者理论 [Analysis of the motivation and resistance to the establishment of a hierarchical diagnosis and treatment system: based on stakeholder theory]. *Chinese Journal of Health Policy*, 9(04), 9-15.

- Wang, S. G. (2006). 中国公共政策议程设置的模式 [A model for setting China's public policy agenda]. *Chinese Social Sciences*, (5), 86-99.
- Wang, Y. (2021). 我国上市许可持有人制度的长期机遇（上） [Long-term opportunities for China's marketing authorization holder system (Part I)]. *China Food & Drug Administration Magazine*, (05), 46-53.
- Weissert, C. S. (1991). Policy entrepreneurs, policy opportunists and legislative effectiveness. *American Politics Quarterly*, 19(2), 262-274.
- Woll, P., & Lewis, E. (1981). Public entrepreneurship: toward a theory of bureaucratic political power: the organizational lives of Hyman Rickover. *The American Political Science Review*, 75(1), 202-203.
- Wright, S. R., & Jenkins, W. (1978). *Policy analysis: a political and organizational perspective*. American Sociological Association.
- Xu, S. Y., & Zhang, Z. X. (2005). 管理问题与理论建立:开展中国本土管理研究的策略 [Management issues and theory establishment: developing Chinese local management research strategies]. *Nanjing Business Review*, (04), 1-18.
- Yang, H. S. (2020). *公共政策学* [Public policy]. China Renmin University Press.
- Yang, Y., Li, X. Y., Liu, J. J., & Ren, Y. (2015). 基于药品管理法修订的药品上市许可制度设计研究 [Research on the design of drug marketing authorization system based on the revision of the drug administration law]. *Chinese Pharmaceutical Journal*, 50(17), 1558-1562.
- Zahariadis, N. (2007). *The multiple streams framework-structure, limitations, prospects: theories of the policy process*. Routledge.
- Zhang, K. (2015). 地方主官异地交流与政策扩散:以“多规合一”改革为例 [Non-local exchange and policy diffusion of local chiefs: a case study of the "integration of multiple regulations" reform]. *Journal of Public Administration*, 8(03), 79-102.
- Zhang, X. W., & Gao, Q. (2020). 乡村治理中的顶层设计与地方实践:如何从试点到推广? [Top level design and local practice in rural governance: what should be done to move from pilot project to widespread practice?]. *Journal of Wuhan University of Science and Technology(Social Science Edition)*, 22(02), 193-200.
- Zhou, L., & Li, S. (2016). 跨体制流动与政策创新:制度环境约束下政策企业家的身份选择——以西南省公益金融创新为例 [Cross-institutional mobility and policy innovation: the identity choice of policy entrepreneurs under the constraints of institutional environment: a case study of public welfare finance innovation in southwest province]. *Journal of Public Administration*, (05), 45-63.
- Zhu, C. K. (2016). *公共政策学* [Public policy]. Qinghua University Press.
- Zhu, Y. P. (2008). 中国住房保障政策: 回顾与前瞻[China's housing security policy: a review and perspective]. *Journal of Public Administration*, (04), 84-109.
- Zhu, Y. P. (2010). 政策创新与政策扩散研究述评 [Review of policy innovation and policy diffusion research]. *Journal of Wuhan University (Philosophy and Social Science Edition)*, 63(04), 565-573.
- Zhu, Y. P. (2012). 政策过程中的政策企业家:发展与评述 [Policy entrepreneurs in the policy process: development and commentary]. *Journal of Sun Yat-sen University (Social Science Edition)*, 52(02), 156-164.
- Zhu, Y. P., & Xiao, D. W. (2015). Policy entrepreneur and social policy innovation in China. *The Journal of Chinese Sociology*, 2(10), 1-1.

Webliography

- Freeman, R. E., & Mcvea, J. C. (2001, March 16). *A stakeholder approach to strategic management*. SSRN. Retrieved August 10, 2023, from https://papers.ssrn.com/sol3/papers.cfm?abstract_id=263511
- GBW. (2015, December 8). *The importance of implementation for parametric release in pharmaceutical manufacturing*. GBW114. Retrieved December 20, 2022, from <http://www.gbw114.com/news/n14323.html>
- Marla, S. (2015, May 20). *Parametric release: a regulatory perspective*. American Pharmaceutical Review. Retrieved May 15, 2023, from <https://www.americanpharmaceuticalreview.com/Featured-Articles/174390-Parametric-Release-A-Regulatory-Perspective/>
- PICS. (2007, September 25). *Recommendation on guidance on parametric release*. PIC/S. Retrieved October 4, 2022, from <https://picscheme.org/docview/3448>
- State Council. (2015, November 4). *Decision of the standing committee of the national people's congress on authorizing the state council to carry out pilot projects of the drug marketing authorization holder system in some localities and related issues*. Central Government of PRC. Retrieved August 1, 2023, from https://www.gov.cn/xinwen/2015-11/04/content_5004817.htm

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Annex A: Questionnaire (Semi-structure interview)

Background Introduction:

1. Brief introduce Parametric release: concept, the significance of Parametric release; the history of development globally, current status in China.
2. The research purposes.

Part 1: (Regarding Parametric Release policy)

1. Please introduce yourself briefly.
2. Do you know China's current common product release method for large-volume injection? What are the pros and Cons?
3. How do you know parametric release? What is your understanding of this policy? What are the pros and Cons?

Part 2:(Research method: Stakeholder theory)

4. Who are the stakeholders of this study? Who are the key stakeholders? Why?
5. What are the roles of each key stakeholder for parametric release policy adoption in China?
6. What is the positive impact as well as concerns / for different stakeholders?
7. As one of the stakeholders, do you see China as ready to adopt and implement parametric release policy? Why?
8. For different stakeholders, do they have common interests and goals, such as NMPA and the advocator of industry? What are they? Do they have a conflict of interest and objective? What are they?
9. Do you have any suggestions regarding how to deal with the potential conflict of interest among different stakeholders?
10. For this project, do you think a partnership can be built among stakeholders with common interests? Can this partnership promote the parametric release policy adoption and implementation in China? What kind of value can be created?
11. In terms of building partnerships among stakeholders, what ways/actions do you think can help achieve the goal?

12. What kind of resources are needed to accomplish the goal?

What are key success factors regarding building partnerships among key stakeholders?