Innovation Economics and Management Research (IEMR)
Volume 11, Issue 2 (2026). ISSN：2949-1304

Referential Significance for China from Clinical Trials of Unlisted Products Initiated by Foreign Researchers

Changhui Liu[1], Jiyin Zhou[2]

[1] *School of Medical Humanities, Hubei University of Chinese Medicine, Hubei Health Industry Development Research Center, Wuhan, China*
[2] *Clinical Medical Research Center, Second Affiliated Hospital of Army Medical University, Chongqing, China*
[2]*Corresponding author. Email: zhoujiyin@outlook.com*

ABSTRACT
Objective: The objective of this paper is to further improve the management level and research quality of clinical research initiated by researchers in China. Methods: The research is conducted by analyzing the current situation of unlisted products used in clinical research initiated by researchers in China and its regulations, and drawing on the regulatory experience and management mode of unlisted products used in clinical research initiated by foreign researchers. Results: Although there are differences in the management regulations and management modes of IIT in different countries, most of them classify the risk of participants according to the research, carry out risk stratification management, and take into account science and ethics. Conclusion: On the basis of drawing lessons from relevant foreign management experience and models, it is necessary for China to continuously improve policies and regulations, strengthen process management, and establish and improve relevant systems. It is also necessary to promote mutual recognition of ethical review, promoted resource integration, establish a management system in line with the actual situation of China at this stage, and further promote the standardization and high-quality development of IIT in China.

Keywords: *Clinical research initiated by researchers, Unlisted products, Management mode, Ethical review.*

1. INTRODUCTION

Investigator-initiated clinical research (IIT) refers to clinical research initiated by researchers. The scope of research is usually areas not covered by clinical trials initiated by pharmaceutical companies, such as rare disease research, comparison of diagnostic or therapeutic methods, new uses of listed drugs, etc.[1] The use of unlisted products for clinical research initiated by researchers was once a common gray area. For example, the specific scheme of unlisted product IIT was designed according to the problems found in the phase I drug clinical trial, and its research results guided the phase II clinical trial.

This paper sorts out the current situation and relevant laws and regulations of unlisted products used in IIT in China, and draws on the regulatory experience of foreign unlisted products used in IIT, and then puts forward relevant suggestions, in order to better provide important reference and valuable experience for unlisted products used in IIT.

2. OVERVIEW OF THE CURRENT SITUATION AND REGULATIONS OF UNLISTED PRODUCTS USED IN IIT IN CHINA

According to the relevant data of drug clinical trial registration and information publicity platform and China Clinical Trial Registry, the number of IIT projects registered in China Clinical Trial Registry in 2014 was only 723, while the number of registrations in 2024 reached 6132. It can be seen that IIT has gradually become an important force to promote the development of clinical medicine in China.

2.1 Current Status

With the gradual improvement of clinical research ability in China, IIT has been paid more and more attention. For example, in 2023, Hunan Provincial Drug Administration approved the second type of medical device attention intensive training software for the adjuvant treatment and rehabilitation training of children aged 6 to 12 years old with attention deficit hyperactivity disorder according to the IIT results. In 2024, the application for clinical trial of iquiolensai injection for refractory generalized myasthenia gravis was approved[2]. Therefore, IIT plays an indirect role in the research and application of drugs and medical devices in China, and even provides an important reference for drug market review.

At present, the clinical research carried out in China includes the evaluation of the efficacy and safety of drugs and medical devices, the study of disease prevention measures and the verification of new treatment methods. Unlike clinical trials, IIT has a wider scope of research, giving researchers greater autonomy and flexibility. This autonomy enables IIT to focus more directly on specific clinical issues, thus playing an important role in improving treatment options and improving diagnostic procedures. Although some top medical and health institutions have strong scientific research capabilities and resources to initiate and complete IIT, the research level of IIT is uneven. Due to limited funds in the design and implementation stages, IIT often faces many challenges.[3]

2.2 Overview of Regulations

In October 2014, the Health Commission issued the "Measures for the Management of Clinical Research Projects in Medical and Health Institutions" (National Health Medical Development [2014]No.80). In 2021, the pilot work of "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions (Trial)" was launched, which was piloted in four provinces and cities: Beijing, Shanghai, Guangdong and Hainan. On September 18,2024, the National Health Commission, the State Administration of Traditional Chinese Medicine and the National Bureau of Disease Control and Prevention jointly promulgated the "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions", which was implemented on October 1, 2024. At present, there are no clear regulations, ethical review guidelines and industry norms for IIT of unlisted drugs, medical devices, formula foods for special medical purposes and other products in China. The "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions" also only allows listed products to be used for IIT, and unlisted products have not yet been included in the IIT category. Therefore, the "Drug Administration Law of the People's Republic of China", "Drug Clinical Trial Quality Management Standard", "Medical Device Clinical Trial Quality Management Standard " and other norms have become the legal regulation basis for pre-market clinical trials of products.

According to Article 19 of the “Drug Administration Law of the People's Republic of China”, all clinical trials involving unapproved drugs must be approved by the State Food and Drug Administration, but there is no specific standard for the approval of clinical studies involving unapproved drugs and medical devices. This simple unilateral approval method for licensing clinical trials has caused regulatory ambiguity, and researchers cannot obtain clear legal support.

At the same time, special management methods are used in some special cases. The "Technical Guidelines for the Addition of New Indications to Cancer Drugs" promulgated in 2012 clearly states that high-quality IIT results can also be used as an important reference to support the approval of new indications. "Notice of the State Food and Drug Administration of the National Health and Family Planning Commission on the Issuance of Management Measures for Clinical Research on Stem Cells (Trial)" (2015) and "Guidelines for Clinical Research on Somatic Cells (Trial)" (2023) allow the development of IIT for unlisted somatic cells, and "Technical Guidelines for the Addition of New Indications to Listed Antineoplastic Drugs (2023 Edition)" allows the development of off-label indications for listed antineoplastic drugs. To a certain extent, these management methods provide important support for accelerating the new research methods of clinical treatment of difficult and complicated diseases. However, clinical research institutions and major researchers should have the corresponding qualifications required by the "Quality Management Standards for Drug Clinical Trials", the approval documents of the ethics committee, detailed research plans, standardized quality management systems and monitoring records, which undoubtedly complicates the

supervision work. IIT-type research is usually reviewed and approved by the scientific review committee and ethics committee of the researcher 's institution, and implemented and supervised after the project is established.

3. THE REGULATORY EXPERIENCE OF FOREIGN UNLISTED PRODUCTS FOR IIT

3.1 United States

From the perspective of regulatory classification, the United States divides IIT into new drug clinical trials (hereinafter referred to as “IND-IIT”) and non-registered clinical trials (hereinafter referred to as “Non-IND-IIT”). IND-IIT needs to submit an IND application. The initiation and implementation of Non-IND-IIT research does not need to be declared to the US Food and Drug Administration (hereinafter referred to as "FDA"). It can only be implemented after review by research institutions such as universities and hospitals. When it comes to the informed consent process, it is necessary to comply with the provisions of the US Federal Regulations on Institutional Review Boards (hereinafter referred to as "21 CFR 56"). In addition, the United States stipulates the scope of application of exempted research and non-exempted research. Commonly exempted studies include single-armΠ phase trials using marketed drugs to treat different cancers, Iphase oncology trials of marketed drugs, studies on new drug combinations, and studies on high-dose treatment of cancer patients; non-exempt studies include adjuvant chemotherapy studies, studies using new drugs with unconfirmed activity, and studies supporting new indications. Among them, for the IIT used in off-label use after listing, whether to submit an IND application can be judged by referring to whether it meets the conditions for exempting IND[4].

From the perspective of the structure of federal regulations, the US FDA does not actually regard IIT as a separate chapter, but integrates it into the relevant chapters of IND (mainly the informed consent requirements of 21 CFR Part 312 and 21 CFR Part 50 and the institutional review requirements of 21 CFR Part 56). Some IITs need to apply for IND, and some can be exempted from IND application. Clinical studies including IIT may be exempted from IND applications on the premise that they are not used for new indications applications, do not involve major changes in drug labels and advertisements, and do not involve other factors that increase the risk of medication.

From the perspective of the application of exemption studies, FDA issued the "Guidelines for New Drug Application Exemptions for Legally Listed Drugs or Biological Products for Cancer Treatment" in 2004 on the basis of 21 CFR Part 312. The purpose is to provide general guidance for the application of new drug exemptions for research on biological products or listed drugs for cancer treatment, that is, to further explain on the basis of 21 CFR Part 312. The key and premise of the exemption still lies in the risk assessment, that is, whether there are “administration routes, dose levels, patient population use or other related factors that may significantly increase the risk of drug use (or reduce risk acceptability)” explicitly mentioned in 21 CFR Part 312.2 (b). At the same time, in the guidelines, FDA requires institutions and researchers to perform IND applications for studies that need to be submitted based on the evaluation results after evaluating whether the study falls within the scope of IND exemption according to the guidelines. The FDA has also issued a supplemental guideline for tumor-specific exemptions from IND. The guideline proposes that clinical trials that are not intended for registration or commercial purposes can be decided by the investigator whether to submit an IND application.

The clinical research management model of Dana Faber/Harvard Cancer Center (DF/HCC) at Harvard Medical School is a typical representative of the management model of IIT institutions in the United States. The center has a large number of clinical trial projects with researchers as the main body, and the clinical research office has a special team of inspectors to undertake the monitoring tasks of such projects [5]. The clinical research office undertakes the responsibility of project coordination, regularly organizes clinical department seminars, follows up on research progress, and timely convenes coordination meetings to optimize workflow and improve operational efficiency. Professional committees such as the Data Security Management Committee and the Scientific Process Review Committee regularly review the implementation of the project. After the clinical research reaches the end point of the trial and the bidder confirms that the project can be concluded, the relevant departments of clinical research can complete the project completion procedures. Through the multi-level and all-round whole-process clinical research management and control system, the center ensures the standardized

and orderly development and smooth implementation of clinical research.

3.2 European Union

The regulatory requirements of EU Regulation 2014/536 on IIT are consistent with clinical trials. It includes two aspects of relevant legal regulations and regulatory policies. Under the regular review of IIT by the independent data monitoring committee, it actively convenes promotion meetings to grasp the safety and effectiveness of IIT projects in the implementation process [6].

The current EU regulations on drug clinical trials include the higher-level law Dir. 2001/20/EC (the "Clinical Trials Directive") issued on April 4, 2001, and Reg. (EU) No 536/2014 (the "Regulation on Clinical Trials of Medicinal Products for Human Use") issued on April 16, 2014, along with related guidelines. The "Regulations on Clinical Trials of Pharmaceuticals for Human Use" has a comprehensive legal framework designed to ensure the scientific and ethical compliance of trials while protecting the rights and interests of research participants. It covers a wide range of contents. The main regulatory elements include approval requirements and procedures, clinical trial status, research participant protection, safety report, research drug management, etc. The regulation proposes "low-intervention clinical trials", which are of vital importance for assessing standard treatment and diagnosis, optimizing the use of pharmaceutical products, and promoting a high level of public health.

From the perspective of regulatory policy, the European Medicines Agency has adjusted the clinical trial data disclosure mechanism. Since January 1,2015, all the drug marketing license declaration materials and related clinical research reports submitted to the bureau have been open to the public and allowed to be applied to academic exploration and non-commercial scientific research activities. It can be seen that under the EU regulatory framework, the clinical research (IIT) initiated by researchers is centered on non-commercial attributes, and the relevant system design has laid a solid foundation for the normalization and standardization of clinical trials. Under the premise of ensuring informed consent and research participant recruitment compliance, research participant reward or compensation, data protection, qualifications of participants and test sites, and damage compensation requirements, [7] member states and all member states of the clinical trial location are jointly assessed.

However, the above application procedures are too cumbersome and strict monitoring requirements, which is not conducive to improving the efficiency of the test, and will greatly damage the enthusiasm of researchers. Therefore, the EU has also considered simplifying the process. For example, 2005/28/EC ("European Commission's Directive on the development of guidelines and detailed guidelines for the quality management of clinical trials for human use in research and its production or import authorization requirements") proposed that member states should take into account the particularity of academic research. For non-commercial research that meets specific standards, the sponsor can submit an application for simplified clinical trials to the drug administration department of the host country. The sponsor only needs to prove that the research meets the requirements of scientific rigor, controllability of risk assessment, and ethical guidelines (such as the "Helsinki Declaration"), and directly submits a streamlined clinical plan to the drug administration agency of the host country, exempting some of the complicated administrative documents required for commercial trials. The member states also need to establish a rapid assessment mechanism, focusing on the review of scientific, ethical compliance and risk management measures to shorten the approval cycle. However, for various reasons, this approach has not been implemented.

The most representative clinical research management model in the EU is the European cancer research and treatment organization model. The European Organization for Research and Treatment of Cancer is a comprehensive clinical research transformation and exchange platform for the entire European medical system, and has long-term cooperation with the National Cancer Institute to fully integrate resources in related fields in Europe and the United States [8]. The European Organization for Research and Treatment of Cancer has given full play to the service support and quality supervision functions of clinical research and maintained the high-level development of IIT.

3.3 United Kingdom

The UK drug clinical trial regulatory system focuses on protecting the rights and interests of research participants, ensuring scientific and reliable test data, and promoting pharmaceutical R&D innovation. The system integrates

international standards and local characteristics, forming a multi-level and multi-link regulatory framework, covering the whole life cycle from experimental design to data submission. After the end of the Brexit transition period in 2020, the British Medicines and Health Products Administration (MHRA) established an independent regulatory system based on the revised version of the "Regulations on Clinical Trials of Pharmaceuticals for Human Use", retaining a high degree of compatibility with EU regulations, while making innovations in the optimization of the approval process. In 2021, the British Medicines and Health Products Administration updated the “Clinical Trial Statistical Guidelines”, which mandated that statistical verification nodes should be preset when adaptive trial design was adopted. At the same time, it was required to complete scientific review within 30 days, focusing on evaluating drug safety, rationality of trial design and risk control measures.

The protection mechanism of participants' rights and interests includes multi-level protection measures. The economic compensation standard is 1.5 times the national minimum wage, and the insurance coverage shall not be less than 2 million pounds per person. The participation of vulnerable researchers in clinical research is subject to review by specific ethics committees (such as the Youth Ethics Committee), and visual aids are mandatory for the informed consent process. The "Research Ethics Committee Standard Operating Procedure (SOP v10.0)" and the "UK Health Research Policy Framework" (2023 Revision) issued by the UK Health Research Authority (HRA) require all trial sites to have a Research Participants ' Rights and Interests Liaison Officer. Its main purpose is to provide independent and reliable supporters and rights spokespersons for research participants (especially vulnerable groups) throughout the research process, so as to more fully guarantee their rights, welfare and dignity, in addition to existing measures such as ethical review and informed consent. This is an important upgrade of the rights and interests protection mechanism of research participants in the United Kingdom.

3.4 Japan

In Japan, all kinds of medical research targeted at human beings need to comply with the provisions of "various medical research targeted at human beings" formulated by the Ministry of Health, Labour and Welfare of Japan in principle, especially non-interventional observational research. This is a basic law and a principled requirement. In 1997, Japan promulgated the "Clinical Trial Quality Management Standard", which stipulated that the highest standard for the implementation of drug clinical trials was clinical trials for the purpose of registration and listing. In 2003, Japan revised the "Drug Administration Law" and clarified the legitimacy and regulatory requirements of IIT. In the same year, Japan formulated the “ethical guidelines related to real-world clinical research”. In 2014, it integrated the “ethical guidelines related to epidemiological research” and introduced the “ethical guidelines related to medical research targeting human beings”. In June 2021, the "ethical guidelines related to life science and medical research for humans" were issued. This policy is an ethical norm formulated by Japan for medical research involving research participants. It integrates a number of previous relevant regulations, such as the "ethical guidelines related to real-world clinical research" in 2003, to adapt to new fields such as human genome and genetic analysis. In April 2018, the Ministry of Health, Labor and Welfare of Japan promulgated and implemented the “clinical research method”, which stipulated the relevant matters of clinical research. These laws and regulations together constitute the core legal basis in the field of Japanese clinical research.

Japan also has two IIT systems, one for IND tests and the other for non-IND tests. The IND trial was conducted in accordance with the "Clinical Trial Quality Management Specification" and the IND application was submitted to the Ministry of Health, Labor and Welfare. These tests are regulated and monitored in the same way as commercial tests and are reported to the Institutional Ethics Committee and the Medicines and Medical Devices Bureau on a monthly basis if safety issues arise. Due to the small number of professionals operating clinical trials, these requirements pose a huge obstacle to the academic community, because they often take time, a large amount of paperwork, and high costs. In contrast, non-IND trials conducted according to the “Clinical Research Guidelines” issued by the Ministry of Health, Labour and Welfare in 2003 do not require application. The requirement of non-IND-IIT is not as strict as that of IND, but it submits a report to the Ethics Committee every year and a report on safety issues to the Ministry of Health, Labor and Welfare. Compared with the IND experiment, these requirements involve shorter time, less paperwork and lower cost. It is easier for academic institutions

to carry out non-IND, even with very few staff. Therefore, due to the non-IND test in the paperwork, research process and quality assurance requirements are not strict, the data quality is poor, so the non-IND test data for the approved research project is basically invalid. Although it may provide some new evidence, it is not useful in clinical practice [9].

4. ENLIGHTENMENT OF FOREIGN REGULATORY EXPERIENCE TO CHINA

4.1 Construction of Clinical Trial Data Sharing Platform

The construction of clinical trial data sharing platform is an important carrier to provide experimental experience. Vivli is a global clinical research data sharing and analysis platform established by Microsoft Azure. It is committed to promoting the open sharing of clinical trial data to promote medical research progress. The platform brings together 4990 research results shared by about 2.7 million participants from 111 countries and 23 institutions, covering more than 20 diseases such as diabetes, cancer, and COVID-19. The non-profit nature of the platform makes it play an important role in the sharing of clinical trial data. Researchers can submit data requests through the platform, and use the high-quality clinical data provided by the platform, including diabetes, cancer, asthma and other diseases, to conduct in-depth research. In China, the level of medical development is different due to the different regional development. Therefore, it is extremely important to establish a nationwide test data specialization platform, and even consider establishing a “multi-level and multi-featured” IIT database in conjunction with neighboring countries or “Belt and Road” countries.

4.2 Multi-oriented Academic Research Management Model

The management of IIT in foreign countries is mainly divided into administrative licensing for the purpose of registration and university management without the purpose of registration. At the same time, it actively seeks a multi-oriented research management model. Some countries have formed a centralized academic clinical research management institution with universities as the core to standardize project support and management [10]. For example, Dana Faber/Harvard Cancer Center, Harvard Medical School, USA, adheres to the strategic orientation of cancer clinical research with cancer as the main core in the whole process of IIT management from planning, auditing, development to completion, adheres to the demand orientation of optimizing treatment and expanding application, and adheres to the quality orientation of strictly supervising all aspects of IIT to meet the standards, so as to provide a reliable basis for clinical decision-making of cancer. In addition, the clinical research centers of Oxford University in the United Kingdom and Duke University in the United States have become the main undertakers in the management of such academic research. Combined with the above functions, they actively seek to adapt to different oriented research methods, which greatly innovates the form of IIT supervision. China should set different orientations according to the types of risks and results of IIT and divide them into different categories.

5. SPECIFIC REFERENCE MEASURES

5.1 Development of Targeted Regulatory Regulations

At present, although the "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions" clarifies the four basic systems of IIT, including the scope of application, institutional responsibility, scientific review and ethical review, and applies classified management together with collaborative supervision, there is a lack of effective management measures. Therefore, China's IIT management agencies can set up a leading group to carry out unified management work, establish an integrated data sharing platform, integrate existing clinical trial registration and regulatory information systems, and improve the data supervision system, which will help to strictly supervise unlisted products IIT. In addition, for high-risk predictive studies involving off-label drug use and clinical application of new medical technologies, specific guidelines can be formulated in the "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions" to guide institutions to reasonably evaluate the scientific nature of research and fully identify and evaluate the risks and benefits of research ; at the same time, researchers should fully respect the right of informed consent of research participants, and explain the research risks and the way of risk-

taking. In the event of serious adverse events, corresponding active treatment measures should be taken in time to fully protect the personal safety of the research participants and report to the ethics committee. This will provide guidance for the standardization of IIT research, and will also help to clarify the direction of IIT supervision of unlisted products.

When formulating targeted laws, we can consider defining the regulatory body, responsibilities and team members and capabilities of IIT. For regions with limited resources, regional ethics committees and academic committees can be established to better assist research teams in carrying out ethical and scientific IIT [11]. After clarifying the definition and responsibilities of each subject, it is necessary to establish a legitimate and appropriate public access procedure. With regard to the legal use of data, the law should clarify the responsibilities of the "Data Security Monitoring Committee" to supervise the disclosure of information, achieve data transparency, and take the initiative to perform the work that the IIT review and inspection results must be disclosed in the integrated data sharing platform, except that the confidentiality study is not disclosed after application [12]. These measures will provide a strong guarantee for the joint supervision of unlisted products.

5.2 Strengthening the Process Management of IIT

A sound risk assessment system is the core of IIT's process management. The United States and the European Union do not manage IIT separately, but integrate IITs that need to declare IND and IITs that do not need to declare IND into the overall clinical research management, and clarify that exceptions can be applied in special cases. For example, the EU's IIT may belong to the "low-intervention clinical trials" part can be appropriately relaxed, but this provision is still based on risk assessment.

Medical and health institutions should establish a risk full-process reporting mechanism for IIT, and fully consider the factors that may cause risks in the research process, such as research program, ethical review, research participant recruitment, adverse events, etc. At the same time, it is also necessary to establish an IIT file management system, clarify the list of documents to be filed, the location and time limit of the file, and ensure the integrity and systematicness of the file[13].

Protecting the rights and interests of research participants is an important concept throughout process management. The existing ethics committee review mechanism should be developed to the research participant protection work system, so as to promote the more comprehensive protection of the rights and interests of the research participants [14]. Therefore, the concept of putting the rights and interests of research participants first should be clearly defined to provide support for the rights and interests of research participants in the whole process management of IIT, and to ensure the timely realization of IIT results.

5.3 Establishing Damage Compensation System

The latest revision of the "Helsinki Declaration" in 2024 is an international ethical principle for medical research involving human research participants, which strengthens the ethical obligation that researchers should provide compensation for research participants who are harmed by participating in research. "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions" Article 37 stipulates that medical and health institutions shall make reasonable compensation or compensation to the damaged research participants in accordance with the agreement or relevant administrative regulations. However, the specific damage compensation system has not been established, and there are few reports on the actual compensation of research participants injured in IIT. In order to provide appropriate compensation, it is necessary to establish specific management systems (e.g. procedures for consultation with the victim, procedures for payment of compensation) and evaluation systems (e.g. assessment of causality and injury levels to determine the amount of compensation). In addition, local government departments can also implement research participant injury compensation insurance. These important measures can not only safeguard the vital interests of research participants, but also provide a guarantee for medical and health institutions to carry out ethical follow-up review.

5.4 The Establishment of Ethics Committee Certification Mechanism

Article 19 of the "Measures for the Administration of Clinical Research Initiated by Researchers in Medical and Health Institutions" stipulates that medical and health institutions have

the right to establish an IIT ethics committee, and the IIT of different medical and health institutions will be reviewed by the ethics committee of different institutions, which will easily lead to different ethical review processes and review standards. In order to continuously optimize the medical ethics review process and improve the quality of review, some regions have carried out pilot projects of regional ethical mutual recognition mechanism. For example, on March 21,2025, the establishment conference of Chengdu Regional Medical Ethics Alliance was held in the Third People's Hospital of Chengdu. Chengdu Third People's Hospital, West China Hospital of Sichuan University, Sichuan Provincial People's Hospital and other 31 medical institutions have achieved mutual recognition of Chengdu medical ethics review. However, regional certification still has great limitations. It is recommended to establish a unified national ethics committee certification mechanism. Under the premise of complying with the ethical principles of the "Helsinki Declaration" and the ethical review normative documents such as the "Ethical Review Measures for Human Life Sciences and Medical Research", it is necessary to clarify the ethical review rules, review standards and review responsibilities, and improve the working system [15].

5.5 Centralizing Resources and Coordinating Provincial Regulatory Forces

IIT often involves many fields and many regions, so the problem of unequal or shortage of resources that may occur in various provinces and cities in China needs to be solved urgently. In this field, with reference to the excellent experience of the EU in collecting the resource advantages of each member state and centralized and unified management, it will help to formulate an IIT regulatory system in line with China's characteristics. It is necessary to establish a provincial IIT management service center, which can be affiliated to the provincial health commission or the drug administration. We can also actively promote the “single ethical review” pilot, that is, the center uniformly accepts the ethical review application of the province's IIT. At the same time, a provincial IIT project library and an electronic supervision platform should be established, and the center should provide professional services such as regulatory consulting, program design, and statistical support. Relevant departments such as the Health Commission, the Drug Administration, the Department of Science and Technology, the Department of Education, the Medical Insurance Bureau, and the Department of Finance should gather the regulatory forces of each province, submit a single set of data, and hold a centralized expert seminar to minimize the time of clinical trials. In addition, provincial health administrative departments can set up an active leading expert committee or a selection ethics specialized agency to comprehensively grasp and analyze the research situation of IIT in the region, and summarize the specific situation in regional statistical agencies. Statistical institutions need to conduct detailed analysis on the diversity of IIT in the jurisdiction (such as basic research, clinical transformation, public health, etc.) and differentiated influencing factors (such as disease field, ethical risk, etc.), and give different supervision and resource allocation for different research orientations and influencing factors. Through this "classified guidance and on-demand supply" regulatory model, the provincial IIT management service center can achieve precise empowerment of different IIT studies, which can not only avoid the rigidity of "one-size-fits-all" supervision, but also concentrate resources to support breakthroughs in key areas of clinical research.

6. CONCLUSION

The core feature of IIT is that researchers carry out research according to clinical needs without considering drug registration and market benefits. Therefore, this research model has a high degree of flexibility and adaptability and can solve key problems in clinical practice. Although there are differences in the management regulations and management modes of IIT in different countries, most of them classify the risk of research participants according to the research, carry out risk stratification management, and take into account science and ethics. On the basis of drawing lessons from foreign relevant management experience and mode, China constantly improves policies and regulations, strengthens process management, establishes and improves relevant systems, promotes mutual recognition of ethical review, promotes resource integration, establishes a management system in line with the actual situation of China at this stage, and further promotes the standardized and high-quality development of IIT in China.

REFERENCES

[1] Liao Hongwu, Hao Chunyi, Zhang Lei, et al., Thoughts on the Supervision and Ethical Review of Investigator-Initiated Clinical Trial [J]. Chinese Medical Ethics, 2019, 32(12): 1518—1521,1534.https://doi.org/10.12026/j.issn.1001-8565.2019.12.08

[2] Nian Honglei, Li Jihong, Zhou Jiyin, Challenges, Countermeasures, and Key Points of Ethics Review in Investigator-initiated Clinical Trials of Unlisted Products [J]. Chinese Medical Ethics, 2025, 38(01): 31-39. https://doi.org/10.12026/j.issn.1001-8565.2025.01.05

[3] Minghuang Hong, Zhao Yan. The Development and Challenges of Investigator-Initiated Trials (IITs) in China [J]. Holistic Integrative Oncology, 2024, 1(3): 57. https://doi.org/10.1007/s44178-024-00123-7

[4] Lingor Paul, Koch Jan C, Statland Jeffrey M, et al. Challenges and Opportunities for Multi-National Investigator-Initiated Clinical Trials for ALS: European and United States Collaborations[J]. A.myotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2021, 5-6(22): 1-7. https://doi.org/10.1080/21678421.2021.1879866

[5] Cao Ye, Systematic introduction about clinical research management of HMS DF/HCC: entire process management of clinical research [J]. Chinese Jounal of New Drugs, 2015, 24(10): 1096-1099. https://doi.org/10.1003/j.cnki.1003-3734.2015.10.006

[6] Shi Jia'na, Lin Sisi, Zheng Xiaowei, et al., Pharmacy Services-related Investigator-initiated Trial Research Design and Practical Experiences [J]. Chinese Journal of Modern Applied Pharmacy, 2024, 41(20): 2879-2883. https://doi.org/10.13748/j.cnki.issn1007-7693.20242274

[7] Wei Fenfang, Sun Yuxin, Leng Jinnuo, Yang Yue, Interpretation and reflection on the Reg. (EU)No 536/2014 of the European [J]. Chinese Jounal of New Drugs, 2017, 26(16): 1865-1872. https://doi.org/10.3760/cma.j.issn.1003-3734.2017.16.018

[8] Kai Jiejing, Lv Duo, Liu Jian, Zhao Qingwei, Discussion on the standardized management of investigator initiated trial [J]. The Chinese Journal of Clinical Pharmacology, 2020, 36(15): 2357-2360. https://doi.org/10.13699/j.cnki.1001-6821.2020.15.058

[9] Tatsuya Ito. Differences in Investigator-Initiated Trials Between Japan and Other Countries Analyses of Clinical Trials Sponsored by Academia and Government in the Clinical Trials.gov Registry and in the Three Japanese Registries [J]. Journal PLoS ONE, 2017, 11(2): e0148455. https://doi.org/10.1371/journal.pone.0148455

[10] Sun Zhe, Xie Li, Hu Tingting, et al., Comparison and analysis of management mode of investigator-initiated trial at home and abroad [J]. Chinese Journal of New Drugs and Clinical Remedies, 2020, 39(2): 83-87. https://doi.org/10.14109/j.cnki.xyylc.2020.02.04

[11] Li Yixuan, Xie Li, Qian Biyun, et al., Regulatory framework of investigator-initiated trials: retrospect and prospect [J]. Chinese Journal of New Drugs and Clinical Remedies, 2020, 39(03): 146-150. https://doi.org/10.14109/j.cnki.xyylc.2020.03.04

[12] Shen Hao, Sun Luning, Wang Xiu, et al., Practice and Thinking of Data and Safety Monitoring Board in IIT Research [J]. Chinese Hospital Management, 2023, 43(7): 68-70. https://doi.org/10.3969/j.issn.1001-5329.2023.07.020

[13] Gong Fulian, Wang Xiaoling, Liang Yuguang, Analysis of management elements of investigator-initiated trial in medical institutions in China [J]. Modern Hospitals Journal, 2022,22(8): 1149-1152+1156. https://doi.org/10.3969/j.issn.1671-7562.2022.08.004

[14] Li Huijuan, Yuan Jie, Wu Yangfeng, Common Ethical Issues in Investigator-initiated Clinical Studies and Regulatory Considerations [J]. Medicine and Philosophy, 2022, 43(7): 6-10. https://doi.org/10.12014/j.issn.1002-0772.2022.07.02

[15] Wang Hongjing, Sun Shuhui, Xu Yumei, Zhou Jiyin, Exploration of Legal Regulations of Investigator-initiated Trials [J]. Medical Ethics Education China, 2025(10): 1306-1314. https://doi.org/10.12026/j.issn.1001-8565.2025.10.11