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Analysis of Major Project Management Problems in the Research and Development of New Biological Products in China

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Abstract

At present, Chinese biomedical enterprises are rapidly developing to product innovation, enterprise scale expanding, management regularization and Research and Development (R&D) cycle shortened, which indicates that most enterprises who cannot quickly complete the transformation to adapt to the development trend of biomedical development, especially small and medium-sized enterprises, will face the risk of being eliminated. In order to solve these difficulties, a scientific and effective new biological products R&D project management system should be established, in addition to the need for continuous scientific innovation and technological upgrading. The general process of new biological products R&D in China as the starting point, the author fully analyzed the main problems of R&D project management of new biological products in this paper. It is proposed that biomedical enterprises should not only solve the problems of project process management in project initiation, planning, execution and changes, abort and closure, but also solve the problems in project enterprise management environment such as human resource allocation, project communication management and performance appraisal. It is suggested that on the basis of fully analyzing the overall R&D process, segmented project management is implemented to establish a scientific and effective project management system based on "systematic management". What the enterprise decision makers need to weigh is that when to start and how much to cost to establish a scientific and standardized R&D project management system, and complete enterprise management upgrading. Transformation is painful, but also imperative.

Keywords: Project Management; General Process of R&D of New Biological Products; Major Project Management Problems

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Opportunities and Challenges Faced by Biomedical Enterprises in China

China's biomedical manufacturing industry is continuing to develop rapidly with the natural growth of China's population, the aggravation of population aging degree and the continuous enhancement of residents' awareness of health care, and with the scope increasing of national medical security coverage [1]. According to the report of Frost & Sullivan [https://baijiahao.baidu.com/s?id=1707335755173573533&wfr=spider&for=pc], China's biomedicine market size reached ¥317.2 billion yuan in 2019. China is expected to further expand its biological drug market to ¥641.2 billion yuan by 2023. With the expansion of medical insurance coverage, with the increase in pharmaceutical R&D investment, the biological drug market is expected to reach ¥1319.8 billion yuan in 2030. Biomedical enterprises have broad prospects [2].

At the same time, Chinese biomedical enterprises still face great challenges in survival and development. Firstly, compared with the international pharmaceutical market, there are a large number of biomedical enterprises in China. From 2007 to 2019, 1,132 newly biomedical enterprises were established in China [http://k.sina.com.cn/article_2401737737_8f279c09001012jlc.html] [3], but the scale of them is usually small. There are few innovative pharmaceutical enterprises with real international competitiveness, and their R&D capacity, production technology and supporting facilities need to be improved urgently. Secondly, comparing with chemical drugs, biological drugs are more complex, with longer R&D cycle, greater capital investment, and higher risk of R&D failure [4]. Thirdly, in the new round of medical system reform in China, the overall price level of biological products is constantly declining, and the operating pressure of many biomedical enterprises is increasingly increasing [5].

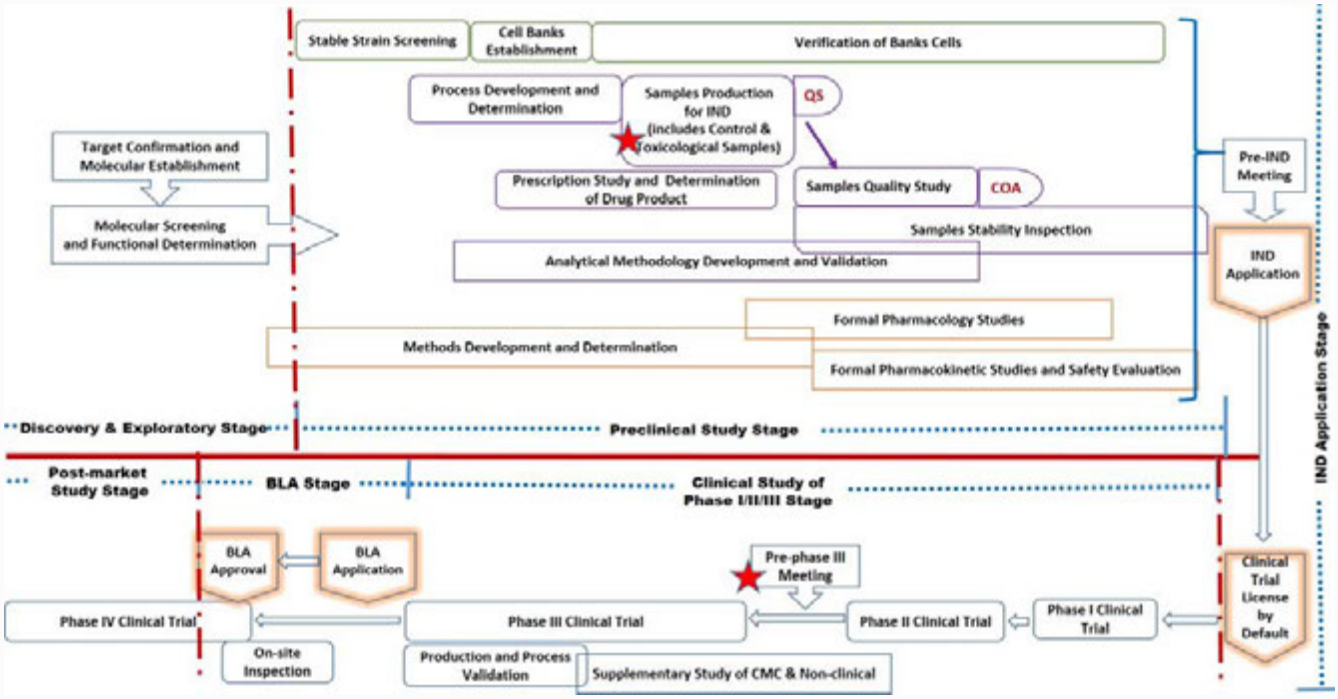

Figure 1: The general process of the R&D new biological product (take the antibody/recombination protein drugs for example).
QS: Quality Specification; COA; Certificate of Analysis

At present, Chinese biomedical enterprises are rapidly developing to product innovation, enterprise scale expanding, management regularization and shortened R&D cycle. Most enterprises that cannot quickly complete the transformation to adapt to the development trend of biomedical development, especially some irregular small and medium-sized biomedical enterprises will face the risk of being eliminated.

Scientific and Effective New Biological Products R&D Project Management is an Important Magic Weapon to Win

The R&D of new biological products is a kind of activity of high technology, high risk, high investment, long cycle, and high yield. In today's rapid development of economy and technology, the competition between the industries is more and more fierce. The competition of R&D ability between each new biological R&D companies is mainly reflected in the management level when the R&D funds is closed, technical ability is similar. To be in a dominant position in the competition, the enterprise must first have the ability to improve the management level. Scientific and effective R&D project management is an important magic weapon to make risk biomedical enterprises quickly reverse the situation of being eliminated and stand out in the fierce competition. Then, to establish a scientific and effective new biological products R&D project management system, the first thing is to understand the process of new biological products R&D and the main problems of its project management.

General Process of R&D New Biological Product and Project Management

General process of R&D new biological product

Take the antibody/recombination protein drugs for the example, the general process of R&D new biological product is divided into new drug discovery and exploratory stage, preclinical study stage, Investigational New Drug (IND) stage, clinical study stage, Biological License Application (BLA) stage, and post-market study stage. It is shown in Figure 1. The primary tasks for each stage are: (1) New drug discovery and exploratory stage: Target confirmation and molecular establishment, molecular screening and functional determination. (2) Pre-clinical study stage: a) stable strain screening, cell banks establishment, verification of banks cells; b) process development and determination, samples production for IND (including stability inspection samples, control sample and toxicology sample); c) prescription and process study of drug product; d) analytical methodology development and validation, quality study and stability inspection of drug substances and drug products; e) Formal pharmacology studies, pharmacokinetic studies, and safety evaluation. (3) Investigational New Drug (IND) application phase: Pre-IND meeting, IND application and default license for clinical trials. (4) Clinical study of phase I/II/III stage: a) clinical trial of phase I, clinical trial of phase II, pre-phase III meeting, clinical trial of phase III; b) supplementary study of CMC and non-clinical, production and process validation. (5) Biological License Application (BLA) stage: BLA, on-site inspection and BLA approval. (6) Post-market study stage: Clinical trial of phase IV. Generally, the whole cycle of R&D new biological product is very longer. Between 2010 and 2020, the FDA approved 440 new drugs, and the clinical development time of the new drug has changed very little in a decade, ranging from 5 to more than 20 years, taking an average of 8.3 years [6,7]. It can be conferred that the whole cycle of R&D a new biological product will take 7~12 years, or even more than 12 years.

Sectioned project management according to the general process of R&D a new biological product

The project management of R&D new biological product mainly consists of five parts: Project initiation, planning (overall study plan), execution (including changes), monitoring and the closure [8]. Then, if the project starts from the target confirmation until the BLA, it

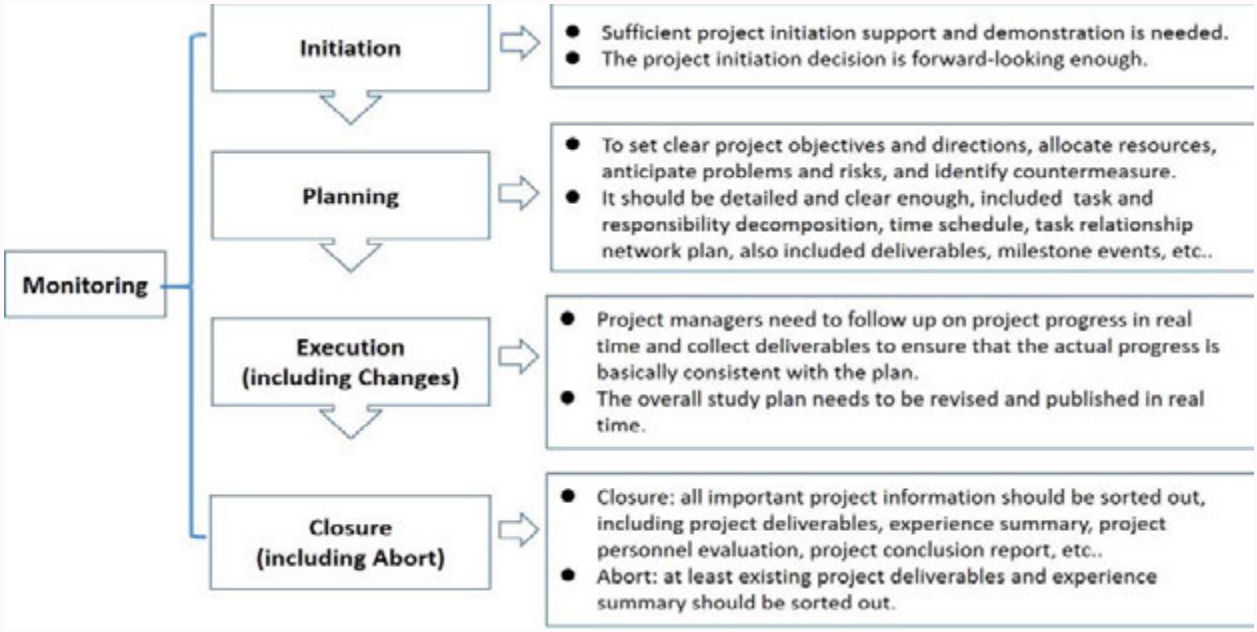

Figure 2: The main problems in the project process management procedure.

is obviously not conducive to the overall project management. The reasons are: (1) The whole cycle of R&D a new biological product is long (normally with 7~12 years) and high failure rate (the average failure rate from clinical phase I to the regulatory decision for marketing was 87.1% over the past decade [https://www.iqvia.com/insights/the-iqvia-institute/reports/2019-r-and-d-achievements/]) [9], so it is obviously unnecessary to equip personnel and materials for clinical trials too early in the new drug discovery and exploratory stage. (2) The entire R&D process requires too high technical and management levels for project leaders that few people can meet the whole process at the same time. (3) The environment for new drug development is changing (many competing products may no longer be allowed to continue to invest in this project). Therefore, the author suggests that the project management leader should divide the R&D project of biological product into multiple projects according to the general R&D stage and important R&D nodes to do projects management respectively. It can be divided into several parts, that (1) by stages (labeled red dotted lines in Figure 1): The overall project can be divided into four projects, they are new drug discovery and exploratory phase project, preclinical study and IND application phase project, clinical trials and BLA application stage project, post-market study stage project; (2) by important nodes (labeled red stars in Figure 1): When taking the starting of toxicology batch production to be the node, the preclinical study phase project can be divided into two projects, they are process development stage and non-clinical study stage projects; when taking pre-phase III clinical study meeting to be the node, clinical trials of phase I/II/III project can be divided into two projects, they are clinical trial of phase I/II project and clinical trial of phase III project. In this way, the project management will be clearer, and easy to promote the overall control and promotion.

Analysis of the Main Problems in the R&D Project Management of New Biological Products in China

Analysis of the main problems in the project process management

Project initiation: The R&D of new biological product is characterized by long cycle, large investment, high risk and high elimination rate [10]. The whole process of new drug research and marketing has high risks, and the failure of the projects will cause huge losses for investors and enterprises. There are serious homogenization problems in the project initiation of biological products in China, such as anti-tumor PD-(L)1 track. According to the analysis of the information released on CDE (Center for Drug Evaluation, NMPA)'s official website, the clinical trials of PD-(L)1 have been arrived 130 only in 2021 in China [https://www.cde.org.cn/main/news/viewInfoCommon/1839a2c931e1ed43eb4cc7049e189cb0] [11]. By the end of March 2022, there were 13 kinds of PD-(L)1 drugs have been launched in China, including 9 domestic drugs [12]. After they were entered the medical insurance catalog, the price of PD-(L)1 was directly dropped from ¥300,000 yuan/year to ¥50,000 yuan/year, or even lower [https://new.qq.com/omn/20220425/20220425A07PL800.html]. Even internationally, the R&D of PD-(L)1 drug is saturated [13]. For biological products R&D enterprises, the profit space is already self-evident. That is to say, except for a very few products with fast R&D speed and obvious competitive advantage with the same target, most products of PD-(L)1 track will die or lose money. Therefore, it is necessary to have a high degree of forward-looking and scientific in the project approval decision.

Therefore, sufficient project approval and demonstration is the first step in the success of the new biological products R&D project, which request enterprises doing comprehensive market research before the project initiation, accurately grasp the actual situation of market demand and competing products. At the same time, the drug enterprise should consider its R&D platform ability and work basis of this project to derive the IND submission, approved time and drug market time. Then, the R&D input and output budget should be done to decide whether to start-up this project [14].

Overall study plan of project: The overall study plan of new biological products R&D project refers to the systematic task arrangement to achieve the project objectives (e.g. obtaining

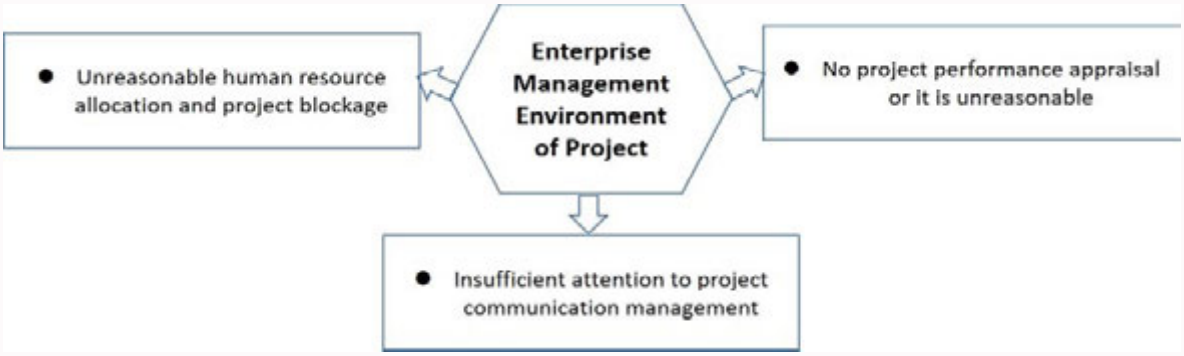

Figure 3: The main problems in the project enterprise management environment.

clinical trials approval), which is the central content of R&D project management. 'Work Breakdown Structure (WBS)', 'Gantt chart' and 'PM software for monitoring schedule' can be used to establish the overall study plan [15]. The main objectives of the overall study plan are to set clear project objectives and directions, allocate resources, anticipate problems and risks, and identify countermeasure. The overall study plan mainly includes task and responsibility decomposition, time schedule plan, task relationship network plan, also includes deliverables, milestone events, etc. [8]. The overall study plan should make the research content coherent and clear, scientific and feasible, with a clear division of labor, and the responsibility of each task should to be the only person.

Execution management and planning changes: Project managers need to follow up on project progress in real time and collect deliverables to ensure that the actual progress is basically consistent with the plan. When reaching the project milestone node, the project leader shall organize the project node meeting to determine the detailed next project plan. If it is inconsistent with the overall study plan, the change of the plan shall be implemented.

The change shall consider its impact and submit the change application. According to the impact of the changes, the changes can be divided into some generations, such as general and major levels. The level of the change approver should also be determined according to the level of the change. The overall study plan needs to be revised and published in real time. New biological products R&D project is a large-scale project coordinated by many departments. Even if only some changes that seem not important are not reported in time, it can easily lead to a serious delay of the overall project.

Project abort and closure: At the end of the project, all important project information should be sorted out, including project deliverables, experience summary, project personnel evaluation, project conclusion report, etc. [8]. At the same time, the success rate of new biological products R&D projects is limited, and most projects are not completed as planned [16]. However, the accumulation of project experience and technical results is still significant for project management, so such projects require at least submitting existing project deliverables and experience summary during project suspension.

The overview of the main problems in the project process management procedure is shown in Figure 2.

Analysis of the main problems in the project enterprise management environment

Unreasonable human resource allocation and project blockage: If you want to ensure the smooth and efficient progress of the R&D projects, you must have an efficient cooperation team. Firstly, the designation of the project leader has an extremely important impact on the success or failure of the overall project. A project without a clear project leader, or with multiple project leaders, will lead to individual problems that are unfound or have no management, affecting the overall progress and quality of the project. Secondly, the task leader is directly responsible for the planning and execution management of the task, and the department head should cooperate with him to establish a matching task team and provide manpower and technical support for him. If all the tasks of all the projects are directly in the charge of each department leader, in the case of multiple projects in parallel, it will inevitably lead to slow project progress feedback, slow project problems discovery, project leader management difficulties and other problems. In serious cases, project blockage may occur.

New biological products R&D is a long-term and multi-stage project, as shown in Figure 1. In order to avoid project blockage, new biological products R&D enterprises need to evaluate the speed limit task of each R&D stage according to their own situation, and evaluate the flux of the speed limit task [17]. If the flux is 5 projects, it is appropriate to keep the projects to be 4 to 6 at this stage as far as possible. Personnel from other project stages can be allocated for up to 5 projects to avoid the waste of human resources. In addition, if multiple R&D projects are opened at the same time (>5), the same research tasks at the same stage in the key R&D path cannot be carried out at the fastest speed. Therefore, multiple projects need to enter the same R&D task at appropriate intervals and avoid opening multiple projects at the same R&D stage.

Insufficient attention to project communication management: Project communication management consists of four parts: Communication planning, information release, performance report and management closing [8]. Managing the project communication well is a crucial part of improving the project success rate [18,19]. According to statistics, more than 70% of the failed projects are not because of the plan not detailed or under inadequate control, but because of some resources of the project cannot be timely and adequately utilized, which is directly related to adverse communication.

A relatively complete communication management plan should clarify the communication needs of the stakeholders, the way of releasing the required information, the time limit and frequency, the scope of personnel to release and receive the information, the reporting time limit and path of the performance report, the list of deliverables, the meeting plan, etc. [8]. Many new biological products R&D

enterprises do not have a complete and clear project communication management plan, and the release of project information is relatively random, which are in a very chaotic communication environment. Some small-sized new biological products R&D enterprises' project leaders can also hold their fewer projects by relying on their previous project communication experience and personal influence without complete communication management plan. However, this method depends on individual ability and influence, belongs to the "rule of man", does not have institutional constraints, and is not suitable for multi-project and systematic project management.

No project performance appraisal or it is unreasonable: Project performance appraisal is the constraint for project leader to urge project members to complete project tasks in accordance with norms, on time and with good quality. If no project performance appraisal or performance appraisal is unreasonable, project leader need to completely rely on personal influence to manage [20,21]. However, new biological products R&D project belong to multiple departments completed project, the person who has such personal influence and can manage R&D project is at least R&D director, which is obviously not suitable for multiple project management. In addition, if the R&D enterprise is in a state of no performance appraisal or unreasonable performance appraisal methods for a long time, the excellent R&D talents cannot be effectively affirmed and promoted. And that will inevitably lead to the loss of excellent talents, which is not conducive to the benign operation of the project and the development of the enterprise.

The overview of the main problems in the project enterprise management environment is shown in Figure 3.

Artificial Intelligence - An Essential Tool to Establish New Biological Products R&D Project Management System

Artificial Intelligence (AI) technology have been predicted to highly impact present and future new biological products R&D project management [22]. According to the actual project management requirements, based on the basis of AI technology, intelligent project management software system is developed to fit the needs of biological products R&D project management. The software system leads project planning and executes of global control by WBS architecture, and follow up the project progress, cost, resources, performance, risk, etc. effectively with the advanced theory of "dynamic management, real-time sharing", solve the project delay or failure questions lead by information lag in project management process. Then it can greatly improve the enterprise R&D project control ability. The software system can also be named biological products R&D project management system. With this system, most of the problems in project process management and in project enterprise management environment can be easily solved. Gartner recently postulated that 80% of the work of today's project managers may be eliminated by 2030 as AI take on traditional PM functions [23].

Discussion

The rise and development of new biological products in China is about ten years. Therefore, compared with developed countries, our current lack of management experience and our management quality is lower. In this paper, the author introduced the general R&D process of new biological products, and fully analyzed the main problems of R&D project management in China. It is proposed that the biomedical enterprises should not only solve the problems of project process management such as project initiation, planning, execution and changes, abort and closure, but also solve the problems in project enterprise management environment such as human resource allocation, project communication management and performance appraisal. It is suggested that on the basis of fully analyzing the overall R&D process, segmented project management is implemented to establish a scientific and effective biological product R&D project management system based on "systematic management". With the rapid development of China's biomedical industry, the enterprises that can survive and develop in the competition must be the enterprises with a scientific and effective new biological products R&D project management system, such as an Artificial Intelligence (AI) project management system [22].

Although a large part of domestic small and medium-sized enterprise decision makers have realized the importance of R&D project management, but because of the fear of its early establishment will lead to larger organizational structure changes, affect personnel stability, and lead to short-term R&D efficiency decreasing, they still struggle to make up their minds to change. They hope one or several of the new biological products can bring stable income, then with the economic backing to establish R&D project management system. On the whole, it's also needs long-term's exploration and optimization on how to establish a professional technology-oriented, systematic new biological product R&D project management system with clear structure, to help enterprises to better complete new biological product R&D, and then achieve enterprise strategic goals. When and how much cost to establish a scientific and standardized R&D project management system and complete the upgrade of enterprise management, is the biomedical enterprise decision makers need to weigh. "Transformation" is painful, but also imperative.

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References

1. Li H. The major achievements of biological products in China. Chin Med J (Engl). 2000;113(10):942-7.
2. Sword refers to the 10 trillion Yuan market, China's pharmaceutical industry set sail. Strategic Emerging Industry Insight. August 06, 2021.
3. Development report of China's biomedical industry in 2020 (simple version).
4. Scheinberg MA, Felix PAO, Kos IA, Andrade MA, Azevedo VF. Partnership for productive development of biosimilar products: Perspectives of access to biological products in the Brazilian market. Einstein (Sao Paulo). 2018;16(3):eRW4175.
5. Li H, Wu Z, Hui X, Hu Y. Impact of local health insurance schemes on primary care management and control of hypertension: A cross-sectional study in Shenzhen, China. BMJ Open. 2019;9(10):e031098.
6. Brown DG, Wobst HJ, Kapoor A, Kenna LA, Southall N. Clinical development times for innovative drugs. Nat Rev Drug Discov. 2022;21:793-4.
7. Hwang TJ, Darrow JJ, Kesselheim AS. The FDA's expedited programs and clinical development times for novel therapeutics, 2012-2016. JAMA. 2017;318(21):2137-8.
8. PMI. A Guide to the Project Management Body of Knowledge (PMBoK Guide) (6th Ed.). Newtown Square, Pennsylvania: Project Management Institute; 2017.
9. IQVIA Institute. 2019 R&D Achievements- New product launches, clinical

trial activity, and investments. 2020.

10. Singh G, Dahlin JL, Walters MA. Risk management in early discovery medicinal chemistry. Methods Enzymol. 2018;610:1-25.

11. CDE. Annual report of clinic trail progress of new drug registration in China. 2021;2021.

12. Tencent. Summary of 13 kinds of PD-(L)1 approved in China. April 25, 2022.

13. Xin Yu J, Hodge JP, Oliva C, Neftelinov ST, Hubbard-Lucey VM, Tang J. Trends in clinical development for PD-1/PD-L1 inhibitors. Nat Rev Drug Discov. 2020;19(3):163-4.

14. Pandey M. Investment decisions in pharmaceutical R&D projects. Drug Discov Today. 2003;8(21):968-71.

15. Fernandes G, O'Sullivan D. Project management practices in major university-industry R&D collaboration programs - A case study. J Technol Transf. 2022;48(1):361-91.

16. Jung YL, Yoo HS, Hwang J. Artificial intelligence-based decision support model for new drug development planning. Expert Syst Appl. 2022;198:116825.

17. Liu M, Shan M, Wu J. Multiple R&D projects scheduling optimization with improved particle swarm algorithm. Sci World J. 2014;2014:652135.

18. Bagnol B, Clarke E, Li M, Maulaga W, Lumbwe H, McConchie R, et al. Transdisciplinary project communication and knowledge sharing experiences in Tanzania and Zambia through a one health lens. Front Public Health. 2016;4:10.

19. Liang J, Warren J, Orr M, Day K. Junior doctor communication systems and the deterioration communication management theory. Stud Health Technol Inform. 2019;263:122-33.

20. Kaye BL. Performance appraisal and career development: A shotgun marriage. Personnel. 1984;61(2):57-66.

21. Metcalf C. The importance of performance appraisal and staff development: A graduating nurse's perspective. Int J Nurs Pract. 2001;7(1):54-6.

22. Schuhmacher A, Gassmann O, Hinder M, Kuss M. The present and future of project management in pharmaceutical R&D. Drug Discov Today. 2021;26(1):1-4.

23. Costello K, Gartner says 80 percent of today's project management tasks will be eliminated by 2030 as artificial intelligence takes over. March 20, 2019.