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Quality Management and Control Strategies in the Development Stage of Biologic Drugs

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Abstract: Although the development of biological drugs brings new hope to human health, it also presents certain challenges, requiring strengthened quality management and control. Key aspects during the research and development phase include: controlling raw materials and equipment; ensuring proper sample management and analysis; safeguarding data recording and security. Control strategies involve establishing a comprehensive quality management system, conducting risk assessment and response, utilizing technical tools, and enhancing personnel training and communication. These elements are critical stages and strategies for ensuring the safety, efficacy, and quality controllability in the development of biological drugs, ultimately providing patients with high-quality medications.

Keywords: Biologics; R&D Stage; Quality Management Control

Introduction

In the field of modern medicine, biopharmaceuticals have become a focal point of the pharmaceutical industry due to their unique therapeutic effects and broad application prospects. The research and development of biopharmaceuticals is a complex and high-risk process that involves multidisciplinary knowledge and advanced technologies. Moreover, the quality of biopharmaceutical development directly impacts drug safety, efficacy, and quality controllability, playing a crucial role in patient health and life safety. However, current biopharmaceutical development faces numerous challenges, such as target specificity and production processes. Therefore, an in-depth exploration of quality management and control strategies during the development phase of

biopharmaceuticals is of great practical significance for improving development quality and advancing the biopharmaceutical industry.

1. Overview of Biopharmaceutical R&D

Biopharmaceuticals are a crucial component of modern medicine, bringing new hope to human health with their unique advantages and immense potential. They primarily include therapeutic antibodies, vaccines, and recombinant protein drugs. Derived from biological materials such as microorganisms, humans, animals, plants, and marine organisms, or synthesized to mimic their natural counterparts through advancements in biology, medicine, and related technologies, these products serve as preventive, therapeutic, or diagnostic medical agents. Compared to traditional chemical



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drugs, biopharmaceuticals offer higher efficacy and specificity, enabling better targeted therapy, reducing side effects, and improving patients' quality of life. The research and development process of biopharmaceuticals is complex and lengthy, typically involving stages such as target discovery, molecular design, screening and optimization, preclinical studies, clinical trials, and post-marketing surveillance^[1]. Target discovery involves using bioinformatics and high-throughput screening to identify biological targets that may exert therapeutic effects; molecular design then constructs biopharmaceuticals with favorable bioactivity and safety based on the target and drug design principles. The development of biopharmaceuticals holds significant value in advancing the pharmaceutical industry, meeting clinical needs, and improving national healthcare standards. However, it also faces numerous challenges, such as insufficient target specificity, difficulties in quality control, and the need to optimize production processes. Therefore, quality management and control in biopharmaceutical development must be strengthened to ensure safety, efficacy, and quality consistency, thereby providing patients with superior medications.

2. Key Quality Management and Control Aspects in the Research and Development Phase of Biologics

2.1 Raw Material Quality Control

The quality of raw materials influences the success or failure of biopharmaceutical research and development, and strict control over raw material quality is key to quality management during the development phase of biologics. (1) Select reliable suppliers: Conduct comprehensive assessments of suppliers' qualifications, production capabilities, and quality control systems, choosing reputable suppliers with standardized production practices to ensure raw material quality at the source. (2) Establish procurement standards and procedures: Define strict requirements and specific procurement standards for raw materials, clarifying quality specifications, standards, and quantities to ensure that all procured materials meet the needs of the research. (3) Strengthen inspection and testing: Perform rigorous inspection and testing of procured raw materials, including appearance, purity, and activity indicators, to ensure

their quality meets required standards. (4) Manage storage appropriately: Set different storage conditions, such as temperature, humidity, and light exposure, based on the characteristics of each raw material to prevent deterioration or damage. (5) Establish a traceability system: Build a comprehensive raw material traceability system to record information on procurement, inspection, and usage, enabling timely tracing and resolution when issues arise.

2.2 R&D Environment and Equipment Management

R&D environment and equipment management serve as a critical pillar for quality control in the biopharmaceutical R&D phase, providing stable and reliable conditions for research work. (1) Environmental cleaning and maintenance: Conduct thorough cleaning and disinfection of R&D laboratories to control levels of contaminants such as dust and microorganisms, ensuring the environment meets the requirements for biopharmaceutical R&D. (2) Temperature and humidity regulation: Install monitoring and regulation equipment to precisely control indoor temperature and humidity based on the needs of different R&D stages, preventing fluctuations from affecting experimental results. (3) Regular equipment calibration: Perform calibration and debugging of R&D equipment at specified intervals to ensure accuracy and stability, such as balances and microscopes. (4) Equipment maintenance: Establish a comprehensive equipment maintenance plan, including daily inspections, cleaning, and upkeep, to promptly identify and resolve equipment malfunctions. (5) Operating procedure training: Provide R&D personnel with training on proper equipment operation procedures, enabling them to master correct methods and avoid issues such as equipment damage or compromised experimental data due to improper use.

2.3 Sample Management and Analysis

The development of biopharmaceuticals is characterized by complex processes, susceptibility of sample activity to degradation, and significant batch variability. Effective lifecycle management and precise analysis of samples are critical for controlling research quality and preventing experimental deviations. Sample management runs throughout the entire process, from small-scale trials and pilot production to process optimization. During development, raw drug substances, intermediates, finished products,

and stability study samples should be stored in separate zones according to type, with warehouse temperature, humidity, and light exposure conditions controlled based on the activity requirements of the biological preparation to avoid sample loss caused by environmental fluctuations. Meanwhile, a unique coding traceability system should be established to record sample collection times, preparation processes, transfer points, and personnel involved, ensuring that each sample is clearly identifiable ^[2]. Before conducting various tests, multiple detection methods must be applied strictly in accordance with pharmacopoeia standards and R&D SOP documents, covering physicochemical indicators, biological activity, and impurity content, to minimize the risk of non-compliant results from single-method testing. All original test data must be archived in real time, with any arbitrary tampering or supplementation of original data strictly prohibited. Non-compliant samples must be sealed, marked, and uniformly destroyed according to regulations. Through systematic sample management and analysis, the interference of sample errors can be effectively eliminated, ensuring the authenticity and reliability of biopharmaceutical R&D experiments and providing accurate data support for subsequent process optimization and clinical trial advancement.

2.4 Data Recording and Security

Experimental data from biopharmaceutical R&D serves as a critical basis for process validation, quality assessment, and regulatory submission. The authenticity, integrity, and confidentiality of this data directly impact the validity of final R&D outcomes and are essential components for establishing and implementing R&D quality management. Throughout the entire R&D process, strict real-time recording measures for original data must be adhered to. Whether operators view, modify, or subsequently supplement, alter, or delete experimental data, paper-based records must maintain consistent content, with all operational traces preserved to meet pharmaceutical R&D data traceability verification requirements ^[3]. For electronic R&D data, reasonable hierarchical access control measures should be implemented, clearly defining the usage permissions of relevant tools for experimenters, reviewers, and managers, while preventing unauthorized individuals from casually browsing, copying, or modifying the primary R&D

data. Additionally, regular database backups and virus prevention measures should be conducted to avoid data loss or leakage due to system failures or cyberattacks. Furthermore, a dual-review system should be established, with designated personnel responsible for cross-checking original experimental data and analysis reports to promptly identify data entry errors.

3. Analysis of Quality Management Control Strategies in the Research and Development Stage of Biologics

3.1 System Construction and Improvement

Establishing and improving a quality management system is one of the key approaches to effectively controlling quality during the research and development (R&D) phase of biologics. For R&D work, it can provide a solid institutional guarantee. (1) Define Standards: Based on relevant international and domestic regulations, guidelines, and specific circumstances, develop comprehensive, detailed, and easy-to-operate quality standards tailored to the characteristics of biologics R&D, covering every aspect of the R&D process. (2) Optimize Processes: Streamline the R&D workflow, eliminate redundant steps, and clearly identify the quality control points and responsible personnel for each step, ensuring efficiency and smoothness. (3) Strengthen the Document Management System: Establish an appropriate document management system to classify, number, store, and update documents generated during production and usage, enabling consistent tracking of relevant documents throughout R&D work, ensuring that required information is reliably guaranteed, with good completeness and traceability. (4) Conduct Training: Actively organize training for employees on quality management knowledge and skills, enhance quality awareness, and familiarize them with the requirements and operational methods of the quality management system. (5) Continuous Improvement: Regularly evaluate and audit the quality management system, and based on the evaluation results, make timely adjustments and improvements to adapt to changes and developments in R&D work.

3.2 Risk Assessment and Response

The lengthy process of biopharmaceutical development, high sensitivity of biological raw materials, and complex process variables result in multiple uncontrollable

quality risks throughout the entire process. Timely assessment and handling of various quality risks, along with the implementation of preventive measures, are crucial for mitigating hidden hazards and reducing the failure rate of research and development. Based on standard operating procedures for cell culture, protein purification, and formulation preparation, combined with failure mode and effects analysis tools, potential risks related to personnel operations, equipment operation, environmental cleanliness, and raw material purity are fully identified and classified according to the probability of occurrence and severity of impact. For areas with relatively higher risk levels, corresponding preventive designs should be implemented—for example, enhancing real-time sterile monitoring and establishing relevant commonly used culture environments to address microbial contamination risks in cell culture^[4]. For common, lower-level risks, periodic inspection mechanisms should be employed to further monitor risk dynamics and drive continuous improvement. A risk review ledger should be established to record risk triggers, treatment measures, and corrective effects. By implementing pre-judgment, in-process control, and post-review throughout the entire risk management process, a dynamic closed-loop quality risk control system for biopharmaceutical development can be achieved, reducing the occurrence of issues such as process deviations and product non-compliance at the source, thereby enhancing the overall stability, orderliness, and rigor of biopharmaceutical R&D.

3.3 Use of Technical Tools

The rational use of technical tools is an important means to enhance quality management and control during the development of biologics, which effectively improves R&D efficiency and quality. (1) Data analysis software: Specialized data analysis software enables in-depth mining and analysis of R&D data. For example, statistical process control software can monitor quality fluctuations in the production process and promptly identify potential issues. (2) Simulation and modeling tools: Computer-based simulation and modeling tools can simulate the R&D process and mechanisms of action of biologics, predict drug performance, and optimize development plans. (3) Automated equipment: Introducing automated laboratory equipment standardizes and normalizes experimental

operations, reduces human errors, and improves the accuracy and reproducibility of experimental results. (4) Quality traceability system: Establishing a quality traceability system using technologies such as barcodes and QR codes to label and track raw materials, intermediate products, and finished products ensures the traceability of product quality. (5) Electronic document management system: Utilizing an electronic document management system to centrally manage R&D documents facilitates the storage, retrieval, and sharing of documents, thereby improving document management efficiency.

3.4 Personnel Training and Communication

R&D personnel are the direct executors of quality control in biopharmaceuticals. Therefore, insufficient professional competence and poor communication between roles can easily lead to a series of human-induced quality risks, such as operational errors, process disconnections, and substandard implementation of protocols. Improving regular personnel training mechanisms and cross-departmental communication channels is essential to implementing quality control throughout the entire process^[5]. Pharmaceutical companies need to conduct targeted training tailored to different R&D responsibilities, stratified by level and focus. For experimental operators, training should emphasize aseptic techniques, standard equipment usage procedures, and quality compliance. For management personnel, the focus should be on process quality control points, risk assessment capabilities, and compliance document management. Regular assessments, case-based teaching, and reviews should be organized, incorporating past quality error cases in R&D to strengthen quality awareness across the board, preventing non-standard actions based solely on experience. Additionally, regular communication channels between R&D, quality control, and analytical departments should be established, along with routine cross-departmental meetings to share progress on R&D and quality issues, promptly addressing conflicts in process coordination, sample submission, and data review.

Conclusion

In the future, quality management and control in the research and development phase of biopharmaceuticals will face more opportunities and challenges. With the rapid advancement of technology, new techniques and

methods will continue to emerge, providing powerful tools and means for quality management and control. At the same time, the quality management system will become more comprehensive, ensuring accurate control from research and development to production. Risk assessment and response will also become increasingly intelligent and efficient, enabling early identification and mitigation of potential risks. The use of relevant technological tools will become more extensive and in-depth, improving both research efficiency and quality. Personnel training and communication will place greater emphasis on personalization and specialization, enhancing the overall competence of the team. Through continuous improvement and innovation, the quality of biopharmaceutical research and development will be greatly enhanced, making greater contributions to human health.

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