Article @ Virology

Standardized Management on Quality Control Equipment of Viral Vaccines Industry in China

Guanjie Wang, Jiashu Zhang, Mai Peng, Bo Liu，Jingli Li

National Institutes for Food and Drug Control, Beijing, 100050, P.R. China

ABSTRACT

Aiming at the equipment used for quality control in the viral vaccine industry, this article sorts out the requirements for equipment management from three aspects: laws and regulations, industry quality management specifications and pharmacopoeia regulations. According to the characteristics of the vaccine industry and the principles and uses of commonly used equipment, the instruments and equipment used for quality control are divided into five categories, and the management characteristics of these categories are explained. It is recommended to refer to the United States Pharmacopoeia and the characteristics of my country's vaccine industry to adopt a 4Q management model for the management of quality evaluation equipment, that is, equipment design qualification (DQ), installation qualification (IQ), operation qualification (OQ), and performance qualification (PQ). Standardized management of equipment is an important guarantee for the accuracy and traceability of quality control of viral products.

Article History: Submitted: 28/09/2017; Revised: 19/11/2017; Accepted: 04/12/2017

DOI:10.21092/jav.v6i4.92

Key Words: Viral vaccines, Equipment, Quality control, Management,Standardization

Introduction

Humans have been fighting against viruses since ancient times. The spread of viral diseases such as smallpox and measles has caused large-scale human deaths. The use of viral vaccines had effectively prevented and controlled the occurrence and prevalence of viral diseases.The discovery of immunization has been a singular improvement in the health of

Corresponding author, Wang GJ , E-mail:wanggj@nifdc.org.cn

Tel.: +86-10-53852042

mankind. Viral vaccines containing infectious agents can be developed by classical techniques (attenuation by repeated passage in cultured cells) or by genetic engineering[1].

As of the end of 2018, there were nearly 100 licensed manufacturers of viral vaccines in China. Vaccines, as a special class of drugs, are different from traditional chemical drugs and have the characteristics of complex molecular structure, diverse biological activities and physical and chemical properties. How to safely and effectively evaluate the quality of vaccine products is a hot issue of public concern [2]. The formulation, revision, and implementa--tion of the "Drug Administration Law of the People's Republic of China" (hereinafter referred to as the "Drug Administration Law") [3] have made "strict supervision to ensure quality" a prominent feature of the industry. Equipment management is the premise and foundation of quality evaluation work, and it is also an effective tool to ensure the quality of virus vaccine products throughout the life cycle.

This article takes the common equipment for quality evaluation in the viral vaccine industry as a starting point, comprehensively summarizes the equipment management needs, and discusses the standardized management of equipment for quality evaluation in this industry.

Legal documents and requirements related to equipment management in the viral vaccine product industry

1.Main legal documents

There are three main legal documents involved in vaccine product industry equipment. The main legal basis for equipment purchase is the "Procurement Management Law of the People's Republic of China" [4], which requires that the purchase intention of equipment be actively disclosed before the purchase to ensure the openness and transparency of the procurement process. The main legal basis for equipment traceability is the "Measurement Law of the People's Republic of China" [5]. At present, the quality control of the vaccine product industry mainly completes the traceability of instruments through calibration and verification. The "Drug Administration Law of the People's Republic of China" emphasizes the configuration of quality control laboratory testing equipment

In terms of equipment safety management, the "Special Equipment Management Law of the People's Republic of China" [6] is the legal basis for the safe use of autoclaved equipment in laboratories to ensure the safe use of such equipment.

2.Quality management practices

Vaccine products are a special class of drugs, and the quality system in the field of R&D, production, and circulation must follow the "Quality Management Practices

for Non-clinical Research of Drugs" [7], "Quality Management Practices for Pharmaceutical Manufacturing" [8], "Preparation Preparations in Medical Institutions" Quality Management Standards" [9] to carry out work. The requirements for equipment management are stipulated in the above three management specification documents, and the specific requirements are shown in Table 1.

It can be seen from the table 1 that the requirements for equipment management in the R&D and production of viral vaccines involve four aspects: equipment configuration, verification, recording, and maintenance.

Table 1: Contents involving equipment management in drug quality management practices

Practices Name	Article Number and main contents
Quality Management Practices for Non-clinical Research of Drugs	Chapter 5, Article 15,16 and17. The performance of the equipment should meet the requirements and be verified regularly; the records should be detailed and archived regularly.
Good Manufacturing Practice of Medical Products	Chapter 5, Article 1-5. Principles of equipment, design and installation, maintenance and repair, use and cleaning, calibration.
Preparation Preparations in Medical Institutions" Quality Management Standards	Chapter 4, Article 26-31,49,59,61. Mainly involves configuration, cleaning, calibration, repair and maintenance, and records.

3. Pharmacopoeia

Pharmacopoeia is the main basis for carrying out quality supervision. At present, the equipment used in the detection method in the fourth general rule of "Chinese Pharmacopoeia" stipulates special verifica--tion indicators such as gas phase and liquid phase, and requires that "the measuring instruments used in the test all meet the requirements of the national standard. Regulations of the Technical Supervision Department"[10]. In terms of equipment management, the "United States Pharmacopoeia" clearly puts forward the 4Q management concept of equipment design confirmation, installation confirmation, operation confirmation and performance confirmation [11]; "European Pharmacopoeia" stipulates the technical indicators of drug testing equipment in Article 2.1 [12] .

Classified management of vaccine quality control equipment

According to the characteristics of the biological product industry and the principles and uses of common equipment, the quality control equipment of the biological product industry can be divided into 5 categories, see Table 2.

The management of biosafety equip--ment must first meet the configuration needs of bio-safety laboratories. For example, bio-safety cabinets need to choose type A or type B according to the design structure of airflow and isolation barriers; regular inspection and maintenance are required in daily work. It's the essentials of device management [13]. Autoclave equipment mainly focuses on sterilization verification and the verification of the entire equipment. The autoclave also needs to meet the management of special equipment in China, such as personnel special equipment operation certificates and safety management personnel certificates, and the safety indicators of the equipment. Condition detection and daily maintenance.

Cold chain management is a notable feature of the biologics industry. In the quality control of biological products, the storage of samples has very clear temperature and humidity requirements, so the regular verification of temperature and humidity equipment is the management point of such equipment, such as the temperature and humidity monitoring of refrigerators and cold storage where vaccines are placed, and the temperature and humidity monitoring probes. Calibration, distribution of temperature throughout the chamber, etc.

Microplate readers in physical and chemical equipment are widely and frequently used in vaccine quality testing. This type of equipment is mainly used for quantitative analysis of some antigens and residual components based on immune binding, such as the detection of bovine serum albumin residues [14], etc. . In addition to regular training for operators, such equipment requires regular maintenan--ce and regular calibration.

Explore on the management mode of vaccine quality control equipment

Quality control equipment management generally considers processes in China such as procurement, acceptance, daily applica--tion, calibration/verification, and asset scrapping. The United States Pharmacopoeia proposed for the first time that the equipment management mode should adopt the 4Q management mode, that is, equipment design confirmation (DQ), installation confirmation (IQ), Operation Qualification (OQ), Performance Qualification (PQ) [15]. It is more suitable for "qualification" in drug

testing institutions. There are differences and connections between the two. Verification focuses more on the method to determine whether the method is compliant; confirmation emphasizes whether the equipment meets the experimental requirements, which are more specific. Regardless of the management model, in fact, the process of equipment purchase, acceptance, calibration/verification, and recording is emphasized in the equipment management process.

The purchase of equipment belongs to the design confirmation in the 4Q management mode. This process emphasizes that the equipment purchase requirements must meet the experimental requirements, and especially emphasizes that the equipment purchase parameters must at least meet the experimental parameter requirements. There are mainly two reference standards for the purchase of quality control laboratory equipment in the biological product industry. Commonly used testing equipment for quality control in the product industry [16].

Table 2: Classification of quality control laboratory equipment in the vaccine product industry

Classification	Representative equipment	Main Function
Biosafety equipment	Biological safety cabinets, clean benches, fume hoods, etc.	Ensuring biosecurity, ensuring the safety of personnel, samples, and more.
Autoclave equipment	Autoclave, fumigation sterilizer, hydrogen peroxide sterilizer, etc.	According to sterilization requirements, test samples, auxiliary utensils, solution culture medium, etc. can be sterilized.
Temperature and humidity equipment	Carbon dioxide incubator, biochemical incubator, refrigerator, ultra-low temperature refrigerator, etc.	Used for cell culture and reproduction; storage or pretreatment of vaccine products and auxiliary reagents.
Physical and chemical equipment	pH meter, microplate reader, UV-visible spectrophotometer, etc.	Qualitative or quantitative analysis of physical and chemical items in vaccine quality testing, such as antigen content.
Medical equipment	Nucleic acid extractor, nucleic acid hybridization instrument, etc.	Quantitative analysis of residual DNA in vaccine quality control.

Installation confirmation mainly refers to whether the installation conditions of the equipment meet the requirements, such as the installation environment directly affects the use of the equipment. Operation confirmation mainly refers to whether the technical indicators meet the procurement requirements during equipment acceptance. In 4Q management, this management is very important and directly affects subsequent use. The technical indicators of operation confirmation basically cover all performance indicators of the equipment.

Performance confirmation refers to whether the technical indicators of the instrument are suitable for the intended use, which is widely used in daily work, such as regular instrument calibration/verification, period check, and irregular verification, etc., all belong to a kind of performance confirmation way. In the performance confirmation, it is necessary to ensure the planning of the work, whether the parameters that have been confirmed by the performance are complete, and whether they meet the experimental requirements. For example, the temperature range of the refrigerator where the sample is placed is (2-8) °C, the daily setting temperature point is 5 °C, the calibration temperature point is 5 °C, and the absolute value of temperature uniformity and fluctuation should be less than 3 °C

In conclusion, Equipment management is an important part of the quality control of biological products, and plays a fundamental role in determining the accuracy and traceability of test results. How to do a good job in scientific and standardized equipment management in the biological product industry is also the direction of further discussion.

Competing interests

The authors declare all financial and non-financial competing interests.

Reference

[1]. Susan Payne.Viral Vaccines,in Viruses[M]. Academic Press, 2017, Pages 73-79.

[2]. WANG J Z. Overview of biopharmaceuticals regulatory science development in China [J]. Chin J New Drugs,2018,27(21):2465-2471.

[3]. Drug administration of the people′s Republic of China. National People′s Congress Standing Committee，issued 2015-04-24.

[4]. Government Procurement Law of the People's Republic of China. National People′s Congress Standing Committee，issued 2002-06-29.

[5]. People's Republic of China Metrology Law. National People′s Congress Standing Committee，issued 2002-06-29.

[6]. Special Equipment Safety Law of the People's Republic of China. National People′s Congress Standing Committee，issued 2013-06-29.

[7]. Quality Management Practice for Nonclinical Drug Research. State Food and Drug Administration，issued 2017-07-27.

[8]. Good Manufacturing Practice of Medical Products. State Drug Administration，issued 2010-10-19.（in Chinese）

[9]. Quality Management Practice for Pharmaceutical Preparations in Medical Institutions. State Food and Drug Administration，issued 2000-12-05.

[10]. Pharmacopoeia of the People's Republic of China. China Pharmaceutical Science and Technology Press，issued 2015

[11]. US Pharmacopeia. General Chapters: <1058> Analytical Instrument Qualification.32nd ed. Rockville, MD: United States Pharmacopeial Convention; 2009.

[12]. Monograph T. European pharmacopoeia[J]. European Directorate for the Quality of Medicine & Health Care of the Council of Europe (EDQM), edn, 2017.

[13]. Wang G, TIAN L, XIANC X. Equipment management experience in the WHO prequalification[J]. CHINA MEDICAL HERALD, 2013,10(2):156-157.

[14]. Zhang K, Song C, Li Q, et al. The establishment of a highly sensitive ELISA for detecting bovine serum albumin (BSA) based on a specific pair of monoclonal antibodies (mAb) and its application in vaccine quality control[J]. Human Vaccines, 2010, 6(8): 652-658.

[15]. Xiang X, Huang H, Zuo N. Establishment of a New Equipment Quality Management System with Performance Management as the Core. CHINA MEASUREMENT & TEST, 2014, 28(7):721-725.