

Considerations on Regulatory Quality Control in Pharmaceutical Industry

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ABSTRACT

With the development of pharmaceutical fields, the quality control of the pharmaceutical industry gets more and more attention. The aims of pharmaceutical industry are manufacturing high quality medicines, identifying the safety of products and assessing the efficacy of medicines. Pharmaceutical industry has to achieve the manufacturing standard which is regulated by the authorities. The industry or company requires to adhere the medicines principles such as Pharmacopoeia, Good manufacturing practice (GMP) or International Council on Harmonisation (ICH) and manufacturing medical products should follow the Standard Operation Procedure (SOP). In order to build a good medical quality supervision system, industry needs to control the monitoring of every step of medicines in production process from many different perspectives. Also, doing the sampling inspection for products to make sure the characterization of medicines could help to achieve the standard. Therefore, this paper will focus on the importance and advantages of regulatory control of medicines, research on the factors that affect the medicines quality in pharmaceutical industry and puts forward some effective ways to improve the quality of manufacturing.

Keywords: *Pharmaceutics, Quality system, GMP, ICH, Pharmacopeia.*

1. INTRODUCTION

There are many different factors that can influence the regulatory control of the products. In order to control the quality level, industry or company could improve quality level from different aspects, such as materials, technology or specialized equipment. The drugs and medicines are used to cure the diseases, prevent the disorders which help humans to get a big step in treatment. The substances inside the medicines will cause the changes in the body of patients and some of them are poison which means they can harm the body of persons. As a result, the control of doses is vital, so that means the quality control of the medicines is important for the whole public health and safety [1].

To be specific, the harm from the drugs or medicines may cause severe adverse reactions, and there are some fake medicines or expired drugs in the market. The government or administration could regulate the medicines by controlling the regulatory quality in pharmaceutical industry [1].

Furthermore, there are many factors that may affect the quality of medicines in pharmaceutical industry. For example, the quality of raw materials, the quality of equipment or human resources may influence the quality system. There is also a whole complete system for production and every step has to be regulated and monitored. Both the materials system, laboratory controls system, facilities and equipment system, production system, packaging and labeling system and the basic part - quality system. Quality system could be the foundation of other five manufacturing systems and all of them are composed of a six-system inspection model [2].

Moreover, there are three main purposes of building quality control system in pharmaceutical industry so as to achieve the optimal quality products standard for patients and consumers, maintain the effective regulatory system and make improvements and good development of medicines system. Finally, completing the good quality should be the main approach for pharmaceutical industry, however, manufacturing technology and equipment should be improved as well. Also, improving the overall quality of employees could help regulation

of products in pharmaceutical industry. Overall, there are some main points show the status situations of pharmaceutical production and give some suggestions of future improvement.

2. DETERMINANTS OF QUALITY CONTROL IN PHARMACEUTICAL INDUSTRY

In low-income countries, poor quality medicines became a big issue among the public health. However, out of standard medicines are not only present in those low-development countries, but also in all different places. To be specific, there is an example of British company which did not follow the manufacturing standard to sell ineffective drugs to consumers and paid for mistakes. From 2001 to 2005, the branch company of GlaxoSmithKline in Boston produced some medicines which are Kytril, Bactroban, Paxil CR and Avandamet and those medicines are claimed as contaminated medicines. The industry of company knowingly selling those contaminated and ineffective products to customers and some of those medicines have no therapeutic effect and did not obey the Food and Drug Administration (FDA) rules. Finally, the company paid 750 million dollars and they had to be responsible for criminal liability [3, 4]. There is another similar event happened in China, a company called Changsheng made substandard rabies vaccines. The Changsheng company used different sizes of fermenters that GMP does not allow to use. After this incident, public security is not guaranteed. If the ineffective rabies vaccine is injected, the harm to the patient is particularly large because once the onset of rabies starts, the death rate is 100%. On the other hand, this case causes lots of public lost the confidence of vaccines and refused to inject the vaccines. The importance of regulatory control in pharmaceutical industry is vital, it not only harms health of public, but also causes the negative social problems [6]. Overall, according to the research, there are more than 106,000 people died each year because of the ineffective and poor-quality medicines [5]. In conclusion, if the public took the counterfeit drugs from pharmaceutical industry, it may cause lots of severe issues. Those medicines may lack therapeutic effect and it could lead to death without correct treatment and likely miss the best treatable stage. It even could bring some worse negative effects, such as poison or adverse reactions, also the credibility of public medical establishment will decrease [8].

According to the resources that appeared above this review, there is a model which contains six components and it called six-system-inspection-model. This model includes six different but connected parts which are materials system, laboratory controls system, facilities and equipment system, production system, packaging and labeling system and the quality system. The whole production process depends on the quality level of those relative systems. Also, there is a big interaction between each of them, they may influence each other.

All of above systems build a whole and complete system for manufacturing process.

2.1 Quality System

First of all, a quality system of a company or an industry should follow the instruction of the authority. Quality system should ensure the observance of the standard such as GMP, Pharmacopoeia and ICH. The main goals of quality system are to provide a maintained and stable system for production, also achieving the better characterization of drugs and improving the development of manufacturing are necessary for the pharmaceutical industry. There are four main elements in the quality system of the pharmaceutical industry: regulatory system of products characterization and quality, corrective action and CAPA system, changing management system and monitoring system of the performance and quality of medicines. Overall, quality system is the basic system for other five systems, and it could be the foundation of them. It connects and links the other five parts to build a whole complete manufacturing operation.

2.2 Material and Equipment System

There are also some factors that may affect the pharmaceutical operations and some of them could be the current issues in pharmaceutical industry. In the process of manufacturing in pharmaceutical industry, material is the key part, it will affect the quality of the whole medicines. It also could be the first part of the whole process, so it decides that if the other systems active well. Some of the pharmaceutical industry did not select a good materials supplier, so that the quality of material will influence next steps. Many companies failed to control the source of the materials or failed to test the poor-quality materials, leads the failure in the manufacturing process. Even it is a long-term-

cooperation-supplier, company required to do sampling inspections regularly because some of suppliers may cut corners to supply low quality [7].

Secondly, the specialized equipment could be another important part in the manufacturing process. Pharmaceutical company have to renew the facilities, enhance the production system and improve the manufacturing quality. It also needs to optimize the manufacturing machine, so that can strengthen the quality of products. However, many companies failed to maintain machines properly, and some medicines may get infected or get contaminated. According to the Good manufacturing practice (GMP), there are 3 main points for pharmaceutical industry to consider. There are Aseptic Manufacturing Facility, Equipment Qualification and Cleaning Validation. Industry has to make sure the cleaning of the material, equipment and place, so that could avoid the contamination of the products. Also, the quantification terms are required such as Installation Qualification (IQ), Operation Qualification (OQ) and Performance Qualification (PQ). What's more, it is necessary to keep equipment clean and maintain the equipment regularly. The position of the equipment, the surface of equipment and prevent contact with some materials and substances. The conditions and environment are important for the operational equipment, for instance, if the room temperature is high, the specialized equipment such as liquid chromatograph would be damaged. Thus, equipment requires a suitable place and environment to run [9]. There are some companies used old and cheap equipment for saving money and hardly renew the machines. In the Changsheng vaccine case that mentioned before, this company used larger size fermenters which are not qualified to produce vaccine and caused a large amount of vaccine lose efficacy [6]. Therefore, maintaining the machines and keeping clean of the laboratory help to improve the quality level of the manufacturing process in pharmaceutical industry.

2.3 Laboratory System

Laboratory system is the one of six parts system. Company should stipulate everything in the laboratory such as sampling, standards, labeling, containers and so on. On one hand, the sampling and testing of the material and other preparation in the laboratory must be prepared. The quality level of those products should achieve the standard of the guideline, such as doing drug stability test,

recording the lab report. On the other hand, some regulations in the laboratory is important as well. For example, the use of lab coats, gloves, goggles and the equipment recording that anytime experimenter have to record after using the lab equipment. There are also have other laboratory rules includes the size of containers, the cleaning times of the equipment. Therefore, a good laboratory system should ensure the correct operation and make sure everything in the laboratory is standard and regular. Also, each step of the manufacturing process in the laboratory should be regulatory [10].

2.4 Production System

In 1906, Food and Drug Administration (FDA) was built in the US and FDA alleged that Good manufacturing practice (GMP) would be the standard for all new drugs for all pharmaceutical industries. Thus, the production system has to follow the GMP guideline completely, otherwise the products would be treated as adulterated drugs. Production system contains many parts of manufacturing production, like dosage form, sampling, testing and validation. The key part of the production and process system is that the quality of the final products. The strength, dosage, quality of the medicines should be tested to provide that the components in the products are safe and pure. The manufacturing process of a drug is very complicated and it has to undergo many procedures such as cultivation, fermentation, purification and analyzation. As a result, experimenters need to avoid the contamination of the products and test many times, then recording the experiments.

2.5 Packaging and Labeling System

In the packaging and labeling system, shipment and storage are very vital parts. The labelling and packaging process go through lots of steps which are records or permission. However, there are some points which need to be considered, the distribution of different medicines during the storage and recalling the substandard drugs. Moreover, labeling is important too, industry should confirm that every medicine has correct labeling. What's more, the packaging and labeling of the medicines should be design as hard to be damaged. The labeling should not be easy to be affected, and they should be important information on it without any missing details. Date of manufacture, expiration date, ingredients and materials and other information should be appeared on the surface.

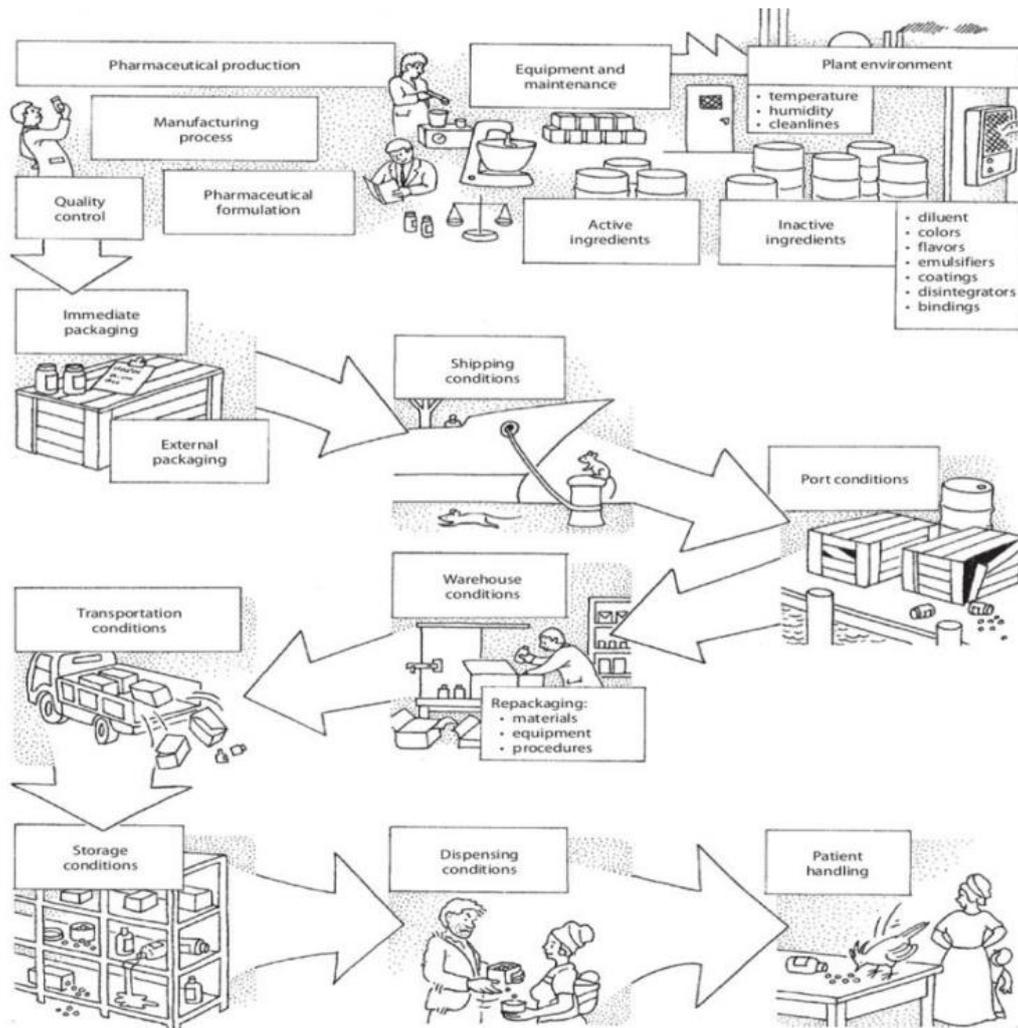


Figure 1 Factors of quality control in the pharmaceutical industry.

The quality control of the pharmaceutical industry is affected by many factors. ("Figure 1") From the conditions in the industry which are materials environment, technology, equipment and so on. Those steps decide the basic quality of the products during process. Then, after the manufacturing process, there are some other determinants many change the quality such as the packaging, shipping and storage. Thus, every step of the whole pharmaceutical operation has to get quality assurance [8].

3. SUGGESTIONS ON MANUFACTURING QUALITY IMPROVEMENT

As a result, the company should complete the whole system and improve the quality control in pharmaceutical products. Also, improving the whole quality of staffs in the company and

improving the production equipment. Finally, improving the production technology level is vital as well.

4. CONCLUSION

In summary, the aims of the quality control system are to make sure that the medicines are safe, effective and have a good standard quality. All the pharmaceutical companies or industries have to follow the regulation from authorities includes the GMP, ICH and other ordinances from the FDA or some others. The final medicine products require the stable characterizations and the effective incidents. However, the quality control process is easy to be influenced by many factors, so that the laboratory tests and sampling inspection are needed. The negative effects from the poor-quality medicines or counterfeit drugs are severe and harmful. Therefore, maintaining the quality level of

pharmaceutical industry is significant and it can be implemented from several aspects. The six-inspection model demonstrates that industry could improve quality level from materials system, laboratory system, facilities and equipment system, production and process system and packaging and labeling system. Each of these systems built a complete manufacturing framework and contributes for the pharmaceutical operation.

AUTHORS' CONTRIBUTIONS

This paper is independently completed by Zihan Xu.

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REFERENCES

- [1] Sanderson, A. Importance of drug regulations. Lfatablepresses.Com; LFA Machines, November 16, 2018. <https://www.lfatablepresses.com/articles/drug-regulations-importance>.
- [2] (N.d.). Fda.Gov. Retrieved September 26, 2021, from <https://www.fda.gov/media/71023/download>
- [3] GlaxoSmithKline to plead guilty & pay \$750 million to resolve criminal and civil liability regarding manufacturing deficiencies at Puerto Rico plant. Justice.Gov. October 26, 2010. <https://www.justice.gov/opa/pr/glaxosmithkline-plead-guilty-pay-750-million-resolve-criminal-and-civil-liability-regarding>.
- [4] Brink, W., & Mollica, M. Poor quality control in the pharmaceutical industry: A report. Brinkzone. Com, January 10, 2019. <https://brinkzone.com/poor-quality-control-in-the-pharmaceutical-industry-a-report/>
- [5] Barbara Starfield, MD, MPH. Medical Errors – A Leading Cause of Death. The Journal of The American Medical Association, 2000: 284:94.
- [6] Liu B, Chen R, Zhao M, et al. Vaccine confidence in China after the Changsheng vaccine incident: a cross-sectional study. BMC Public Health. 2019;19(1):1564. Published 2019 Nov 27. doi:10.1186/s12889-019-7945-0.
- [7] Wheelwright, S. M. (2013, May 22). Recent quality issues in pharmaceutical compliance: Lessons from warning letters. Pharmoutsourcing. Com. <https://www.pharmoutsourcing.com/Featured-Articles/137533-Recent-Quality-Issues-in-Pharmaceutical-Compliance-Lessons-from-Warning-Letters/>
- [8] (N.d.-b). Msh.Org. Retrieved September 26, 2021, from <https://www.msh.org/sites/msh.org/files/mds3-ch19-qualityassurance-mar2012.pdf>
- [9] (N.d.-c). Fda.Gov. Retrieved September 26, 2021, from <https://www.fda.gov/media/92841/download>
- [10] (N.d.-d). Fda.Gov. Retrieved September 26, 2021, from <https://www.fda.gov/media/92835/download>
- [11] Cder, F. / O. (n.d.). The pharmaceutical quality system (PQS). Fda.Gov. Retrieved September 26, 2021, from <https://www.fda.gov/media/92818/download>