European Journal of Pharmaceutical Science and Research

Journal homepage: www. http://mcmed.us/journal/ejpsr

BASIC PRINCIPLES IN THE VALIDATION OF STERILE PRODUCTS

Ankith Kumar Reddy B*, Subhashis Debnath, Niranjan Babu M

Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh- 517 561, India.

Article Info

Received 20/10/2013
Revised 14/11/2013
Accepted 15/11/2013

Key words: Aseptic Technique, End-product Testing, Sterile Products, Equipment, Compounding, Quality assurance, Sterile products, Sterile products, Quality assurance.

ABSTRACT

The focus on developing, implementing and using quality systems during pharmacy preparation of sterile products has never been important than it is today. United States Pharmacopeia (USP) Chapter <1206> ("Sterile Drug Products for Home Use") can be used as the standard for compounding sterile preparations. The focus of this article is to emphasize that the operating standards described in the American Society of Health-System Pharmacists Guidelines on Quality Assurance for Pharmacy-Prepared Products and/or USP Chapter <1206> should be reviewed and followed by responsible pharmacy personnel who prepare sterile products and to identify operating metrics that can be used to design a quality system for the preparation of sterile products in a pharmacy. The authors discuss process simulation testing, development of a dynamic environmental monitoring program, routine cleaning and sanitizing procedures, validation of aseptic technique, validation of compounding equipment and end-product testing. Figures provide information about types of activities validated by process simulation testing, pharmacy cleanroom environmental sampling locations and sample environmental monitoring scheduling. Tables cover baseline alert and action-limit values for pharmacy cleanroom environmental sampling, characteristics of cleaning and sanitizing agents and a sample cleaning plan for controlled work areas. A sample validation plan is also provided.

INTRODUCTION

Generally, five basic steps are necessary to validate any manufacturing process

1. Written documentation
2. Manufacturing parameters
3. Testing parameters
4. In-process controls
5. Final product testing

In sterile product manufacturing, five major steps are involved in approaching the validation of a sterile process. These are outlined below using thermal sterilization as the example process.

1. Select or define the desired attributes of the product. Example: The product will be sterile.
2. Determine specifications for the desired attributes. Example: The product will be sterilized by a sterilization process sufficient to produce a probability of non - sterility of one out of 1 million containers.
3. Select the appropriate processes and equipment. Example: Use microbial kinetic equations to determine the probability of non-sterility. Select cleaning equipment and container component procedures designed and validated to reduce the product bioburden to the lowest practical level. Select an autoclave that can be validated in terms of correct operation of all mechanical controls. Use the appropriate types of thermocouples, thermal sensing devices, biological indicators, integrated chemical indicators, and culture media to conduct the validation tests.
4. Develop and conduct tests that evaluate and monitor the processes, equipment, and personnel.

Examples:

a. Determine microbial load counts prior to container filling.

Corresponding Author

Ankith Kumar Reddy B
Email:- ankithpharmaline0002@gmail.com

b. Determine D and Z values of biological indicator organism.
c. Perform heat distribution studies of empty and loaded autoclave.
d. Perform heat penetration studies of product at various locations in the batch.
5. Examine the test procedures themselves to ensure their accuracy and reliability.
Examples:
a. Accuracy of thermocouples as a function of variances in time and temperature.
b. Repeatability of the autoclave cycle in terms of temperature and F value consistency.
c. A challenge of the sterilization cycle with varying levels of bioindicator organisms.
d. Reliability of cleaning processes to produce consistent low-level product bioburdens. Each validation process should have a documented protocol of the steps to follow and the data to collect during the experimentation. As an example,App. I presents a protocol for the validation of a steam sterilization process. Upon completion of the experimental phase of validation, the data are compiled and evaluated by qualified scientific personnel.

- Once a process has been validated, it must be controlled to assure that the process consistently produces a product within the specifications established by the validation studies, documentation should present original validation records, a schedule of revalidation dates, and data from the revalidation studies. The interval between validation studies strictly depends on the judgment of the validation team based on the experience and history of the consistency of the process.
- There are five basic methods—heat, gas, radiation, light, and filtration. The first four methods destroy microbial life, while filtration removes micro-organisms. Vali-dation approaches and procedures used for most of these methods will be addressed in the remainder of this chapter. Gaseous validation and radiation validation approaches will be focused on ethylene oxide and gamma radiation, respectively. The other gaseous and radiation methods, however, generally will follow the same principles as those discussed for ethylene oxide and gamma radiation. Some extra coverage will be given to vapor phase hydrogen peroxide because of its increased application, particularly in the sterilization of barrier isolators.

REFERENCES

1. Berrebi H. (2001). The bottle-pack system for the pharmaceutical industry. Rommelag AG, Hintere Bahnhofstrasse, 78.
2. Leo F. (1987). Chapter in Aseptic Pharmaceutical Manufacturing - Technology for the Olson and Groves. Interpharm Press.
3. Sharp JR. (1987). Manufacture of sterile pharmaceutical products using 'blow-fill-seal' technology. *Pharmaceutical Journal*, 239, 106.
4. Sharp JR. (1988). Validation of a new form-fill-seal installation, Manufacturing Chemist, 22.
5. Zimmerman L. (1984). Technical measures for aseptic packaging of liquids with the bottle pack-aseptic-system. *Drugs made in Germany*, 41, (2), 56.