

Sterility Assurance of Parenteral Products – Major Deficiency for Recall

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Received date: March 13, 2017; Accepted date: March 17, 2017; Published date: March 24, 2017

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Editorial

Sterility is one of the most important Critical Quality Attribute (CQA) for all parenteral drug products as they are intended to circumvent body's defense mechanisms and rapidly enter blood circulation. When the sterility of such products is compromised, it leads to microbial contamination of the drug product and/ or presence of particles leading to serious adverse events including death.

Lack of sterility assurance is a leading contributor to safety alerts and product recalls by Food and Drug Administration (FDA). Table 1

summarizes the safety alerts to parenteral products and drug manufacturers in 2016 [1]. Lack of sterility assurance can be product specific (probably caused by container closure integrity leakage) or manufacturing site specific (caused by poor facility and engineering or improper manufacturing practices) affecting all the drug products manufactured in the affected site. Such instances lead to major deficiencies during FDA facility inspections sometimes even leading to ceasing of all manufacturing operations until rectified [1-5].

| Drug Product | Manufacturer | Reason for Recall |
|--|--------------------------------|-----------------------------------|
| 5% Dextrose Injection USP in PAB Container | B. Braun Medical Inc. | Leakage and/or Particulate Matter |
| Eye Wash/Eye Irrigating Solutions | United Exchange Corp | Microbial Contamination |
| Eye Saline Eye Wash | Honeywell | Microbial Contamination |
| Lyophilized HCG and Sermorelin | Talon Compounding Pharmacy | Lack of Sterility Assurance |
| Human and Animal Sterile Drug Products | I.V Speciality Ltd | Lack of Sterility Assurance |
| Sterile Drug Products | Cantrell Drug Company | Lack of Sterility Assurance |
| Sterile Drug Products | Medaus Pharmacy | Lack of Sterility Assurance |
| Sterile Drug Products | Pharmakon Pharmaceuticals | Lack of Sterility Assurance |
| Sterile Drug Products | Tri-coast Pharmacy | Lack of Sterility Assurance |
| Sterile Human and Animal Compounded Products | Abbott Compounding Pharmacy | Lack of Sterility Assurance |
| Sterile Compounded Products | Well Care Compounding Pharmacy | Lack of Sterility Assurance |
| Sterile Products | Wells Pharmacy Network | Lack of Sterility Assurance |

Table 1: FDA safety alerts for drugs and biological products with compromised sterility in 2016.

Correction of sterility related deficiencies is usually time consuming and as it involves a team of facility engineers, manufacturing personnel, validation engineers and product development scientists to come together and fix the root cause of the problem. Hence, maintaining sterility of parenteral drug products throughout the product lifecycle and prevention of sterility related deficiencies is of utmost importance. Administrative bodies including FDA [6,7] and International Conference on Harmonization (ICH) [8,9] have developed set of guidance's and reference procedures to be followed for successfully developing and testing a finished product with sterility assurance.

Various methods of sterilization including moist heat sterilization, dry heat sterilization, ethylene oxide sterilization or sterilization by aseptic filtration are available and a mode of sterilization is selected based on product specifications. As a general rule of thumb, terminal

sterilization is the most preferred method of sterilization unless the container/closure system or drug product is not deemed to be suitable for terminal sterilization procedures [10,11].

Sterility of a finished product is assessed by monitoring microbial growth or turbidity as per USP <71> at product release and annually on stability throughout product shelf life [2]. Additionally, Bacterial Endotoxin Test (BET) is evaluated for all parenteral products as per USP <81> to monitor bio burden of the drug product [3]. Furthermore, Container Closure Integrity Testing (CCIT) is also evaluated on all drug products at release and on stability to ensure sterility of the drug products [4,5]. In addition to ensuring product sterility, care has to be taken to ensure appropriate environmental and engineering controls at the manufacturing site to develop a product with acceptable sterility assurance [6].

In conclusion, maintaining sterility of drug products intended for parenteral administration is of utmost importance and current good manufacturing practices to ensure sterility assurance has to be followed throughout product lifecycle.

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