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A Sotera Health company

The Effect of Gamma and Ethylene Oxide Sterilization on a Selection of Active Pharmaceutical Products (APIs) for Ophthalmics

Increasingly stringent product sterility requirements and guidance are being included in global regulatory documents issued by regulatory bodies such as the European Medicines Agency (EMA) and the Food and Drug Administration (FDA). These sterility requirements and guidance can be met by the following methods:

1. Terminal Sterilization
2. Aseptic Processing
3. Aseptic Processing and Terminal Sterilization

Terminal Sterilization

Terminal sterilization predominately focuses on applying heat, ionizing radiation, or different gasses to the final drug product. The product is sterilized in its final packaging or final assembled form, which highly reduces subsequent sterility risk. Terminal sterilization provides a Sterility Assurance Level (SAL) that is possible to calculate, validate and control. This helps reduce product waste, recalls and patient risk from non-sterile products that are more likely to occur when aseptic processing is used.

Aseptic Processing

Aseptic processing focuses on assembling previously sterilized components in an aseptic environment. During final product assembly, it is critical to maintain the sterility of the sterile components and product. Sterilizing and sterility testing pre-filled devices and combination products after aseptic filling helps to significantly reduce the risk of sterility or contamination issues which today account for approximately a third of FDA recalls.

Practical Application

Ophthalmic products, where the drug product requires application directly into the eye either by injection, ointment/drop, or implant, are one of the leading therapeutic areas subject to heightened regulatory scrutiny.

The overarching objective of the study was to apply sterilization to APIs in a therapeutic area that is prone to using aseptic processing, to demonstrate the ability to use terminal sterilization. Five GMP Quality Ophthalmic Active Pharmaceutical Ingredients (APIs) were tested using Gamma and Ethylene Oxide sterilization modalities. The following ophthalmic preparations were studied: dexamethasone, acyclovir, tetracycline hydrochloride, triamcinolone, and methylprednisolone.

The findings demonstrated that the application of Gamma (where suitable) and Ethylene Oxide on APIs did not adversely impact drug content, nor did it result in significant detectable impurities.

In addition, for Gamma applications, multiple factors were tested including varying the absorbed dose and temperature applied to the product during the study. The understanding of the impact of these factors allows for better process optimization.

Conclusions

The key findings of this research study help inform pharmaceutical companies developing these APIs about the benefits of terminal sterilization and/or aseptic processing: an underexplored research field in the broader scientific literature. The detailed description of the methodology and processes applied, whether through radiation (Gamma) or gas (Ethylene Oxide), provide a template for the replication of such sterilization modalities applied to additional APIs, Therapeutic Areas, and Key Indications.

With the global rise of biopharmaceuticals whose primary mode of administration is injection (Prefilled Syringe, Auto Injector, On Body Injector, Pen Injector), these sterilization modalities are poised to dominate an ever-growing share of the pharmaceutical market worldwide.