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Points to Consider for Sensitivity to Oxidation by Peroxide

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PDA Points to Consider for Sensitivity to Oxidation by Peroxide Team

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1.0 Introduction and Scope

The potential for drug products, especially biologics, to oxidize when they are processed within systems that have been decontaminated with hydrogen peroxide is an important concern. This primarily applies to isolator systems, where vapor phase hydrogen peroxide (VPHP) or vaporized hydrogen peroxide (VHP) is used to decontaminate the system. However, it could also apply to restricted access barrier systems (RABS) or to conventional areas where liquid cleaners containing hydrogen peroxide or other oxidizing agents are used as sporicides. The advent of rapid methods to decontaminate isolator systems, including nebulized and ionized hydrogen peroxides, as well as recent changes in equipment and system design have made the use of isolators with oxidation-sensitive products more feasible.

In order to determine the effects of VHP on oxidation-sensitive products, the industry needs instrumentation capable of measuring the entire range, from the high ppm-level exposures during a decontamination cycle to the lower ppb levels required for oxidation sensitive products at the end of aeration. Current instrumentation used to test for VHP at levels lower than 1.0 ppm is difficult to calibrate, maintain, and operate in a production facility.

Summarizing current issues and approaches to consider for an oxidation-sensitive product, industry experts outline best practices for developing a manufacturing process for drug product. This review starts from initial spiking studies and includes the common approaches to correlating the amount of hydrogen peroxide (H_2O_2) that could reach the product, considering product path and worst-case conditions, when product could be exposed during aseptic filling processes. Uptake studies should be conducted to determine the stoppage time when empty containers may have accumulated too much H_2O_2 (starting with the highest concentration that might be encountered by the end of aeration) and should no longer be filled. Similarly, the stoppage time should be determined at which a filled, unclosed container can be exposed and, if exceeded, those units should be rejected. Special situations, such as partially stoppered vials in lyophilization, also need to be considered.

This document addresses aspects to consider in the design, development, processing, instrumentation, materials, and equipment specific to issues with products sensitive to oxidation when exposed to H_2O_2. General topics related to sterility assurance and development of the VHP decontamination process are not included, nor is cycle development from a sterility standpoint. Concurrently, a *PDA Points to Consider on Aseptic Processing of Sterile Pharmaceutical Products in Isolators* to address general isolator considerations is in publications along with the revision efforts for PDA TR34***(1)***.

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