NON-AEROSOL STERILE IPA 28 DAY STERILITY VALIDATION STUDY

Summary:

The sterility of sterile 70% Isopropyl alcohol (IPA) solution (Cidehol ST Decon # 8316), equipped with a non-aerosol trigger spray delivery device, was monitored over a 28 day period. The IPA had been previously rendered sterile by a process which includes 0.22µ filtration, double-bagging in a class 100 cleanroom, and gamma irradiation to a SAL (Sterility Assurance Level) of $1x10^{-6}$. Two sets of sterile product were opened and used in either a controlled, Class 100 cleanroom, or uncontrolled (benchtop) environment for a consecutive 28 day period. Sterility was validated using USP 24 sterility testing at days 14, 21, and 28 and environmental monitoring of both settings was conducted using air settling plates. Both the controlled and uncontrolled sample sets remained sterile throughout the study duration. The uncontrolled (benchtop) sample set is significant since sterility of the product was maintained despite the presence of bacterial contamination in the environment as evidenced by a mean bacterial count of 11.5 CFU/5 plates per day.

Background:

The use of sterile disinfectants is a regulatory requirement for Class 100 cleanrooms employed in the manufacture of sterile products. Sterile 70% isopropyl or ethyl alcohol is often used as a final step in the disinfection in aseptic processing areas since it is an effective broad spectrum disinfectant, evaporates quickly, and leaves no residue. In keeping with efforts to control contamination in aseptic areas, the process of disinfection itself is being evaluated and revised due to a concern that reagents, such as the disinfect itself, may provide a potential source of contamination. The primary criterion of all disinfectants used in these environments has been the integrity of the product with respect to sterility and pyrogen content. As a result of these new concerns, this primary criterion is being superceded by concerns regarding potential contamination problems with the delivery format of the product. For example, many manufacturers of sterile, concentrated disinfectants are switching to a single dose format to minimize handling (dilution, mixing etc…) and reduce the possibility of contamination of the opened vessel. Similarly, the delivery system of sterile alcohol solutions has been examined and adapted. It has been suggested that a pressurized aerosol can maintains the sterility of its contents better than a non-pressurized (trigger spray) container. The argument being that the aerosol can utilizes a propellant to maintain a positive pressure within the container whereas the trigger sprayer aspirates room air into the container, providing a potential source of contamination to the remaining contents. While this issue represents a genuine concern, within the context of use within a Class 100 cleanroom, the issue of room air contamination does not seem probable. The current sterility validation study demonstrates that sterile IPA in a non-pressurized, trigger spray bottle remains sterile when used for a 28-day period in both a controlled (class 100 cleanroom) and uncontrolled environment.

FDA standard 209E guidelines demand that a cleanroom be maintained at a specified level of contamination control depending upon class. When used in such an environment the only possibility of contamination of the contents of a non-pressurized container would be the environment of the cleanroom. In other words, the source of the problem is with the cleanroom itself. Even if a cleanroom were contaminated with spores for instance, the likelihood of those spores contaminating the contents of non-pressurized containers is very minimal due to the positive laminar air flow, incorporated into all cleanroom design. The laminar flow of air from floor to ceiling prevents the suspension of airborne contaminates within the cleanroom which prevents the contaminants from being “sucked” into the bottle. Even when used (spraying and aspiration) in an uncontrolled, non-laminar flow area, the non-pressurized, trigger sprayer showed no signs of contamination even though air settling plates confirmed the presence of bacterial contamination.

Description:

A total of 30 samples of sterile 70% isopropyl alcohol solution in 16 oz bottles, equipped with a trigger spray head (Decon Labs Cidehol ST 70, cat# 8316) were used in this study. The samples had been previously rendered sterile by 0.2μm filtration, double bagging in a Class 100 cleanroom, and subjected to terminal sterilization using gamma irradiation to a SAL (sterility assurance level) of $1X10^{-6}$. Half of the samples (15 bottles) were placed in a controlled (Class 100 cleanroom) environment, and half (15 bottles) in an uncontrolled (laboratory benchtop) environment. The bottles were used in a manner to simulate normal usage: Each bottle was sprayed one complete aspiration twice per day for a consecutive 28 day period and the fully adjustable trigger nozzle remained in a open position for the entire period. Environmental monitoring was conducted by placing five aerobic and five yeast/molds bioburden settling plates within each environment. The plates were opened for approximately one hour, closed and incubated as necessary. Sampling was performed every second day for the duration of the study. On day one of the study, both sample sets were placed in their respective environments, removed from their sterile double-bagged packaging and used as described. On days 14, 21, and 28, five bottles from each sample set were removed and tested for sterility using USP 24 <61> Sterility testing membrane filtration.

Results and Discussion:

Both the controlled (class 100 cleanroom) and uncontrolled (benchtop) sample sets remained sterile throughout the study duration. Environmental monitoring of the class 100 cleanroom revealed a mean count of 0 cfu/5 plates bacteria and 0 cfu/5 plates yeast/molds. The uncontrolled (benchtop) environment had a mean count of 11.5 cfu/5 plates bacteria and 0 cfu/5 plates yeast/molds. Thus despite evidence of bacterial contamination of room air and it's subsequent aspiration into the vessel via the trigger spray mechanism, the contents of the bottles in the uncontrolled environment remained sterile.

Conclusion:

The concern that the packaging and delivery mechanism of sterile disinfectants might represent an additional contamination risk in aseptic processing (Class 100 cleanroom) areas was the motivation for the current study. There has been a movement away from the trigger spray dispensing of sterile 70% alcohol solution and toward pressurized aerosol cans due to a concern that former requires the aspiration of room air into the vessel and represents a possibility for contamination. While these adaptations are intended to preserve the integrity of the sterile product, they have come at a price for the end user. The change from a trigger spray dispenser to an aerosol can represents a 40% increase in cost to the end user with absolutely no difference in product quality (with respect to sterility and endotoxin limits). Aerosol product pricing aside, this does not include the inevitable waste that occurs with any aerosolized product: The majority of the volume of the container is propellant, not product and the propellant frequently runs out before the entire product is used up.

The current study was undertaken to address the issue of whether the trigger spray delivery format preserves or compromises the sterility of the remaining product when sterile 70% IPA is used during a consecutive 28 day period. The results clearly demonstrate that this product, when delivered using a trigger spray mechanism, remains sterile for at least 28 days despite the necessity of aspirating room air into the container. In fact this product, when used in our "worst case scenario" uncontrolled benchtop environment, remained sterile despite the aspiration of contaminated room air. Thus, when used in a class 100 cleanroom, appropriately maintained with respect to particle limits and laminar flow requirements, sterile 70% Isopropyl alcohol delivered in trigger spray delivery format should represent no additional contamination threat than the same product delivered using a pressurized aerosol can and provides significant cost savings when compared to aerosol cans.

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