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Actril® Cold Sterilant

Research Report: The use of Actril Cold Sterilant for Periodic Sporicide Disinfections as well as Daily Disinfections in Pharma Production Facilities under USP<1072> Guidelines.

Introduction

A sound cleaning and sanitization program is needed to prevent microbial contamination in controlled environments used for the manufacturing of products. Disinfectants need to meet varying requirements based on the market of final use (healthcare, food or pharma manufacturing). The United States Pharmacopeia chapter <1072>[1] addresses the testing required to ensure proper control of Pharmaceutical Cleanrooms.

Tests According To USP <1072>

Use-Dilution Tests

Extensive use-dilution tests have been performed with Actril® Cold Sterilant, diluted Actril with ClearKlens VH5 against a wide range of organisms including:

Spores: B. subtilis2, C. sporogenese[2], C. difficile[3],

Mycobacteria: Mycobacterium bovis[2],

Viruses: Polio Virus Type 2[4], Herpes Simplex Type 1 & 2[4], HIV[4],

Fungi: Trychophyton mentagrophytes[2],

Vegetative Bacteria: P. aeruginosa[2], S. choleraesius[2], S. aureus[2] and MRSA[5].

These tests were conducted according to AOAC protocols or modified.

Surface Challenge Tests

The selection of suitable disinfectants and the verification of their effectiveness in surface challenge testing are more representative to reality and are critical in the development of a cleaning and sanitization program. The challenge is conducted by inoculating 2 x 2-inch coupons made from the material desired to be tested and the organism of interest. A disinfectant is evaluated for the ability to be bactericidal, virucidal, fungicidal and sporicidal. The germicide must demonstrate at least a 2-log reduction for bacterial spores, 3-log for bacteria, fungus and viruses at a time point of 10 minutes or less. Inside vented Pharmaceutical production rooms, most proper wiped surfaces will not remain wet after 10 minutes.

Terminology

Chemical Disinfectant – A chemical agent used on inanimate surfaces and objects to destroy infectious fungi, viruses, and bacteria, but not necessarily their spores. Sporicidal and antiviral agents often categorized as high-level, intermediate-level, and low-level by medically oriented groups based upon their efficacy against various microorganisms.

Cleaning Agent – An agent for the removal from facility and equipment surfaces of product residues that may inactivate sanitizing agents or harbor microorganisms

Decontamination – The removal of microorganisms by disinfection or sterilization.

Disinfectant – A chemical or physical agent that destroys or removes vegetative forms of harmful microorganisms when applied to a surface.

Sanitizing Agent – An agent for reducing, on inanimate surfaces, the number of all forms of microbial life including fungi, viruses, and bacteria.

Sporicidal Agent – An agent that destroys bacterial and fungal spores when used in sufficient concentration for a specified contact time. It is expected to kill all vegetative microorganisms.

Sterilant – An agent that destroys all forms of microbial life including fungi, viruses, and all forms of bacteria and their spores. Sterilants are liquid or vapor-phase agents.[1]

Disinfectants, Materials & Detergents

Microorganisms differ greatly in their resistance to disinfection agents. The general order of resistance to chemical disinfectants from most to least is Spores → Mycobacteria → Nonlipid-coated viruses → Fungi → Vegetative bacteria → Lipid-coated viruses. The addition of a detergent can aid a disinfectant in reducing the time needed to inactivate microbes. The type of surface being disinfected can also affect the time required by the chemical disinfectant.

The Benefits Of PAA Technology

Actril Cold Sterilant uses the Peracetic Acid Technology (PAA) which is successfully used for more than 10 years by many FDA audited Pharma Production Facilities all over the world. At a very low PAA concentration (0.06%) Actril® is documented as a Cold Sterilant and potentially destroys all microbiological life including vegetative forms, virus and endospores.

Diluted Actril at 0.012% PAA has been confirmed as a very effective agent against all vegetative forms. In pharma production facilities less chemistry applied on the surfaces better it is in term of potential interference/residue, corrosion, rinsing time and of course cost. The use of Actril® on surfaces leaves no H2O2/PAA/AA residue behind after exposure[8].

Experimental Procedure

According to the USP<1072> Surface Challenge Test Protocol, the trials evaluated Actril® Ready To Use (RTU), Diluted Actril® (1:5) and both on stainless steel and Lexan® (plexiglass) surfaces and with and without the addition of a detergent (0.3% ClearKlens Plus VH5) to the Actril® solution. The tests were conducted at room temperature (~22°C) and were composed of bacteria, mycobacteria, fungi, viruses and spores. For several tests, the inoculum containing the microbial challenge also had 3% or 5% fetal bovine serum contamination to represent the organic challenge faced by surface disinfectants. Testing performed in triplicates at ATS Labs in Eagan, MN–USA, at Henkel in Germany (EU) and at Medivators is referenced in the different tables to show the results.

Results & Discussion

Disinfectants are evaluated and selected from the following list of important criteria:

1. A wide spectrum of activity 2. A fairly rapid action time 3. Not neutralized by residual organic matter 4. Environmental conditions 5. Compatibility with the surface to be disinfected 6. Compatibility with detergents used 7. Sporicidal properties and 8. Range of formats available[7]. Actril®, depending on the use protocol (Ready to Use, Diluted, with our without detergent), provided the needed level of log reduction required by the USP<1072>.

Actril® Ready To Use (RTU) for periodic disinfection

Tables 1[8] and 2 show Actril® used as a Ready To Use solution is a very effective broad spectrum agent destroying the vegetative forms of bacteria, mycobacteria, virus, fungi as well as endospores. The measured Log Reduction after 5 minutes contact time is over 5 log on viruses, over 4 log on vegetative forms (3 log required) and over 3 log on endospores (2 log required). There is no observed difference between efficacy trials on clean surfaces or surfaces contaminated by organic materials. Table 2 confirms additionally the use of 0.3% ClearKlens Plus VH5 detergent in Actril® is not inhibiting the Actril® efficacy.

Table 1: Actril® RTU Average Log Reduction @ 5 minutes
Clean Surfaces

Organism	Description	Lex-	S/S	ATS
P. aeruginosa	Bacteria Vegetative	5	4.2	A07017
B. atrophaeus (subtilis)	Bacteria Spore	3.5	3.6	A07017
A. brasiliensis (niger)	Fungi Spores	4.6	4.8	A07017
Poliovirus type 1	Virus Human Non Enveloped	3.8	3.9	A07017
M. terrae	Mycobacteria	4	5	A07017

Table 2: Actril® RTU & Actril® RTU + 0.3% ClearKlens VH5 detergent average Log Reduction @ 5 minutes
Surfaces contaminated with 5% Fetal Bovine Serum

Organism	Description	Actril®		Actril® + 0.3% Clear-		ATS Test #
		Lexan	S/S	Lexan	S/S	
S. aureus	Bacteria Vegetative	>4.63	>4.59	>4.53	>4.59	A13572
P. aeruginosa	Bacteria Vegetative	>4.63	>4.66	>4.53	>4.59	A13571
B. atrophaeus (subtilis)	Bacteria Spore Aerobic	3.47	3.59	NA	NA	QP202104
C. sporogenes	Bacteria Spore Anaerobic	>4.38	>4.36	>4.38	>4.36	A13573
A. brasiliensis (niger)	Fungi Spore	>4.83	>4.82	>4.83	>4.82	A13570
Porcine Parvo PPV	Virus Animal Non Envelopped	5.25	6.2	>7.77	>8.52	A13512
Poliovirus type 1	Virus Animal Non Envelopped	>5.38	>6.00	>5.70	>6.00	A13513
M. bovis	Mycobacteria	4.33	4.33	4.09	4.37	A13542

Actril® diluted 1:5 for daily disinfection against viruses and vegetative forms

Table 3 shows 1:5 diluted Actril® complies with the USP<1072> requirement for daily disinfection; on both Lexan® and stainless steel surfaces the log reduction is over 3 log on all the vegetative forms of bacteria, fungi and virus.

Table 3: Actril® Diluted 1:5 + 0.3% ClearKlens VH5 average Log Reduction @ 5 minutes

Organism	Description	Lexan	S/S	Henkel Test #
P. aeruginosa	Bacteria Vegetative	>3.96	>4.0	13-15414
S. aureus	Bacteria Vegetative	>4.09	>4.15	13-15414
C. albicans	Fungi Vegetative	>3.71	>3.57	13-15414
Poliovirus type 1	Virus Human Non Envoloped	>4.50	3.97	13-15414
Murine Parvovirus	Virus Animal Non	>3.3	>3.15	13-15414

Table 4 shows that similar to full strength Actril®, the diluted version is neither more nor less effective with or without ClearKlens on S. aureus. This confirms the results comparing the Tables 1 and 2; there is no interference from the addition of the detergent.

Table 4: Actril® Diluted 1:5 Average Log Reduction @ 5 minutes

Organism	Description	Lexan	S/S	Henkel Test #
S. aureus	Bacteria Vegetative	NA	>4.19	13-15414

In addition to the test results included in this report, Medivators has conducted a number of other tests relevant to clean room disinfection including: AOAC Use Dilution Tests, Residuals and Material Compatibility. Figure 1 & 2 demonstrates that the addition of 0.3% ClearKlens Plus VH5 detergent does not affect the stability of the active ingredients in Actril® Cold Sterilant in RTU version over extended periods of time. Actril® in the diluted form has to be prepared daily for use.

Figure 1: Stability of Hydrogen Peroxide

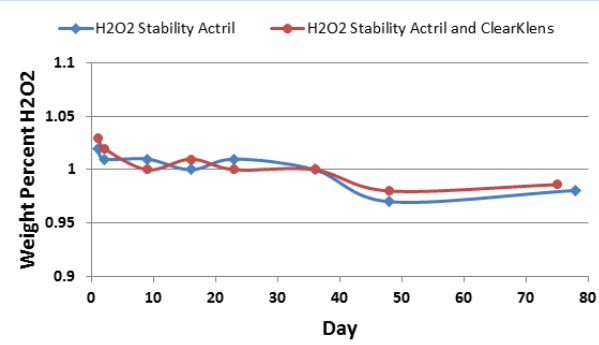
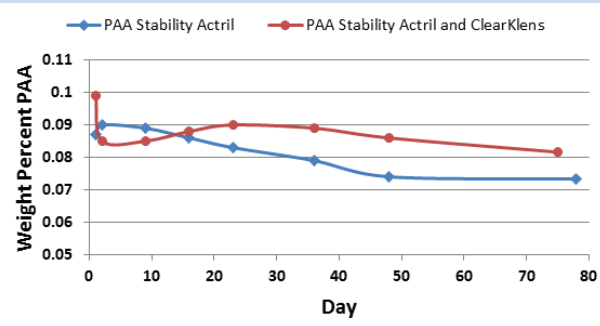


Figure 1: Stability of Peracetic Acid



Conclusion

In order to achieve microbial control in cleanrooms, the use of defined cleaning techniques together with the application of detergents and disinfectants, is of great importance. Selecting appropriate detergents and disinfectants is an important choice for the cleanroom manager and the microbiologist to make. A review of the data in this report shows that Actril and diluted Actril with a detergent satisfy all the important aspects of a disinfectant to the highest level.

As already demonstrated by many FDA audited Pharma production facilities worldwide, Actril® Cold Sterilant's efficacy conforms to the USP<1072> requirements with a contact time of 5 minutes or less (Table 1). According to a separate study and report, Actril® does not leave any H2O2/PAA/Acetic Acid residue behind on the surfaces[6]. Actril® Cold Sterilant can be used as a Ready To Use solution as periodic broad spectrum and effective sporicide agent applied on surfaces in Pharma Production facilities.

Actril® Cold Sterilant can be used, after dilution (1:5) by the user, for daily disinfection of large surfaces, floor, wall, ceiling, in aseptic areas. Diluted (1:5) Actril® is effective against viruses and vegetative forms and complies with USP<1072> (Table 2). In a diluted form, it still shows a noteworthy sporicidal activity about 0.5 or 1 log reduction. This data suggests that the daily use of the diluted

solution can also be effective at controlling spores, a capability that other disinfectants are not able to do. Using Actril® Cold Sterilant in both full strength and diluted form will allow the cleanroom staff to stock 1 product, making validation, storage and use much more convenient.

In both daily and periodic use a detergent, ClearKlens Plus VH5, can be added to Actril® without any negative impact on the efficacy for cleaning and disinfecting the surfaces in one unique step. Using diluted Actril and ClearKlens together simplifies the cleaning/disinfecting validations and use procedures. Actril® Cold Sterilant meets the international criteria for clean room disinfections and is a valuable tool for Pharma Clean Room Quality people, Clean Room Managers and Microbiologists.

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