

ROOM DECONTAMINATION WITH HYDROGEN PEROXIDE VAPOR

INTRODUCTION

During the 1990s, many types of operations requiring aseptic conditions were moved from clean rooms into sophisticated glove boxes or isolators. In the pharmaceutical industry, both quality control testing and manufacturing processes have employed isolation technology. Research applications involving a need for containment of dangerous biological organisms or protection of Specific Pathogen Free (SPF) animals have also used isolation technology. In the pharmaceutical area, the predominant sterilant has been hydrogen peroxide gas (Lysfjord and Porter, 1998). The majority of these installations are using STERIS VHP® Systems to generate the hydrogen peroxide gas. In research applications, which are most often non-GMP, manual sprays and wipe downs with sporicidal agents are common.

In some cases, it is not practical to move a manufacturing operation or research application into the confines of an isolation system, so they remain in classified clean rooms or biological safety laboratories. Periodic decontamination* of these areas with a highly sporicidal gas can be desirable. In many cases, people would traditionally use formaldehyde gas as a fumigant. This paper is an attempt to categorize and review room applications that are currently using STERIS VHP 1000 series generators as their sanitizing system. Eighteen room applications are summarized. The list of applications is not all-inclusive, but provides a good cross-section of the range of uses.

In general, rooms that require periodic decontamination can be categorized by production and research applications. In most cases, production applications involve the manufacturing of sterile pharmaceuticals or medical devices in an aseptic clean room. The primary concern is the prevention of contamination of products from environmental microorganisms. Research applications usually involve work with pathogens, and the primary concerns are the safety of the researchers and the elimination of cross contamination between experiments. In some research applications, the reduction of environmental microbial contamination is also a concern such as in the care of SPF animals.

Rooms being decontaminated with hydrogen peroxide vapor can also be roughly divided into 3 categories based on how they are used. The first category may be defined as general work space. In production applications, this would normally include rooms used for the manufacturing or filling of aseptically processed products. An extensive description of the application for decontaminating a vial filling area was documented at a German pharmaceutical company (Jahnke and Lauth, 1996, 1997). In the research areas, rooms that are decontaminated with hydrogen peroxide can include research labs or animal cage areas (Krause et al., 1999).

Material pass-through rooms are the second general category. This would include supplies needed for the production of pharmaceutical products or the care of SPF animals. One application, for which hydrogen peroxide vapor has replaced the traditional use of formaldehyde, is the decontamination of chicken eggs used for viral vaccine production (Gruhn et al., 1995). The efficacy of hydrogen peroxide vapor on animal viruses and the gentleness of the vapor on a variety of materials and equipment has also been documented (Heckert et al., 1997).

The third general category of applications involves rooms built for equipment decontamination. In both production and research applications, this involves the gassing of equipment that may be contaminated with pathogens in a room built specifically for that purpose. In a production environment, this would typically be done at a centralized repair facility (Anonymous, 1998). A central repair facility would normally decontaminate a room full of equipment daily or weekly. Equipment decontamination at a research facility is done on an as-needed basis, before equipment is removed for repair from level 3 or 4 Biological Safety Laboratories (BL-3 or BL-4). Equipment decontamination rooms can be built with a single entrance door or a double door, pass-through configuration.

A summary of the general categories of rooms that are decontaminated with hydrogen peroxide vapor is listed in Table 1.

Table 1. Summary of Room Application Categories

CATEGORY	PRODUCTION	RESEARCH
Work Space	Aseptic Processing and Filling	Pathogen Research Labs and Animal Care Rooms
Materials/Supplies	Rubber Stoppers, Plastic Bottles, Cleaning Supplies	Sterile Animal Bedding and Feed
Equipment	Central Repair Facility, Frequent Use	Exit from Biological Safety Lab, Used Periodically

MATERIALS OF CONSTRUCTION

The materials used for room construction vary widely with these applications. In most cases, the fresh air make-up for the ventilation system to the rooms is shut off during the decontamination process. In some cases, the ventilation system is manipulated to help maintain the desired pressure balance in the room during decontamination. In many cases, the air handling system is activated at the end of the cycle to assist the aeration of the room. Some of the labs are built without any special construction. For periodic decontamination of this type of space, duct work and doors may be sealed with duct tape. Pharmaceutical work spaces are most often classified as cleanrooms and therefore have been built with cleaning in mind. Pass-through rooms are usually built specifically for that purpose and often include stainless steel walls and doors with inflatable seals. Equipment decontamination rooms have been built using materials typical of walk-in refrigerators or freezers. Regardless of the materials of construction used, the room must be well sealed during the decontamination to prevent worker exposure in adjacent work spaces. In the United States, a limit of 1 ppm for an 8 hour time weighted average for worker exposure to hydrogen peroxide vapor has been established by the federal government.

General recommendations for materials of construction for new projects are listed below in Table 2. Contact a STERIS VHP Process Engineer to discuss the safety and applicability of using hydrogen peroxide vapor on existing rooms.

Table 2. Recommended Materials for New Construction

MATERIAL/COMPONENTS	COMMENTS
Heating, Ventilation, and Air Conditioning (HVAC) unit ¹	Make-up air intake should have positive shutoff or be controlled to provide small airflow for pressure balance. All piping exposed to gas should be well sealed.
Humidification Systems	Have positive shut off
Dehumidification System	Can expedite cycle. Desiccant Wheels: - Need positive shutoff or isolation during sterilization to avoid leakage or damage to wheel Cooling Coils: - Need to be at room temperature before injecting H ₂ O ₂ - Stainless steel preferred over copper
Ductwork	- Leak tight stainless steel or aluminum - PVC pipe: cost effective, easy to seal, may cause slightly longer cycles due to high absorption
Circulation	Conventional Fans HVAC Systems
Walls	Plaster board with reinforced plastic wall covering; Stainless steel; Concrete block or steel with epoxy paint ²
Doors	Frequent use: Inflatable seal doors Moderate use: Freezer-type doors Infrequent use: Conventional, use duct tape to seal
Windows	Glass preferred
HEPA filters	Standard glass fiber; aluminum frames; if gel sealed, use silicone based
Gaskets	Silicone, Viton, Norprene
Sealants	Silicone based
Plastics / Polymers	Most compatible except for Nylon

¹Note: Not approved for US HVAC applications

²Note: Care should be taken to avoid condensing Hydrogen Peroxide vapor on epoxy coatings or blistering may occur. Consult with your STERIS VHP Process Engineer for more details on development of safe, effective, cycle development.

PRODUCTION EXAMPLES

A summary of production or manufacturing rooms being decontaminated with hydrogen peroxide gas is listed in Table 3. This is followed by specific examples in more detail.

Table 3.
Summary of Rooms at Manufacturing Companies using hydrogen peroxide vapor decontamination

COMPANY	LOCATION	APPLICATION	VOLUME
Pharma Hameln	Germany	Aseptic Filling	56 m ³
Ferring	Sweden	Aseptic Filling (10 Rooms)	9 m ³ to 89 m ³
Confidential	Scotland	Aseptic Filling (2 Lines)	140 m ³
Confidential	Germany	Tablet Production	150 m ³
Roche Diagnostics	Germany	Aseptic Filling (7 Rooms)	15 m ³ to 90 m ³
Dr. Kade	Germany	Aseptic Filling	40 m ³
Oncotec	Germany	Aseptic Filling	30 m ³
Confidential	USA	Filling Supplies	27.2 m ³
Lohmann Animal Health	Germany	Eggs for Vaccines	40 m ³
Janssen	Belgium	Cleanroom Supplies	9 m ³
Bayer Diagnostics	USA	Equipment Decontamination	21.5 m ³
Bayer Diagnostics	Ireland	Equipment Decontamination	10 m ³

Production / Processing Room Examples

Pharma Hameln: 56 m³ (1977 ft³) Aseptic filling room

Located in Hameln Germany. This application has been well documented in literature (Jahnke and Lauth, 1996, 1997). The air handling system provides an initial low humidity level in the room. During decontamination, the air handling system is turned off, and two fans are placed in the room prior to the use of the hydrogen peroxide vapor. During the most successful decontamination run documented, all 105 *Bacillus stearothermophilus* biological indicator strips were sterilized, except for those placed in gloves where a 3 to 4 log reduction was achieved. The cycle parameters for the most successful cycle are as follows.

Dehumidification:	None (Done Prior)	
Condition:	Airflow:	34 m ³ /hour (20 scfm)
	H ₂ O ₂ Injection:	10 g/min
	Time:	40 minutes
Sterilize:	Airflow:	32 m ³ /hour (19 scfm)
	H ₂ O ₂ Injection:	6 g/min
	Time:	80 minutes
Aerate:	Airflow:	38 m ³ /hour (22 scfm)
	Time:	4 hours

The parameters above yielded a six-hour cycle time. Microbial monitoring and media fill challenges have been conducted to provide further verification of the biological effectiveness

Ferring Pharmaceuticals: 10 rooms, various sizes from 9 m³ (317 ft³) to 89 m³ (3142 ft³)

This ambitious application involves the decontamination of 10 rooms, which are used for vial filling, ampule filling, syringe filling, sterile filtration, cold storage and gown changing. With the exception of the cold storage room, which has its own recirculating air handling unit (AHU), the other areas have single-pass air through the rooms, i.e. 100% fresh air. This created the opportunity to reconfigure the AHU so that an individual room could be isolated while the other rooms remained "on line." The AHU was modified slightly so that the exhaust from the room being decontaminated could be sealed while the air supply was used to slightly pressurize the area. The air pressure difference regimen could be maintained to enable the decontamination of a room while allowing work to be carried out in the other areas. This application is being validated with 105 *Bacillus stearothermophilus* biological indicator strips.

Cycle information for an example of an 85 m³ Sterile Filtration room is shown below. Dehumidification is done beforehand with the air handling unit; however, a short dehumidification phase is programmed into the STERIS VHP 1001 system to warm up the hoses.

Dehumidification:	Airflow:	32 m ³ /hour (19 scfm)
	Time:	15 minutes
	Humidity:	6.9 mg/l (30% RH @ 25°C)
Condition:	Airflow:	32 m ³ /hour (19 scfm)
	H ₂ O ₂ Injection:	9 g/min
	Time:	20 minutes
Sterilize:	Airflow:	32 m ³ /hour (19 scfm)
	H ₂ O ₂ Injection:	7 g/min
	Time:	100 minutes
Aerate:	Done with Air Handling System	

Production Material Pass-Through Room Example

Confidential: 27.2 m³ (960 ft³) Clean Room Pass-through

This application is located in the United States at a pharmaceutical company. The pass-through room was built to decontaminate bags of supplies, such as rubber stoppers that need to be introduced into the aseptic filling area of a large clean room. The stoppers are sterilized with gamma radiation in triple bags. The bags are loaded onto full-size carts and wheeled into the pass-through room, which can accommodate nine carts at one time. A minimum of a 3 Log reduction of *Bacillus stearothermophilus* was validated by direct inoculation of the bags followed by recovery studies. After implementing the pass-through, a notable drop in viable bioburden was observed during routine environmental monitoring, proving that the system was a significant improvement over the previous manual wipe down procedures. The room is specially built with stainless steel walls, inflatable seal doors, an external dehumidification system, and a large air handling system to shorten the aeration time. The complete cycle time validated was 65 minutes.

RESEARCH EXAMPLES

A summary of rooms at research institutions that are being decontaminated with hydrogen peroxide gas is listed in Table 4. This is followed by specific examples in more detail.

Table 4.
Summary of Rooms at Research Institutions using hydrogen peroxide vapor decontamination

INSTITUTION	LOCATION	APPLICATION	VOLUME
Max Planck Institute	Germany	Animal Care Rooms	63 m ³
Solvay Pharma	Germany	Animal Care Rooms	45 m ³
Confidential	Germany	Animal Care Rooms	45 m ³
UKE, Hamburg	Germany	SPF Animal Supplies	15 m ³
National Cancer Research Institute	USA	AIDS Research Equipment Decontamination	11.3 m ³
National Institutes of Health	USA	Equipment Decontamination for BL-4 Lab	10.2 m ³

Research Laboratories / Animal Room Example

Max Planck Institute, Göttingen: 63 m³ (2225 ft³) Animal Care Rooms

This application was documented in a presentation by Krause et al. (1999). The Max Planck Institute for Experimental Medicine in Göttingen, Germany has rooms where Specific Pathogen Free (SPF) mice are housed in ventilated cage racks. Rooms with clean, empty cages are decontaminated before housing the rodents. Tests were done to demonstrate that a cage blower unit can be successfully decontaminated using hydrogen peroxide vapor. The blower unit is left running in the room during the decontamination process. The installation was challenged with 10⁵ *Bacillus stearothermophilus* biological indicators. In three trials, 21 out of 24 indicators were sterilized, with the positive ones being placed in a barely accessible gap of 5 mm. Contact plates were also used after the fumigation and always showed less than 10 colony forming units per 100 cm². The VHP 1000 generator runs for 10 minutes of dehumidification, 15 minutes of conditioning, and 75 minutes of sterilization. The normal air handling system assists with aeration to produce a total cycle time of about 3 hours.

Research Material Pass-Through Rooms

UKE, Hamburg: 15 m³ (529 ft³), Material Transfer for Specific Pathogen-Free Animal Lab

This application is also for SPF animal care at the University Hospital - Eppendorf, Hamburg, Germany. This transfer room has double doors with pneumatic seals. These doors have no threshold, which allows carts with supplies, tools, etc. to be wheeled into the room and decontaminated. Animal supplies may include bags of presterilized feed and bedding. Gassing the outside of the bags can reduce the amount of bioburden that is introduced to the animal rooms. Ventilated cage racks can also be left running to sanitize the filtration systems in the blower units.

Research Equipment Decontamination Rooms

National Cancer Research Institute: 11.3 m³ (400 ft³) AIDS Research Equipment Decontamination

This facility is located at Fort Detrick, Maryland. The room was originally built to decontaminate equipment being removed for servicing or repair from an AIDS research laboratory. A wide variety of equipment has been decontaminated over the years. The room is specially built for low gas permeation and is sufficiently leak tight so that the VHP 1000 system can control a slight negative pressure in the room to ensure that hydrogen peroxide vapor does not leak to adjoining laboratories. The construction includes leak tight electrical outlets and lighting fixtures. A conventional door is used so some duct tape is employed to reduce air leakage around the weather strip seals. Automatic leak proof dampers are used in the normal air supply and return so aeration can be assisted after the decontamination process.

SUMMARY

Hydrogen peroxide vapor is being used successfully for many types of room decontamination applications. Of the 18 installations surveyed, 10 are located in Germany. The popularity of the technique in Germany may be due to the excellent publications and presentations that have been made by German scientists and engineers on this subject, combined with strict government regulations on the use of formaldehyde gas. Since hydrogen peroxide breaks down into oxygen and water, many people view the technique as a safe and effective alternative to formaldehyde fumigation. Many research laboratories are currently investigating or converting their sanitizing methods from formaldehyde or other manual wipe-down procedures to hydrogen peroxide gas. A gaseous agent saves labor and is much more repeatable than manual cleaning with liquid disinfectants. Operators of STERIS VHP systems also have a high level of personal satisfaction that they are enhancing workplace safety with a process that is environmentally friendly.

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*When using VHP equipment with Vaprox Hydrogen Peroxide Sterilant in the United States, the term biodecontamination referred to in this document is defined as sterilization of exposed porous and non-porous surfaces in a pre-cleaned, dry, sealed enclosure. Any reference to biodecontamination as it relates to the use of this equipment in the United States does not impart additional claims of effectiveness beyond that approved in the EPA-registered labeling of Vaprox Hydrogen Peroxide Sterilant.

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