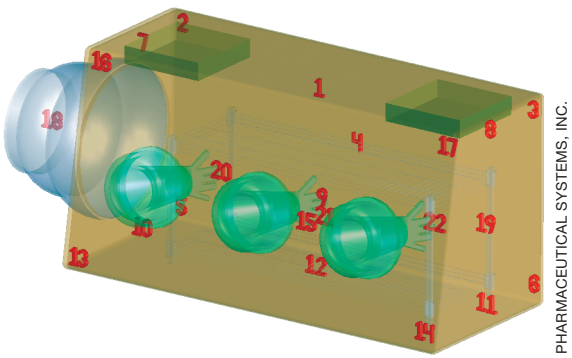
Comparing and Contrasting Barrier Isolator Decontamination Systems

Jim Fisher and Ross A. Caputo*



A discussion of the validation and operation of two commercially available vapor-phase hydrogen peroxide decontamination systems is presented, based on a hands-on examination of both systems.

Ross A. Caputo, PhD, is the CEO of Pharmaceutical Systems, Inc. (PSI), 909 Orchard St., Mundelein, IL, 60060, tel. 847.566.9229, fax 847.566.4960, rcaputo@pharmsustems,com. **Jim Fisher** is the vice-president of engineering at PSI.

*To whom all correspondence should be addressed.

In recent years, the use of barrier isolators in a variety of applications has increased. In 1998, R. Friedman called isolator technology a "promising technology [that] may represent a significant stride forward in aseptic processing" (1). Isolators have become the approach of choice for sterility testing (2, 3) and vapor-phase hydrogen peroxide (VHP) has become the sterilant of choice. According to a survey conducted by Lysfjord and Porter, 75% of surveyed participants indicated that they used VHP for their decontamination processes (4). In this context, a comparison was made of the validation, operation, and performance of two VHP generators, the "STERIS VHP 1000ED" biodecontamination system and the BioQuell's "Clarus 'C'" H_2O_2 gas generator shown in Figure 1.

Isolator equipment and decontamination systems

Isolators. An isolator uses a biological barrier concept in which the analyst or operator is physically isolated from the environment. The isolator is maintained under positive or negative pressure (depending on the application) by HEPA-filtered air. Using a glove port or half-suit, the analyst performs manipulations in the isolator but is physically separated from the product environment, so the risk of contamination during the procedure is minimized.

The choice of positive or negative pressure depends on the application. If the contents of the isolator are carcinogenic or radioactive, negative pressure is maintained to protect the user. However, in most aseptic processing situations, positive pressure is maintained to protect the contents from contamination by the user. The US Food and Drug Administration (FDA) aseptic processing guidance offers some basic guidelines for validating isolators. According to these guidelines, the isolator interior must maintain a Class 100 environment or better, and the room surrounding an aseptic processing isolator should be classified to ensure a consistent bioburden for the isolator's decontamination (5).

The isolator's control system maintains process set points such as the working pressure of the unit. Older isolators typically had dials that adjusted the fan speed and the pressure differential. Modern isolators generally have a programmable logic controller (PLC) or a computer, and generally need less user supervision because the controllers can maintain various set

points such as pressure and temperature. The controller also can alert the user of any alarm conditions through audio and visual alarms, and can communicate with a VHP generator during the decontamination cycle.

VHP generators. A VHP generator has its own PLC or computer controller that manages the various cycle set points and phase parameters, and communicates with the isolator. The generators generally have four distinct phases of operation. Although the nomenclature of the four phases differs from one manufacturer to the next, they function in essentially the same way. These four phases are conditioning, ramping, decontamination, and aeration.

The conditioning phase of the generator cycle prepares the isolator environment for biodecontamination. Conditioning the isolator environment consists of drawing air from the isolator through the generator to increase the temperature and adjust the relative humidity (RH) to required levels. The target conditions of temperature and RH differ in the two generators studied; both generators, however, condition the isolator environment to a desired temperature and relative humidity.

The second phase, ramping, uses elevated hydrogen peroxide (H_2O_2) injection rates to rapidly raise the concentration of VHP inside the isolator to the desired limit. This phase of VHP decontamination is analogous to the "come-up" time in a steam sterilization application.

When the second phase is completed, the decontamination phase begins. During the decontamination phase, the generator maintains a specified VHP concentration in the isolator by reducing the H_2O_2 injection rate. It is this phase of the generator cycle that organisms are inactivated. During validation, this phase is often cut short to demonstrate overkill of the decontamination cycle. The final phase of the VHP generator cycle is the aeration phase, during which the VHP is removed from the isolator after decontamination.

Materials

In this comparison study, a la Calhène three-glove transfer isolator was used. The isolator is a rigid-walled (glass and stainless steel) component with PLC control (7) and was located in a Class 10,000 environment.

The isolator contents used for this comparison are typical sterility-testing contents, including a "Steritest" device. The load contents were placed on stainless steel wire racks to reduce the amount of surface-to-surface contact within the isolator.

The two VHP generators studied use different methods to achieve biological inactivation. Although they both supply VHP to the interior of the isolator, the generators have different VHP and water concentration goals. The manufacturer of the Claris "C," BioQuell Pharma, states that the formation of microcondensation is the primary method of causing the decontamination (8–10), which requires a high level of air saturation. In contrast, the STERIS system targets higher VHP concentrations while avoiding condensation of any kind in the isolator (11,12).

To achieve these goals, the two generators use different cycle parameters, which are based on the four basic generator phases. The specific phases, as described by the manufacturers, are as follows:

STERIS VHP1000ED biodecontamination system

- Phase 1: Dehumidification. The water concentration in the isolator is reduced to the specified set point.
- Phase 2: Conditioning. A hydrogen solution is injected into the air stream to rapidly increase the VHP concentration.
- Phase 3: Decontamination. Hydrogen is injected into the system to maintain the concentration necessary for decontamination.
- Phase 4: Aeration. All the VHP and water are removed.

BioQuell Clarus "C" H_2O_2 gas generator

- Phase 1: Conditioning. The generator adjusts the relative humidity and increases the temperature.
- Phase 2: Ramp gassing. Hydrogen peroxide solution is injected into the air stream to increase the VHP concentration.
- Phase 3: Dwell gassing. Hydrogen peroxide is injected into the system to maintain the concentration necessary for decontamination.
- Phase 4: Aeration. All the VHP and water are removed.

IQ and OQ validation tests

As with all processing equipment, installation qualification (IQ) must be performed on any new VHP gas generator. During the IQ, all of the purchase orders, mechanical specifications, and drawings for the equipment should be reviewed and all the instruments must be calibrated. If the equipment has a PLC or computer control, the version of the control software should be verified. Users should conduct a software validation assessment to determine the extent of software validations necessary. All of the isolator's materials of construction should be verified for safe use with hydrogen peroxide. Finally, all of the supplied utilities (*i.e.*, supplied electricity, compressed air, and exhaust systems) should be checked to ensure that they are within the manufacturer's specifications.

In addition to the standard operational qualification (OQ) tests to ensure the equipment's operational functionality (*i.e.*, alarm and interlock testing, functionality testing, *etc.*), the OQ must include specific testing of the generator and isolator. Such testing includes leak-rate determination, pressure-differential testing, and ammonium hydroxide testing. Finally, the interrelationship between the generator and isolator must be tested. If the generator and isolator control systems communicate with each other, this communication must be challenged. Further more, the OQ must include a test that will determine if the generator progresses through all four phases of operation without any alarms.

Both VHP generator suppliers offer validation services. In both instances, it was found that additional supplemental testing was necessary to meet corporate guidelines for equipment validation. The purchased vendor validation package, however, did cover many aspects of the equipment validation that would not need to be repeated in the supplemental validation package. It is recommended that supplier validation be included with a new purchase of a gas generator, especially if it is the first system of its kind being used by the owner.

Operational tips and observations

In an effort to aid the industry with further validations of both generator systems and to improve their use, a list of tips and observations is included below.

- The pressure fluctuations of the STERIS VHP 1000ED can be large enough to set off alarms when using small volume isolators (<30 ft^3).
- A proporational integral derivative (PID) control algorithm in the VHP 1000ED controls pressure fluctuations in the isolator. The factory PID settings for this control algorithm yielded pressure fluctuations in the test isolator from −0.05 to 1.5 in. of water control. PID settings are adjustable by the user and will yield a stable pressure fluctuation when properly adjusted. In several instances, however, the PID control settings were not stored in the internal memory of the VHP 1000ED after user adjustment.
- A software bug was found on the VHP 1000ED during the validation process that causes a valve to remain open during the dehumidification phase, allowing the machine to occasionally inject VHP into the isolator, causing condensation in the interior of the isolator. Under these conditions, the cycle should be aborted. STERIS was contacted and made aware of the issue the company has made changes to the software to correct this bug. It is suggested that the most current version of the software be installed on the VHP 1000ED to eliminate this problem.
- The temperature profiling of the isolator interior is critical to a successful decontamination cycle. Successful temperature mapping will identify isolator chill plates, which are areas of the isolators interior or walls that do not increase in temperature as fast as the rest of the unit. For example, the surface of the isolator where the legs of the isolator connect to the body could become a chill plate: because the floor area above the leg contains a large mass of steel that needs to be heated, this area may be cooler than the rest of the isolator, causing localized condensation.
- During the validation of an isolator system, biological indicators (BIs), chemical indicators (CIs), and thermocouples should be hung throughout the isolator. Tape or adhesive must be placed carefully. Masking, autoclave, and electrical tape will leave a sticky residue on the surface of the isolator, and can affect the integrity of flexible PVC if it is left in the isolator for several cycles. Experience has shown that "3M Command" adhesive strips and hooks work well for hanging thermocouples, BIs, and CIs.
- The surface area of the load and the material is more important than the volume and contents of the load. Because VHP only interacts with the outside surfaces of the load content, volume has little effect on the decontamination cycle. The volume of the load containers, however, does affect the temperature response of the containers. For example, if a container holds 100 mL of liquid, the surface of the container will heat more slowly than if the same container holds 50 mL of liquid. The load containers should hold the maximum amount of liquid during the validation cycles to present the worst-case thermal load for the isolator.
- The material properties of the load contents should be checked to ensure compatibility with VHP. Cellulosic and paper materials and some flexible plastics absorb VHP. This will lower the VHP concentration in the isolator and cause the aeration phase to be extended as a result of off-gassing of the VHP by the material. VHP has a minimal effect on materials such as glass, stainless steel, aluminum, and many hard plastics such as nonwoven high-density polyethylene and polyvinyl chloride.
- Sufficient water content is required if Dräger tubes are used to measure residual VHP concentration after aeration is completed to ensure that the VHP concentration is <1 ppm. The Dräger tubes require 3–10 mg/L of water vapor in the air to give an accurate reading. If the air in the isolator is too dry, a small petri dish of water can be placed into the isolator such that the readings can be taken directly above the water.
- A glove-holding device and half-suit hangers should be used to keep gloves and half-suits from contacting any surfaces during decontamination. Gloves and half-suits are the primary method of transport of samples and test instruments within the isolator. Therefore, great care should be taken to ensure that every surface is decontaminated thoroughly.
- The room surrounding the isolator should be temperature controlled. Fluctuations in room temperature will cause fluctuations in the temperature of the isolator's exterior surface, leading to condensation on the isolator's interior surfaces. Fluctuations in the isolator's exterior surface can be caused by localized flow from the HVAC system or general fluctuations in room temperature. Therefore, it is important to consider both the temperature control of the room and the location of the HVAC vents.
- The STERIS VHP1000ED has a regeneration-scheduling feature programmed into the controller. The user can schedule the VHP 1000ED to automatically run a regeneration cycle at a specified time. This feature allows the unit to be regenerated during off-peak hours. It is suggested that users carefully consider the timing of the regeneration cycle to reduce the possibility of requiring the use of the machine during the regeneration cycle.

Equipment operational differences

The Clarus "C" and VHP 1000ED generators have many features that are similar although not identical. Both store multiple cycles, provide printouts, have alarms and safeties, and can send and receive remote input and output. The most important differences in the operation of the two machines include the methods for VHP and water removal; the use of single or dual airflow loops; the availability of a parametric gassing option; and the use of a wet or dry cycle.

VHP and water removal. Both isolators use a heavy-metal catalytic converter to break the VHP down into water and oxygen. The VHP 1000ED uses a desiccant dryer unit that absorbs and holds the water removed from the isolator until the unit is regenerated. When the unit goes through its regeneration cycle, it heats up the dryer and passes heated air through it to remove all moisture from the desiccant material. This cycle takes four to five hours to complete and must be done after approximately 1000 g of hydrogen peroxide have been injected. The Clarus "C" unit uses refrigeration principles to withdraw the water from the isolator. This system does not require regular regeneration.

Single versus dual air flow loops. The Clarus "C" has two airflow loops. One loop includes the catalyst and refrigeration unit for removing moisture and VHP from the air, and is used for the conditioning and aeration phases. The second loop is for the ramping and decontamination phases. The second loop does not include the catalyst or refrigeration units, so the VHP and water content are not removed from the isolator. The generator vaporizes additional VHP and injects it into the stream of air that already has VHP entrained.

The VHP 1000ED uses a single-loop system. As a result, the generator removes all VHP and a majority of the water content from the air stream that the generator draws from the isolator.

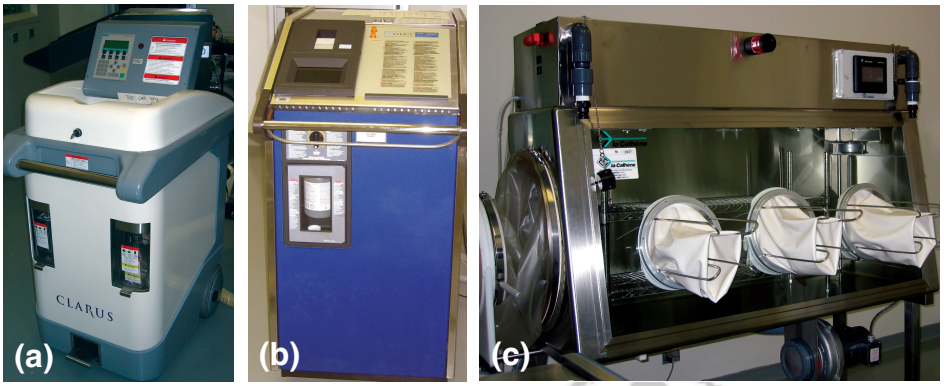


Figure 1: (a) The BioQuell Clarus "C" H_2O_2 gas generator, (b) the STERIS VHP 1000ED biodecontamination system, and (c) the la Calhène isolator used in the study.

Figure 2: Transfer isolator load.

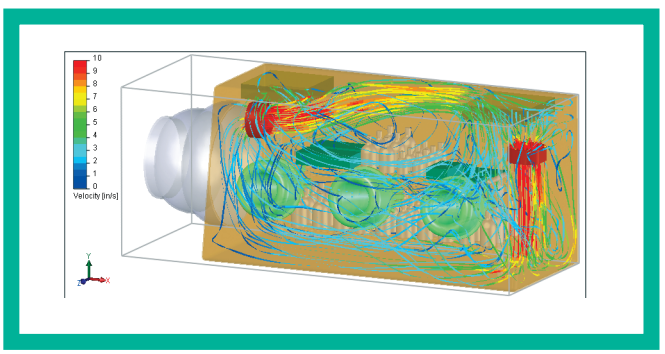


Figure 3: Flow trajectory plot.

During the ramping and decontamination phases, the unit injects VHP into this stream of dry air to maintain the VHP concentration within the isolator.

Parametric gassing. The Clarus "C" has a parametric gassing option that allows the generator to monitor the decontamination cycle and adjust parameters to meet decontamination objectives. BioQuell offers a condensation monitor that can automatically adjust the ramp gassing time based on the conditions inside the isolator. This ensures the desired VHP and water concentration levels have been reached before the dwell-gassing phase begins.

Wet versus dry decontamination cycle. The major difference between the two systems is that one uses a wet decontamination cycle and the other uses a dry cycle. The STERIS VHP 1000ED operates on the principles that dry air holds more VHP, and that the higher the VHP concentration, the higher the kill rate. Because the air inside the isolator can only hold a finite amount of VHP and water before condensation begins, the VHP 1000ED dries the air before gassing. This decontamination method, known as the dry cycle, allows the unit to produce a higher VHP concentration without condensation.

The biodecontamination method of the BioQuell Clarus "C" uses a wet-cycle with microcondensation. When hydrogen peroxide and water condense out of air they do not condense at equal rates. In fact, the hydrogen peroxide condenses at a faster rate than the water, creating a high hydrogen peroxide concentration condensate. This condensate is believed to kill organisms more quickly than VHP alone.

The microcondensation is purported to occur in extremely small droplets that are invisible to the human eye, and is required over every surface of the isolator. A challenge in validating a wet cycle is showing that every surface has conditions sufficient to yield microcondensation. Because of the high saturation level of the air, and the fine line between micro- and macro-condensation and temperature control of the room is critical if a wet cycle is used.

Performance qualification (PQ)

The objective of PQ testing in an isolator decontamination application is to demonstrate that the generator consistently biodecontaminates the isolator using a specified cycle. During PQ, decontamination is tested at the maximum and minimum isolator load conditions.

The current aseptic processing guidance have left room for interpretation in reference to the biological challenge during validation, stating, "[Decontamination] cycles should be developed with an appropriate margin of extra kill to provide confidence in robustness of the decontamination processes. Normally, a four- to six-log reduction can be justified depending on the application" (5). Even though the type of biologic challenge has not been addressed in the guidance, *Geobacillus stearothermophilus* spores have become the industry-accepted organism for the decontamination challenge (6). A rather conservative approach was used in this biodecontamination validation. The cycles used in the validation are intended to provide a minimum six-log reduction of a resistant biological indicator (BI) when exposed to an overkill decontamination cycle. *G. stearothermophilus* spores were used with a minimum initial concentration of 10^6 spores per indicator. The inactivation of 10^6 spores at the three-quarter decontamination cycle time provides a theoretical total organism reduction of 10^8 organisms for a full cycle.

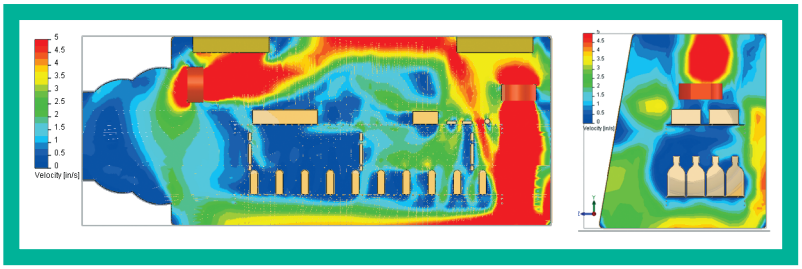


Figure 4: Velocity cut plots. (Left) 10.5 in. from rear wall. (Right) 40 in. from left wall.

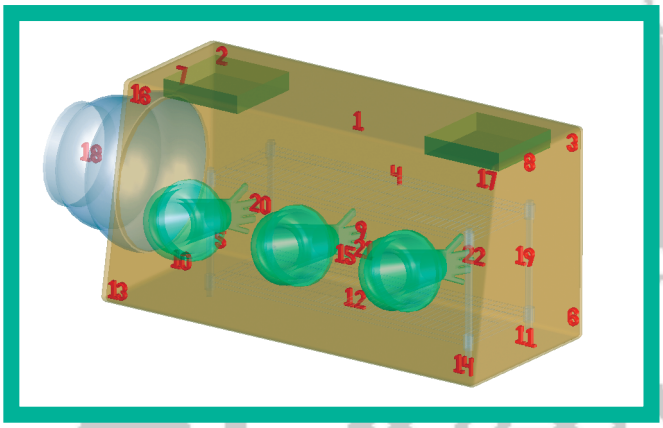


Figure 5: Location of thermocouples, biological indicators, and chemical indicators.

Table I: Settings used for each cycle during performance qualification.

Steris VHP 1000ED biodecontamination system	
Airflow 20 SCFM	
Phase I: Dehumidification	15 min and RH <4.6 mg/L
Phase II: Conditioning	2 min at 5.6 g/min
Phase III: Decontamination	34 min at 3.5 g/min
Phase IV: Aeration	2 to 5 hours
Bioquell Clarus "C" H_2O_2 gas generator	
Airflow 500 L/min (~18 SCFM)	
Phase I: Conditioning	10 min and 40% RH
Phase II: Ramp gassing	15 min at 1.5 g/min
Phase III: Dwell gassing	12 min at 1.1 g/min
Phase IV: Aeration	2.5 to 3 h

The cycle times listed above are the full cycle times. During the PQ, the VHP 1000ED's Phase III and the Clarus's Phases II and III were run at three quarters of the times listed above.

Several tests must be completed in an isolator PQ. The first step is to define the isolator load conditions for both minimum and maximum loading. Next, the user must conduct a computational fluid dynamics analysis (CFD) and/or smoke studies to determine the "worst case" airflow locations in the isolator. The last step of the PQ is the biological challenge at both the minimum and the maximum loads to prove that the stated goals of 10^6 spore reduction in a cycle time are met.

Defining the load. As with most other decontamination or sterilization processes, load determination is critical to the efficacy of the cycle. In VHP decontamination, the surface conditions of the load are the most critical factors to consider because VHP is a surface-decontamination process. The first surface condition to consider is the compatibility of the surface material with VHP. Ideally the load contents should not react with, absorb, or adsorb the VHP. Secondly, the more surface area the VHP has to interact with, the longer it will take to decontaminate all of the surfaces. Another concern is overloading the isolator. If the load is packed too tightly, there may be areas of low VHP concentration within the load resulting from to reduced airflow through the load.

The final consideration for loading an isolator is to avoid surface-to-surface contact between items or parts of the load itself, and between the load and the isolator. Areas where surface-to-surface contact occurs are less likely to receive sufficient VHP concentration, and therefore can pose a potential for contamination. To help avoid areas of surface-to-surface contact, everything should be placed on stainless steel wire racks.

The load used to test the VHP 1000ED consisted of forty-six 250-mL bottles of rinse fluid and samples, eight 100-mL vials of media, two "Steritest kits," scissors, forceps, pens, and a Dräger pump with tubes. A similar load was used to test with the Clarus "C" generator. The majority of the 250-mL bottles were placed on the bottom shelf of the two-shelf rack. The rest of the items were placed on the top shelf. The loading configuration is shown in Figure 2.

Conducting CFD and smoke studies

CFD is a finite element analysis for determining air patterns and temperature distributions around or inside a given model. The most recognizable use for this software is in the automobile and aerospace industries, where air patterns around a car or over the wing of an airplane can be modeled and analyzed. This technology can be used to analyze air patterns inside an isolator. Once the patterns are established, the areas of worst flow or temperature can be found.

There are four basic steps in conducting a CFD analysis on an isolator. The first step is to create a three-dimensional solid model of the isolator, its components, and the placement of load inside the isolator. Once the system's physical shapes and dimensions are defined, the initial fluid conditions must be established. These initial fluid conditions include properties such as temperature and flow rates of the inlet, the exhaust, any distribution fans, the isolator walls, and the air itself. When all the initial conditions have been defined, the analysis is performed.

The flow trajectories, the flow velocities, and the temperatures throughout the isolator are the three most important results of a CFD in an isolator application. VHP is distributed through the isolator by two methods: it can be directly carried on the air stream, and it also can be spread by diffusion from areas of high concentration to areas of low concentration. It is preferable for the VHP to be carried on the air stream to the decontamination site because it is distributed faster this way.

The airflow trajectory plot generated from the CFD analy-

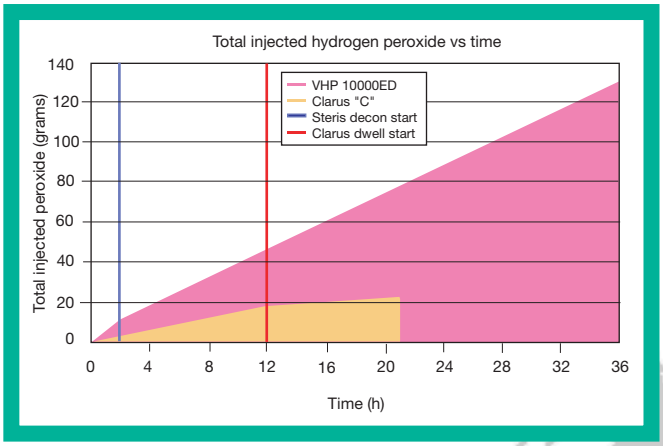


Figure 6: Total injected aqueous H_2O_2 versus time.

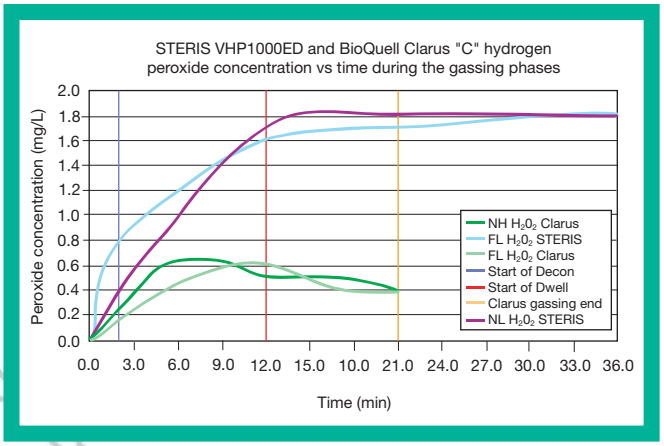


Figure 7: VHP concentration versus time.

sis, showed the approximate paths of air through the isolator and its velocity at each point (see Figure 3). The plot shows that the airflow tends to travel around the outer perimeter of the isolator, around the load, and does not flow much into the rapid transfer port (RTP).

To obtain more detailed information, air velocity cut plots were then generated at points showing the low flow areas of the isolator identified in the airflow trajectory plot. From velocity cut plots (see Figure 4), it was determined that the locations of worst flow were on the left side of the bottom shelf in between the left and middle gloves, in the RTP, and inside the sleeves of the gloves. In the velocity cut plot, higher velocity flows are shown in red while darkening shades of blue show low flows.

Smoke studies were conducted to provide a physical confirmation of the CFD analysis. During these studies, the loaded isolator was mapped with visible smoke, and the established smoke patterns were analyzed to determine the worst-case flow locations. In both generators studied, the airflow entered and exited at the same places at a similar volumetric flow rate, 20 standard ft^3/min. The smoke studies for generators yielded similar worst-case points for airflow as those seen in the CFD analysis.

Placement of thermocouples, biological indicators, and chemical indicators

Twenty-two calibrated thermocouples, biological indicator (BIs), and chemical indicators (CIs) were placed at standard locations throughout the isolator. Additionally, four thermocouples, BIs, and CIs were placed in the worst-case locations determined in the CFD and smoke studies. Worst-case points were defined as the area of lowest flow and/or lowest temperature. The BIs and CIs covered the entire interior of the isolator, with a concentration of approximately one BI and CI per cubic feet. Figure 5 shows the placement of the thermocouples, BIs, and CIs.

G. stearothermophilus was used as the BI for the PQ of both generators. The BIs were commercially prepared on a stainless steel carrier and placed into a nonwoven high-density polyethylene pouch. Because the PQ of the two machines was executed more than six months apart, two different lots of BIs, from a single manufacturer, were used. The manufacturer's certified D-value for both lots of BIs was approximately two minutes with an initial population of 2.2×10^6. An in-house confirmation of the initial population was performed according to *USP* Chapter ⟨55⟩, and it was verified that the BIs were within acceptable population limits at 1.1×10^6 organisms per carrier.

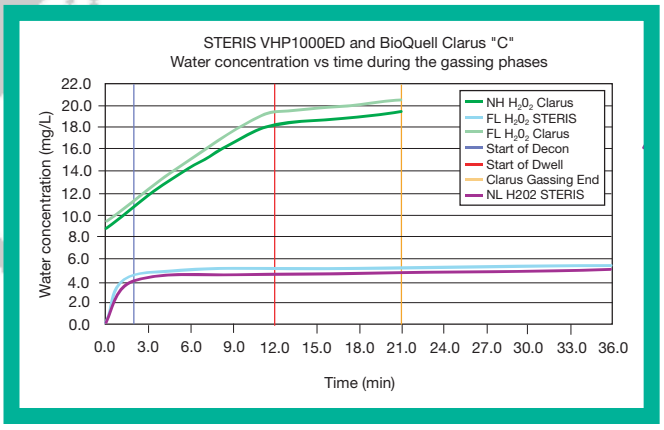


Figure 8: Water concentration versus time.

The D-value of the BIs was also tested, using a VHP biological indicator evaluator resistometer (BIER) unit (VhyPer, PSI) to expose the BIs to a controlled concentration of VHP and water vapor under a constant controlled temperature (13). This test was conducted using a square wave shuttle over various timed exposures at 32 °C with a VHP concentration of 2.0 mg/L. The test identified the D-value of the BIs as 0.2 min. This is lower than the manufacturer's specifications, probably because the VhyPer allows for more exact determination of the D-value.

Results and equipment performance differences

Separate performance qualification tests were conducted for the VHP 1000ED and the Clarus "C". Both generators' cycles passed the acceptance criteria of 100% inactivation of the biological challenge for both the minimum and maximum load conditions on three consecutive runs each. During PQ, several performance differences were noticed. The Clarus's cycle is shorter and uses considerably less hydrogen peroxide solution. In addition, the VHP and water concentration profiles differ significantly because of the differences in their methods of operation (wet versus dry).

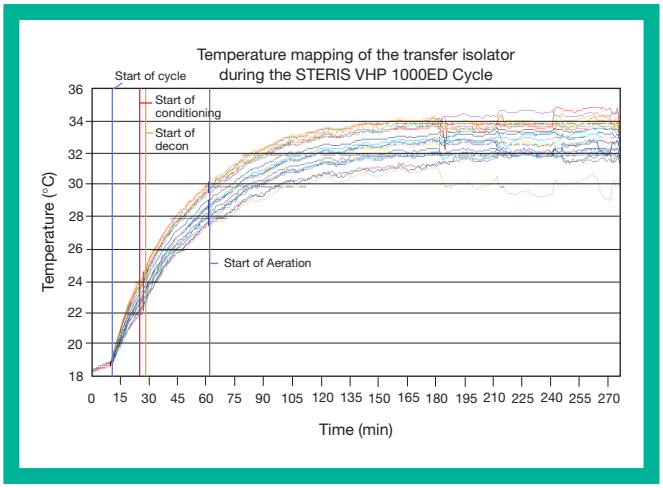


Figure 9: STERIS temperature profile.

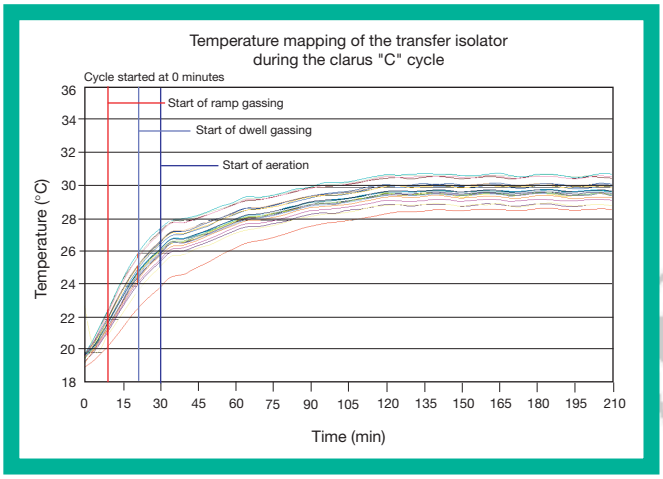


Figure 10: Clarus "C" temperature profile.

Compared biodecontamination cycles

The cycles that were programmed into each generator are listed in Table I. Aeration was continued until the isolator environment was <1 ppm VHP, as read by a Dräger pump and tube, to meet OSHA permissible exposure limit guidelines for acceptable hydrogen peroxide contact levels (14). Once the VHP level was below this limit, the cycle was considered complete and the BIs and CIs were harvested.

The first three phases (conditioning, ramping, and decontamination) of the VHP 1000ED totaled 62 min with an additional 3 to 5h of aeration, for a total cycle time of 4 to 6h. The first three phases of the Clarus "C" totaled 37 min with 2.5–3h of aeration, for a total cycle time of 3 to 3.5. Because the Clarus "C" has a shorter cycle time and lower hydrogen peroxide injection rates, it uses less hydrogen peroxide during a cycle. During the two three-quarter cycles, the Clarus "C" used 22.5 g of hydrogen peroxide whereas the VHP 1000ED used 130.2 g.

Water and hydrogen peroxide concentrations and temperatures

To monitor the concentration of VHP and water vapor in the isolator, a guided wave vapor monitor was used. The adsorption, absorption, and decomposition of VHP in an isolator will cause VHP and water concentrations to vary from the theoretical concentrations as calculated by a mass balance (15). The guided wave vapor monitor uses near infrared spectroscopy to measure the actual VHP and water vapor concentrations in mg/L (15). The guided wave's probe was positioned in the approximate center of the isolator to determine the concentrations in and around the load. Because the guided wave measures VHP and water vapor continuously, these concentrations can be measured over time during the generator decontamination cycle. Figures 6 and 7 show the concentration profiles of VHP and water vapor during the gassing cycles. In both instances the maximum and minimum load conditions are plotted. The readings gathered from the guided wave guaranteed that the isolator and load had similar vapor concentrations profiles from run to run.

Because the VHP 1000ED and the Clarus "C" use different biodecontamination methods (wet versus dry) VHP and water levels were different in the two generators (see Figures 8 and 9). The VHP 1000ED had significantly higher VHP concentrations throughout the cycle than the Clarus "C." In contrast, the VHP 1000ED has significantly lower water concentrations throughout the cycle. The similarity between the maximum- and minimum-loaded conditions demonstrates that the load contents had little effect on the VHP concentrations during the gassing cycle.

The temperature profiles for the two generator systems are shown in Figures 9 and 10.The temperature profiles for the two generators are very similar. In other generators, the temperature increased continuously during the decontamination phase and did not reach a steady state temperature until the aeration phase.

Conclusion

After completing an installation qualification, operational qualification, and performance qualification, and comparing the operation and performance of the STERIS VHP 1000ED Biodecontamination System and BioQuell Clarus "C" H_2O_2 gas generator, it can be concluded that both units can be validated, and are capable of effectively decontaminating an isolator. There are differences between the two systems; however, these differences do not affect the effectiveness of either unit to decontaminate an isolator system.

References

1. R. Friedman, "Design of Barrier Isolators for Aseptic Processing: A GMP Perspective," *Pharm. Eng.* **18** (2), 28–33 (1998).
2. J.C. Lyda, "Regulatory Aspects of Isolator/Barrier Technology," PDA Pharm. Sci. Tech., 49 (6), 200–304 (1995).
3. C.M. Wagner and J. Raynor, "Industry Survey on Sterility Testing Isolators: Current Status and Trends," *Pharm. Eng.* **21** (2), 124–140 (2001).
4. J. Lysfjord and M. Porter, "Barrier Isolation History and Trends, A Millennium Update," *Pharm. Eng.* **21** (2), 142–145 (2001).
5. Food and Drug Administration, *Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing–Current Good Manufacturing Practice* (FDA, Rockville, MD, 2001).
6. "Hydrogen Peroxide Vapour Biological Efficacy," V2.5 (BioQuell Pharma, Andover Hampshire, United Kingdom, February 2003).
7. "La Calhène Three Glove Transfer Isolator User's Manual," (La Cal-

hène, Vendome, France).
8. R. Watling and C. Parks, "Theoretical Analysis of the Condensation of Hydrogen Peroxide Gas and Water Vapour as Used in Surface Decontamination," *Pharm. Sci. Tech.* **56** (6), 291–299 (2002).
9. Clarus "C" User Manual, STD2000-005, Rev. 4 (BioQuell Pharma, Andover Hampshire, United Kingdom, 2002).
10. Cycle Development Guide, STD2000-006, Rev. 1, (BioQuell Pharma, Andover Hampshire, United Kingdom, 2002).
11. VHP 1000ED Biodecontamination System Operator Manual, (STERIS Corporation, Erie, PA, 2002).
12. VHP 1000ED-C Biodecontamination System Maintenance Manual, (STERIS Corporation, Erie, PA, 2003).
13. D. Khorzad *et al.*, "Design and Operational Qualification of a Vapor-Phase Hydrogen Peroxide Biological Indicator Evaluator Resistometer (BIER) Uni," *Pharm. Technol.* **27** (11), 84–90 (2003).
14. M. Ebers, MSDS No. A121, "Hydrogen Peroxide Solution (31%–35%)", STERIS, 19 February 2002.
15. G.P. Brown, et al.,"Calibration of Near-Infrared (NIR) H_2O_2 Vapor Monitor," *Pharm. Eng.* **18**, (6), 66–76, (July–August 1998).

FYI

AAPS announces 2004 fellows

The American Association of Pharmaceutical Scientists (AAPS, Arlington, VA, www.aapspharmaceutica.com) has unveiled its annual list of AAPS Fellows. This year, 24 people were honored for professional excellence in the pharmaceutical sciences:

Kevin D. Altria, PhD
Jeffrey S. Barrett, PhD
Ronald R. Bowsher, PhD
Richard N. Dalby, PhD
John W.A. Findlay, PhD
Joseph C. Fleishaker, PhD
Joseph A. Fix, PhD
Andrea Gazzaniga, PhD
Bruno C. Hancock, PhD
Guenther Hochhaus, PhD
Jin-Ding Huang, PhD
Peter F. Kador, PhD
Peter Kleinebudde, PhD
Ah-Ng Kong, PhD
Jean W. Lee, PhD
Hans Lennernäs, PhD
Joyce J. Mordenti, PhD
Ram B. Murty, PhD
Fridrun Podczeck, Dr. sc. nat. habil
Joseph W. Polli, PhD
Jagdish Singh, PhD
Tetsuya Terasaki, PhD
Peter Veng-Pedersen, PhD
Lawrence X. Yu, PhD