ADVANCED BARRIER
CONCEPTS, INC.
BE SECURE WITH OUR KNOWLEDGE

Corporate Capabilities

Advanced Barrier Concepts, Inc. promotes scientific and technical excellence through consulting relationships with world-class corporations, establishing best practices in advanced aseptic manufacturing and testing.

For solutions to isolation or advanced aseptic processing challenges, contact …

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Advanced Barrier Concepts, Inc. is a scientific and technical services firm dedicated to the advancement of state-of-the-art barrier isolation, aseptic processing, and sterilization system technologies for the pharmaceutical, biotechnology, and medical device industries.

Advancing Scientific Practice Standards

Today, the use of isolators in the laboratory has become standard practice for sterility testing activities. The FDA's September 2004 publication "Pharmaceutical cGMPs for the 21st Century" brings isolation technology to the manufacturing environment citing regulatory support and encouragement for the early adoption of new technical advances for the pharmaceutical and biotechnology industries. The ability to decontaminate the exposed surfaces of an isolator and its production equipment to a high level using reproducible and validated methods is a major reason for regulatory support because of the increase in the SAL of an aseptically filled sterile product using this technology. A well-designed isolated system provides an aseptic processing environment as well as a barrier against human and environmental contamination.

Selecting the Right Partner

Transforming from conventional aseptic processing to an Isolation Solution is an important decision. For you to efficiently and effectively transform your operation to take full advantage of all the benefits isolation technology offers, you need someone you can trust… an organization with broad scientific, technical and regulatory knowledge that can do the job right.

Advanced Barrier Concepts, Inc. is that partner…

- We have been a pioneer and a leader in the application of isolation technology to advanced aseptic processing equipment since 1994, the earliest stages of industry development.
- Our ongoing process of innovation – and our ever-expanding knowledge base – continues to refine, redefine and open up an exciting world of opportunities and abilities for all our clients.
- We offer the exceptional levels of experience and skills required to successfully lead your company through the implementation process from initial concept through validation.

CONTENTS:

Company Principals

James R. Rickloff, MS
Partner / Scientific Director

William C. Little, BME
Partner / Technical Director

Leading the team at **Advanced Barrier Concepts, Inc.** are Jim Rickloff and Bill Little, both experts in the application of isolation technology into aseptic processing and sterilization systems. Their expertise has been obtained through experience working with leading equipment vendors along with pharmaceutical and biotech end users of the technology. Their background encompasses research and development on these systems as well as implementing them on a broad range of domestic and international projects.

Advanced Barrier Concepts, Inc.'s professional alliances allow the company to provide a team capable of providing specific client application solutions necessary for a successful integration of your isolator system into your sterility testing or advanced aseptic processing application. The Advanced Barrier Concepts, Inc. and its team of professionals will be there to support the client's needs from process definition through system qualification.

Advanced Barrier Concepts, Inc. utilizes a GAMP® management structure that ensures systematic project control and documentation traceability from user requirement specifications thru the execution of the performance qualifications. This structure will help to make certain that the detail for the packaged process equipment will be fully addressed. It will also provide project control from start to finish that will allow personnel changes without affecting project integrity. Work with experienced partners who can guide you through all phases of concept development through project implementation and validation execution.

Services

Advanced Barrier Concepts, Inc. offers the complete spectrum of support services required for the implementation of isolated sterility testing and aseptic filling applications. Services range from feasibility and conceptual design to planning and project management to validation and operator training.

User Requirements Specifications

Accurately define your requirements to improve system performance, set clear client/vendor expectations, minimize change orders, control cost, and maintain schedule.

Systems Integration

Work closely with client and equipment manufacturers to select, integrate, and validate the equipment required to support aseptic processing and sterility testing isolation applications.

Facility Planning

Ensure that the isolators and associated decontamination equipment, safety systems, exhaust systems, and facility layout provide for smooth installation and optimal system performance.

Validation Planning

The development of a good manufacturing system requires planning not just for the technical details of the engineering, but also from a regulatory perspective. A validation master plan, which is developed properly during the early phases of project planning, can provide a significant savings in time and resources and lead to faster facility licensing. Advanced Barrier Concepts, Inc. has the experience to integrate key design decisions and important validation strategic decisions into a comprehensive document relating the design rationale to the validation strategy. This seamless approach to validation takes the guesswork out of developing a realistic equipment and process validation schedule

Vendor Management

A key to successfully executing a project is to clearly communicate and educate each vendor regarding the technical expectations, project timeline milestones, and documentation requirements unique to each client. This includes regular project meetings, periodic design reviews (including isolator mock-ups that challenge the ergonomics and operation of the system), plus drawing and documentation reviews. Advanced Barrier Concepts, Inc. can assist in the professional management of isolation and aseptic equipment related projects from start to finish. Acting as a customer advocate, we can coordinate complex vendor relationships and ensure that the right scientific, validation, and engineering questions get answered before the equipment arrives on plant site.

Factory Acceptance Testing

The more thoroughly the system is tested in the factory, the greater the assurance that the system will operate as intended in the field, thereby facilitating installation, validation, and start-up. Advanced Barrier Concepts, Inc. will test total systems (both mechanical and microbiological parameters) before they leave the factory floor to eliminate unpleasant surprises during start-up and validation. At the same time, equipment vendors will become educated on the principles of pharmaceutical processing, isolator system design, sterilization, client documentation standards, and current or proposed good manufacturing practices.

Site Acceptance Testing

The system is challenged under field conditions, plus factory test punch list items are finally reviewed and closed in preparation for validation.

Installation and Operational Qualification

Testing a system per your quality system and the most current industry standards will provide you with the most consistent comprehensive equipment validation program throughout your plant. ABC can address individual equipment validation issues as well system-wide interface challenges.

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Process Development / Cycle Development
Optimize the decontamination cycle of the qualified equipment to provide the most efficient turn-around times or the decontamination cycle can be tuned to achieve certain process specific goals.

Performance Qualification
Properly and efficiently challenge your isolator decontamination process to account for your unique process characteristics plus comply with the best practices on current US and European systems.

SOP Development
In-house existing procedures may need to be adapted to isolated equipment or you may need guidance on writing new documents. ABC has a broad range of experience in the best industry practices

Operator Training
Provide proper documentation and hands-on teaching to ensure that your operators are thoroughly trained to understand and embrace the new technologies that they will be working with on a daily basis.

Annual Requalification
ABC knows how to set-up and execute an annual re-qualification program that keeps your system in compliance but still maximizes efficiency to keep you up and running in production.

Advanced Barrier Concepts, Inc. is the trusted resource of many of the world's leading pharmaceutical manufacturers. Their repeated confidence reflects our ability to continually set benchmark standards of quality and service. We invite you to review some of our completed projects for our valued clients.

AAI, Inc. (Wilmington, NC)

- Performed Factory Acceptance Testing and Site Acceptance Testing for a SKAN Bioburden Testing Isolator System / Sterility Test System.
- Performed the IQ, OQ, and developed the PQ testing protocols.
- H_2O_2 gas D-value determination of test carriers.
- Executed Cycle Development and Performance Qualification protocols for the decontamination process on both isolators.
- Developed the SOP for the set-up and operation of the sterilant generator to support the execution of a validated isolator decontamination cycle.
- Sterile challenge protocol development and execution support.

Abbott (Barceloneta, PR)

- Developed the User Requirement Specifications, Equipment Specifications, and Factory Acceptance Testing Specifications for a Bioburden Testing Isolator System.
- Reviewed / specified the facility's requirements for the isolated system.
- Developed the Validation Master Plan that determined the requirements for the qualification of the processes associated with the Bioburden Test Isolator System.
- Developed IQ, OQ, and PQ testing protocols.
- Executed Cycle Development and Performance Qualification protocols for the decontamination process.
- Developed the SOP for the set-up and operation of the sterilant generator to support the execution of a validated isolator decontamination cycle.

Acambis, Inc. (Canton, MA)

- Provided conceptual design support for a production aseptic processing fill/lyophilize manufacturing facility. The following three designs were explored for this project: conventional aseptic processing in a clean room, a totally isolated filling system, and an aseptic processing design that utilized the RABS (Restricted Access Barrier System) technology.
- Provided current technical information regarding the validation of an isolator and a RABS system.
- Provided input for the FDA's 2004 initiative, "Pharmaceutical CGMPs for the 21st Century", relative to how a specific aseptic processing design will impact the Agency's procedure regarding facility reviews.

Acambis, Inc. (Rockville, MD)

- Reviewed / revised the URS, DDS, mock-up procedures, and the FAT and SAT protocols for a la Calhéne lyophilizer interface isolator and an autoclave/depyrogenation oven interface isolator.
- Executed the mock-up, FAT, and the SAT for the two interface isolators.
- Developed the commissioning protocols for the two interface isolators and for an IsoTech filling isolator, three IsoTech transfer isolators, and two VHP1000 Biodecontamination systems.
- Executed the commissioning protocols.
- Reviewed / revised the SOPs for the set-up and operation of the equipment.

Acambis, Inc. (Rockville, MD)

- Qualification of a lyophilized aseptic filling isolator system consisting of a filling isolator (IsoTech), lyophilizer interface isolator (la Calhéne), autoclave/depyrogenation oven interface isolator (la Calhéne), and three transfer isolators (IsoTech) decontaminated using a VHP1000 Biodecontamination System.
- IQ/OQ/CD/PQ protocol development and execution for the six isolators and two VHP1000 H_2O_2 generators. Equivalency testing performed for two transfer isolators and the second VHP1000 generator.
- BI resistance testing using a transfer isolator.

Agracetus, Inc. / Auragen, Inc. (Middleton, WI)

- Sterile process development for Phase 1 Clinical DNA Product and system validation of an Isolation Technologies rigid wall isolator, sterile transfer systems, autoclave, and VHP1000 generator.
- Environmental monitoring of the isolator, laminar flow hoods, and the manufacturing area. Revalidation performed after equipment modifications
- Participation in SOP development and reviews.

Allergan, Inc. (Waco, TX)

- Facility design review and optimization (HVAC air exchanges, temperature control).
- Validation protocol development and execution of a la Calhéne flexible wall sterility test isolator system and VHP1000 Biodecontamination System.
- H_2O_2 gas D-value determination of test carriers.

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Allergan, Inc. (Irvine, CA)

- IQ/OQ/CD/PQ protocol development and execution for an IsoTech HemiSphere half-suit isolator, an IsoTech IsoSphere isolator, and a VHP1000 Biodecontamination System.
- BI resistance testing using the IsoSphere isolator.
- Sterilant intrusion and residue effects protocol generation and execution to determine if H_2O_2 can penetrate into product containers and environmental monitoring supplies at levels that could lead to false negatives.

Amgen Limited (Juncos, Puerto Rico)

- Qualification of a Carlisle Barrier (Walker Barrier) sterility testing system that consisted of two rigid wall 3-glove transfer isolators, a rigid wall dual half-suit workstation isolator, and two STERIS VHP1000ED-AB generators.
- Validation master plan, URS, and operational SOP development.
- BI D-value resistance testing in a transfer isolator protocol development and execution.
- Advanced decontamination cycle development testing.
- IQ/OQ/PQ protocol development and execution.
- Sterilant intrusion and residue effects protocol generation and execution to determine if H_2O_2 can penetrate into product containers and environmental monitoring supplies at levels that could lead to false negatives.

Amgen (Providence, RI)

- Qualification of a Walker Barrier sterility testing system that consisted of two rigid wall 3-glove transfer isolators, a rigid wall dual half-suit workstation isolator, and two STERIS VHP1000ED-AB generators
- Provided a technical review (GAP Analysis) of the original validation and determined that the testing was not properly conducted (validation short-falls) to support repeatable and robust decontamination cycles.
- VHP1000ED-AB User Requirements Specifications (URS) development
- VHP1000ED-AB IQ/OQ protocol development and execution
- BI D-value resistance testing in a transfer isolator protocol development and execution.
- CD/PQ protocol development and execution.
- Sterilant intrusion and residue effects protocol generation and execution to determine if H_2O_2 can penetrate into product containers and environmental monitoring supplies at levels that could lead to false negatives.
- Maintenance of Asepsis within the Workstation Isolator protocol generation and execution to verify a 30-day hold time period between decontamination cycles.
- SOP development
- Operator training to provide an overall understanding of the capabilities and limitations of the equipment.

Amgen (Thousand Oaks, CA)

- Validation Planning and Execution Support for two (2) Walker Barrier sterility test single half-suit isolators with adjoining airlock and two (2) VHP1000ED-AB Biodecontamination systems.
- Equipment and facility final design reviews and optimization (HVAC air exchanges, temperature control, sterilant manifold).
- Process equipment and isolator User Requirements Specifications (URS) development.
- Mock-up evaluation and pre-FAT to properly assess the design, construction, and test plan.
- FAT and Commissioning protocol development and execution.
- IQ/OQ/CD/PQ protocol development and execution for the process equipment and isolator systems.
- SOP development and operator training.
- TOP (Turn Over Package) generation.

Apotex (Richmond Hill, ON)

- Validation Planning and Execution Support for an isolated vial filling system that consists of a la Calhéne Filling isolator, Accumulation isolator, Transition isolator and two (2) STERIS VHP1000 Biodecontamination systems.
- Validation master plan development.
- Facility design review and optimization (HVAC air exchanges, temperature control).
- Process equipment and isolator User Requirements Specifications (URS) development
- FAT/SAT protocol development and execution
- Process equipment and isolator system validation (IQ/OQ/PQ)
- Process development involving isolation and hydrogen peroxide gas decontamination.
- SOP Development

Apotex (Richmond Hill, ON)

- Provided technical support for the upgrade of a 1995 la Calhéne 4-isolator aseptic filling system to incorporate 21st century isolation and sterilization technologies, which included current system evaluation and viable upgrade design concepts.
- Interfaced with equipment vendors to ensure that the proposed designs would provide the required operational parameters and could be easily integrated to provide a system that could be validated.

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APP, Inc. (Grand Island, NY)

- IOQ and Validation protocol development and execution of a la Calhéne two half-suit flexible wall sterility test workstation isolator, two 3-glove flexible wall transfer isolators, and two STERIS VHP1000ED Biodecontamination systems.
- Successful revalidation of decontamination cycles and equivalency testing on second VHP1000ED-AB.
- Performed D-value testing on test Biological Indicators for validation testing.
- Developed the Cycle Development and Performance Qualification test protocols for a SKAN ARIS Sterility Test System.
- Executed Cycle Development and Performance Qualification protocols for the decontamination process.

AstraZeneca, Inc. (Westborough, MA)

- Facility design review and optimization (sterilant generator manifold).
- Validation protocol development and execution of a rigid wall sterility test isolator system, including autoclave-interface and VHP1000.
- H_2O_2 gas D-value determination of test carriers.
- SOP Generation.
- Annual revalidation services, including BI resistance testing.

AstraZeneca, Inc. (Westborough, MA)

- Reviewed / revised the URS, FRS, DDS, and FAT for a new sterility testing isolator system that was comprised of two 3-glove la Calhéne soft-wall transfer isolators, a dual half-suit soft-wall workstation isolator and two STERIS VHP1000ED-AB Biodecontamination Systems.
- Reviewed / revised isolator and P&ID drawings.
- FAT execution team member for both isolator systems.
- Supervised isolator system installation at client facility.
- Designed VHP circuit to allow the decontamination of the complete isolator system using either of the two hard piped (stationary) VHP 1000 generators. The design included heat taping and insulation of the supply and return piping with a temperature feedback circuit.
- Designed a Dräger H_2O_2 gas monitoring system where the sensors when activated send a signal to a Dräger QuadGard controller to activate a warning strobe light and audible alarms, abort the decontamination cycle, and send an alarm signal to the security guard station.
- IQ/OQ/CD/PQ protocol development and execution for the three la Calhéne isolators and two VHP1000 generators.
- Sterilant intrusion and residue effects protocol generation and execution to determine if H_2O_2 can penetrate into product containers and environmental monitoring supplies at levels that could lead to false negatives.
- BI resistance testing using a transfer isolator.
- Developed the SOP for the set-up and operation of the equipment.
- Provided a one-day combined classroom / hands-on training session to provide an overall understanding of the capabilities and limitations of the technology.
- Annual revalidation services, including BI resistance testing.

Aventis Pasteur Clinical Manufacturing Area (Swiftwater, PA)

- FAT protocol development for clinical filling facility isolators.
- IQ/OQ/PQ protocol development and execution on VHP1000 and clinical filling facility isolators.
- H_2O_2 gas D-value determination of test carriers.
- Environmental qualification and monitoring plan development.
- Media fill / sterile challenge protocol development and execution support.

Aventis Pasteur Production Facility (Swiftwater, PA) *

- Validation planning and execution support for an isolated high speed vial filling system that consisted of a Despatch Industries MAFS® isolator designed with Infeed, Filler, and Outfeed sections and was decontaminated with a single STERIS VHP1000 Biodecontamination system.
- IQ/OQ protocol development and execution for the VHP1000 generator.
- CD/PQ protocol development and execution.
- BI resistance testing of spore suspension directly inoculated onto stainless steel carriers.
- UV D-value determination of test carriers.
- UV pass-through chamber Cycle Development and PQ protocol generation and execution.
- Media fill / sterile challenge assistance.
- Drafted Regulatory Licensing documents.
- Provided operator training on all process equipment in formal training program
- System annual revalidation testing.

* ONE OF THE INITIAL ISOLATED ASEPTIC FILLING LINE INSTALLATIONS (1997) IN THE USA.

Aventis Pasteur (Toronto, Ontario)

- VHP1000 cycle optimization and successful revalidation in an existing sterility test lab.
- VHP1000 PQ and equivalency protocol development and execution in a relocated sterility test lab.

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Baxter Healthcare Corp. (Boulder, CO)

- STERIS VHPM1000 modular generator IQ/OQ, Cycle Development, and PQ protocol development and execution on a Metall + Plastic clinical filling isolator.
- VHP1000 and sterility testing isolator IQ/OQ and PQ protocol development and execution.
- H_2O_2 gas D-value determination of test carriers.

Biopure, Inc. (Cambridge, MA)

* System specification and design review of a rigid wall IsoTech 2-glove IsoTransfer® sterility test isolator system.
* H_2O_2 gas D-value determination of test carriers.
* IQ/OQ and PQ protocol development and execution on VHP1000 and sterility testing isolators.
* Design review of hydrogen peroxide liquid, hydrogen peroxide spray/fog, hydrogen peroxide gas, and steam sterilization processes for a Form-Fill-Seal machine used for IV solution filling.

BioReliance Corporation (Rockville, MD)

- Facility review, design consultation, and process development for a sterile batch injectable clinical filling line that consisted of an IsoTech rigid wall filling isolator, a Hemisphere® soft wall depyrogenation oven interface isolator, three 3-glove rigid wall transfer isolators, and two STERIS VHP1000 Biodecontamination systems.
- Validation Master Plan support.
- IQ/OQ protocol development and execution for the two VHP1000 generators.
- CD/PQ protocol development and execution for the five isolator systems.
- BI resistance testing in a transfer isolator.

Bristol Myers Squibb (New Brunswick, NJ)

- Validation planning and execution support for an isolated filling/lyophilization system that consisted of a SKAN Filling isolator, a SKAN Lyo Loading isolator, a Carlisle Barrier (Walker) Formulation isolator, and a VHP1000 Biodecontamination system.
- Review and revise process equipment and isolator User Requirements Specifications (URS).
- VHP1000 cycle development testing for the Formulation isolator.
- IQ/OQ/PQ supplemental protocols to vendor qualification packages when required or in lieu of these packages when not provided by the process equipment manufacturers.
- Isolated equipment mock-up support.
- FAT/SAT protocol development and execution.
- Process equipment and isolator system validation (IQ/OQ/PQ)
- Process development involving isolation and hydrogen peroxide gas decontamination.

Bristol Myers Squibb (Devens, MA)

- Validation execution support for a bioburden test isolator system that consisted of two Walker Barrier 3-glove flexible wall isolators and a portable STERIS VHP100S-P Biodecontamination system.
- CD/PQ protocol development and execution.
- Sterilant intrusion and residue effects protocol generation and execution.

Covidien (Raleigh, NC)

- Walker Barrier 4-glove rigid wall Sterility Test Isolator IQ/OQ protocol development and execution.
- VHPM100-ABX IQ/OQ, cycle development, and PQ protocol development and execution.
- BI resistance testing.
- Sterilant intrusion and residue effects protocol generation and execution to determine if H_2O_2 can penetrate into product containers and environmental monitoring supplies at levels that could lead to false negatives.
- Operator training.

Eisai, Inc. (Research Triangle Park, NC)

- Walker Barrier 4-glove rigid wall sterility test isolator.
- VHP1000ED Cycle Development testing to determine “Nominal” H_2O_2 exposure and “Production” aeration parameters.

Genentech, Inc. (Hillsboro, OR)

- Validation execution support for an isolated aseptic liquid filling system that consisted of a SKAN Filling isolator; an isolated aseptic lyophilization system that consisted of a SKAN Filler isolator, Buffer isolator, and Loader isolator; and two SKAN ARIS sterility testing isolator systems.
- Smoke testing protocol generation and execution for the three isolation systems.
- BI resistance protocol generation and execution using a SKAN ARIS isolator.
- CD/PQ protocol development and execution for the two SKAN ARIS sterility testing isolator systems.
- CD/PQ protocol development and execution for the two SKAN aseptic processing isolator systems.

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Genzyme (Framingham, MA)
- GAP analysis to verify that the VHP®1000ED decontamination cycles developed for both an IsoTech IsoTransfer™ and Hemisphere™ In*terface isolators incorporated regulatory and industry guidelines.
- VHP® Sterilization Technology training for Validation and Quality personnel.

Glaxo-Wellcome (Research Triangle Park, NC)
- Facility design review and optimization (HVAC air exchanges, exhaust systems).
- Validation protocol reviews and validation execution assistance for a flexible wall sterility test isolator with autoclave interface system.

Intarcia Therapeutics (Hayward, CA)
- Validation execution support for three Walker Barrier aseptic filling isolator systems interfaced with a VHP®1000 Biodecontamination System.
- CD/PQ protocol development and execution.
- BI resistance protocol development and execution.

Janssen Biologics BV (Leiden, Netherlands)
- Determined the cause(s) for H_2O_2 gas concentration reduction and provided a recommended corrective action plan for a Getinge flexible wall workstation isolator integrated with a VHP®1000ED.

Jubilant HollisterStier Corp. (Spokane, WA)
- Validation planning and execution support for a Walker Barrier rigid wall 4-glove aseptic filling isolator integrated with a Bioquell IG-1 hydrogen peroxide generator system.
- H_2O_2 cycle development protocol generation and execution for the FAT and SAT (triplicate testing of cycle defined during the FAT), which included aeration studies to ≤1.0ppm.
- BI resistance protocol development and execution.

Lancaster Labs (Lancaster, PA)
- IQ/OQ/PQ protocol development and execution of a la Calhéne flexible wall sterility test isolator system.
- Facility design review for isolator external exhaust optimization and room control (# air exchanges, temperature).
- Successful revalidation of decontamination cycles and equivalency testing on second VHP1000.
- New laboratory design review, exhaust system design/qualification and post-relocation equivalency revalidation studies of the sterility test isolator suite.
- H_2O_2 gas D-value determination of test carriers.
- IQ/OQ and PQ protocol development and execution of a double-door autoclave and adjoining interface isolator.

McGaw (B. Braun), Inc. (Irvine, CA) *
- Validation planning and execution support for a sterile liquid and powder high speed filling process that consisted of an IMA 4-isolator filling system and two STERIS VHP1000 Biodecontamination systems.
- Isolator design consultation (e.g. sterilant port locations, generator/isolator control issues).
- CD/PQ protocol development and execution.

  * ONE OF THE INITIAL ISOLATED ASEPTIC FILLING LINE INSTALLATIONS (1997) IN THE USA
- CD/PQ protocol development and execution for the second sterile liquid and powder high speed filling process (duplicate of initial line).
- CD protocol development and execution for the third sterile liquid and powder high speed filling process (same design as lines 1 and 2).

Merck & Co., Inc. (Elkton, VA)
- Design consultation and process development including sterilant manifold systems into the production areas for a sterile bulk powder filling application in rigid wall isolators (Total Process Containment) decontaminated using STERIS VHP1000 Biodecontamination systems.
- Sterilizable transfer system development assistance for bulk powder transport and delivery in disposable bags.
- VHP1000 IQ/OQ and FAT cycle development.
- H_2O_2 gas D-value determination of test carriers.
- PQ protocol development and execution on 5 isolators and 5 VHP1000s, including successful equivalency studies on the multiple generator system.

Merck & Co., Inc. (Elkton, VA)
- Generated a *CONCEPTUAL DESIGN STUDY* that explored the viability of three different concepts that incorporated only available technology that would convert an existing sterile powder filling operation inside isolators, which had product packaging manufacturing stages that did not support asepsis operations, into a completely closed aseptic process from fill through final bulk product packaging.
- Identified all the equipment and components required to implement each viable design.
- Performed a risk analysis for each of the viable designs.
- Provided cost estimate for each of the viable designs.

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Merck & Co., Inc. (West Point, PA) *

- Barrier technology prototype research, development, and feasibility testing.
- Peroxide Plus™ (steam/H_2O_2) sterilization methods development and testing.
- Factory Acceptance Testing, IQ, and OQ protocol development and execution of an isolated (Despatch Industries isolator system integrated with a Peroxide Plus sterilization process) high speed TL filling system that consisted of a vial washer, depyrogenation tunnel, filler, stoppering and capping systems, and related systems (i.e. isolator CIP, product pathway CIP/SIP, sterilizable transfer ports, stopper lift system).

* ONE OF THE INITIAL ISOLATED ASEPTIC FILLING LINE INSTALLATIONS (1997) IN THE USA

Merck & Co., Inc. (West Point, PA: BTMC- Biotechnology Manufacturing Complex)

- Leak remediation of prototype seed lab isolator system.
- VHP1000 IQ/OQ/CD and PQ protocol development and execution of a seed lab isolator system that consisted of two (2) Total Process Containment rigid wall isolators and a STERIS VHP1000 Biodecontamination system.

Merck, Sharpe & Dohme, Inc. (Clermont-Ferrand, FRANCE)

- Design consultation and process development for a sterile batch ophthalmic isolated filling line that consisted of three la Calhéne rigid wall isolators, a flexible wall transfer isolator, and three STERIS VHP1001 Biodecontamination systems.
- VHP1001 FAT cycle development testing on filling line isolators at la Calhéne (France) and IMA (Italy).
- IQ/OQ and PQ protocol development and execution for three (3) rigid wall isolators, one (1) soft wall isolator and three (3) VHP1001s.
- H_2O_2 gas D-value determination using spore suspension inoculated on test carriers manufactured from the system's materials of construction.
- Successful revalidation of decontamination cycles.

Merck, Sharpe & Dohme, Inc. (Clermont-Ferrand, FRANCE)

- H_2O_2 gas D-value determination using spore suspension inoculated on stainless steel carriers.
- IQ/OQ and PQ protocol development and execution for the second sterile batch ophthalmic isolated filling line (duplicate of initial line).

Merck, Sharpe & Dohme, Inc. (Clermont-Ferrand, FRANCE)

- Design consultation and process development for an isolated sterile filling/lyophilization line that consisted of three (3) rigid wall la Calhene filling isolators, six (6) rigid wall lyophilizer isolators, one (1) rigid wall inspection isolator, one (1) rigid wall capping isolator and ten (10) Steris VHP1001 Biodecontamination systems. The filling line was supported by two (2) la Calhene flexible wall transfer isolators, decontaminated using an eleventh STERIS VHP1001 generator, to aseptically transfer presterilized supplies, tools, and/or machine components required for the manufacturing process. The filling line was also supported by a sterility testing suite that consisted of a la Calhene flexible wall workstation isolator, a flexible wall transfer isolator and a twelfth STERIS VHP1001 generator.
- VHP1001 cycle development protocol generation and execution for the three filling/lyophilization line isolator systems, the two support transfer isolator systems, and the sterility test isolator system.
- VHP1001 equivalency testing using the Guided Wave NIR sensor technology protocol generation and execution.
- IQ/OQ and PQ protocol development and execution for the three filling/lyophilization line isolator systems, the two support transfer isolator systems, the sterility test isolator system, and the twelve (12) STERIS VHP1001 generators.
- Sterilant intrusion and residue effects protocol generation and execution.

Millennium Pharmaceutical (Cambridge, MA)

- Designed and oversaw fabrication of an isolated integrated mammalian cell culture and purification system.
- Integrated process equipment with isolators
- Developed and executed environmental monitoring plans
- Validated (IQ/OQ/PQ) all process equipment and decontamination processes.

Monsanto (Augusta, GA)

- Design consultation and process development for an isolated sterile syringe filling line and support processes that consisted of a Carlisle (Walker) Barrier rigid wall filling isolator with integrated STERIS VHP M1000 modular Biodecontamination system, a rigid wall combination isolator with integrated STERIS VHP M1000, and five (5) rigid wall support isolators including a sterility test isolator that were individually decontaminated using a STERIS VHP1000 mobile generator.
- Facility design review for isolator external exhaust optimization and room control (# air exchanges, temperature).
- FAT protocol execution at isolator vendor.
- H_2O_2 gas D-value determination of test carriers.
- IQ/OQ and PQ protocol development and execution for the seven (7) filling and support isolator systems, the two (2) modular STERIS VHP M1000 generators and the multiple VHP1000 mobile generators.
- IQ/OQ and PQ protocol development and execution for the IC Technologies UV transfer port for the syringe barrels.
- UV D-value determination.

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Novex Pharma, Inc. (Richmond Hill, Ontario)

- Hydrogen peroxide gas manifold system development for a production ophthalmic barrier filling system.
- Hydrogen peroxide gas manifold system for a clinical injectable barrier filling system.
- Protocol development and execution for VHP1000 cycle development on three (3) rigid wall isolators comprising the injectable barrier filling system with oven and autoclave interface.
- H_2O_2 gas D-value determination of test carriers.
- Design review, protocol development, and execution H_2O_2 gas cycle development studies on a high speed injectable filling line interfaced to 2 VHP1000's in parallel.

Pharmacia (Kalamazoo, MI)

- Hydrogen peroxide gas process development, validation strategy consultation, and cycle development on a high-speed barrier filling system.
- Joint project management of clinical filling facility incorporating isolation technology.
- Development of validation master plan for all new equipment.
- IQ/OQ/PQ protocol development and execution of equipment, filling system isolators and VHP1000.
- Design consultation and process development for a sterile bulk powder filling operation that included a centrifuge, two Fitzmills, one powder cooler, and an exit chute using hydrogen peroxide gas decontamination.
- VHP1000 cycle development testing.
- IQ/OQ/PQ protocol development and execution for the powder fill system and one VHP1000.

PSGA / Johnson & Johnson (Buenos Aires, Argentina)

- Facility design review for isolator external exhaust optimization and room control (# air exchanges, temperature).
- IQ/OQ/PQ protocol development and execution for a Carlisle (Walker) Barrier rigid wall sterility testing isolator, a rigid wall transfer isolator, and a STERIS VHP1001 Biodecontamination system.
- H_2O_2 gas D-value determination protocol development and execution.
- Sterilant intrusion and residue effects protocol development and execution.
- SOP Generation.

PSGA /Janssen Cilag (Mexico)

- Facility design review for isolator external exhaust optimization and room control (# air exchanges, temperature).
- IQ/OQ/PQ protocol development and execution for a Carlisle (Walker) Barrier rigid wall sterility testing isolator, a rigid wall transfer isolator, and two (2) STERIS VHP1001 Biodecontamination systems.
- H_2O_2 gas D-value determination protocol development and execution.
- Sterilant intrusion and residue effects protocol development and execution.
- SOP Generation.

SAIC (Fredrick, MD)

- Process development involving isolation and hydrogen peroxide gas decontamination.
- CD and PQ protocol development and execution for an isolated pilot filling process that consisted of a Walker Barrier rigid wall filling isolator, a rigid wall oven interface isolator, a rigid wall 4-glove transfer isolator, two (2) rigid wall 3-glove transfer isolators , two (2) STERIS VHP1000ED Biodecontamination systems, and one (1) STERIS VHP1000 Biodecontamination system.
- H_2O_2 gas D-value determination protocol development and execution.
- Sterilant intrusion and residue effects protocol development and execution.

SAIC (Fredrick, MD)

- FAT and SAT protocol development and execution for a Walker Barrier combined rigid wall sterility testing isolator/airlock system integrated with a STERIS VHP M100-ABX modular Biodecontamination system.
- IQ/OQ protocol development and execution for the VHP M100-ABX generator.
- H_2O_2 gas D-value determination protocol development and execution.
- CD/PQ protocol development and execution for the isolator's main chamber only decontamination cycle and the airlock only decontamination cycle.
- Sterilant intrusion and residue effects protocol development and execution.

Samsung Biotech (Incheon, Korea)

- IQ/OQ protocol development and execution for a STERIS VHP M100-S Biodecontamination system integrated with Comecer rigid wall 4-glove isolator with an adjoining pre-chamber.
- H_2O_2 gas D-value determination protocol development and execution.
- CD and PQ protocol development and execution for the combination isolator main chamber and pre-chamber decontamination cycle and the pre-chamber only decontamination cycle.

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- Sterilant intrusion and residue effects protocol development and execution.
- Aseptic Maintenance protocol development and execution to verify that the isolator will remain germ-free and under ISO Class 5 conditions following the execution of the previously validated combined enclosure decontamination cycle for a minimum period of seven (7) days.

TEVA Pharmaceutical Works (Gödöllö, Hungary)

- Decontamination cycle development (CD) and PQ protocol review and execution support for an IMA filling cRABS (closed RABS) and a Lyo/Capping cRABS with integrated STERIS VHPM100-SX Biodecontamination systems.
- Generated final reports.
- FDA audit support.

Wyeth (Carolina, Puerto Rico)

- Facility design review and optimization for a sterility test suite that consisted of a Carlisle (Walker) Barrier rigid wall single half suit autoclave interface isolator, a rigid wall two half-suit workstation isolator, two (2) rigid wall 3-glove transfer isolators, and two (2) STERIS VHP1000ED Biodecontamination systems.
- Validation master plan development.
- FAT/SAT protocol review and execution for the four isolator systems.
- IQ/OQ protocol development and execution for the four (4) isolator systems and the two VHP1000ED generators.
- CD/PQ protocol development and execution.
- H_2O_2 gas D-value determination protocol development and execution.
- Sterilant intrusion and residue effects protocol development and execution.
- Operational SOP Development.

Wyeth (Pearl River, NY)

- Design consultation, process development, and validation planning for an isolated containment clinical filling line that consisted of a vial washer; a depyrogenation tunnel; a Carlisle (Walker) Barrier isolator system that enclosed the vial accumulator, filler, lyophilizer loading/unloading system, capper, and the external vial washer that was decontaminated using two (2) Bioquell Clarus “C” hydrogen peroxide generators.
- Validation master plan development.
- URS (User Requirement Specification) and FS (Functional Specification) development for the isolator system.
- FAT and SAT support for the isolator system and selected process equipment.
- Designed a sterilant manifold system to allow isolator decontamination in a variety of combinations or separately.
- IQ/OQ/CD/PQ protocol development and execution for the isolators and sterilant generators.
- Operational SOP development for the isolators and sterilant generators and operator training.

Wyeth (Marietta, PA)

- Facility design review and optimization for a sterility test suite that consisted of a la Calhéne flexible wall single half suit autoclave interface isolator, a flexible wall two half-suit workstation isolator, four (4) flexible wall 3-glove transfer isolators, and two (2) STERIS VHP1000 Biodecontamination systems.
- IQ/OQ protocol development and execution for the seven (7) isolator systems and the two VHP1000 generators.
- CD/PQ protocol development and execution.
- H_2O_2 gas D-value determination protocol development and execution.
- Sterilant intrusion and residue effects protocol development and execution.
- Operational SOP development for the isolators and sterilant generators and operator training.

Wyeth (West Chester, PA)

- Process development, feasibility testing, and validation of surface decontamination of a centrifuge / rotary vacuum dryer system using a single STERIS VHP1000 Biodecontamination system that incorporated a ABC designed sterilant delivery manifold.
- IQ/OQ protocol development and execution for the VHP1000 generator.
- CD/PQ protocol development and execution for the VHP1000 generator connected to the centrifuge / rotary vacuum dryer system.
- H_2O_2 gas D-value determination protocol development and execution using a transfer isolator.

Wyeth Biotech (Sanford, NC)

- CD/PQ protocol development and execution for a sterility test system that consisted of la Calhene flexible wall single half suit workstation isolator, a rigid wall 2-glove transfer isolator and a STERIS VHP1000 Biodecontamination system.
- H_2O_2 gas D-value determination protocol development and execution using the transfer isolator.
- Sterilant intrusion and residue effects protocol development and execution.

Wyeth Biotech (Sanford, NC)

- Validation support for a sterility testing suit that consisted of two (2) CPS (Walker) Barrier rigid wall 4-glove sterility testing isolators and two (2) STERIS VHP1000ED-AB Biodecontamination systems.
- IQ/OQ protocol development and execution for the two isolator systems and the two VHP1000ED generators.
- CD/PQ protocol development and execution.

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- H_2O_2 gas D-value determination protocol development and execution using the transfer isolator.
- Sterilant intrusion and residue effects protocol development and execution.
- SOP development and operator training.

Publications and Presentations

As recognized leaders in advanced aseptic processing in the pharmaceutical and biotech industries, Advanced Barrier Concepts' team members are widely published and entertain many industry conference speaking engagements.

Presentations

These and other presentations are available for viewing and downloading at our website http://www.advancedbarrier.com

The Use of Nitrogen Dioxide Gas for Isolator Decontamination Applications

Rickloff, J. R., PDA Global Conference on Pharmaceutical Microbiology, October 22-24, **2012**.

A new decontamination technology is being developed and a review of preliminary breadboard testing on an isolator was presented.

Historical Perspective on the Decontamination of Isolators Using Hydrogen Peroxide Gas

Rickloff, J. R., ISPE Barrier Isolation Technology Conference, June 6-7, 2005.

A 15-year look back at how hydrogen peroxide gas generators were developed and implemented into isolator systems was provided along with a synopsis on how to properly validate the decontamination process and how variable BI resistance can effect the revalidation of such systems.

The Use of Abbreviated Decontamination Cycles to Prevent False Negative Sterility Test Results

Rickloff, J. R., PDA SciTech Summit, March 10, 2004.

Reviewed the current methods and past data involved in the validation of sterility testing isolators and discussed the value of using abbreviated decontamination for some product containers to prevent sterilant penetration.

Implementing Validation Strategies for Isolator-Based Systems

Rickloff, J. R., Barnett International's 4th Annual Isolator Conference, January 27-28, 2003

This workshop thoroughly reviewed the overall strategies and basic validation methodologies for isolator system validation utilizing gaseous decontamination methods. Facility design and qualification, equipment qualification, performance qualification, and process simulation testing was reviewed, with practical examples and demonstrations of key methods and techniques.

H_2O_2 Gas Decontamination Cycle Comparisons Between Rigid and Flexible Wall Isolators

Rickloff, J.R., la Calhène AUDITS 101 Conference, October 3-4, 2002.

This presentation provided an overview on the decontamination cycle and regulatory expectations for the process. Past flexible wall data and its' implications are reviewed and how new trends in validation techniques are implemented to reduce them. The benefits of rigid wall isolator construction are also discussed.

Microbiological Monitoring in Isolators

Rickloff, J.R., bioMerieux Industrial Microbiology Seminar, September 18, 2002.

This presentation reviewed the principles of microbial monitoring in isolators, current US and European regulatory requirements for monitoring, and the means to achieve and maintain a germ free environment. The current means to monitor the air and surfaces in isolators is also touched upon.

Practical Validation Strategies for Isolated Sterility Testing Labs - Part I

Rickloff, J.R., Barnett Isolator Conference, June 13-14, 2002

This workshop thoroughly reviewed the overall design process and equipment qualification methodology for isolator systems utilizing gaseous decontamination methods. Key learning objectives included determining your capacity requirements, developing a validation master plan, facility classification requirements, and qualifying your isolators and related process equipment.

Presentations

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Practical Validation Strategies for Isolated Sterility Testing Labs - Part II

Rickloff, J.R., Barnett Isolator Conference, June 13-14, 2002.

The second part of the Workshop focused on the Performance Qualification studies that are needed to properly validate the gaseous decontamination method in sterility test isolator systems. Practical examples, a discussion of acceptance criteria, and the demonstration of test methods were included. Key learning objectives included determining a D-value for your BIs, developing and qualifying decontamination cycles, isolator aeration, sterilant ingress methods, and creating a meaningful process simulation (no false negative) study.

Current Trends in Controlled Environments

Rickloff, J.R., AAPS Annual Meeting, October 29, 2000.

An overview of conventional aseptic processing was presented, and it addresses the key issues that corporate decision makers are faced with when implementing isolation technology, such as regulatory requirements and equipment validation focus areas.

Isolator Sterilants: Common Issues and Differences

Rickloff, J.R., PDA Conference, October 16-17, 2000.

This presentation discussed the similarities and differences of the current chemical germicides used for isolator decontamination in the pharmaceutical industry with emphasis placed on validation issues and safety considerations.

Current Trends and Concepts in Validating Sterility Testing Isolators

Rickloff, J.R., Serentec Workshop for Sterility Testing, May 25-26, **2000**.

Past practices & current trends in validating sterility testing isolators were reviewed with an emphasis on productivity. Although the key validation criteria remain the same, i.e. no false negatives, improvements to the overall system design have permitted the optimization of the decontamination cycle.

Publications

These and other publications are available for viewing and downloading at our website http://www.advancedbarrier.com

Hydrogen Peroxide Gas Decontamination

Rickloff, J.R., *in* Advanced Aseptic Processing Technology, Informa Healthcare, London, England, **2010**.

This chapter provided an overview on the basics of H_2O_2 gas decontamination and on how the sterilant should be applied to isolator systems. In addition, the latest in validation techniques and sterilant monitoring requirements were discussed from a user and regulatory perspective.

Chemical and Biological Aspects of Hydrogen Peroxide Gas

Grignol, George[1], Don Eddington[1*], Ph.D., Dave Karle[1], and James Rickloff[2], ISPE Barrier Isolation Technology Conference, Arlington, VA, June 5-6, 2000.

The interactions of hydrogen peroxide concentrations and surface temperatures are studied in an isolator using chemical and microbiological techniques. These tests verify commonly accepted theories of the gaseous properties of flash vaporized hydrogen peroxide that have recently been challenged.

Key Aspects of Validating Hydrogen Peroxide Gas Cycles in Isolator Systems

Rickloff, J.R., Journal of Validation Technology, 5:61-71, 1998.

The purpose of this paper is to revisit some essential validation aspects of sanitizing isolators with hydrogen peroxide gas in order to assist the industry in demonstrating reproducibility of the process under worst-case conditions.

Hydrogen Peroxide Gas Sterilization Trials Performed on A Prototype Enclosed Vial Filler

Rickloff, J.R. and D. Eddington, PDA/ISPE Conference, January 17-18, 1995.

Testing was performed on a prototype vial filler isolator at TL Systems Corp. in Minneapolis, MN, to determine the feasibility of incorporating hydrogen peroxide gas sterilization into the system. Carrier sterilization, isolator aeration, and water fill residual data was presented.

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"Modern Trends in Sterilization of Enclosures"

Rickloff, J.R. and L. M. Edwards, Chapter in Isolator Technology: Applications in the Pharmaceutical and Biotechnology Industries, edited by Carmen Wagner and James Akers, Interpharm Press, 1995.

"Engineering and Project Management Issues for a Hydrogen Peroxide Sterilized Filling System"

Rickloff, J.R. and L. M. Edwards, Chapter in Isolator Technology: Applications in the Pharmaceutical and Biotechnology Industries, edited by Carmen Wagner and James Akers, Interpharm Press, 1995.

Hydrogen Peroxide Gas Sterilization: A Review of Validation Test Methods

Rickloff, J.R., J. Dalmasso, and L.W. Lyhte, PDA Annual Meeting, 1992.

The importance of performing temperature distribution studies, the use of chemical and biological indicators in optimizing and verifying proper gas distribution, a technique to easily perform square-wave D-value determinations, and a means to quantitatively monitor aeration efficiency when using a prototype VHP1000 was reviewed.

Resistance of Various Microorganisms to Vaporized Hydrogen Peroxide in a Table Top Sterilizer

Rickloff, J.R. and P. Orelski, ASM Annual Meeting, **1989**.

A great deal of information is available in the literature on the relative resistance of microorganisms to aqueous hydrogen peroxide; however, the same cannot be said for hydrogen peroxide in the gaseous state. *Bacillus stearothermophilus* spores were found to be the most resistant to the sterilant, and the presence of organic soil did not affect the ability of hydrogen peroxide gas to sterilize stainless surfaces.