PHARMACEUTICAL CASE STUDY COMPILATION

STERAMIST™
POWERED BY BINARY IONIZATION TECHNOLOGY

MARCH 2016

TOMI™ ENVIRONMENTAL SOLUTIONS
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New Technology Achieves Unparalleled Efficacy in Pharmaceutical Spaces without the Need to Wipe or Rinse Leaving No Residues

Groundbreaking disinfection/decontamination system, SteraMist™ powered by Binary Ionization Technology® (BIT™), is streamlining pharmaceutical disinfection/decontamination protocols because it offers greater material compatibility and boasts significant efficacy compared to older disinfection/decontamination options. Whether utilized for processing areas, clean rooms, or for materials transfer, SteraMist™ BIT™ meets the disinfection/decontamination requirements for all pharmaceutical spaces; from communal rooms to the most stringently guarded areas. It's the unique science behind the technology that makes this system so versatile and effective.

About SteraMist™ BIT™

A patented two-step process, SteraMist™ BIT™ activates and ionizes a low percent hydrogen peroxide solution after it passes through an atmospheric high voltage cold plasma arc. This creates a fine mist called Activated Ionized Hydrogen Peroxide (AIHP), which contains a high concentration of Reactive Oxygen Species (ROS). Consisting mostly of hydroxyl radicals, ROS damages and disrupts the cell wall of pathogenic organisms through oxidation of proteins, carbohydrates, and lipids. This cellular disruption and/or dysfunction allows for disinfection in targeted areas and large spaces.

Utilizing SteraMist™ BIT™, pharmaceutical facilities can achieve complete room disinfection/decontamination including high touch surfaces, sensitive equipment, walls and floors, making whole room disinfection/decontamination easier. **Here are recent case studies featuring top global pharmaceutical companies that have integrated SteraMist™ BIT™ into their current disinfection/decontamination protocols:**

Case Study: Custom Pass Box Developed Utilizing AIHP and Integrated Using an Existing HVAC System

Overview: An Italian manufacturing plant that produces sterile injection products, non-sterile liquids and semi solids. It's one of the main Contract Manufacturing Organization (CMO) partners for national and international companies and is specifically authorized to work with the following:

- **Injectable Production Lines** (liquid in vials and in ampoules, manufactured in asepsis or terminally sterilized; sterile powder in vials aseptically filled);
- **Semisolid Product Lines** (gels, creams, ointments);
- **Non Sterile Liquid Line** (liquids and solutions, suspensions, syrups, eardrops).

Situation: In June 2013, the facility went through a complete renovation of one of the sterile departments with the objective of guaranteeing that material and personnel flows followed Good Manufacturing Practices (GMP) and safety norms.

Solution: Rearrange the existing department which could not be enlarged to create a more streamlined material and personnel flow. Integrate SteraMist™ BIT™ as a permanent disinfection system to guarantee the highest level of microbiological and quality control. SteraMist™ BIT's AIHP is used utilized to disinfect materials moving into the sterile department and to protect the sterile room from potential contamination from adjacent non-classified areas. To accomplish this, a custom pass box was developed utilizing AIHP and integrated with the existing HVAC system.

Materials loaded into Pass Box Utilizing AIHP

All case study results and implications featured in this paper utilizing SteraMist™ powered by Binary Ionization Technology® (BIT™) were conducted with international pharmaceutical partners/clients headquartered in Italy.

Evaluation Criteria:

Parameter	Objective	Verification Method
Diffusion of the AIHP Solution	Agent's diffusion is homogeneous, reaching every surface of the entering materials.	Chemical Indicators
Disinfection/decontamination level	SAL = 10^6 in every sampling spot.	Geobacillus stearothermophilus ATCC 12980 e/o ATCC 7953 Bioindicators on a metal support
Generated fog condensation	Avoid an excessive condensation on surfaces (do not overcome the saturation point of the fog).	Visual check
Cycle time	Considering all the other parameters, sterilization is reached in the shortest period of time possible.	Device's timer

Results: SteraMist™ BIT™ was put through the standard phases of validation for equipment qualification. During these phases of validation, SteraMist™ BIT™ treated materials made of steel and packed materials moving through the custom autoclave. The requested Sterility Assurance Level (SAL) 10^6 reduction was achieved throughout all sampling spots.

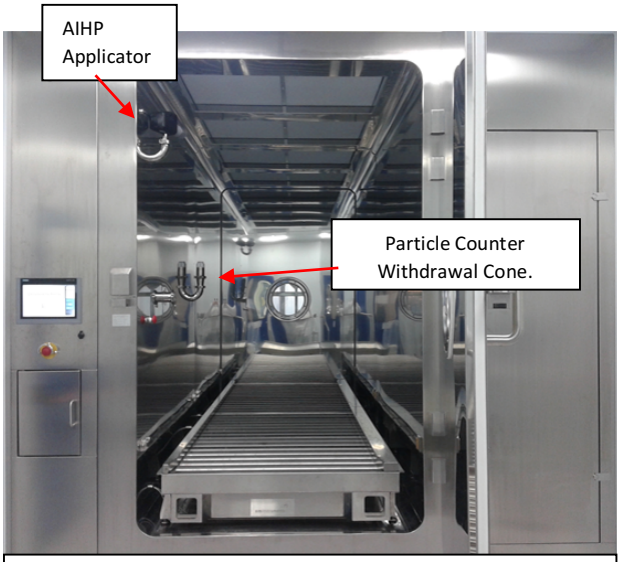
Case Study: Custom Pass Box Utilizing AIHP is Installed in a Compulsorily Sterile Products Department

Overview: A global manufacturing company headquartered in Italy produces pharmaceutical products for human and veterinary use as well as medical devices; for sterile and non-sterile liquid products, in single-dose or multi-dose primary containers. The HEALTH & BEAUTY Division guarantees the highest standards of safety in the preparation and packaging of cosmetic products, and healthcare and non-sterile medical manufacturing, filling and packaging of liquid products, gels and creams in single-dose and multi-dose plastic containers.

Situation: The company needed to quickly and efficiently transfer numerous packaging materials from class D to class B rooms where aseptic filling activities are performed.

Solution: A custom pass-box utilizing SteraMist™ BIT's AIHP is installed in the compulsorily sterile products department. The device is a ventilated pass-through chamber; the air comes from the air outlet and is released into the room through 4 HEPA filters H14, which achieve the environmental class ISO 5 (Class A according to cGMP). The material transfer cycle goes through multiple phases including:

- Preliminary Control: critical process parameters are checked to confirm they receive a positive evaluation.
- Loading Pass Box: materials included primary boxes, gamma-ray sterilized and packed into PE bags.
- Disinfection: this stage includes many phases from preparation of the pass box, initiating the system, priming to charge the hydraulic circuit, fogging until desired concentration is reached, contact time, aeration and particle sampling.



Custom Pass Box Utilizing SteraMist™ BIT's AIHP.

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- Validation: Once disinfection has been validated (no alarm sounds), the pass box door can be opened and boxes can be unloaded.

Results: The efficiency of the cycle has been demonstrated by positioning 20 biological indicators inoculated with 10^6 G. Stearothermophilus spores. All indicators resulted in full 10^6 reductions.

Case Study: Feasibility Study to Support Integrating the Use of the SteraMist™ Environment System

Overview: Established in Italy since 1947, this pharmaceutical manufacturing company specializes in the production, distribution and promotion of medical devices, nutritional supplements, as well as therapeutic drugs used in oncology, neuropathy, and internal medicine in Italy and abroad. This case study focuses on the manufacturing plant that specializes in:

- **Injectable forms** (lyophilized powders, ready to use solution), small and large volumes
- **Capabilities:** include freeze drying, filling (liquids & solids), packaging

Situation: The company conducted a feasibility study to support integrating SteraMist™ Environment System into its current GMP protocols for disinfection. The areas of interest included the Lyophilization department (cleanroom & lyophilizer) and Dust Micro-dosing and Macro-dosing equipment. The requested Sterility Assurance Level (SAL) was a 10^6 reduction.

Solution: Twenty biological indicators and chemical indicators were placed throughout the Lyophilization department to assess homogeneous distribution of AIHP during the fogging cycle as well as efficacy.

Lyophilizer Room & AIHP Applicators (circled)

Evaluation Criteria:

Parameter	Objective	Verification Method
Diffusion of the H_2O_2 solution	Agent's diffusion is homogeneous all over the area	Chemical Indicators
Decontamination cycle efficacy in the cleanroom	SAL = 10^5 in every chosen sampling spot	Biological Indicators/tri-scale ($10^{4\text{-}5\text{-}6}$)
Decontamination cycle efficacy on the lyophilizers	SAL = 10^6 in every chosen sampling spot	Biological Indicators/tri-scale ($10^{4\text{-}5\text{-}6}$)
Cycle time	Considering all the other parameters, sterilization is reached in the shortest period of time possible.	Device timer

Results: Full 10^6 reduction on all biological indicators and homogeneous diffusion of AIHP, SteraMist™ BIT™ was implemented into Biomedica Foscama's disinfection protocols for the pharmaceutical manufacturing plant.

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Case Study: Feasibility Study to Support Integrating the Use of the SteraMist™ Environment System

Overview: A global pharmaceutical company focused on developing, manufacturing and commercializing branded pharmaceuticals, generic and over-the-counter medicines, and biologic products. Overall representing 1000 generic, branded generic, established brands and OTC pharmaceutical products and +35 specialty branded products focusing principally in the Women's Health, Urology, Gastroenterology and Dermatology therapeutic categories. Product portfolio includes:

- **Sterile Cytotoxic Parenterals**, including freeze dried ones
- **Sterile non Cytotoxic Parenterals,** including freeze dried ones
- **Injectable solutions**
- **Prefilled Syringes**

Situation: Actavis conducted a feasibility study to support integrating the SteraMist™ Environment System into its current GMP protocols for disinfection. The study was concentrated in two manufacturing departments and the requested Sterility Assurance Level (SAL) was a 10^6 reduction.

Solution: Conduct disinfection in two targeted departments for a three-hour duration to assess homogeneous distribution of AIHP during the fogging cycle as well as efficacy. Sensitive electronic devices remained in the room to also be disinfected.

Evaluation Criteria:

Parameter	Objective	Verification Method
Diffusion of the H_2O_2 Solution	Agent's diffusion is homogeneous all over the area	Chemical Indicators
Decontamination cycle efficacy	SAL = 10^6 in every chosen sampling spot.	Biological Indicators
Generated fog condensation	Avoid an excessive condensation on surfaces (do not overcome the saturation point of the fog), preventing any influence on the sensitive electronic devices.	Visual check
Cycle time	Considering all the other parameters, sterilization is reached in the shortest period of time possible.	Device's timer

Results: Full 10^6 reduction on all biological indicators and homogeneous diffusion of AIHP. Sensitive electronic devices in the rooms were not affected by the disinfection process, even if some machine casing were open. SteraMist™ BIT™ was implemented into plant disinfection protocols for their pharmaceutical manufacturing plant.

Case Study: Integration of the SteraMist™ Environment System to Disinfect Surfaces Used in the Production of Oral Solids Containing Biological APIs

Overview: This case study features a strategic pharmaceutical center for the production, packaging and distribution of oral solids.

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Situation: The strategic center has created a new department that is completely dedicated to the production of oral solids containing biological Active Pharmaceutical Ingredients (APIs). The microbial evaluation of the ingredients used in the new department, also considering their nature, caused a persistent contamination on the analysis area (which is dedicated and isolated from the rest of the Quality Control (QC) area).

Solution: Utilizing the SteraMist™ Environment System, three fogging applicators were utilized to achieve complete room disinfection of two rooms in the micro-laboratory as well as adjacent rooms. Ten biological indicators and seven chemical indicators were placed throughout the laboratory and adjacent rooms to assess homogeneous distribution of AIHP during the fogging cycle as well as efficacy. Computers, keyboards, fridges and sensitive electronic devices remained in the laboratory during disinfection.

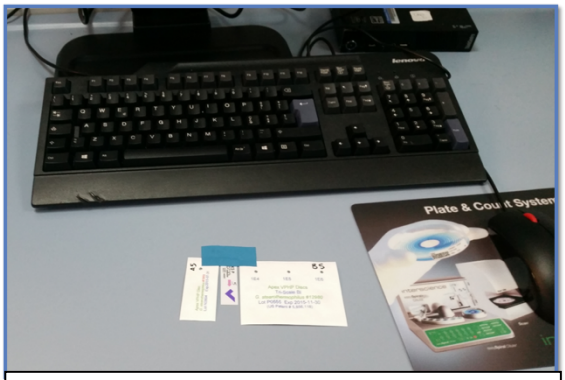
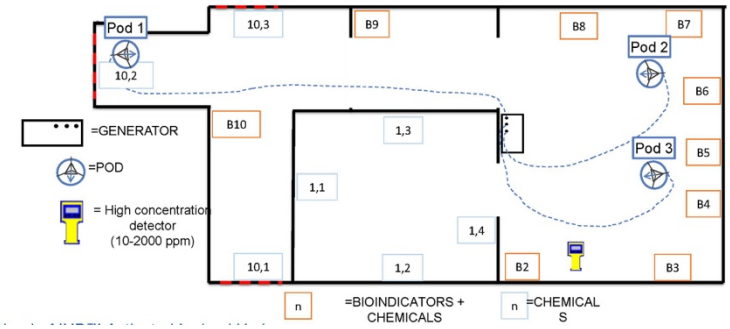


Photo of Keyboard after Disinfection

Evaluation Criteria:

Parameter	Objective	Verification method
Diffusion of the H_2O_2 Solution	Agent's diffusion is homogeneous all over the area	Chemical Indicators
Decontamination cycle efficacy	SAL = 10^5 in every chosen sampling spot.	Biological Indicators tri-scale ($10^{4\text{-}5\text{-}6}$)
Generated fog condensation	Avoid an excessive condensation on surfaces (do not overcome the saturation point of the fog), preventing any influence on the sensitive electronic devices.	Visual check
Cycle time	Considering all the other parameters, sterilization is reached in the shortest period of time possible.	Device timer

Results: SteraMist™ powered by Binary Ionization Technology® (BIT™) exceeded the efficacy objective achieving a 10^6 reduction in every chosen sampling spot. There was no condensation on surfaces and sensitive electronic devices in the laboratory were not affected adversely.



Room layout including positioning of AIHP applicators (Pods), biological indicators and chemical indicators.

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