Discontinuation of LpH and Vesphene Sanitization Agents and Implementation of Vesta Syde SQ 128 RTU Disinfectant Agent

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Abstract *— Disinfectants play a critical role in our daily lives and are particularly crucial in pharmaceutical industries due to the importance of maintaining high cleanliness levels and preventing the spread of contaminants. These substances or solutions are designed to kill or inactivate microorganisms on surfaces or in the environment. They are used in various settings such as homes, hospitals, schools, public spaces, and industries to maintain a safe and healthy environment. STERIS communicated in 2022 that LpH and Vesphene phenolic disinfectants will be discontinued in July 2023. Many sites across the Merck network are impacted; this is a Global situation: LpH and Vesphene are the LPO-qualified disinfectant agents for walls and ceilings; A new disinfectant must be qualified for sanitizing at LPO.*

Keywords *— Disinfectant, LPO, Merck, Sanitize.*

PROBLEM STATEMENT

STERIS communicated in 2022 that LpH and Vesphene phenolic disinfectants will be discontinued in July 2023.

- Many sites across the Merck network are impacted, and this is a global situation.
- LpH and Vesphene are the LPO-qualified disinfectant agents for walls and ceilings.
- A new disinfectant must be qualified for LPO.

Immediate Action Taken

- LpH inventory strategy was designed to cover site sanitizations up to 2 Qt 2024.

RESEARCH DESCRIPTION

This research will adopt a mixed-methods approach, combining qualitative and quantitative methods. Primary data will be collected through observations, while secondary data will be gathered from academic literature, industry reports, and regulatory documents. The research will focus on Merck-LPO, considering locations and regulatory environments to ensure a comprehensive understanding of quality assurance practices.

RESEARCH OBJECTIVES

- The major changes that will be implemented in Mar/03/2023 are:
- Implementation of Vesta Syde SQ 128 RTU disinfectant agent to sanitize walls.
- Eliminating Vesphene for manufacturing procedures but maintaining LpH to consume current inventory.
- The sanitation of ceilings will be eliminated.
- Sanitization of rolling doors will be eliminated.
- Modification of the sanitization frequency and environmental monitoring samplings of Micro. Laboratory, QC In-Coming, and PU3 areas from monthly to quarterly
- Elimination of Temodar/Temodal rooms and Isolator sanitization and sampling from the environmental monitoring program
- Format and wording modifications.
- Vesta Syde's open container expiration date is 3 months.
- LpH open container expiration date is 56 days.
- Include verified in the sanitization form to comply with documentation practices and to align with laboratory and In-coming sanitization documents.

RESEARCH CONTRIBUTIONS

The elimination of a sanitizing agent and the implementation of another can make significant

contributions to the field of sanitation and hygiene. Researchers can provide valuable insights into selecting the most suitable option for various settings and purposes by investigating the effectiveness, efficiency, and safety of different sanitizing agents. This research can improve sanitation practices in various industries, leading to enhanced health and safety. Also, studying the effects of different sanitizing agents on microbial populations can help develop strategies to control and prevent the spread of infectious diseases and product contamination. The research may also explore the environmental impact and sustainability aspects associated with the use of different sanitizing agents, paving the way for more environmentally friendly solutions.

BACKGROUND

Merck & Co. was founded in the U.S. on January 1, 1891. George Merck, age 23, established the company to distribute fine chemicals throughout New York City and the neighboring areas. For more than 130 years, Merck has brought hope to humanity through the development of important medicines and vaccines. They foster a diverse and inclusive global workforce and operate responsibly daily to enable a safe, sustainable, and healthy future for all people and communities. Their values represent the core of our character and guide every decision and action we take.

- Patients first
- Respect for people
- Ethics and integrity
- Innovation and scientific excellence

The areas of focus of Merck are:

- Oncology
- Vaccines
- Infectious diseases
- Cardio-metabolic disorders
- Immunology
- Neuroscience

Merck has well-established Compliance Program reflects Merck's longstanding commitment to compliance with the laws and regulations governing pharmaceutical and vaccine marketing and selling activities in the United States [1]. Merck's Compliance Program is also consistent with the recommendations set forth in "Compliance Program Guidance for Pharmaceutical Manufacturers" published by the Office of Inspector General U.S. Department of Health and Human Services (the "HHS- OIG Guidance") and the provisions of the Code on Interactions with Healthcare Professionals created by the Pharmaceutical Research and Manufacturers of America [1]. It is regulated by Food and Drug Administration, Occupational Safety and Health Administration, European Medicines Agency, Pharmaceuticals and Medical Device Agency, and Drug Enforcement Administration [1].

Sanitization

Sanitization is a process that involves reducing, eliminating, or controlling the number of microorganisms, such as bacteria, viruses, and fungi, to a safe and acceptable level. It is an essential practice in various industries and settings, including healthcare facilities, food processing plants, laboratories, and public spaces, to prevent the spread of infections and maintain hygiene standards.

The concept of sanitization revolves around the use of various techniques, methods, and sanitizing agents to achieve the desired level of microbial reduction. Some commonly used sanitizing agents include disinfectants, sanitizing solutions, heat, and ultraviolet (UV) radiation. These agents work by damaging the cell structure or disrupting the metabolic processes of microorganisms, rendering them inactive or unable to reproduce.

Sanitization practices may involve cleaning surfaces, equipment, or objects with water, detergent, or other cleaning agents to remove visible dirt and debris. Once the cleaning step is complete, the application of a proper sanitizing agent follows further to reduce the microbial load to a safe level. Factors such as contact time, concentration, and specific application methods are crucial in ensuring effective sanitization [2].

Disinfectants

STERIS' LpH® III Disinfectant is specifically formulated for the routine disinfection of hard, non-porous surfaces. At a use dilution of rate of 0.8% v/v (1:128), the LpH III Disinfectants kill a broad spectrum of common bacteria and fungi. The acidic LpH III Disinfectant formulation can be used alone or in rotation with the Vesphene III Disinfectants. These products have an extensive documentation package to meet your validation objectives and are supported by the STERIS Technical Services team for individualized application and validation assistance [3].

Vesphene is a commonly used sanitizing agent in healthcare and laboratory settings [2]. It is a brand name for a quaternary ammonium compound (quat) sanitizer and disinfectant. The specific formulation of Vesphene can vary depending on the manufacturer, but it typically contains a combination of quaternary ammonium compounds and other ingredients. Vesphene sanitizing agents are effective against a broad spectrum of microorganisms, including bacteria, viruses, and fungi. They are commonly used for surface disinfection in healthcare facilities, laboratories, and cleanrooms. Vesphene products are designed to be used on hard, non-porous surfaces and can be applied via spraying, wiping, or soaking methods [4].

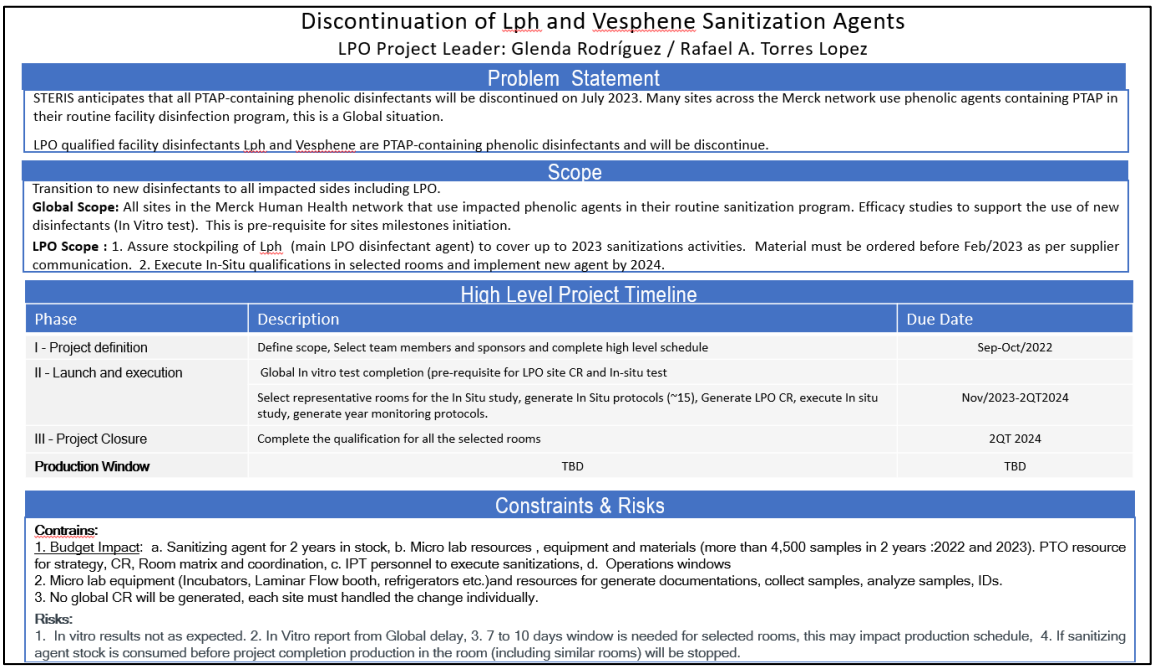
Vesta Syde SQ 128 RTU is a ready-to-use quaternary ammonium compound (quat) sanitizing agent and disinfectant. It is a brand name product typically used for surface disinfection and sanitization in various industries, including healthcare facilities, food processing plants, and institutional settings [5].

- Quaternary Ammonium Compound: Vesta Syde SQ 128 RTU contains quaternary ammonium compounds as its active ingredients. Quats are effective antimicrobial agents that can kill a broad spectrum of microorganisms, including bacteria, viruses, and fungi.
- Ready-to-Use: Vesta Syde SQ 128 RTU is formulated as a ready-to-use product, meaning it does not require dilution before use. This convenience allows for immediate and easy application without the need for additional mixing or measuring.
- Surface Disinfection: Vesta Syde SQ 128 RTU is designed for use on hard, non-porous surfaces. It can be applied through spraying, wiping, or other appropriate methods to thoroughly disinfect and sanitize surfaces, helping to reduce the risk of infection transmission.
- Efficacy and Safety: Vesta Syde SQ 128 RTU has demonstrated efficacy against various microorganisms when used according to the manufacturer's instructions. It is important to follow the recommended contact time and concentration for effective sanitization. Additionally, ensure proper ventilation and use of personal protective equipment (PPE) as recommended on the product label.
- Compliance: Vesta Syde SQ 128 RTU may comply with relevant regulatory standards and guidelines, such as those set by the Environmental Protection Agency (EPA) for disinfectants or other appropriate regulatory bodies depending on the region or industry [1]. Disinfectants play a critical role in our daily lives and are particularly crucial in pharmaceutical industries due to the importance of maintaining high levels of cleanliness and preventing the spread of contaminants. Disinfectants are substances or solutions that are designed to kill or inactivate microorganisms on surfaces or in the environment. They are essential in our daily lives as they help prevent the spread of harmful pathogens, reduce the risk of infections, and promote overall hygiene and cleanliness. Disinfectants are used in various settings such as homes, hospitals, schools, public spaces, and industries to maintain a safe and healthy environment.

In the pharmaceutical industry, where the production of medicines and healthcare products takes place, the use of disinfectants is of utmost importance. Here are a few reasons why

disinfectants are essential in pharmaceutical industries:

- Contamination Control: Pharmaceuticals need to be manufactured in controlled environments to ensure product safety and efficacy. Disinfectants help control microbial contamination in manufacturing facilities, cleanrooms, and equipment to prevent the introduction of unwanted microorganisms into the products. This is crucial to maintain the quality and integrity of medications and prevent contamination-related issues.
- Compliance with Regulatory Standards: Pharmaceutical industries are regulated by strict guidelines and standards to ensure product quality, safety, and efficacy. Disinfection procedures and protocols are essential for compliance with these regulations. Using effective disinfectants and following proper disinfection practices helps meet the requirements set by regulatory authorities.
- Prevention of Healthcare-Associated Infections (HAIs): In healthcare settings, where pharmaceutical products are administered and used, prevention of healthcare-associated infections is paramount. Disinfectants are used to clean and disinfect surfaces, medical equipment, and patient care areas to reduce the risk of HAIs. This helps protect patients, healthcare providers, and visitors from microbial pathogens, ultimately saving lives and reducing healthcare costs.
- Employee and Public Safety: Disinfectants contribute to the safety of pharmaceutical industry workers and consumers. By effectively killing or inactivating microorganisms, disinfectants minimize the risk of exposure to harmful pathogens, including viruses, bacteria, and fungi. This is especially crucial in settings where contact with hazardous substances or infectious materials is common.



Discontinuation of Lph and Vesphene Sanitization Agents

LPO Project Leader: Glenda Rodríguez / Rafael A. Torres Lopez

Problem Statement

STERIS anticipates that all PTAP-containing phenolic disinfectants will be discontinued on July 2023. Many sites across the Merck network use phenolic agents containing PTAP in their routine facility disinfection program, this is a Global situation.

LPO qualified facility disinfectants Lph and Vesphene are PTAP-containing phenolic disinfectants and will be discontinue.

Scope

Transition to new disinfectants to all impacted sides including LPO.

Global Scope: All sites in the Merck Human Health network that use impacted phenolic agents in their routine sanitization program. Efficacy studies to support the use of new disinfectants (In Vitro test). This is pre-requisite for sites milestones initiation.

LPO Scope : 1. Assure stockpiling of Lph (main LPO disinfectant agent) to cover up to 2023 sanitizations activities. Material must be ordered before Feb/2023 as per supplier communication. 2. Execute In-Situ qualifications in selected rooms and implement new agent by 2024.

High Level Project Timeline

Phase	Description	Due Date
I - Project definition	Define scope, Select team members and sponsors and complete high level schedule	Sep-Oct/2022
II - Launch and execution	Global In vitro test completion (pre-requisite for LPO site CR and In-situ test	
	Select representative rooms for the In Situ study, generate In Situ protocols (~15), Generate LPO CR, execute In situ study, generate year monitoring protocols.	Nov/2023-2QT2024
III - Project Closure	Complete the qualification for all the selected rooms	2QT 2024
Production Window	TBD	TBD

Constraints & Risks

Contrains:

1. Budget Impact: a. Sanitizing agent for 2 years in stock, b. Micro lab resources , equipment and materials (more than 4,500 samples in 2 years :2022 and 2023). PTO resource for strategy, CR, Room matrix and coordination, c. IPT personnel to execute sanitizations, d. Operations windows
2. Micro lab equipment (Incubators, Laminar Flow booth, refrigerators etc.)and resources for generate documentations, collect samples, analyze samples, IDs.
3. No global CR will be generated, each site must handled the change individually.

Risks:

1. In vitro results not as expected. 2. In Vitro report from Global delay, 3. 7 to 10 days window is needed for selected rooms, this may impact production schedule, 4. If sanitizing agent stock is consumed before project completion production in the room (including similar rooms) will be stopped.

Figure 1

Discontinuation of LpH and Vesphene Sanitization Agents Project

Project Title: Discontinuation of Lph and Vesphene Sanitization Agents
Leader: Glenda Rodriguez / Rafael Torres Lopez **Sponsor** M. Bruno

Situation:
STERIS anticipates that all PTAP-containing phenolic disinfectants will be discontinued on July 2023. Many sites across the Merck network are impacted, this is a Global situation. LPO qualified facility disinfectants Lph and Vesphene are PTAP-containing phenolic disinfectants

Solution / Scope:
Transition to new disinfectants
Global: All sites that use impacted phenolic agents in their routine sanitization program. Efficacy studies (In vitro test) to support the use of new disinfectants

LPO: Execute In-Situ qualifications in selected rooms and implement new agent by 2024.

Status: OCT/2023

Overall Status	
Time	Cost
Scope	Resources

Key Assumptions:

Implementation at site will start without Sanitization agent qualification (In-Vitro testing completed). Global Micro will provide a document to justify the starting of the implementation.

Original Project Escalations / Risks

What	Impact on...	Probability (L,M,H)	Support Needed
Regulatory inspections concern due to In situ tests starts before the In vitro report	Compliance	M	Approve strategy. Change management process will prevent implementation without In vitro report.
Budget /resources constrain. Project with high volume of samples/testing.	Cost	M	Prioritize windows so executions in sequential and not simultaneous
In vitro test results not pass. Budget impact: cost of materials and resources. Time constrain to qualification of other agent (global impact)	Cost	L	Approve matrix strategy to reduce amount of executions
In vitro test results not pass: New strategy definition (e.g alternate sanitizing agent) must be considered	Time/ Cost	M-L	Prioritize windows so executions in sequential and not simultaneous
Pharmacy project delay	Time	L	Implementation at site will start without Sanitization agent qualification

Figure 2
Original Escalations and Risks – Discontinuation of LpH and Vesphene Sanitization Agents Project

Project Title: Discontinuation of LPh and Vesphene Sanitization Agents
Leader: Glenda Rodriguez / Rafael Torres Lopez **Sponsor** M. Bruno

New Escalations / Risks

What	Impact on...	Status	Support Needed
Malfunction of Lab microbial identification equipment (Microseq)	Time	Microseq equipment out of service from AUG/12/2022 to SEP/02/2022. This delayed In situ and annual monitoring execution microbial identifications. Isolates were sent to Accugenix for IDs.	None Equipment was fixed but time were impacted.
Events reported during the In Situ execution (Out of limits results, microbial identification issues etc.)	Compliance/ Time	Two Out of acceptance criteria reported in noncritical surfaces. Microbial identifications received from Accugenix did not match the microscopic description of isolates. Three QNs and 1 Complaint to Accugenix were generated.	None Complaint and QNs were closed on Oct/15/2022 but time was impacted.
Events reported during Annual monitoring study in Pharmacy rooms	Compliance/ Time	Coliform bacteria were identified from samples collected in the gowning rooms and one material transfer area of Pharmacy rooms 250 and 251.	Investigation is in process.
Safety Issues with disinfectant application techniques	Time	In Situ studies were executed using spraying technique for disinfectant application. Safety concerns due to explosive risks (Vesta Sycle contains 10% of IPA). Qualification using Mopping technique was required.	Investigation is in process.
Several documents must be generated and approved during November 2021 (Document CR, Midas documents, In Stu reports , etc.)	Time	Documents generation in progress.	Micro Lab resource for document generation. Quality , Safety and IPT resources for document revision and approval.

Figure 3
New Escalations and Risks – Discontinuation of LpH and Vesphene Sanitization Agents Project

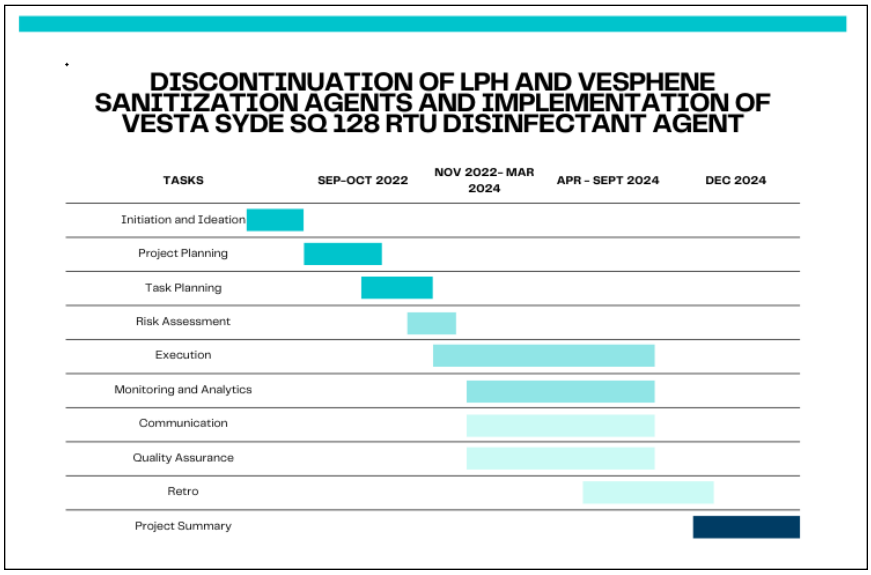


Figure 4

Gantt Chart – Discontinuation of LpH and Vesphene Sanitization Agents Project

ANALYSIS TECHNIQUES

Stage I: Readiness and pre-execution documentation.

- Define a plan for stocking (at least 2 years).
- LPO CR for the implementation strategy.
- Execution strategy definition and room selection.
- New disinfection agent receiving protocol.
- Protocol for the laboratory media neutralization study.
- In Situ Execution protocols (5 selected rooms).
- Annual monitoring protocol for Pharmacy Rooms selected as the worst case for execution.

Stage II: Execution (from March 2023 to October 2024).

- Media neutralization - 7 microorganisms, 54 runs.
- In situ executions - 3 protocols, 5 rooms, 11 executions.
- Annual Monitoring for Pharmacy rooms - 1 protocol, 2 rooms, more than 12 executions completed. Execution is still in progress until Dec/2023.

Stage III: Implementation.

- Media neutralization study report.
- Technical document for the sanitization frequency modification from 1 to 3 months.
- In Situ reports (3).
- CR for revision of site documents – 13 documents impacted by new disinfectants from Micro lab, manufacturing, and QCIC areas.
  - 5 SOPs
  - 6 Forms
  - 2 Labels

What will be Implemented?

All documents are approved. The major changes that will be implemented in Dec/2024 are:

- Implementation of Vesta Syde SQ 128 RTU disinfectant agent for the sanitization of walls of production rooms. In the coming area and Microbiology laboratories facilities.
- Elimination of sanitization with LpH and Vesphene for Micro lab and QCIC.
- Eliminate Vesphene for Manufacturing procedures but maintain LpH to consume current inventory.
- The sanitation of ceilings will be eliminated.
- Sanitization of rolling doors will be eliminated.
- Modification of the sanitization frequency and environmental monitoring samplings of Micro.

Laboratory, QC In-Coming, and PU3 areas from monthly to quarterly.

- Eliminating Temodar/Temodal rooms and Isolator sanitization and sampling from the environmental monitoring program.
- Grey Zones will be added to the Environmental Monitoring (EM).
- Sanitization procedures for the 3 areas were aligned.

RESULTS AND DISCUSSION

- No global CR was generated for new disinfectant implementation.
- Cross-functional project that involved: Micro Laboratory, Safety, Purchasing, Warehouse, PTO, and IPTs.
- LPO has more than 30 rooms in the manufacturing areas. A strategy was needed to simplify the qualification execution. Only 4 production rooms were selected for execution.
- Activities were managed by current area personnel. No additional resources were assigned.
- The new disinfectant agent and application technique presented new safety risks.
- Delays in microbial identifications due to malfunction of Lab microbial identification equipment (Microseq). The equipment was out of service for 1 month. Contract lab Accugenix was used.

Investigations

- Two out of the acceptance criteria were reported on non-critical surfaces.
- Accugenix IDs did not match the LPO macroscopic assessment for isolates (1 complaint was also generated).
- Coliform bacteria were identified from samples collected during the execution of the annual monitoring protocol.
- Changes in the sanitization process also impacted the microbial environmental monitoring program.

Vesta Syde SQ was selected as the new disinfectant agent to be used for the disinfection or sanitization of the wall and other non-floor surfaces at the Merck GMP areas after the supplier discontinuation of the currently in used LpH and Vesphene agents. The LPO new disinfectant Vesphene introduction and implementation was covered by a Change Request.

The effectiveness of the Vesta Syde SQ was challenged against normal site flora and selected microorganisms with satisfactory results. Demonstrating that it has adequate antimicrobial properties when in contact with the surface for 5 to 10 minutes for walls and other non-floor construction materials.

LPO sanitization In -Situ qualification was executed using disinfectant Vesta Syde SQ 128 Ready-to-use formulation following instructions depicted in the following approved protocols:

1. Vesta Syde SQ Disinfectant Qualification Protocol and In-situ Testing for Pharmacy Rooms
2. Vesta Syde SQ Disinfectant Qualification Protocol and In-situ Testing for Manufacturing Rooms
3. Vesta Syde SQ Disinfectant In-situ Testing for Microbiology Rooms

During the execution of the above-listed protocols, the Vesta Syde was applied to walls, doors, and other applicable surfaces with an atomizing pump. Therefore, the disinfectant was prayed directly to the surface. To ensure adequate contact time with the surface, re-applications were executed until the surface remained wet for 10 minutes. Results reported for all the executions complied with the protocol acceptance criteria.

As part of the Vesta Syde introduction project implementation phase, an alternative to the Vesta Syde application technique challenged during the In Situ studies was requested due to safety recommendations. Based on that, an evaluation of mopping as an application technique for the Vesta Syde was required and documented in this technical memo.

OBJECTIVE/ SCOPE

This evaluation intends to provide justification to support the change in the application technique and determine the impact (if any) on the sanitization process qualification.

This will cover the following evaluation:

- Instructions on the current LPO sanitization procedure.
- Comparison of both application techniques: Spraying and Mopping.
- LPO facility and production type.

Current LPO Sanitization Procedures

Instructions to execute the sanitization process of the GMP areas at LPO are included in different documents used at LPO. Environmental monitoring samples are collected by the Microbiology Evaluation Monitoring Program with a pre-established frequency. No variability in the results was reported that would lead to differentiation in the techniques. Thus, both techniques are adequate to effectively sanitize the LPO facilities using the currently approved disinfectant agents.

LPO Sanitization Requirements

LPO is a non-classified controlled oral solid dosage manufacturing facility. All the products manufactured at LPO are considered to have low microbial susceptibility. Product water activity is below 0.6 aW. The sanitization or disinfection of the walls of the LPO facility type is not required. Therefore, the change in technique is considered a low risk for the LPO environmental control requirements.

CONCLUSIONS

Both application techniques, Mopping and Spaying, are acceptable and can be applied for the sanitization of the GMP areas. Both techniques maintain the contact time of the disinfectant with the surface to guarantee microbial reduction. The In Sit qualifications were executed as part of demonstrating the effectiveness of the Vesta Syde in LPO facilities to control the microbial growth in the environment below acceptable levels. An additional In Situ qualification execution is not required to approve the implementation of the mopping technique for the sanitization of rooms at LPO. However, one execution in a selected room is recommended as a verification run to provide data supporting the evaluation conclusion.

The following actions are recommended:

1. The protocol should be amended to include one sanitization execution on one of the rooms included in the protocol. This document covers the execution of larger rooms, thus representing the worst case for the execution process. Sampling locations, acceptable limits, and general strategy will be maintained as per the original protocol. Only applicable changes, including the mopping technique, will be made in the execution.
2. Summary reports for studies can be approved before the amendment. However, the implementation of the mopping application technique for the rooms covered in the protocols cannot be implemented until the additional sanitization executions covered in the amendment are completed.
3. Satisfactory results of the additional sanitization executed using the mopping technique will be representative of all the GMP areas, and the technique can be applied.
4. Environmental monitoring protocol for the Pharmacy rooms must be amended to include the mopping technique in the current instruction checklists. The specific technique to be used in future monitoring executions will be based on safety area recommendations.

REFERENCES

[1] Merck. (2024, June 24). *Products* [Online]. Available: https://www.merck.com/products/.

[2] WebstaurantStore Blog. (2022). *Cleaning, Sanitizing, Disinfecting: What's the Difference?* [Online]. Available: https://www.webstaurantstore.com/blog/3208/cleaning-sanitizing-disinfecting.html?srsltid=AfmBOopPN6BuP9NVRKFtkRjKIGfDyocKo_sMzJSK6YiaAYlmDzJjDp2.

[3] STERIS Life Sciences. (2024*). LpH III se Phenolic Disinfectant* [Online]. Available: https://www.sterislifesciences.com/products/surface-disinfectants/pharmaceutical-disinfectants/lph-iii-se-phenolic-disinfectant.

[4] STERIS Life Sciences. (2024). Vesphene III st Phenolic Disinfectant *[Online]. Available:* https://www.sterislifesciences.com/products/surface-disinfectants/pharmaceutical-disinfectants/vesphene-iii-st-phenolic-disinfectant.

[5] STERIS Life Sciences. (2024). *Vesta-Syde SQ Quaternany Ammonium Disinfectant [Online].* https://www.sterislifesciences.com/products/surface-disinfectants/pharmaceutical-disinfectants/vesta-syde-sq-disinfectant.