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Qualification studies at SAT acceptance stage of the pharmaceutical containers washing machine

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Abstract. In pharmaceutical practice, glass containers are subject to mandatory cleaning before filling. The presence of dust, microorganisms or other contaminants significantly affects the quality of the medicinal product, in particular, reducing its effectiveness. Proper preparation of containers ensures the safety of medicines and their preservation throughout the entire shelf life. The purpose of the study was to evaluate the effectiveness of glass vial preparation on an automatic washing machine as part of qualification tests to confirm its compliance with production standards. The preparation of vials for bottling included disinfection, soaking, rinsing, washing, drying, depyrogenation, and sterilisation using automated washing machines. Site Acceptance Tests ensured that the equipment worked properly after installation. They included an analysis of the technical documentation, parameters of communication systems and control units of the washing machine. Residual contaminants such as sodium chloride, alkalis, and riboflavin were tested to assess the efficiency of the washing process. Based on the results, a seven-step procedure was defined, which included ultrasonic cleaning, rinsing with purified water, and a final rinse with injection water. These cycles have proven to be effective in the preparation of sterile drug containers. Recommendations for optimising process parameters, such as duration, temperature, chemical composition, and mechanical action, have helped to maximise productivity and minimise maintenance costs. A modern approach in compliance with international ISO standards ensured the high quality of vial preparation. The automated washing machine proved its efficiency, optimised the cleaning process, reduced the risk of contamination, and guaranteed the reliability of packaging preparation for sterile medicines

Keywords: glass containers for pharmaceutical use; bottle washing machine; site acceptance tests (SAT); user requirement specification (URS); fluorescence test for cleanability

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Introduction

Modern pharmaceutical developments are focused on ensuring the safety and high quality of parenteral medicines and biopharmaceuticals. One of the key stages in this process is the preparation of containers for sterile products. Proper treatment of the containers helped to reduce the risk of contamination and ensure that the quality of the products is maintained throughout their shelf life. In the context of the implementation of GMP principles and cost optimisation in the Ukrainian pharmaceutical industry, the study of validation and qualification of equipment for washing, drying, and depyrogenising containers has become particularly relevant. However, the scientific literature insufficiently covers the aspects of acceptance testing (AT), which leads to gaps in theoretical knowledge and practical application.

Innovative developments in the pharmaceutical industry use processes such as aseptic manufacturing to ensure the safety and high quality of parenteral products and biopharmaceuticals for patients with various medical conditions. K. Sampathkumar & B.A. Kerwin (2024) noted that to accelerate development, ensure compatibility between formulation and storage container, and reduce production costs, pharmaceutical companies can use predefined container/sealant systems that are compatible and prequalified for use with filling lines at manufacturing sites. S. Panighello & G. Pintori (2024) highlighted that the pharmaceutical industry depends on reliable and efficient packaging to ensure the integrity, safety and efficacy of its products, and glass packaging has long been a key material in pharmaceutical packaging. In pharmaceutical practice, glass containers must be washed before being filled with the drug. The presence of dust, pathogens, and other contaminants can significantly affect the quality of the medicinal product, reducing its effectiveness. The proper preparation of pharmaceutical containers should ensure the safety and quality of the product throughout the entire shelf life.

S. Yoneda *et al*. (2021) noted that containers supplied by manufacturers, even if they are manufactured to high quality standards, may contain various particles that need to be removed before filling. Therefore, containers intended for sterile products are handled differently depending on the material and type of product being prepared. F. Liu & R. Hutchinson (2024) highlighted that the presence of particles, endotoxins, and chemical contaminants in parenteral medicinal products (PMPs) poses a significant risk to the safety and efficacy of the product. Even if containers are manufactured to high standards, they may still contain particles that need to be removed before filling. These contaminants, if not removed properly, can lead to serious adverse reactions in patients. Therefore, sterile product containers must be handled with great care, considering factors such as the material and type of product being prepared. Effective removal of particles is essential to ensure the safety of both humans and animals, which underlines the need for strict quality control in the preparation and handling of these products.

Researchers F. Jameel *et al*. (2021) also noted that additionally, during the drying and depyrogenation stages of vial preparation and washing, static charges can form on the surface of vials, potentially affecting dosing during filling, mechanical visible and invisible particles, surface changes in curved glass vials, coating failure, alkali depletion in the glass structure, and alkali ingress into the drug product environment.

Researcher W.G. Lindboe (2021) studied the evolution of approaches to container preparation inspection in the pharmaceutical industry. He noted that these approaches have undergone significant changes, from conventional methods to innovative solutions driven by advances in technology and the type and level of contamination of containers. In his paper, W.G. Lindboe described in detail the stages of vial preparation, which may include disinfection, soaking, rinsing, washing, drying, depyrogenation, and sterilisation. The researcher paid special attention to the use of automated washing machines, which significantly increase the efficiency and accuracy of these processes.

The selection of appropriate pharmaceutical equipment for the preparation of sterile product containers and the proper qualification of washing machines are necessary steps to ensure and guarantee the quality of sterile and parenteral medicines and biopharmaceuticals for patients with various medical conditions. Washing and sterilisation (depyrogenation) machines for containers are among the pharmaceutical equipment that requires qualification – documentary evidence that a particular equipment works correctly, reproducibly, and produces the expected results.

The authors O.O. Saliy *et al*. (2019) emphasised that the pharmaceutical industry, where GMP principles are mandatory, is also gradually moving to lean manufacturing. In the context of the current Ukrainian economy, this approach is aimed at reducing operating costs while maintaining the proper quality of medicines. Y. Chen *et al*. (2023) also noted that the development of a combined and optimisation approach to minimise energy consumption while maintaining product quality will lead to improving energy efficiency and reduce the cost of qualification studies without adversely affecting production or product quality. According to FDA recommendations, "containers and closures for drugs must be clean and, if required by the nature of the product, sterilised and treated to eliminate pyrogenic properties to ensure fitness for intended use" (U.S. Food and Drug Administration, 2024).

Site Acceptance Tests (SAT) are a critical quality management stage conducted "on-site." Testing occurs when a washing machine is accepted at its site. These final tests are essential as they confirm the washing machine's performance after installation and adjustment, ensuring it is functional as a complete unit. Scientific literature has scarcely covered approaches, best practices, results, and challenges in qualification testing of pharmaceutical equipment, including washing, sterilisation, and depyrogenation machines for glass containers,

particularly at the SAT acceptance stage at pharmaceutical production sites.

The purpose of this study was to conduct SAT qualification studies for a pharmaceutical vial washer designed for sterile formulations.

Materials and Methods

The study was conducted at a pharmaceutical enterprise Ukraine equipped with a new line for washing, sterilising, and depyrogenating glass vials for sterile formulations manufactured by Ambica Pharma Machines Pvt. Ltd, India. The line included a vial washing machine and a sterilisation/depyrogenation tunnel. Depyrogenation methods, such as heating tunnels, address pyrogenicity issues, but residual particles, endotoxins, and chemical contaminants may cause adverse reactions in humans or animals. Therefore, vial washing machines are identified as critical devices, and validation qualification studies, conducted according to available guidelines such as EU GMP Annex 15 (European Commission, 2013-2014), are essential for their effective and compliant operation.

Studies on SAT stage:

Visual inspection. The analysis of the documentation included a check Design specifications, Electrical Wiring Diagrams, Installation Instructions, Operation Manual and Functional Specifications, Maintenance Instructions, Material Certificates, IQ Protocol, OQ Protocol, FAT Protocol and Report, SAT Protocol, Instructions for Key Machine Components, Functional Specification, Equipment Design Specifications, Supplier test documents, Cleaning Instructions. The enterprise carried out a check of the connection of systems and identification of control points to confirm compliance of the equipment with technical specifications (EU guidelines for good manufacturing practice…, 2015). Acceptance criteria: Compliance with user requirements specification (URS) and purpose of application (Shoturma, 2024).

Qualification studies were performed on an automated linear continuous-motion washing machine, where vials undergo various cleaning stages, including pre-washing, main washing, and rinsing. ISO 8362-1 Type I 100R glass vials with a 20 mm neck diameter, manufactured by Bormioli Pharma S.p.A., Italy, were used for tests.

Washing and preparation process for vials for sterile formulations. The automatic vial washing machine was designed for external and internal cleaning of glass cylindrical containers with volumes of 50 and 100 ml. Vials, packed in polyethylene wrapping, were transported to a "D"-class cleanroom where the washing machine and sterilisation/depyrogenation tunnel were installed. Vials were unpacked and placed on the feed tray/conveyor of the washing machine, from where they were transported to the washing zone and underwent all stages of cleaning including: Ultrasonic cleaning; Washing with recirculated water; Washing with purified water (PW); Final rinsing with water for injection (WFI). The vials were unloaded from the washing machine and transported via a conveyor to the sterilisation/depyrogenation tunnel, where they underwent the following sterilisation stages: preheating – wet vials were preheated and dried; sterilisation/depyrogenation: the vials were exposed to high temperatures to ensure sterility and the removal of pyrogens; cooling: the vials were cooled to 20°C.

Considering the martial law in Ukraine, the conduct of FAT tests online, and the impossibility of conducting SAT tests in the presence of specialists from the equipment manufacturer, as part of the SAT acceptance, tests for soluble substances were conducted to confirm that the equipment can function as intended. Qualification studies included testing for the absence of contaminants on the surfaces of vials and inside them after completing a washing cycle in the machine. For these tests, a predetermined amount of each contaminant was applied to test vials, and the number of residues was determined after the washing cycle. The reduction in contaminants was used to evaluate the machine's performance.

Sodium chloride challenge test (soluble substances). A 30% aqueous solution of sodium chloride was prepared, and 0.1 ml was applied to the inner surface of 10 test vials. The vials were rotated to coat their inner surfaces and allowed to air-dry at room temperature. The test vials were marked and loaded into the washing machine along with uncontaminated vials. The test vials were placed at the beginning, middle, and end of the washing cycle. After washing cycle, the vials were carefully removed to avoid environmental contamination.

The vials were rinsed with distilled water, and the residual amounts of sodium chloride in the rinses were examined by a qualitative reaction. 0.2 ml of 1.0 M silver nitrate and 1 ml of dilute nitric acid were added. The procedure was repeated for flushes from containers not contaminated with sodium chloride. Acceptance criteria: all vials should be free of sediment, opalescence, or turbidity. The amount of chloride ions was determined by direct argentometry with potentiometric determination of the equivalence point (Pearson & Elstob, 1970). Acceptance criteria: absence of sodium chloride in the rinses from the inner surface of the vials after washing.

Test for the absence of chemicals (with alkali). An aqueous solution of alkali of known concentration was prepared and 10 vials were contaminated, subjected to a washing cycle, and the wash water was collected similarly to the test with sodium chloride. The alkali content of the wash water was determined by titration with a standard solution of sulphuric acid until the colour of the phenolphthalein indicator changed (Dhoke, 2023). Acceptance criteria: absence of alkali in the rinses from the inner surface of the vials after washing.

Chemical contamination (riboflavin testing). The use of fluorescent riboflavin allowed for clear visualisation of areas that were difficult to clean (edges, corners, etc.) (Salo *et al.*, 2008). An aqueous solution of riboflavin (Hubei Guangji Pharmaceutical Co., Ltd., China) was prepared at a concentration of 0.2 g/L as a test residue of the chemical. The aqueous solution was applied to the surface of 10 test vials

to be loaded into the washing machine. Riboflavin is highly soluble in water and has an ultraviolet fluorescence at 385-395 nm. The contamination had a fluorescent yellow colour that was easily visualised (VDMA, 2007). The test vials were placed between the other vials so that they would enter the washing machine at the beginning, middle, and end of the washing cycle. After the washing cycle, the test vials were carefully removed to avoid other contamination from the environment. The cleaning efficiency was evaluated based on the presence of any residual contamination by visual assessment and under UV light at 360 nm to detect any signs of riboflavin contamination by fluorescence. The criterion for machine compliance was the absence of riboflavin fluorescence on the inner surfaces of the vials after washing.

Results and Discussion

The washing and preparation machine for sterile vials is a relatively simple device used to clean containers during pharmaceutical manufacturing. The first acceptance test (SAT) was conducted at the pharmaceutical enterprise. During SAT acceptance, only installation qualification (IQ) and operational qualification (OQ) of the machine were performed, as no regulatory requirements explicitly specify that washing machine performance must be qualified.

***Table 1**. Documentation review for proper installation and operation of the vial washing machine*

No.	Parameter	Available or not?		
		Yes	No	Undetermined
1.	Design specifications (DS) Drawings of the general location	+		
2.	Electrical Wiring Diagrams	+		
3.	Installation Instructions	+		
4.	Operation Manual and Functional Specifications (FS)	+		
5.	Maintenance Instructions	+		
6.	Material Certificates	+		
7.	IQ Protocol	+		
8.	OQ Protocol	+		
9.	FAT Protocol and Report	+		
10.	SAT Protocol	+		
11.	Instructions for Key Machine Components	+		
12.	Functional Specification	+		
13.	Equipment Design Specifications	+		
14.	Supplier test documents such as welder qualifications, welding records, roughness checks	+		
15.	Cleaning Instructions	+		
16.	Original Instructions and Qualification Certificate for Key Components	+		

***Source:** based on authors' own research*

The SAT included documentation review, system connectivity verification, and control point identification. The results are summarised in Table 1. Documentation was critical for successful commissioning and verification.

The analysis of the documentation for the installation and operation of the vial washing machine revealed that most of the necessary materials were available, ensuring that the machine could be properly installed, operated, and maintained. Key documents, such as the Design Specifications (DS), including the general layout drawings, were present, providing the foundational framework for the installation. The availability of Electrical Wiring Diagrams ensured proper electrical connections, which is crucial for ensuring safe operation.

Additionally, Installation Instructions were available, detailing the setup process for the machine, while the Operation Manual and Functional Specifications (FS) provided guidance on how to operate the machine and its expected performance. Maintenance instructions were also included, helping to ensure the longevity of the equipment and its proper upkeep. The presence of Material Certificates guaranteed that the materials used in the construction of the machine met the required quality standards. Furthermore, the IQ Protocol (Installation Qualification) and OQ Protocol (Operational Qualification) documents were available, which were essential for verifying that the machine was correctly installed and functions as intended.

Cleaning Instructions is also critical, as proper cleaning procedures are necessary to maintain hygiene standards, particularly in environments dealing with pharmaceutical or medical equipment. Without these documents, certain aspects of the installation and operation may not fully comply with regulatory standards or best practices. The machine's design and functional characteristics met the User Requirements Specification (URS). Table 2 shows the results of the verification of the electrical system parameters of the sterile vial washer machine. It lists the parameters required to ensure the proper installation and operation of the vial washer.

***Table 2**. Verification of utility supply systems parameters of the vial washing machine for sterile forms*

No.	Parameter	Expected Result		
		Accept	No	Undetermined
1.	Total power load 15.7 kW (380 V, 50 Hz, 3 phases, 5 wires)	√		
2.	Compressed air 50 [L/min] at 6-7 [bar]	√		
3.	WFI pressure [bar] 3-4 [bar]	√		
4.	WFI temperature [°C] 70-80 [°C]	√		
5.	WFI consumption [m^3/h] 1.0 [m^3/h]	√		
6.	Length (mm) To be specified on site	√		
7.	Width (mm) To be specified on site	√		
8.	Height (mm) To be specified on site	√		
9.	Weight (kg) To be specified on site	√		

***Source:** based on authors' own research*

The table lists the various electrical systems and physical characteristics that need to be verified. For each parameter, the expected result is given and the verification status is indicated as "Accept", "No" or "Undetermined". The parameters are critical to the operation of the machine, especially in a sterile environment where precise conditions are required. Compressed air is a critical utility for the functioning of the washing machine, typically used to power certain components or assist with the cleaning process. The expected flow rate is 50 L/min at a pressure of 6-7 bar. The WFI system is used to provide water of the highest purity, necessary for sterilisation processes. The expected pressure range for WFI is 3-4 bar. The machine's WFI pressure has been verified as within the expected range. The temperature of WFI is critical for ensuring effective sterilisation. The expected temperature range for WFI is between 70-80°C. The consumption of WFI is expected to be 1.0 m^3/h. This is an important metric for determining water usage and efficiency.

The verification results for most of the utility supply parameters indicate that the vial washing machine is in compliance with the expected specifications. All key utilities, such as total power load, compressed air, WFI pressure, temperature, and consumption, have passed the verification, showing that the machine can function as intended within the provided operational environment. The location environment of the bottle washing machine was also checked, namely the available space in the production room (the room plan was assessed), the available ceiling height, the requirements for drains (pH neutralisation, wastewater cooling), and the maximum noise level allowed (dBA). The verified parameters confirm that the Installation Qualification (IQ) has been successfully completed. The automated vial washing and preparation machine has been installed as specified in the URS, and the utility systems were sufficient to support its operation and ensure proper functionality of the equipment.

Verification of Control Units for the Vial Washing Machine for Sterile Forms provides a comprehensive overview of the control systems and safety parameters for the vial washing machine. Table 3 lists various operational conditions and failure scenarios, specifying whether the system is set to display, stop, signal, or reset (either manually or automatically) in response to each condition. The parameters are critical for ensuring the machine's safe operation, particularly in a sterile manufacturing environment.

***Table 3**. Verification of control units for the vial washing machine for sterile forms*

No,	Parameter	Requirements						Result	Remarks
		Customise	Display	Stop	Signal	Manual reset	Automatic reset		
1.	Performance and applications	◆	◆					+	
2.	Low compressed air pressure		◆	◆	◆	◆		+	
3.	Low pressure WFI		◆	◆	◆	◆		+	
4.	Low recycled water pressure		◆	◆	◆	◆		+	
5.	Vials min. accumulation at the power supply station		◆	◆	◆		◆	+	

Table 3. Continued

No,	Parameter	Requirements						Result	Remarks
		Customise	Display	Stop	Signal	Manual reset	Automatic reset		
6.	Pump overloading		◆	◆	◆	◆		+	
7.	Low water level		◆	◆	◆		◆	+	
8.	Low water temperature		◆	◆	◆		◆	+	
9.	Engine overloading		◆	◆	◆	◆		+	
10	Feed from the next machine is blocked or malfunctioning		◆	◆	◆		◆	+	

Source: *based on authors' own research*

The system is appropriately configured to address a wide range of fault scenarios and operational issues that could occur during the machine's use. Each fault condition is set to activate the necessary safety measures, including display alerts, stoppage of operation, signalling the issue, and automatic resets where applicable. These safety measures are crucial in ensuring the machine operates within the required standards, preventing any potential damage or failure.

The configuration ensures comprehensive monitoring of vital processes such as air pressure, water levels, pump and engine load, and any potential malfunctions related to the feed from the next machine. The automatic reset feature in many cases is particularly valuable in maintaining continuous operation and reducing the need for manual intervention.

The control units for the vial washing machine have been properly configured to address a variety of operational faults and performance issues. The system's comprehensive safety and alert mechanisms, including display, stop, signal, and automatic reset functions, provide adequate protection for both the machine and the process. The verified results demonstrate that the machine's control systems are fully prepared to ensure safe and efficient operation in a sterile production environment. Washing Cycles and Utilities Systems Applied to the Sterile Vial Washer provides an overview of the various washing cycles involved in the operation of the sterile vial washer, along with the corresponding utility systems required for each cycle.

Therefore, the results of the site acceptance test (SAT), which included installation qualification (IQ), were satisfactory and can guarantee that the washing machine, once installed and configured, will perform according to URS design parameters and the prepared containers will meet expectations for cleanliness, identity, safety and quality. Based on the results of the SAT acceptance, the vial washing cycles were determined, as shown in Table 4.

Table 4*. Washing cycles and utilities systems applied to the sterile vial washer*

No. of washing cycle	Cycles	Utilities systems
1	Ultrasonic cleaning	Compressed air + tap water
2	Pre-washing of vials	Recycled water (recycled water)
3	Vial blowing	Compressed air, tap water
4	Washing of vials	Purified water (WP)
5	Vial blowing	Sterile compressed air
6	Rinsing vials	Water for injection (WFI)
7	Drying of vials	Sterile compressed air

Source: *based on authors' own research*

Each row represents a distinct step in the vial washing process, specifying the cycle type and the utility systems used during that step. The utility systems include compressed air, tap water, recycled water, purified water (WP), sterile compressed air, and Water for Injection (WFI), all of which play a critical role in ensuring the effectiveness of each washing step. As can be seen from Table 4, the preparation of compressed air and its supply to the vial washing machine has a significant impact on meeting the requirements for the preparation of non-sterile primary packaging. Cleanliness is achieved by the machine's option of inverting the container under the influence of gravity and the use a filtered compressed air for cleaning process.

The table below shows that a variety of utility systems are employed across different cycles, each serving a specific purpose in the cleaning and sterilisation process. The washing cycles outlined in Table 4 demonstrate a well-structured and efficient approach to vial cleaning, with careful consideration of the utility systems required at each stage. The use of appropriate utilities, such as recycled water for pre-washing and WFI for final rinsing, ensures both cost-effectiveness and compliance with the highest standards of sterility. The combination of compressed air and sterile compressed air for drying and blowing also contributes to maintaining the vials' cleanliness and sterility throughout the process. Overall, the system is well-designed to meet the stringent requirements of sterile vial washing in pharmaceutical manufacturing.

Test vials were prepared and vial washing cycles were performed. The riboflavin test is designed to provide a

preliminary demonstration that the proposed wash cycles clean the vials. The results of the evaluation of the cleaning and preparation of pharmaceutical containers after the washing cycle are presented in Table 5.

***Table 5**. Results of qualification tests for cleaning and preparation of pharmaceutical containers after the washing cycle*

Qualification tests	Total number of vials	Number of test vials	Number of contaminated vials	
			Visual assessment	Evaluation under ultraviolet light
Sodium chloride challenge test (soluble substances)	300	30	Not detected	-
Test for the absence of chemicals (with alkali)	280	28	Not detected	-
Chemical contamination (riboflavin testing)	300	30	Not detected	Not detected

***Source:** based on authors' own research*

This successful run of a full cleaning cycle demonstrated that all systems were functioning correctly and confirmed that all sensors and probes were calibrated, operational, and compliant with the requirements outlined in the URS. Contaminant testing had been conducted on both the surfaces and interiors of the vials post-wash cycle, with predetermined amounts of various contaminants applied to test vials prior to washing. Post-cycle evaluations detected no residual contaminants, highlighting the high performance of the machine. Additionally, riboflavin testing was employed to identify critical cleaning points that could have posed hygiene risks or structural defects. Based on these results, the Operational Qualification (OQ) was successfully completed.

Glass remains the preferred primary packaging material for parenteral medicines, primarily due to its chemical resistance, inertness, strength, and transparency (Schaut *et al.*, 2014). The most commonly used glass vials are ISO 8362-1 type I 6R, 10R and 100R with 20 mm diameter elastomeric stoppers coated with fluoropolymer. These vials are available in baths, pre-washed and depyrogenated, ensuring that they are treated in the same way as during drug manufacturing. The stoppers are also available pre-washed and ready to be sterilised before use, which minimises the necessary preparation steps and brings them closer to the manufacturing process (Teska *et al.*, 2016). The use of fluoropolymer-coated stoppers guarantees the integrity of the vials and prevents contamination from external sources, making them ideal for sensitive pharmaceutical products.

In pharmaceutical practice, glass containers must be washed before filling with the drug. The presence of dust, pathogens and other contaminants can significantly affect the quality of the medicine, reducing its effectiveness. Proper preparation of pharmaceutical containers ensures the safety and preservation of products within the established shelf life (Kuzmina & Strokan, 2013). According to the authors, even minor traces of contamination can lead to instability of the dosage form, which can negatively affect its therapeutic efficacy. Therefore, ensuring that containers are thoroughly cleaned is a critical step in the pharmaceutical manufacturing process.

Mechanical visible and invisible particles, surface changes in curved glass vials, coating breakdown, alkali depletion in the glass structure and release of alkali into the drug product environment (Ditter *et al.*, 2018). The research highlights the crucial role of maintaining the integrity of glass containers to avoid interactions between the packaging and the pharmaceutical product. Even small changes to the glass surface, such as alkali release, can alter the chemical composition of the medicinal product, affecting its safety and efficacy. Therefore, proper washing protocols are essential to prevent such problems and ensure product quality.

Scientific publications provide data on the regulatory framework governing laboratory equipment and metrological qualification work, and also propose approaches to the classification of equipment for determining the scope of qualification work. M.M. Nesterchuk *et al*. (2009) discussed the need to develop clear qualification standards to ensure that laboratory equipment, including cleaning systems, performs in accordance with established regulatory requirements. They emphasised the importance of periodic testing and certification of equipment to minimise the risks associated with non-compliance and to maintain consistency in the production process. This approach is critical to meeting the stringent safety and quality standards required in the pharmaceutical industry.

V.K. Yakovenko *et al*. (2015) identified key features and opportunities for qualification of spectrophotometric equipment in pharmaceutical analytical laboratories. The researchers focused on the importance of proper qualification of spectrophotometric equipment to ensure accurate measurements in pharmaceutical analysis. Their study illustrated how qualification procedures for such equipment can improve the accuracy of analytical results, which is essential for the safe production of pharmaceutical products. Proper qualification of analytical equipment ensures that measurements are consistent and reliable, thereby supporting the overall quality control process.

Reviews of vial and rubber stopper washers include tests for insolubles, solubles, and endotoxins by S.J. Shinde *et al*. (2014) emphasised the importance of testing cleaning solutions for impurities that may contaminate pharmaceutical products. In their study, the researchers emphasised that the water quality and purity of the chemicals used in the washing process are vital to maintaining

the safety and stability of the final medicinal products. The researchers recommended comprehensive testing protocols to detect endotoxins and other contaminants that may be present in cleaning solutions, ensuring that the cleaning process does not result in the release of harmful substances into the packaging.

P. Lopolito *et al*. (2017) demonstrated how process parameters such as time, temperature, chemical composition, coating, and mechanical action affect the performance of automated vial washing systems. The researchers found that optimising these parameters led to a significant increase in cleaning efficiency and a reduction in the risk of contamination. They also emphasised that variations in these parameters can affect the quality of the cleaning process, highlighting the importance of careful control of the washing conditions. Their study illustrated how fine-tuning process variables in automated systems can minimise the need for manual intervention, thereby improving productivity and safety in pharmaceutical manufacturing.

In summary, qualification studies of pharmaceutical equipment are limited, but in the rapidly evolving global pharmaceutical market, understanding the basics of cleaning helps optimise automated systems and avoid common mistakes that reduce cleaning efficiency, productivity and increase maintenance costs. The results of these studies contribute to ongoing efforts to refine cleaning procedures, improve automation systems, and ensure safe pharmaceutical production. Proper equipment qualification and process optimisation play a key role in achieving high standards of purity and ensuring the long-term stability of medicines.

Conclusions

Based on the results of the on-site acceptance testing (SAT-acceptance), including documentation review, system connections, and control unit verification, it has been established that the equipment, its configuration, and spare parts comply with the technical specifications outlined in the contract. Key documents, such as the Design Specifications (DS), including the general layout drawings, were present, providing the foundational framework for the installation. The availability of Electrical Wiring Diagrams ensured proper electrical connections, which is crucial for ensuring safe operation. The equipment meets the preselected design parameters. The results obtained are satisfactory and confirm that, after installation and setup, the washing machine will function properly, ensuring that the washed and prepared containers meet expectations for cleanliness, identity, safety, and quality.

The communication systems and washing/preparation cycles for pharmaceutical vials intended for sterile medicinal forms have been defined. All key utilities, such as total power load, compressed air, WFI pressure, temperature, and consumption, have passed the verification, showing that the machine can function as intended within the provided operational environment. The verified parameters (the room plan), the available ceiling height, the requirements for drains (pH neutralisation, wastewater cooling), and the maximum noise level allowed (dBA) were confirm that the Installation Qualification (IQ) has been successfully completed. It is confirmed that the system control units is appropriately configured to address a wide range of fault scenarios and operational issues that could occur during the machine's use. Each fault condition is set to activate the necessary safety measures, including display alerts, stoppage of operation, signalling the issue, and automatic resets where applicable.

Contaminant testing on vial surfaces and interiors after the machine's washing cycle, using test contaminants such as soluble substances (sodium chloride), chemical agents with alkali, and riboflavin, followed by post-wash evaluations, confirmed the absence of contaminants. This indicates the high performance of the machine and the effectiveness of the selected washing cycle. Further research is also focused on optimising testing protocols for evaluating the machine's performance in removing biological contaminants under varying operational conditions and container specifications. Additionally, studies evaluating the effectiveness of the washing cycle on non-standard or challenging vial geometries, and testing for the removal of biological contaminants and endotoxins, would provide a more comprehensive validation of its capabilities.

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None.

Conflict of Interest

None.

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Кваліфікаційні дослідження на стадії SAT приймання машини для миття та підготовки фармацевтичних контейнерів

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Анотація. У фармацевтичній практиці скляні контейнери підлягали обов'язковому миттю перед розливом препарату. Наявність пилу, мікроорганізмів або інших забруднень суттєво впливає на якість лікарського засобу, зокрема зменшуючи його ефективність. Належна підготовка контейнерів забезпечує безпеку препаратів і їх збереження протягом усього терміну придатності. Дослідження було спрямоване на оцінку ефективності підготовки скляних флаконів на автоматичній мийній машині в рамках кваліфікаційних випробувань для підтвердження її відповідності виробничим стандартам. Підготовка флаконів до розливу включала дезінфекцію, замочування, ополіскування, миття, сушіння, депірогенізацію та стерилізацію із використанням автоматизованих мийних машин. Гарантію належної роботи обладнання після встановлення забезпечували приймальні випробування (Site Acceptance Test – SAT). У їх межах проводили аналіз технічної документації, параметрів систем комунікації та вузлів контролю мийної машини. Для оцінки ефективності миття тестували залишкові забруднення, такі як хлорид натрію, луги та рибофлавін. На основі отриманих результатів визначили семистадійну процедуру, що включала ультразвукове очищення, промивання очищеною водою та остаточне промивання водою для ін'єкцій. Ці цикли підтвердили свою ефективність у підготовці контейнерів для стерильних лікарських засобів. Рекомендації щодо оптимізації параметрів процесу, таких як тривалість, температура, хімічний склад і механічна дія, дозволили досягти максимальної продуктивності та мінімізувати витрати на обслуговування. Сучасний підхід із дотриманням міжнародних стандартів ISO забезпечив високу якість підготовки флаконів. Автоматизована мийна машина підтвердила свою ефективність, оптимізувала процес очищення, знизила ризики забруднення та гарантувала надійність підготовки упаковки для стерильних лікарських засобів

Ключові слова: скляні контейнери для застосування у фармації; машина для миття флаконів; приймальні випробування на місці (ПВМ); специфікація вимог користувача (СВК); флуоресцентний тест для перевірки здатності до очищення