Buffer Formulation Vent Filter Re-Use at Parenteral Manufacturing Plant

Jorge Figueroa-Rodríguez
Master in Manufacturing Competitiveness
José A. Morales, PhD
Industrial and Systems Engineering Department
Polytechnic University of Puerto Rico

Abstract *— For sterilization-in-place cycles that used vent filters as a redundant non-contact product, the filter membranes could be re-used several times without impacting their integrity neither compromising the sterilization cycle. At a parenteral manufacturing plant in Puerto Rico, the vent filter is discarded after exposed to a one-single sterilization-in-place cycle. With the implementation of this project, the vent filter used during the sterilization-in-place as part of the buffer formulation at Manufacturing Plant can be re-used up to 50 times. With DMAIC (Define, Measure, Analysis, Improve and Control) quality strategy, the use of vent filters during buffer formulation at Manufacturing Plant was improved. Under DMAIC, the sterilization conditions of the filter's manufacturers was identified as the worst-case sterilization scenario. Also, validation activities were executed to confirm no moisture residual particles were found in the vent filter membrane after multiples consecutives sterilization cycles. At the end, this project implementation will provide better manufacturing flexibility and cost-savings for up to USD 105,000 yearly.*

Key Terms *— reuse filter, steaming, sterilization-in-place, vent filter*

PROBLEM STATEMENT

As part of manufacturing process improvements, it was identified an opportunity that could provide more flexibility in the manufacturing process and cost savings. Currently, the use of vent filters during the manufacturing process is one time only and is a non-product contact part. Vent filters are used in buffer preparation fixed tanks during Steam-In-Place (SIP) cycle after the preparation of buffer solutions. When finished, vent filters are discarded. This practice provides high costs to the manufacturing process.

Research Description

For the purpose of this research, the industry under investigation will be identify through this research paper as Manufacturing Plant, parenteral industry in Puerto Rico.

Currently, the plant buffer vent filters are one time use only. Buffer vent filters are used as part of the buffer fixed tanks. The primary function of the vent filters (hydrophobic membranes) is to protect the tanks' internal volume from the environment while exchanging air from the manufacturing room. Vent filters protect the tanks internal volume when air moves toward the tank's interior, but also protect the environment when air is expelled out of the tank's head space. These filter membranes and housings are not direct product contact elements.

The reason of this research is to provide substantial evidence that the vent filter used during the SIP cycle as part of the buffer preparation can be re-used up to 50 times. Using vent filter manufacturer's data, it was found that the life-time of the vent filters is longer than the time-use during the SIP cycle in Manufacturing Plant. Calculations were performed to convert the maximum time-use of the manufacturer to the Plant SIP cycle using a safety factor. Based on the calculations, 50 times was determined. Validation activities are required to ensure that no humidity presence is found in the vent filter after SIP cycle; the humidity presence in the vent filter could cause problems in subsequent SIP cycles.

Research Objectives

The objectives of this research are:

- Report empirical evidence to re-use the vent filter used during the SIP cycle as part of the buffer preparation activities.

- Compute the new life-time of the vent filters to be used in the manufacturing plant.
- Determine the presence of humidity particles in the vent filters after Manufacturing Plant SIP cycle.
- Implement vent filter's re-use project in Manufacturing Plant using Project Management methodology.

Research Contributions

Research conducted in parenteral industries will help to extend the life-time of vent filters during the SIP cycle as part of the buffer preparation activities from on-single use to 50 times. Also, by using Project Management methodology, manufacturing process will be developed to reuse the vent filters following the medical regulations; this guarantees the quality when manufacturing buffer solutions. This research will provide manufacturing flexibility in the formulation of biomedical products, more manufacturing capacity and cost savings up to 105,000 USD yearly.

LITERATURE REVIEW

Sterilization describes the process that eliminates all forms of microbial life. Steam under pressure, dry heat, hydrogen peroxide gas plasma, ethylene oxide (EtO) gas and liquid chemicals are the principal sterilizing agents used in the industry [1]. Another similar concept is cleaning, cleaning is the action of remove visible soil from objects and surfaces and normally is performed manually or mechanically using water with detergents or enzymatic products. Unlike cleaning, the sterilization focused at a microorganism's level.

To ensure sterility of product contact surfaces from the start of each operation, the entire path of the sterile processing stream should be sterilized [2]. Also, to ensure the correct sterility level, the sterilization needs to be validated by either biological and chemical indicators and/or physical measurements [3]. The term "sterile" is defined as "free of all viable organisms". The most frequently-used sterilization type is the steam sterilization. Steam sterilization is nontoxic, inexpensive, rapidly microbicidal and sporicidal. Steam is considered water in the vapor state [2].

The basic principle of steam sterilization is to expose to direct steam contact at the required temperature and pressure for the specified time. These are the 4 key parameters: steam or moisture, temperature, pressure and time, validated whether by chemical and biological indicators or physical measurements. Biological indicator is a population of microorganisms inoculated onto a suitable medium and placed within the appropriate sterilizer load locations to determine the sterilization cycle efficacy of a physical or chemical process. The "challenge microorganism" is selected based upon its resistance to the given process [4].

Per [5], steam sterilization principles consisted on six factors continuously monitored during the sterilization:

- **Time:** The exposure sterilization time is the minimum sterilization time required to eliminates the presence of microorganisms.
- **Temperature:** The temperature of the saturated steam is directly related to time and pressure. In case of time, the steam sterilization temperature increases when reduces the time of the sterilization.
- **Moisture:** The moisture level during the steam sterilization has the ability to denature or coagulate proteins. Saturated steam in the system to be sterilized is in equilibrium with heated water at the same pressure, which means it contains the maximum amount of moisture without liquid condensate present.
- **Direct Steam Contact:** To consider sterile, all surface in the system needs to be contacted with the steam. When steam has contact with the surface the energy stored is transferred to the surface. The energy stored in steam is much higher than dry air or water at the same temperature.
- **Air Removal:** No air is required to sterilize the system. Thus, the air is vacuumed in the system during the pre-conditioning phase.

- **Dry:** System shall be properly dried after sterilization completion. Condensation is the natural result of steam contact with the cooler surfaces of the system during the heating and exposure phases. The presence of condensation can cause re-contamination of the system.

During the steam sterilization, the temperature has a direct relationship with pressure. Increasing the steam pressure allows an increase in the temperature of the pressurized steam. To assure sterility level, it is recommended that a temperature of 121 °C (249.8 °F) be maintained at least 30 minutes. To maintain this temperature, the pressure recommended is 15.95 psig [6].

Steam sterilization has many advantages, it a simple, rapid, effective, safe environment-friendly and low-cost sterilization method. Typically, the steam sterilization cycles consisted on the following phases [7].

- **Pre-Conditioning:** During this phase, the air is removed from the system.
- **Exposure:** During this phase, the system is exposed to programmed temperature. Also, this phase instead of use programmed recipe parameters, it can be controlled by biological or chemical indicators. Biological indicators (BIs) are considered the best test for sterilization. In case of chemical indicators, provide immediate evidence of steam penetration, not necessary of sterilization.
- **Post-Conditioning:** During this phase the dry system is cooled.

As temperature increases beyond the range where biological activities occur at an optimum rate, cellular metabolism begins to slow down. For each type of cell there is a temperature limit above which vital proteins, enzymes and nucleic acids are permanently damaged and irreversible death occurs [8].

SIP processes help to provide enhanced sterility assurance for aseptically filled products. The advantage of SIP lies in the fact that the system is sterilized as a complete unit eliminating aseptic assemblies whereby points of contamination may result. SIP is a critical process because enables the entire processing system to be sterilized as a single entity thereby reducing the need for aseptic connections [9]. The SIP process consisted to apply heat on use saturated steam – water mixture in which the steam is in equilibrium with the condensate—resulting in de-saturation or "superheating". Since the sterilization aims to eliminate the presence of microorganisms is more effective when saturated steam contacts the microorganism. Presence of liquid water is required for the effective sterilization through denaturalization of proteins in the cell wall at temperatures in the range of 121 °C [10]. The saturated steam undergoes a phase change to the liquid state at which time the heat of condensation is released. The condensation is released through an exit system that consists mainly in an exit line with a vent filter.

Based on [11], the vent filter includes a housing coupled to the container. The housing includes a first opening communicating with an interior of the container and a second opening communicating with an exterior of the container. The housing defines a gas flow path between the first and second openings. A filter is coupled to the housing and disposed across the gas flow path such that gas flowing between the openings flows through the filter. The filter includes a porous metal hydrophobic filter medium. The components of the assembly may be fabricated from materials that are durable and resistant to deterioration due to elements stored within the container, as well as environmental elements. To achieve reproducible sterilization conditions and to avoid damage to the installed filter cartridges, the sterilization process needs to be performed at controlled and monitored conditions.

Then sterilization process should be developed and validated at controlled condition, thus any component from the system to be sterilized is damaged. Following are general principles when a system with filter cartridges is steam sterilized [5].

- **Condensate:** No condensate should be in the filter cartridges after steam sterilization

because the resistance produced to the flow that will generate increased differential pressure across the filter at elevated temperatures. Thus, this will cause maximum stress and possible damage to the filter cartridge.

- **Particulate:** Steam lines can suffer corrosions over a prolonged time-period. Pipe corrosion can result in the presence of particulate consisting of metal fragments, which can be carried by the steam to the filter. These fragments will be retained by the filter resulting in accelerated blockage of the filter and may resulting a damaged filter.
- **Chemical Additives:** Chemicals are often added to the feed water in steam generators. These chemicals will form part of the steam and, therefore, will contact the filter cartridge being steam sterilized.

During steam sterilizations, as steam is applied to the filter, air is purged from the system which that saturated steam contacts and heats all the filter surfaces. As the steam heats and subsequently flows through the cartridge filter, there will be an inherent resistance to that flow. The amount of resistance to the steam flow is measured as a drop-in pressure across the filter and is called the differential pressure (dP). In other words, the differential pressure is the upstream steam pressure minus downstream steam pressure.

When filter cartridge is heated to 121 °C (249.8 °F) or higher, significant stress is placed on the filter due to physical properties changes. Therefore, in order to perform a steam sterilization at 121 °C (249.8 °F) the differential pressure recommended is 0.3 psid in the forward direction, otherwise dP above this level may cause filter damage [5] [10].

While saturated steam behaves as a gas and so flows easily through the filters, contact with any cool surface will produce condensate as the steam cools. When the steam leaves the boiler area it will begin to condense. This condensate first collects on the walls of the system in droplet form the accumulates to for a film that gravitates to the bottom of the system. When high velocities are involved this film can begin to build up into waves, the peaks of which break off, throwing water droplets into the steam flow. This result in a wetter steam that tends to condense even more and having a bigger water accumulation that could damage the system [6].

When designing the systems that needs to be steam sterilized, it is recommended to design the filter housing locations far from the bottom of the system. Also, create as part of the system a condensate drainage system which pipelines should have fall in the direction of flow and with a condensate trap at each low point. Per [12], the Branch lines connections as part of the drainage system is commonly used. The pipeline branch arrangement forms a “Y” at the intersection with the trunk line and is oriented vertically relative to the trunk line. The condensate trap is a mechanical valve to remove condensate. They are located at points upstream and downstream of the filter where condensate would collect. The condensate traps work on the principle that, as condensate collects, the temperature at the trap falls below that required for effective steam sterilization 121 °C (249.8 °F). At this point the valve opens, drains the condensate and draws in live stream from the steam supply.

Steam sterilization under controlled conditions is an acceptable operation for filter cartridges, however, this could lead to filter damage. Thus, is recommended that filter cartridges are integrity testes in-situ after the steam sterilization. This ensure the sterilizing grade filters in aseptic processing. Integrity tests, such as bubble point, diffusive flow or pressure hold test, are non-destructive tests, which are correlated to a destructive microorganism challenge test. Filter Integrity Test (FIT) can be performed before and after SIP cycle. To admit sterilization grade filtration would not be admitted to a process. FITs is seen to stand between certainty and potential failure. The use of hydrophobic filters prevents problematic moisture residues. The filters in the system to be sterilized serves as sterile boundaries.

Thus, the integrity test after the steam sterilization is recommended to ensure the maintaining of the sterility grade. As recommended by the FDA, the integrity testing be conducted after filtration to detect any filter leaks that might have occurred during the filtration [13].

As established by [14], Bioburden is the sum of the microbial contributions from a number of sources, including raw materials, manufacturing of components, assembly process, manufacturing environment, assembly/ manufacturing aids, cleaning processes and packaging of finished products.

Per vent filter's manufacturer biological information, the vent filters under this research can be processed up to 150 SIP cycles using the pressure, time and temperature parameters at extreme conditions. This confirms the reliability of the vent filter that after being exposed up to 150 SIP cycles at extreme conditions can maintain their integrity. Using the vent filter manufacturer's life-time of 150 SIP cycles at extreme conditions, the safety factor of one-third was used to calculate the new vent filter lifetime.

Evaluating the data from the vent filter's manufacturer and calculations, the lifetime of the vent filters for Manufacturing Plant SIP cycle can be extended from one single use to up to 50times. The project methodology to be used during this research is using Project Management tools, project plan was generated to monitor each key activity to accomplish research objectives. Per [15], the Project Management methodology is a strictly defined combination of logically related practices, methods and processes that determine how best to plan, develop, control and deliver a project throughout the continuous implementation process until successful completion. Also, project management processes are established to track cost, schedule, and functionality.

METHODOLOGY

Methodology tools used during this research project are DMAIC Model and Project Management. Using DMAIC model a framework for problem solving which breaks down the process into five steps: Define, Measure, Analyze, Improve, and Control. For this research, the DMAIC model is as follows.

Define

Vent filters used during the SIP cycle as part of the buffer formulation completion activities in Manufacturing Plant are discarded after one-time usage generating high costs and lack of flexibility during manufacturing process.

Measure

Currently, the vent filters used during the SIP cycle after the buffer formulation process in Manufacturing Plant is discarded after one-time usage.

Analysis

As part of the analysis of this project, 3 main activities were identified: SIP condition comparison between vent filter manufacturer versus Manufacturing Plant, calculations to determine the new vent filter life-time and develop a Test Run protocol with the objective of measure the residual moisture content present in the vent filter after consecutives SIP cycles.

After vent filter manufacturer's validation activities, the SIP conditions were compared against the plant SIP cycle. The comparison consisted on identify the key parameters settings during the vent filter manufacturer's validation exercise and manufacturing plant validated SIP cycle. The sterilization key parameters are time, pressure and temperature. Also, parameter as steam flow direction was compared as part of this research.

Using the vent filter manufacturer's life-time of 150 SIP cycles at extreme conditions, the safety factor of one-third was used to calculate the new vent filter lifetime to be used during the buffer formulation process in manufacturing plant. (1) was used to calculate the new vent filter life-time.

(Maximum SIP Cycles) x (Safety Factor) (1)

Validation activities were performed to challenge post SIP residual moisture content of vent filters. Five consecutives SIP cycles were performed in the buffer formulation tanks, Tank A and Tank B. Both tanks, Tank A and Tank B, are mechanically equivalent, the difference consisted in the tank size; Tank A is three times bigger than Tank B. This validation exercise was executed through a test run protocol as data gathering purposes. The main purpose of the test run protocol is to confirm no residual moisture content in the vent filters after SIP cycle.

As part of the test run protocol execution, one vent filter was weighted prior and after each SIP cycle using a calibrated scale. The activities were executed after 5 consecutive SIP cycles using each tank, Tank A and Tank B. (2) details the computation required in the validation activities.

$$\text{Weight Difference} = \text{Weight}_{\text{After SIP Cycle}} - \text{Weight}_{\text{Prior SIP Cycle}} \quad (2)$$

Improve

SIP conditions of the vent filter manufacturer were compared against SIP validated at manufacturing plant. After comparison, it was found that all key parameters, such as time, pressure and temperature, were set a higher value in vent filter manufacturer's SIP cycle than the manufacturing plant. For the non-key parameter as steam flow direction, vent filter manufacturer and manufacturing plant have the same parameter setting. This finding as part of the comparison allows to establish the worst case of the vent filter manufacturer's SIP conditions.

Based on the vent filter manufacturer's Biological Information during the vent filter validation activities, it was determined that the maximum SIP cycles allowed without impacting the integrity of the vent filter is 150 cycles. Since the SIP conditions from the vent filter manufacturer are considered the worst case, a new lifetime was determined using a safety factor of one-third. Using (1), the new lifetime of the vent filters at Manufacturing Plant is fifty times greater.

Validation activities will be required to verify if there is residual moisture content in the vent filter after a SIP cycle. This allows the re-use of the vent filter with the empirical data which shows that no residual moisture content was found after the SIP cycle and, therefore, no bioburden issue will be found. For this reason, a Test Run protocol was generated to establish the required validation activities to confirm if the vent filter is humid after a SIP cycle. As part of the Test Run protocol, weighing the vent filter before and after a SIP cycle with a calibrated scale was required. Five consecutives SIP cycles were performed during the Test Run execution. Each weighting was performed using each buffer formulation tank size, Tank A and Tank B. Using (2), the vent filter weight difference before and after a SIP cycle was determined. After completing the Test Run, it was concluded that no residual moisture content was found during SIP cycles performed in each tank (A and B).

Control

After identifying the new lifetime for the Manufacturing Plant's vent filters, new controls need to be implemented in the manufacturing process to follow the re-use of the vent filter up to 50 times following quality practices and federal regulations. The manufacturing procedures established for the buffer formulation activities will be revised to include the step-by-step activities to implement the project of reuse the vent filters. Also, electronic batch records related to the buffer formulation process will be revised to maintain the counting of the SIP cycles in the vent filter and systematically block the vent filter after the completion of the 50th SIP cycle.

Another model used as part of this research methodology is the Project Management. Using Project Management tools, a project plan was generated to monitor each key activity to accomplish research objectives. Table 1 details the project plan established with all key activities with their corresponding expected completion date, activity owner and current status.

Table 1
Proposed Project Plan

Activities Description	ECD	Owner
Pre-implementation Stage		
Change Request Submission	2019 Q3	Manufacturing Plant Change Control Owner
Vent Filter Manufacturer's Validation Evaluation	2019 Q4	Vent Filter Manufacturer
Implementation Stage		
Manufacturing Plant New Vent Filter Lifetime Calculation	January 2020	Project Owner
Manufacturing Plant – Validation Activities	2020 Q1	Project Owner
Test Run Protocol Generation	January 2020	External Contractor
Test Run Execution	February 2020	External Contractor
Test Run Report Generation	February 2020	External Contractor
Test Run Report Approval	March 2020	Manufacturing Plant Quality Representative
Manufacturing Procedures Revision	April 2020	Manufacturing Plant Formulation Process Owner
Post-implementation and Closing Stage		
Implement Project and Close Change Control	April 2020	Manufacturing Plant Change Control Owner

RESULTS AND DISCUSSION

As part of the vent filter manufacturers validation exercise, the vent filter was subjected to different validation testing to assure the integrity after exposing it at multiples SIP cycles at extreme conditions. Table 2 details the SIP parameters used in this evaluation.

Table 2
SIP Key Parameters – Filter Manufacturer vs. Manufacturing Plant

Parameter	Vent Filter Manufacturer	Manufacturing Plant
Cycles	150	1
Temperature, (°C)	100	80
Differential Pressure, (psid)	6	3
Time, (min)	100	50
Steam Flow Direction	A	A

Table 2 results were modified to protect confidentiality from both companies, vent filter manufacturer and Manufacturing Plant. Based on Table 2, each SIP key parameters during the vent filter manufacturer's validation exercise was set at a higher value in comparison with Manufacturing Plant SIP validated cycle. Regarding to the steam flow direction parameters, both companies used the same condition. Data from Table 2 demonstrate that the Manufacturing Plant validated SIP cycle will cause less damage or cannot compromise the integrity of the vent filter than the extreme conditions performed by the vent filter manufacturer's validation activities. Therefore, after evaluation, Table 2 supports the re-use of the vent filter during the buffer formulation process.

With the maximum allowed SIP cycles of 150 times as per vent filter manufacturer's validation exercise, the safety factor of one-third was used to calculate the new life-time of the vent filter in Manufacturing Plant during the buffer formulation process. Using (1), the new life-time of the vent filters at Manufacturing Plant is 50 times.

Validations activities were performed in Manufacturing Plant through a Test Run protocol to confirm the humidity presence in the vent filter after SIP cycle. The Test Run protocol was executed as data gathering purposes. Each vent filter was weighted using a calibrated scale prior and after SIP cycle. Five consecutive SIP cycles were performed during the Test Run protocol execution. Tables 3 and 4 details the results obtained during the execution of the validation activities using both tank sizes, Tank A and Tank B.

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activities using both tank sizes, Tank A and Tank B. For both tables, results were modified to protect confidentiality of Manufacturing Plant.

Results obtained during the execution of the Test Run protocol as established in Table 3 and Table 4 were analyzed using Minitab V18.0. Two Hypothesis Tests were performed: "2-Sample T Test" and "2-Sample Standard Deviation". The purpose of this data analysis using Minitab is to determine if there is a significant difference from the mean and standard deviation values from both samples; Sample #1 from Tank A results and Sample #2 from Tank B. Figure 1 details the 2-Sample T Test for Tank A and Tank B samples results. Figure 2 details the 2-Sample Standard Deviation Test for Tank A and Tank B sample results.

Table 3
Test Run Execution Results – Tank A

Run	Weight Results (Prior SIP Cycle)	Weight Results (After SIP Cycle)	Weight Difference
1	10.2 g	10.1 g	- 0.1 g
2	10.1 g	10.1 g	0.0 g
3	10.1 g	10.2 g	0.1 g
4	10.2 g	10.2 g	0.0 g
5	10.2 g	10.2 g	0.0 g

Table 4
Test Run Execution Results – Tank B

Run	Weight Results (Prior SIP Cycle)	Weight Results (After SIP Cycle)	Weight Difference
1	10.5 g	10.5 g	0.0 g
2	10.5 g	10.6 g	0.1 g
3	10.6 g	10.7 g	0.1 g
4	10.7 g	10.6 g	- 0.1 g
5	10.6 g	10.6 g	0.0 g

For figure 1, even though the sample size of n=5 is a small sample size, the p-value obtained from the 2-Sample t Test with a 95% of confidence is 0.695, greater than 0.05, which indicates that the mean from Sample #1 and Sample #2 is not significantly different from each other. The difference observed for each Sample is -0.02. The Hypothesis Test was performed to determine if the hypothesis of Sample #1 mean value is different from Sample #2 mean value is met or not. Based on the analysis the hypothesis is not met.

In case of figure 2, using the same sample size of n=5, the p-value obtained from the 2-Sample t Test with a 95% of confidence is 0.717, greater than 0.05, which indicates that the standard deviation from Sample #1 and Sample #2 is not significantly different from each other. The Hypothesis Test was performed to determine if the hypothesis of Sample #1 standard deviation is different from Sample #2 mean value is met or not. Based on the analysis the hypothesis is not met.

Test Run execution results did not show humidity presence in the vent filters after exposing during multiple SIP cycles. During the five consecutive SIP cycles, the vent filter maintained the initial weight. Also, data analysis using Minitab shown that no significant difference was identified for samples results obtained using both tank sizes, Tank A and Tank B.

CONCLUSIONS

Based on the project plan, the activities established to implement the project of re-use the vent filter during the buffer formulation process up to 50 times were properly implemented. All activities within the change control from the different stages were completed satisfactorily.

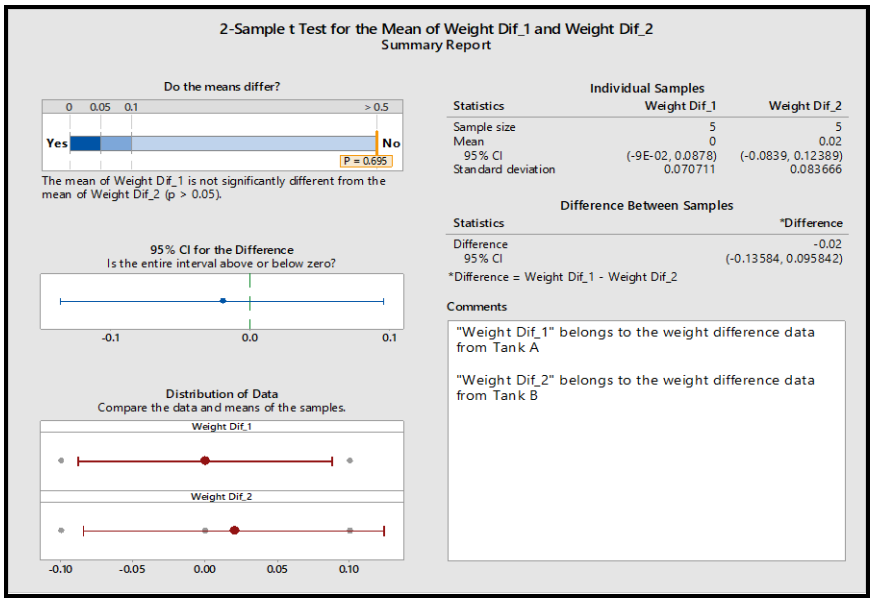

Figure 1
2-Sample t Test for Mean of Weight Difference Tank A and Tank B

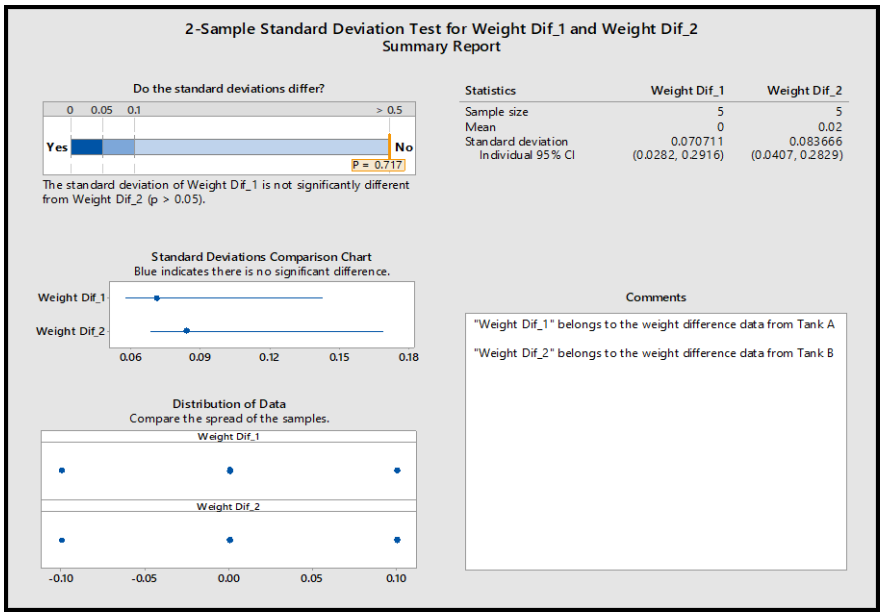

Figure 2
2-Sample Standard Deviation Test for Mean of Weight Difference Tank A and Tank B

After SIP comparison from vent filter manufacturer and Manufacturing Plant, the vent filter will maintain its integrity during the multiple Manufacturing Plant SIP cycles. Vent filter manufacturer shows with empirical data that the SIP conditions to which the vent filter is exposed 150 times are more extreme than SIP conditions validated in Manufacturing Plant. For this reason, the sterilization conditions from the vent filter's manufacturer are considered the worst-case sterilization scenario.

Using the safety factor of one-third, the established lifetime of the vent filter to be used during the buffer formulation process at the Manufacturing Plant is up to 50 SIP cycles. Since the vent filter manufacturer's SIP conditions are more extreme than the Manufacturing Plant's validated SIP, the vent filter can be re-used up to 50

times with the certainty that it will maintain its integrity up to the fiftieth SIP cycle.

As per [2], the results obtained during the execution of validation activities through a Test Run protocol shows that there was no impact in the vent filter due to repetition of several SIP cycles. Also, no residual humidity was observed in the vent filter during the execution. This is consistent with [15]: all system after SIP cycle need to be properly dried to avoid re-contamination issues.

Hypothesis Test analysis using Minitab shows that no significant difference was identified for samples results obtained using both tank sizes (A and B). Therefore, vent filter re-use up to 50 times at the Manufacturing Plant can be performed using all tanks used during the buffer formulation.

The implementation of this project to re-use the vent filters up to 50 times during the buffer formulation allows the Manufacturing Plant to have greater flexibility in manufacturing areas. Also, it is a cost-saving project that provides savings related to the vent filter re-use for up to $105,000 yearly. Based on these benefits, new proposals have been generated to expand the scope of this project to a different manufacturing area. Using the validated sterilization cycle at the Manufacturing Plant, any manufacturing process that uses the vent filter as a redundant non-product contact filter can consider implementing this project.

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