BACHELOR THESIS

VARIATION REDUCTION THROUGH PMC INTEGRATION AND EVALUATION

Student

D. F. Boekhoudt

Industrial Engineering and Management

University of Twente

FIRST COMPANY SUPERVISOR:

Bram Roffel - Manager Process Engineering

SECOND COMPANY SUPERVISOR:

Boris Novaković - Process Engineer

FIRST UNIVERSITY SUPERVISOR:

Dr.Ir. Marco Schutten - Programme Director BSc and MSc Industrial Engineering and Management & Associate professor

SECOND UNIVERSITY SUPERVISOR:

Matteo Brunetti – PhD Candidate Industrial Engineering and Management

DATE : 1-5-2023

Abbott

PREFACE

Dear reader,

This bachelor thesis: “Variation reduction through PMC integration and evaluation” describes the research conducted for the implementation of process monitoring and control at one of the liquid production lines of Abbott Zwolle.

I would like to thank the ARTH team for their great help during this research and willingness to cooperate. I would especially like to thank Boris Novakovic and Bram Roffel, who served as my supervisors from Abbott Zwolle.

Through the feedback from my supervisors at the University of Twente, Dr.Ir. Marco Schutten and Ir. Matteo Brunetti, I have learned a great deal on writing a scientifically well-structured report. I would like to thank them for their input and feedback.

Daan Boekhoudt

Enschede, May, 2023

MANAGEMENT SUMMARY

This research is conducted at Abbott Zwolle on behalf of the Process Engineering department. Abbott Zwolle is part of the Abbott Nutrition branch and produces a wide range of science-based nutrition products to support the health and wellbeing of people of all ages worldwide. This study is focussed on the Aseptic Ready to Hang (ARTH) line of Abbott Zwolle, which produces ready-to-hang bottles used for tube feeding. Within Abbott, Process Monitoring and Control (PMC) is used variably but mainly by Process Engineers. Abbott wants to change this, and thus the objective of this research is the following: *To design, implement and evaluate Process Monitoring and Control for Abbott Zwolle's filler of the Aseptic Ready to Hang line.*

Within this research, we make a distinction between the evaluation of PMC within Abbott Zwolle and the evaluation and implementation of PMC for the filler of the ARTH line. Through the literature and experience gained during this research, we give some methodological recommendations regarding the use of PMC within Abbott Zwolle. Next to the methodological recommendations, we give practical recommendations as a result of this study. By integrating and evaluating PMC at the filler of the ARTH line, several obstacles and improvement points were encountered that should be tackled and prevented in upcoming PMC projects. The three most important recommendations are:

1. Sensor validation within PI is crucial before starting a PMC project to ensure accurate data representation, prevent errors, and reduce computational time.

2. Abbott should consider moving their PMC activities to a new IT system like SEEQ due to PI Processbook's outdated nature and limited capabilities.

3. The proposed methodology for PMC integration should be tested. Hopefully, this fits Abbott's traditional project approach while focusing on the crucial methodological aspects relevant to PMC integration.

In this research, the current use of PMC within Abbott Zwolle is critically evaluated and compared to the available literature on the topic. The goal of PMC is to spot, analyze and reduce special cause variation within the production process. The distinction is made between normal and special cause variation, where normal cause variation is induced by uncontrollable factors such as humidity or temperature fluctuations. Special cause variation is variation where a cause can be assigned to the shift within the process performance. An example of such a cause could be a clogged pipe or a heating element not working properly. Problems like these are a major problem for Abbott Zwolle when they occur. They impact the sterility of the end product, which could mean significant downtime and even batch rejects. An example is the FIQ098 parameter which has breached its specification limit over 3150 times during one year. A breach could mean that the machine waits a few seconds for the parameter to get back to the right level, but it could also last several minutes, or even a new cleaning cycle might be needed.

PMC aims to spot the change in variation before it can cause major problems to the line. Currently, PMC is only used by Process Engineers to monitor parameters that are known to cause problems or to analyze the root cause of problems that have already occurred. This is almost always a case of reactive use. One approach that Abbott wants to explore is the use of PMC by operators on the shop floor.

We start the research by selecting a long list of process parameters. This is done through discussions with the line's Front Line Leaders, Process Engineer, and Mechanical Excellence Engineer. This resulted in

a long list of 20 process parameters. Most focus on the sterility of the machine or product, and one focuses on the crashes that occur at the filler intake. From there, 2 years' worth of data is collected using a time-based 1-minute sampling interval (whenever possible). The data for the process parameters are tested for normality, descriptive statistics are generated, and the results are compared to the specification limits given by Abbott. This enables us to rank the 'performance' of the process parameters against their specification limits. For a company to be a world-class producer, one should aim to have a Defects Per Million Opportunities (DPMO) count even lower than Six Sigma, which corresponds with a DPMO of 3.4. The DPMO is very large for most process parameters in this study. This is mainly due to the step change delay that is seen within the PI data architecture. This results in a discrepancy between reality and registered data, which can be seen as noise in the data set. From there, the process parameters are ranked on their level of control. 6 parameters are marked as drastically out of control, showing significant sources of variation, or breaching the specification limits set by Abbott relatively often. 11 parameters are marked as out-of-control but not crucial. These parameters show special cause variation (E.g., long-term up or down trending) but move relatively well within their specification limits. The remainder of the parameters are marked as in control and show little to no variation. These parameters are ready for more complex control charts, and distributions can be fitted to the data set.

Due to the nature of the data of these parameters, and the lack of normality for the data set, the Individuals control chart is the only valid option for control charting. Through an empirical reference distribution, control limits for the process parameters are determined to have an out-of-control probability similar to a normally distributed three-sigma control chart. The six most critical parameters are visualized in two dashboards. One dashboard is used during the morning meeting, and the other is made for monitoring on the shop floor. One big problem, however, with this approach is that the PI sensors used in this research have not been validated. This means the PI data tags cannot be used for all the "official" applications, like validating a batch or doing a batch work order check.

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GLOSSARY OF TERMS

Abbreviation	Description
ARTH	Aseptic Ready to Hang
CIP	Clean-in-Place
CUSUM	Cumulative Sum Control chart
DMAIC	Define, Measure, Analyze, Improve, and Control
ERD	Empirical Reference Distribution
EWMA	Exponentially Weighted Moving Average
HMI	Human Machine Interface
OCAP	Out-of-Control Action Plan
PAT	Process Action Team
PMC	Process Monitoring and Control
SCADA	Supervisory Control and Data Acquisition system
SPC	Stochastic Process Control

1. INTRODUCTION

This chapter introduces the research assignment. Section 1.1 provides a concise introduction to Abbott Zwolle, while Section 1.2 establishes the relevance and motivation behind this research. Then, Section 1.3 provides the problem statement, and Section 1.4 provides the research objective. Finally, Section 1.5 defines the research questions for this report, while Section 1.6 provides the outline of the report.

1.1 ABBOTT ZWOLLE

Abbott is one of the leading pharmaceutical companies in the world. Abbott is divided into six branches: Cardiovascular care, Diabetes care, Diagnostics, Neuromodulation Care, Nutrition, and Branded generic medicines. In these branches, they possess a market-leading position.

Abbott Zwolle is part of the Nutrition branch. The plant in Zwolle produces and markets a range of nutritional products for people of all ages, including infant formula, pediatric nutrition, adult nutrition, and medical nutrition (see Figure 1). Abbott Nutrition is known for its high-quality products, backed by scientific research and formulated with a focus on taste, convenience, and ease of use. The company's most popular brands include Similac, Ensure, and PediaSure.

Figure 1 - Product range Abbott Zwolle

Abbott Zwolle is the most complex production plant of the nutritional division, producing powder and liquid products for various countries. Next to the drinkable and powder consumer products, Abbott Zwolle also produces tube-feeding products. These bottles are ready to hang on a post to feed people who cannot drink/eat their food. Since the product is (mostly) consumed by people who are severely ill, a clean and safe product is of utmost importance. This means that Abbott Zwolle takes special care in ensuring a sterile product.

1.2 RELEVANCE AND MOTIVATION OF THE RESEARCH

This research focuses on the Aseptic Ready To Hang (ARTH) line of Abbott Zwolle. The filler of the production line takes the empty bottles, fills them, and seals them in a sterile environment. The filler is the most complex and crucial part of the production line and is the focus of this research. The line produces three kinds of tube-feeding bottles and is the liquid priority line of Abbott Zwolle due to the high demand for the products. In its strive to become a world-class producer, Abbott Zwolle continuously seeks ways to improve its production processes. They aim to reduce downtime at the production lines due to damage, quality defects, and batch rejects and increase the production lines' total output. They are currently approaching this through Process Monitoring and Control (PMC). PMC aims to reduce variations within the production process, increasing the process's quality and capability. Process Engineers use PMC to monitor the production processes, and various projects have started using PMC. This research focusses on the evaluation and integration of PMC at the ARTH filler and how Abbott Zwolle can further improve its use of PMC within the production facility.

1.3 PROBLEM STATEMENT

Currently, PMC is used by Process Engineers to monitor the process parameters of the production line. This is almost always a case of 'reactive' use. The process shows an increase in variation, and PMC is used to search for the possible cause of the variation. The problem that Abbott Zwolle is facing is that Operators on the work floor do not have enough insight into the production process. The tools at their disposal only display real-time values of the line and are not clearly formatted. There are no preventive measures in place, and Operators take action when a problem arises by either resolving it themselves or escalating it to a Process Engineer or Mechanical Specialist. Abbott wants to change this and enable Operators to review the production process, which might help mitigate problems before they occur. Several projects have been started using Process Monitoring and Control and that is something that Abbott further wants to explore at the ARTH department. We formulate the core problem as follows:

There is insufficient insight on the shop floor on the performance of the ARTH filler.

Section 1.4 provides the research objective of this problem statement. In Section 1.5, we define the research questions.

1.4 RESEARCH OBJECTIVE

This research aims to design, implement and evaluate Process Monitoring and Control charts at the Aseptic Ready to Hang (ARTH) filler of Abbott Zwolle. The scope of this research is to develop these charts for the ARTH-filler and to review the use of PMC within Abbott Zwolle.

With this in mind, we define the research objective as follows:

To design, implement and evaluate Process Monitoring and Control for Abbott Zwolle's filler of the Aseptic Ready to Hang line.

In Section 1.5 we define several research questions to achieve the research objective. Every research question is answered in a separate chapter and broken down into sub-questions. These sub-questions are answered in a corresponding section within the chapter.

1.5 RESEARCH QUESTIONS

The first part of this research maps out the current situation of Abbott Zwolle concerning their use of PMC. Furthermore, the way products are produced and data is collected is examined.

1) What is the current situation at the ARTH line of Abbott Zwolle?
    1.1. What does the production process at the ARTH filler look like?
    1.2. How is data currently collected and used at the ARTH line of Abbott Zwolle?
    1.3. How does Abbott Zwolle currently use Process Monitoring and Control?

Second, we review the literature on PMC. It is interesting to review the use of PMC within Abbott, compared to the common practice of PMC use in literature. This gives insight into what the critical aspects of PMC are and how it can benefit Abbott Zwolle.

2) How is Process Monitoring and Control used in literature?
    2.1. How can a change in variation be identified?
    2.2. What are the data requirements for PMC?
    2.3. What type of control charts are available in the literature?

2.4. How can Process Monitoring and Control be implemented within Abbott Zwolle?

Third, the process parameters that should be monitored to increase insight on the shop floor should be determined.

3) How can the process parameters of the ARTH filler be visualized to increase the insight on the shop floor?

Furthermore, we identify the critical parameters, and the performance of these parameters and how these parameters can best be visualized is determined. For this, several subquestions are defined.

3.1. What are the critical process parameters during a production run at the filler of the ARTH line?
3.2. How should the raw dataset of the parameters be filtered and subgrouped?
3.3. What level of control do the process parameters show?

Fourth, the application of process monitoring and control within Abbott Zwolle is discussed. Here several points are discussed; how this project is implemented, and what the limitations are of this approach, and possible improvements that can be made concerning the use of PMC within Abbott Zwolle.

4) How should Abbott Zwolle apply process monitoring and control?

1.6 OUTLINE OF THE REPORT

The remainder of this report is organized in the following manner. In Chapter 2. the current situation of Abbott Zwolle is described, where the answer to research question 1 is provided. In Chapter 3, a literature review is performed where research question 2 is answered. In Chapter 4, the process parameters of the line are evaluated, and the filtering needed and the level of control of the parameters is discussed. In this chapter, research question 3 is answered. The application of PMC within Abbott Zwolle is discussed in Chapter 5, where research question 4 is answered. In Chapter 6 we draw conclusions and recommendations on this research for Abbott Zwolle.

2. CURRENT SITUATION

This chapter provides insight into the current situation at Abbott Zwolle. Section 2.1, elaborates on the production process at the ARTH filler. How data is currently collected and used is described in Section 2.2. Then the use of PMC within Abbott Zwolle is elaborated in Section 2.3. We end this chapter with conclusions on the current situation in Section 2.4.

2.1 CONTEXT ON THE PRODUCTION PROCESS

The filler of the Aseptic Ready To Hang (ARTH) production line is quite complex and can fill various recipes of liquid products into three bottle sizes, as seen in Figure 2. These products are sold to a wide range of countries, which also means that in some cases, recipes or specifications for the product might change a bit from the usual production due to regulations from that country. For example, China products are regulated stricter than EU or US products. The production process of these different types of bottles is almost the same during the production steps but differs on a few accounts.

Figure 2 - Ready To Hang bottles (500mL, 1000mL, 1500mL L to R)

The nature of an aseptic production line is that the product and the containers are sterilized separately. For the ARTH line, this means that the liquid product is sterilized separately from the packaging material. The liquid product is sterilized in a Utlra High Temperature (UHT) processing machine. Here the product is heated over a period of time until the product is sterile. This depends on the flow rate of the product, the temperature in the UHT, and the time spent under the sterilization temperature. Figure 3 displays how the liquid product is sterilized.

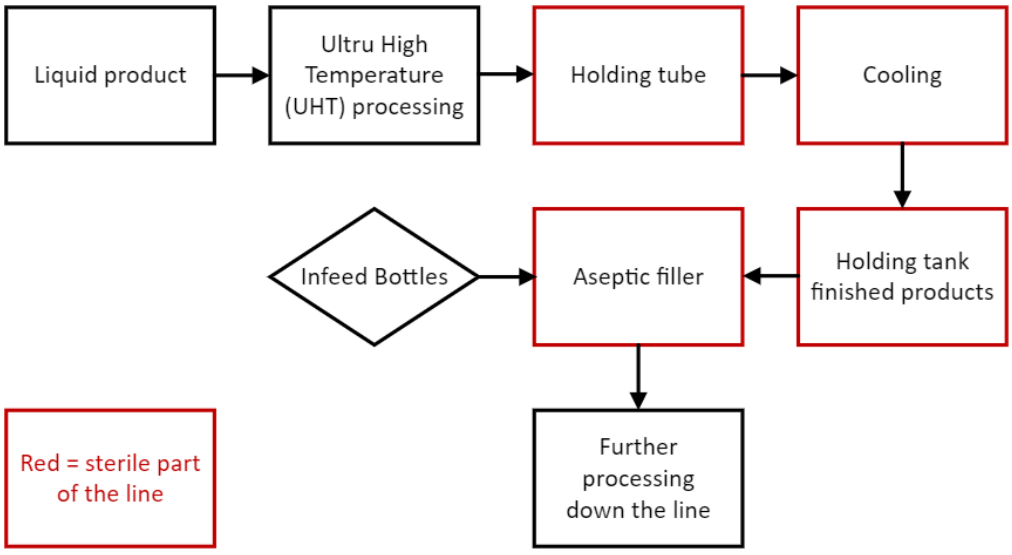


Figure 3 - Sterilization of liquid product

The liquid is pumped through a holding tube from the UHT onwards and cooled to the desired temperature. From there, it is stored in the finished product holding tank. Here the product is kept in a sterile environment, ready to be used in the filler of the ARTH line.

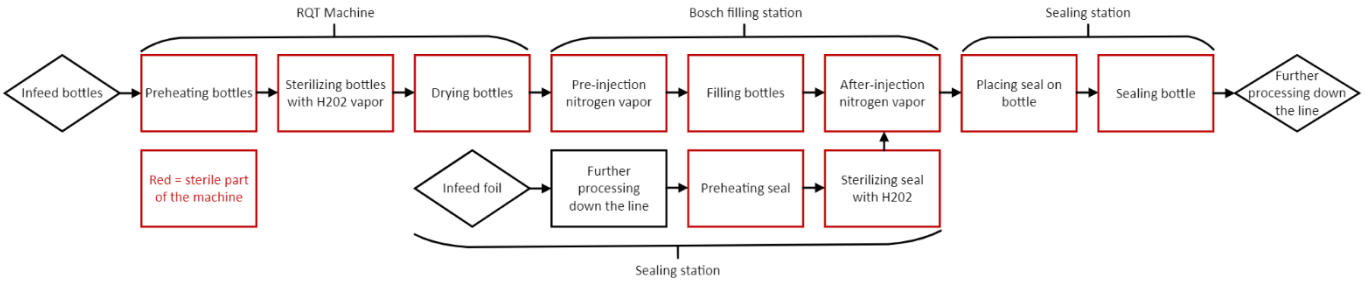


Figure 4 - Production steps of the ARTH filler

The production processes of the different liquid production lines within Abbott Zwolle are almost entirely automated. The process starts in Abbott's warehouse, where the empty, ready-to-hang bottles are stored on pallets. These pallets are taken by Automated Guided Vehicles to the infeed of the production lines. The pallets are placed on a conveyor belt that partially functions as a buffer where multiple pallets can be stored and which feeds the pallets into the depalletizer. One row at a time, the bottles are pushed off the pallet onto another conveyor belt that aligns the bottles in the right direction. When the entire pallet is emptied, it is automatically discarded, and a new pallet is fed into the machine. The buffer area on the conveyor belt ensures that there are always bottles available at the entrance of the filler. Figure 4 displays the production steps of the ARTH filler, where the red steps are in the aseptic module of the machine.

From the depalletizer, the bottles are transported to the intake of the sterilization machine called the RQT. This is also seen as the entrance of the filler and is where the aseptic environment of the production line starts. The entire filling area of the production line is kept under overpressure to the outside environment, which forms a pressure wall that keeps out microorganisms and other forms of contamination.

At the RQT machine, the bottles are placed in an upside-down position. The bottles enter the machine in groups of ten, and these ten bottles stay as a batch during the entire filling process. After being placed upside down, the bottles are heated with sterile hot air before the outside is sprayed with hydrogen peroxide (H2O2) vapor. The preheating of the bottles is needed to make sure the entire bottle is covered evenly with H2O2. If the bottles are not preheated, the warm H2O2 vapor (approx. 82 °C) will condense on the cold plastic bottle. This would mean that the bottles are not evenly coated, and a sterile product cannot be ensured.

After spraying the outside of the bottles with hydrogen peroxide, they are sterile on the outside and are transported further into the machine. The inside of the bottles is slowly warmed with sterile hot air, after which the inside is sprayed with H2O2 vapor. The inside of the bottles is dried off by hot sterile air that follows a three-step cooldown pattern from 80 °C to 20 °C, which cools the bottle to the filling temperature. This is a crucial step because insufficient drying might lead to residue peroxide in the bottles, which might cause a food-safety issue.

The bottles are now entirely sterile and are fed into the Bosch filling station. Here the bottles are pre-injected with nitrogen gas which replaces the air present in the bottles. This step is needed because the oxygen in the air will react with the product, which will speed up the degradation of the ingredients (e.g., vitamins). After the preinjection of nitrogen, the bottles are filled with the liquid product that is transported from the finished product holding tank, which is located above the filling station.

When the bottles are filled, they are rinsed with an after injection of nitrogen gas to replace possible air left at the top of the bottle. After the nitrogen injection, the bottles move to the sealing section of the machine. The seals are stamped out from a film roll and heated and sterilized before moving into the sterile filler environment. Here they are placed on top of the bottles and fused.After the sealing, the bottles leave the filler and the aseptic module and continue to the buffer area of the production line. The bottles pass through various quality-checking machines and are labeled and packaged. After packing the bottles into boxes, they are placed onto pallets and transported by automated guided vehicles to the warehouse where they are stored for transport.

The buffer areas in front and after the filling machine are very important for the operation of the line. The buffer area after the filler can store a significant number of bottles before the filler stops due to a lack of capacity. This buffer area gives Operators time to fix problems or errors further down the line while still being able to produce bottles. The buffer area in front of the filler ensures that there are always bottles present at the infeed of the production line. If the filler itself cannot operate, and the buffer area after the filler is empty, then the remainder of the line also stops. The line produces 24/7 for approximately 40 weeks a year. It is only stopped during the summer plant shutdown when extensive maintenance and cleaning occurs or during a 'Cleaning in Place' (CIP), where the machine is cleaned before resuming production.

The aseptic nature of the line means that the product is only sterile when the bottle is sealed, and all steps before that have taken place with sterile parts and under a sterile environment. This means that if anything in the filler goes wrong before the bottle is sealed, the product might get contaminated, posing a quality threat to Abbott. Various systems are in place in the filler to ensure that the sterile environment is maintained. Most of the time when an error occurs at the filling station of the ARTH line, a sterile environment can be maintained. The machine either needs to wait for a parameter to come back up to its threshold level, or a part of the machine needs to be cleaned while keeping the rest of the filler under a sterile environment. However, sometimes the filler becomes unsterile; this is the case when for example, the overpressure within the filler falls below a certain threshold. Then there is the possibility that microorganisms have gotten into the filler, and thus the machine needs to be thoroughly cleaned. Depending on where the sterility breach has taken place in the filler, the cleaning can take between 1 and 10 hours. Every hour of downtime is a significant expense for Abbott due to the labor hours and missed revenue from production. One of the main contributors to this is FIQ098, a sensor that measures the flow of hot air needed to sterilize the bottles. This flow parameter has had over 3150 occasions in the past year that have been out of specification. Every time this parameter is out of specification, the machine waits until it is within spec again before continuing production.This can be a matter of seconds, but there are also instances where the machine has to be restarted, which takes up much longer.

2.2 MONITORING AT THE FILLING MACHINE

This section describes how the filling machine is currently monitored. Section 2.2.1. discusses how data is gathered at Abbott Zwolle and how the machine is currently monitored. Section 2.2.2 elaborates on the checks on the ARTHs fillers' performance that take place.

2.2.1 Data gathering and monitoring

The Supervisory Control and Data Acquisition (SCADA) system controls and monitors the ARTH filler. SCADA is a combination of hardware and software that enables the automation of industrial processes

by capturing real-time data. The SCADA system connects sensors that monitor industrial equipment like pumps, valves, or motors to an onsite/ remote server. The main benefits of this SCADA system are that it enables Abbott, first of all, to control the operational performance of the machine. In the system, setpoints and ranges for production variables can be altered. This is important because a 500 ml bottle does not need as much H2O2 for sterilization as a 1500 ml bottle. In the system, various combinations of bottle sizes and recipes are stored, which are selected for the corresponding item that they are producing at that time. Next, it can control various valves and motors or production speeds that need to be altered due to circumstances.

Furthermore, it has an alarm function built-in. This function is triggered when a process is in a particular step of production, and a sensor goes outside of its specification limits for that production step. The alarm either causes a stop or needs to be deleted or checked by an operator. The specification limits are based on experience, regulations, and required machine settings.

Finally, it serves as a data acquisition tool. The real-time data acquired from the sensors is stored on a server where it can be accessed for further use. For this, Abbott uses Osisoft PI for this application. OSIsoft PI is a software system that is specialized in collecting, historicizing, finding, analyzing, delivering, and visualizing data.

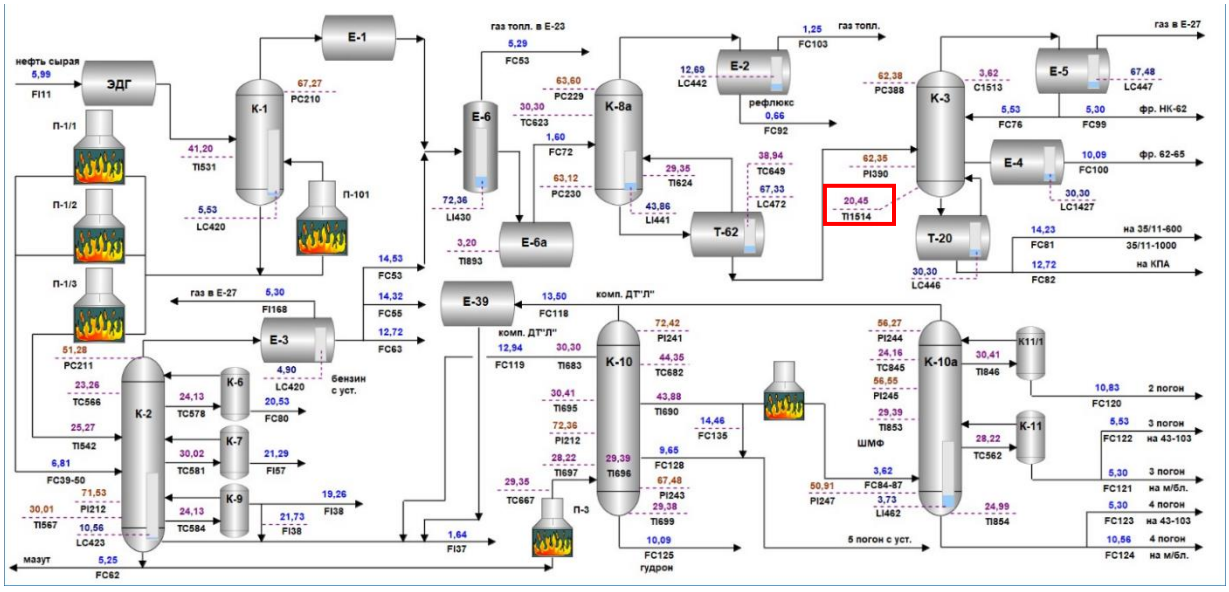


Figure 5 - Example of HMI interface

The SCADA system of Abbott has a Human Machine Interface (HMI) next to the filler; this is essentially a monitor that displays the real-time values of the machine. This HMI also functions as an interface from which changes to the production process can be made. The HMI interface displays the real-time value of a lot of sensors, motors, and valves, as can be seen in the example displayed in Figure 5 (*note that this is not an HMI interface of Abbott, due to confidentiality, this is left out of this study.*) This is also one of its limiting factors. The HMI displays the technical drawings of certain parts of the ARTH filler. These drawings are pretty complex, and the real-time values are hard to find and read. This is because it is not designed for real-time monitoring but for controlling the machine when needed. An example of a parameter that could be monitored is outlined in the red box in Figure 5. Figure 5 is selected as a comparable figure to one of the SCADA HMI interfaces of Abbott Zwolle at the ARTH line.

The PI interface analyzes the data points of the various sensors, motors, valves, et cetera, collected through SCADA. The PI interface is set up for each sensor with compression and exception settings. Compression and exception settings use basic math to compare the current measurement to the previous measurements. These settings determine if a measured point is worthwhile to store or not. With proper compression and exception settings, disk space and network traffic can drastically be reduced and thus, the overall performance can be increased while maintaining high-level data. The compression and exception settings serve as a filter; they determine whether a data point is meaningful. The definition of meaningful data depends on the sensitivity of the settings, but in general, it is data that says something about a shift in the process. If, for example, a sensor shows a linear upward trend for 1 hour, there is no use in storing all data points for that sensor. There is only the need to store the starting point of the linear uptrend and the end of the linear uptrend. Using interpolation, the value of a sensor during any moment between those points can then be determined. The exception setting is a horizontal band with length x and width y. PI takes the last measured point, draws a horizontal band with dimension x,y from it, and evaluates if all newly generated data points fall in the box. If this is the case, the data point is rejected and removed. If the data point falls outside of the x,y box, it is classified as meaningful data and set as the new data point from which a new x,y box is constructed. X is the Exdev setting, or the width of the box, and Y is the ExMax setting, or the box's length (time interval).

The compression setting takes the degree of deviation into account. It takes the last archived data point and draws a cone shape to the newly generated data point. The cone's width is the data point + /- half of the Compdev setting (e.g., if the Compdev = .1 and the data point has a value of 1, the cone has a width of 0.95 to 1.05). The maximum length before a data point is stored is the CompMax setting. For example, a value is stored, and a new data point is generated called point 1. From point 1, a cone is drawn with width Compdev. A new data point is generated called point 2, which falls within the boundaries drawn from point 1. Point 2 is then accepted and point 1 is then deleted from the data set. From there, a new cone is drawn with the width of Compdev. Again a new point is generated called point 3. This point does fall outside the boundaries of the cone and thus is stored and set as the newly archived data point from where the new cone is drawn.

The larger the compression and exception settings, the less sensitive the PI interface is; thus, fewer data points are stored. The smaller the settings, the more sensitive the PI interface is; thus, more data points are stored on the server.

This, however, also poses a risk. If the compression and exception settings are not correctly set up, then there is a risk that meaningful data is lost. In general, all PI data points can be assumed to display a correct representation of reality. This, however, does not mean that all sensors are ideal for Stochastic Process Control purposes. Some produce a lot of data events due to the oscillation of a sensor between two variables. Suppose the exception and compression settings have not been set up correctly. In that case, this can mean that a sensor produces a lot of ‘grass,’ switching back and forth between two values while the shift might be minimal, for example, a temperature gage oscillating between 56 and 57 when the actual value is 56,49 and 56,51. However, this should not be a substantial problem for this research. Wheeler (2017) states the following concerning the quality of a measurement system: “Measurement errors will inflate the limits of any process behavior chart, however until you get to the point of no longer finding any signals of exceptional variation on your process behavior charts, you do not need to check on the quality of your measurement system.”

After passing through the PI interface, the filtered values are stored on the PI server. From there, the data can be extracted with various applications. The most commonly used application for this is PI Processbook (a tool that allows us to plot and display data) and PI Datalink. PI Datalink allows us to retrieve data from the PI server for specific sensors, timeframes, and conditions (like bottle type or different steps during production) and export it to Excel.

From PI, data can be retrieved using a time-based or an event-based sampling method. Time-based sampling collects data at regular intervals, regardless of whether there is a change in the data's value (recall the interpolation function of OSIsoft). If data is sampled every minute, it takes interpolated values from events (archived values) that correspond to the minute requested. Event-based sampling only retrieves the events (archived values) from PI when requesting data. If 24 hours of data is requested for a certain parameter, a sample of 1140 data points is retrieved from the PI server when using time-based sampling. Using event-based sampling, the number of points might be drastically lower, depending on the sensitivity of the exception and compression settings of the parameter. Time-based sampling is generally better suited for frequently changing data and continuous monitoring (e.g., temperatures, pressures, or flow rates). Whereas event-based sampling is better suited for collecting data that is triggered by specific events (e.g., machine failures or alarms).

2.2.2 Checks on machine performance

There are several moments during the day when the performance of the filler is discussed. First of all, the alarms built into SCADA that are checked by Operators when they occur. Next to that, there are regular moments throughout the day when a check on the performance of the line is done. Four central moments are essential: the *shift handover*, the *morning meeting*, the *Root Cause Analysis (RCA) meeting*, and the *Batchworkorder checks*.

During the shift handover meeting, the past performance and all notable events of that shift and previous shifts are discussed between the leaving and starting teams. Abbott works with a five-shift roster, meaning once every two days, a team starts working after four days of leave. They need to be filled in with the necessary details on the operational performance of the filler during their leave. Currently, this is done through the discussion of the logbook where all notable events are registered. During this meeting, there is no way of seeing the past performance of the critical parameters of the filler over the last four days or of the last 16 - 24 hours when the operator had his leave.

The morning meeting is a get-together of one or two operators, the Mechanical Excellence Engineer, the Mechanic, the Front Line Leader, the Quality officer, and optionally the Liquid OG manager and the Process Engineer. They discuss the Overall Equipment Effectiveness (OEE) of the past day, any maintenance that is due during that day, and any notable events that might have happened outside of office hours.

Furthermore, there is the RCA meeting where problems encountered on the line are analyzed and root causes and solutions are identified.

One of the ways that Operators currently use SCADA is the hourly Batch Work Order check. The purpose of the Batch Work Order check is to let Operators have a periodic review of the process performance. The work order contains 19 parameters that are checked, for which the specification limits and the setpoints are given. For example, a nitrogen flow parameter has a specification limit of 5 to 10 cubic meters per hour and a setting of 8 cubic meters an hour. Operators are expected to write down the

parameter's current value and compare it to its specification limits. To do this, Operators have access to multiple dashboards. These dashboards are complex technical drawings that display the entire filler. See, for example, Figure 5. It is a schematic overview, and all parameters are placed according to their position on the filler. This, however, is not very clear. The parameters are tough to find and are not in a logical order when compared to the Batch Work Order. One example of a parameter that could be written down is marked by a red box in Figure 5. For operators, this means that they have to click through four different screens to write down the different values for the entire Batch Work Order.

2.3 PROCESS MONITORING AND CONTROL WITHIN ABBOTT ZWOLLE

This section looks into the current use of Process Monitoring and Control (PMC) within Abbott Zwolle. Before looking at the current use of PMC within Abbott, the concept of PMC is elaborated on.

PMC, also called Stochastic Process Control (SPC), is a tool for monitoring and reducing process variation. Every production process shows variation. However, it is interesting for a production company to identify whether the variation is 'normal' or 'special cause' variation. In the case of Abbott, variation could occur through a slightly different composition of the raw materials or a different season of the year, which causes the humidity to be a bit higher. These are examples of little changes that can be the cause of variation within the production process. This is normal and should not influence the end product that much. However, sometimes a shift in variation occurs, or a process shows a linear up or down trend. The process is not behaving within the 'normal' bandwidth and thus is showing special cause variation. This is an indication that something somewhere in the production process has significantly changed the way the process is operating. PMC aims to identify and eliminate the causes of variability in the process (Montgomery, D.C., 2009). To achieve this, statistical analysis can be used to separate the potential signals from the probable noise (Wheeler, D.J. 2010). The variability of a process has a direct relation to the quality and performance metrics of a process. By reducing variability, there will be fewer breakdowns or rejected products that do not meet quality specifications.

In its strive to become a world-class producer, Abbott is searching for ways it can continuously improve its processes. One way they are currently approaching this is through PMC. This initiative has been around for some time now. The first project using PMC was started in 2017. Since then, it has slowly got a small amount of traction within the organization. In 2019 a steering committee was started that was responsible for the implementation and integration of PMC for Abbott Zwolle. This steering committee has defined goals for Abbott Zwolle regarding the widespread use of PMC in the organization. Furthermore, several projects were started in 2019 trying to implement PMC on various lines.

Currently, PMC is still mainly used by Process Engineers. They use PMC to monitor critical parameters and ensure they do not exceed specification limits. Furthermore, they use PMC during root cause analysis, where they systematically analyze data to find causes for problems and deviations on their production line.

Within the Abbott Nutrition division, PMC is used variably. Some sites are pretty far in the implementation of PMC, whilst others have a long way to go. Abbott Zwolle is one of the leading sites with regard to PMC compared to the rest of the nutrition division. This, however, is a crude view; the targets set by the overarching PMC group of Abbott Nutrition are not realistic when compared with the actual performance of the sites. The target for the past year was that each site would create three control charts. Abbott Zwolle currently has over 250 control charts available for its site. The target of

creating charts is not something that should be monitored. Many charts within Abbott Zwolle are not up to date, and thus the control limits might not be valid anymore. The goals of the global PMC group should focus more on the proper use and integration of charts instead of creation. Within Abbott Zwolle, the ownership is also ill-defined. Currently, the Process Engineers are the 'owners' of PMC. However, they have no explicit time assigned to update PMC in their work week. Next to that, no clear policies are in place for when and how to update the existing charts. Furthermore, no one within the Site Leadership Team is steering for PMC integration. They know about PMC and have seen several projects using PMC, but there is no clear, distinct push from senior leadership to integrate PMC company-wide.

2.4 CONCLUSIONS ON THE CURRENT SITUATION

In this chapterwe discussed the current situation at the ARTH filler. The production process of the ARTH filler is discussed, and the importance of a sterile production environment within the filler is elaborated. The sterility of the machine is currently monitored by a SCADA system that generates alarms when a process parameter exceeds its specification and causes the machine to stop. Furthermore, the SCADA system functions as a control panel for the line, and it collects the sensors' data on the ARTH filler. The collected data is used in the Human Machine Interface, where Operators can view the current values of the process parameters and alter machine settings such as speed, temperature, and pressure. The data is then sent to the OSIsoft PI application, which stores the data after filtering it with compression and exception settings. The performance of the line is discussed during various moments of the day. First of all, during the shift handover where a new production team replaces the previous one. Next to that, during the daily morning meeting where all relevant stakeholders are present. Furthermore, the performance is checked on an hourly basis by Operators on the HMI, and a Batch Work Order is filled in. Within Abbott Zwolle, Process Monitoring and Control is mainly used by Process Engineers who use it to evaluate the process parameters of their line critically. The use of PMC within Abbott Zwolle is mainly reactive, where a problem occurs, and then monitoring is set in place. The current way of monitoring the critical process parameters is not sufficient. There is currently no way of preventively spotting out-of-control situations which can cause significant problems.

3. LITERATURE REVIEW

This chapter reviews the literature on various topics related to Stochastic Process Control (SPC). In Section 3.1, we elaborate on how changes in variation can be identified. This encompasses special and chance causes of variation, run rules to increase sensitivity within control charts, and the different phases of SPC. In Section 3.2 we review the need for probability distributions within control charting applications and the importance of subgrouping within the data set. In Section 3.3 we discribe the most used control charts during Phase I and Phase II of SPC. In Section 3.4 we look into various ways SPC can be implemented within an organization and what lessons can be learned from there.

3.1 IDENTIFYING CHANGES IN VARIATION

This section is composed of three subsections that aim to determine when a process is in statistical control. First, Section 3.1.1 discusses special cause and chance cause variation. In Section 3.1.2, the run rules for control charts are explained. Section 3.1.3 discusses control charting during Phase I and Phase II.

3.1.1 Special cause and chance cause of variation

According to Woodall (2000), a process is said to be "in statistical control" if the probability distribution representing the quality characteristic is constant over time. If there is some change over time in this distribution, the process is said to be "out of control." Montgomery (2009) states that a process is in statistical control when it is operating with only *chance causes* (or normal causes) of variation. Chance causes of variations are natural variability, the cumulative effect of many small, essentially unavoidable causes of variation. If a process shows assignable cause variation or special cause variation, it is said to be out-of-control. There are major non-random patterns present within the data that can be due to machine failure or human interference. According to Shewhart (1931), a process is considered under control when predictions can be made about how a phenomenon will vary in the future using experience. This prediction may not be exact, but it allows us to estimate the probability of the observed phenomenon falling within certain limits.

To do this, Shewhart (1931) proposes the control chart to determine whether a process shows common or special cause variation. The Shewhart Control chart is the most basic control chart and displays the process's average output with an *upper control limit* (UCL) and a *lower control limit* (LCL). Special causes of variation will fall outside of the control limits and thus are easily identified as out-of-control situations. Common causes of variation lie inside the control limits; thus, the chart is said to be in a state of statistical control.

3.1.2 Run rules to increase sensitivity

Western Electric introduced the run rules for control charts to increase the sensitivity of a control chart and better identify out-of-control situations. These rules specify non-normal behavior within control charts and mark these as out-of-control situations. Shewharts control charts, as seen in Section 3.3.1, only link the probability that a data point lies beyond a particular value to an out-of-control or in-control state which are set by the historically measured values. The Western Electric handbook (1956) suggests 3 additional basic decision rules that classify patterns as non-normal or non-random.

These additional rules speak of zones within a control chart. This is something also introduced in the Western Electric handbook. The area between the upper and lower control limit is divided into three categories: zone A, zone B, and zone C. These zones are distributed one sigma (zone C), two sigmas (zone B), and three sigmas (zone A), respectively from the centerline as can be seen in Figure 6. The centerline is the average of all measurements. One sigma is one standard deviation.

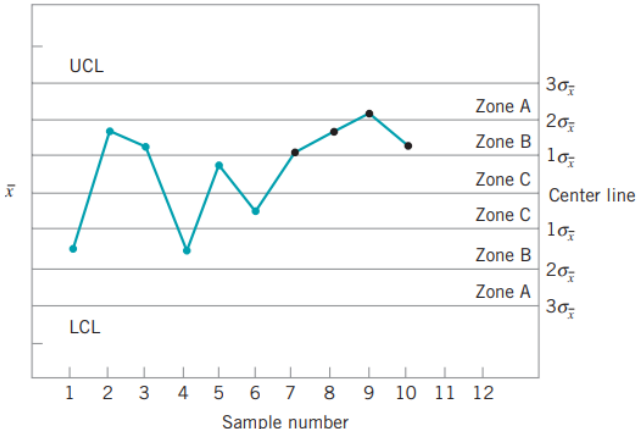


Figure 6 - Western Electric or zone rules

The 3 additional rules are:

1. One point lies outside the three-sigma control limits. (*General Shewhart control chart*)
2. Two out of three consecutive points lie beyond the two-sigma warning limits. *(Western Electric rule)*
3. Four out of five consecutive points lie at a distance of one sigma or beyond from the center line. *(Western Electric rule)*
4. Eight consecutive points lie on one side of the center line. *(Western Electric rule)*

These rules were established to increase the sensitivity of a control chart. It helps detect nonrandom patterns earlier. Montgomery (2009) expands upon these rules with six additional rules to spot a nonrandom pattern:

5. Six consecutive points are steadily increasing or decreasing.
6. Fifteen points in a row are plotted in zone C (above or below the centerline)
7. Fourteen points in a row are alternating up and down
8. Eight points in a row lie on both sides of the center line, with none in zone C.
9. An unusual or nonrandom pattern in the data,e.g., cyclic behavior.
10. One or more points are near a warning or control limit (the warning limit might be closer to the centerline than the 3sigma limit).

Every rule included in the control chart increases the sensitivity of the chart. According to Montgomery (2009), care should be exercised when using multiple decision rules simultaneously. This is due to the increased chance of a Type I error. A Type I error occurs when it is assumed that a process is out of control when in reality, the process is in control. If *k* decision rules are used and that criterion *i* has Type I error probability α_i, then the overall Type I error or the chance of a false alarm of the decision criteria is $\alpha = 1 - \prod_{i=1}^{k}(1 - \alpha_i)$. The more that rules are applied to a chart to identify nonrandom patterns, the greater the chance of a defined out-of-control situation that is actually in control.

3.1.3 Phase I and II of process control

The above-stated rules help us identify data points that are out of control. However, they do not tell us if the process itself is in or out of control. A two-step procedure is recommended in the standard literature to determine the state of a process and bring it into a state of control. According to Atalay et al. (2019), in the first phase, also known as Phase I, the goal is to analyze the process by examining past data and using iterative statistical calculations to estimate unknown parameters. The end goal of Phase I is to

have a reasonable estimation of the parameters that will be used in the Phase II application of control charts.

A Phase I study sets preliminary control limits for a fixed-size sample. From there, a basic Shewhart control chart, as seen in Section 3.3.1, is plotted to analyze the data compared to the preliminary control limits. If all the data points of the sample fall within the control limit, the process is said to be in control. When values are outside the control limits, an iterative study of the process is started. Each data point outside of the control limits is analyzed. Suppose the cause for the out-of-control situation is found. In that case, the decision is made if the cause of the variation is process specific or if it is a form of normal variation detected as an out-of-control situation. The result of this research will be a decision to include or exclude the data point. Afterward, new control limits will be calculated, and the process will be repeated. When eventually all points fall within the control limits, the process is said to be in control during that period of time, and the estimated parameters resulting from the sample can be used for the application of Phase II charting.

During Phase II of charting, it is assumed that the process is in control and that a relatively good estimation of the process parameters is made. The goal of Phase II is focused on process monitoring, making sure that the in-control process stays in control and picking up small sources of variability. Suppose the Phase I study of SPC has been done right. In that case, all significant sources of ugly noise should have already been filtered out, and only minor sources of variation should remain. During this phase, more complex charts will be applied to the processes that are more sensitive to slight deviations and which should detect the remaining causes of the special cause variation.

3.2 DATA REQUIREMENTS FOR PMC

This section discusses the requirements for a valid data set for PMC applications. In Subsection 3.2.1, the need for distributions for control charts is discussed. Next, the importance of subgrouping data is discussed in Subsection 3.2.2.

3.2.1 The need for distributions

When reviewing the literature, there are some contradictions in how one should approach control charting. Shewhart (1931) proposes two different approaches for analyzing data. Starting off, he describes the generic statistical approach that any statistician might be inclined to use. The statistical approach has four steps: It starts with fitting a probability model to the data, which then can be used for later analysis. Step 2 is choosing a probability or a risk that a false alarm will occur. Step 3 is finding the exact critical values for the selected probability of false alarms or transforming the model to match the known critical values. Step 4 uses the obtained critical values in further analysis. This approach is generically valid when looking at statistics, but Shewhart rejects this approach when looking at control charting. He points out that there will never be enough data to identify a specific probability model when collecting data. According to him, probability models are limiting functions for infinite sequences, and therefore they can never be said to apply to a finite portion of that sequence.

Shewhart proposes a different approach. His approach, also consisting of four steps, is more generic. Starting with choosing some generic critical values for which the probability of a false alarm will be reasonably small regardless of what probability model is chosen and using these critical values for further analysis. His generic approach uses three-sigma limits.

Wheeler (2009) verifies the approach of using three-sigma limits. In his study, he analyzed six different probability distributions ranging from uniform to exponential distributions (and three others). He concludes that 98 to 100% of the area under each probability distribution can be covered using three-sigma limits. In practice, this means that the probability of a point falling outside these three-sigma limits is relatively small, and thus, it is more likely that the point is a signal of process change.

Shewhart (1939) emphasizes an essential point regarding his approach: when using run rule 1 (i.e., three-sigma limits) to detect assignable causes, it is crucial to divide the original sequence into subgroups of relatively small size. Failure to do so may result in overlooking the presence of assignable causes. If subgroups are too large, out-of-control points will be suppressed by the majority of in-control data points.

This view of Shewhart and Wheeler is questioned by Khakifirooz et al. (2021). Khakifirooz et al. agree with Shewhart and Wheelers' approach when analyzing baseline data in Phase I applications. However, they reject the approach for monitoring associated with Phase II, in which the use of a process model can be helpful. They recommend fitting an appropriate probability model for Phase II control charting applications.

There is a clear distinction between Phase I and Phase II charting applications. The use of probability distributions in Phase I charting is generally rejected. Phase I charting aims to filter out the probable noise for which Wheeler (2009) and Shewhart (1931) have proven that three-sigma limits are sufficient. Phase II applications focus more on keeping a process in control and early identifying in-control situations. For this, Khakifirooz et al. (2021) recommend the use of probability models.

3.2.2 Subgrouping

One critical assumption concerning PMC is that the items produced are under relatively homogeneous conditions when the process is stable (Zwetsloot et al., 2021). This is an important note to consider when trying to analyze a parameter using PMC. If a parameter is known to perform differently under certain situations, that should be considered during the analysis. According to Wheeler (2022), most statistical techniques are built on the assumption that the data are homogeneous. However, in reality, data are rarely homogeneous. The process behavior chart is a crucial tool for examining data for homogeneity, and it is the premier technique for this purpose in data analysis.

Abbott Zwolle can produce 500, 1000, and 1500 mL bottles with one machine. Some production settings differ for the different bottle sizes. This is very logical since a 1500 mL bottle is larger than a 500 mL bottle and thus logically needs more hydrogen peroxide to be sterilized. These differences will become obvious when plotting data in a process behavior chart, even without prior knowledge of the system. And this is the main benefit of a process behavior chart. It is effortless to spot process shifts during production in a behavior chart, whether it is an increase in variation, a cycle during production, a step-change or linearity (See Appendix I).

When data does not appear to be homogenous when plotting it on a process behavior chart, rational subgrouping can be considered. Zwetsloot (2021) states that if items are produced under conditions that change at known times, then the principle of rational subgrouping can be applied to break up the data sequence into more meaningful subsequences. In the case of Abbott Zwolle, this would mean rationally subgrouping the data into the different bottle sizes and even the different production steps. How data

should be sampled can best be answered by a Process Engineer who thoroughly understands the system's behavior.

3.3 CONTROL CHARTS

This section discusses a selection of the different types of control charts. In Subsection 3.3.1, various Phase I control charts are discussed, and in Subsection 3.3.2, various Phase II control charts are discussed.

3.3.1 Phase I charts

As described earlier, there is a clear distinction between Phase I and Phase II charting applications. During Phase I, the most used charts are the Shewhart control charts. These charts can be subdivided into two subcategories. First, control charts for continuous data (variable data charts), and second, charts for discrete data (attribute data charts). For this study, almost all parameters are continuously monitored; thus, this research is mainly focused on the variables charts.

The Shewhart control charts are the most commonly used charts within organizations and the most simple to construct. One of the significant benefits of these charts is that it does not take a statistician by trade to understand and apply them. The combinations of Shewhart Variables Control Charts and when to use them are depicted in Table 1.

Shewhart Variables Control Chart	**Subgroup size**
$\mathrm{I}-\mathrm{MR}$ chart	*Subgroup = 1*
$\bar{X}-R$ *chart*	*Subgroups between 2 and 10*
$\bar{X}-S$ *chart*	*Subgroup ≥ 11*

Table 1 - Shewhart Variables Control Chart

Another reviewed chart type is the Emperical Reference Distribution (ERD) chart. This chart can be applied when data is not normal, or another distribution cannot be fitted to the data set.

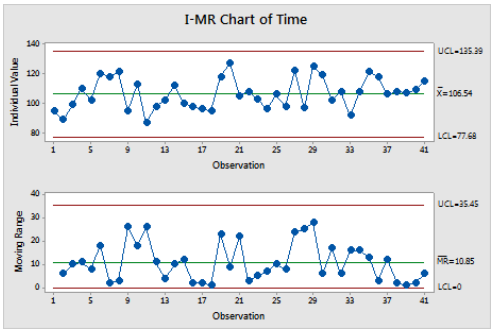


Figure 7 - I-MR chart

I – MR Chart:

The I, or Individuals, chart is used to monitor the process mean when measuring individual values at regular intervals of a process. It collects single observations of a process over time. The MR, or Moving Range, chart is used as a complementary chart to the Individuals chart (see Figure 7). Where the Individuals chart monitors the process mean over time, the Moving Range chart tracks the process variation by comparing each measurement to its previous measurement. The mean of the process is calculated by the formula $\bar{X} = \frac{\sum_{i=1}^{k} x_i}{k}$ where k represents the number of subgroups and x_i the value of the process at point i. Since it is an Individuals chart, every data point is its own subgroup, and thus k represents the number of measurements in the sample. The moving range is calculated by the formula $\overline{MR} = \frac{\sum_{i=2}^{k} |x_i - x_{i-1}|}{k-1}$, this formula divides the sum, of the absolute value, of the current point minus the previous point, by the number of subgroups minus one. The corresponding control limits are then calculated by multiplying the moving range with a control chart constant (*Appendix II*) and adding them to the process mean. These constants are calculated for each *n,* where *n* is the number of observations taken into account in the calculation. For an individual's chart, n is always equal to 2 since it compares the current state with the previous state. The formulas for the control limits are given in Table 2.

Chart	Upper Control Limit	Center Line	Lower Control Limit
I-Chart (Individuals)	$UCL = \bar{X} + E_2\overline{MR}$	$CL = \bar{X}$	$LCL = \bar{X} - E_2\overline{MR}$
MR-Chart (Moving Range)	$UCL = D_4\overline{MR}$	$CL = \overline{MR}$	$LCL = D_3\overline{MR}$

Table 2 - Control limits for I-MR charts

$\overline{\mathbf{X}} - \mathbf{R}$ chart:

The Xbar control chart plots the average change in the process over time from the different subgroup values. The limits of the Xbar chart are derived from the R-chart. That is why Montgomery (2009), among others, states that the first step when interpreting patterns on the Xbar chart is determining whether the R-chart is in control. It is not advisable to interpret the Xbar chart if the R-chart indicates that the process is out of control. If the R-chart is not in control, the limits of the Xbar chart will not be valid either. To construct the Xbar chart, each sample's average is calculated, and the range of the data points within that sample is determined. From there, the overall average value of all samples and the overall range of all samples are calculated. These metrics are then used for the construction of the control limits.

One of the benefits of using an Xbar chart is that it takes the sample average and plots it as one point. This makes the chart less sensitive to anomalies and thus reduces the chance of over-adjustment of the process.

$\overline{\mathbf{X}} - \mathbf{S}$ Chart:

The Xbar S chart is comparable to the Xbar R chart. The S-Chart is used when the sample size is greater than or equal to 10. Shewhart (1931) suggests collecting between 20 and 25 samples within a subgroup size of 10 and above. The S chart is an approximation of the Average standard deviation of the data set. Wheeler (2010) provides a study explaining why the use of a Global Std. Dev and other forms of computing control limits are wrong (see Appendix III), there he shows the calculated control limits for each form of approaching the standard deviation of various datasets. The method of Average Range (described above) and the method of Average St. Dev (Xbar – S chart) are the most robust when calculating control limits and are, by default, integrated into statistical software packages like Minitab or R.

Shewhart attribute control charts:

Shewhart also proposed four different attribute control charts, which focus on the nonconformities of the production process. He introduced the np chart to monitor the *number* of nonconforming units when measuring subgroups at regular intervals. The p chart is used to monitor the *proportion* of nonconforming units when measuring subgroups at regular intervals. The c chart is comparable to the np chart, which monitors the total number of nonconforming units when measuring subgroups at regular intervals. Furthermore, the u chart is used to monitor the average number of nonconformities per unit when measuring subgroups at timely intervals. These charts are mainly used for batch approvals and quality assurance of the produced product, where the producer accepts a threshold of non-conformities.

Empirical Reference Distribution control chart:

The ERD is introduced by Willemain and Runger (1996). This paper provides an approach for control charting in the absence of an assumed normal distribution. The empirical reference distribution can be used to set up control limits for non-normal data, given that sufficient historical data is present. In

stochastic process control, the ERD can be used to estimate the probability of extreme events by extrapolating the ERD beyond the range of the observed data. This approach assumes that the observed data is representative of the underlying probability distribution of the process parameter.

To obtain the ERD, Willemain and Runger (1996) specify the following: let Y denote the sample statistic obtained from a subgroup for which the process parameter is deemed operating under normal conditions. These standard conditions are determined during the Phase I analysis and confirmed by the line's Process Engineer. The probability density function and cumulative distribution function of Y are denoted as $f(y)$and $F(y)$, respectively. Let y_i, $1 \leq i \leq m$, be the independently observed values of Y computed over m subgroups. Here m is set as the number of observations during the in-control period. These observations are then used to calculate the control limits.

Let $Y(k)$ be the kth-order statistic in the sample, with $Y(m)$ being the largest. By convention, $y_{(0)} = -\infty$ and $y_{(m+1)} = \infty$. The m order statistics divide the possible values of Y into $m+1$ random-length sections known as "statistically equivalent blocks." The first block extends from $-\infty$ to $y_{(1)}$, the second from $y_{(1)}$ to $y_{(2)}$, and so forth, with the $(m+1)$st block extending from $y_{(m)}$ to ∞. Let P be the probability that Y falls within any set of b blocks, say those between $y_{(k)}$and $y_{(k+b)}$; then $P = \Pr[y_{(k)} \leq Y \leq y_{(k+b)}] = F(y_{(k+b)}) - F(y_{(k)})$ for $0 \leq k \leq m$ and $1 \leq b \leq m+1-k$. Now from here, control limits can be chosen empirically such that, $LCL = y_{(k)}$and $UCL = y_{(k+b)}$, where P then is equal to the probability of a future point falling within the set control limits.

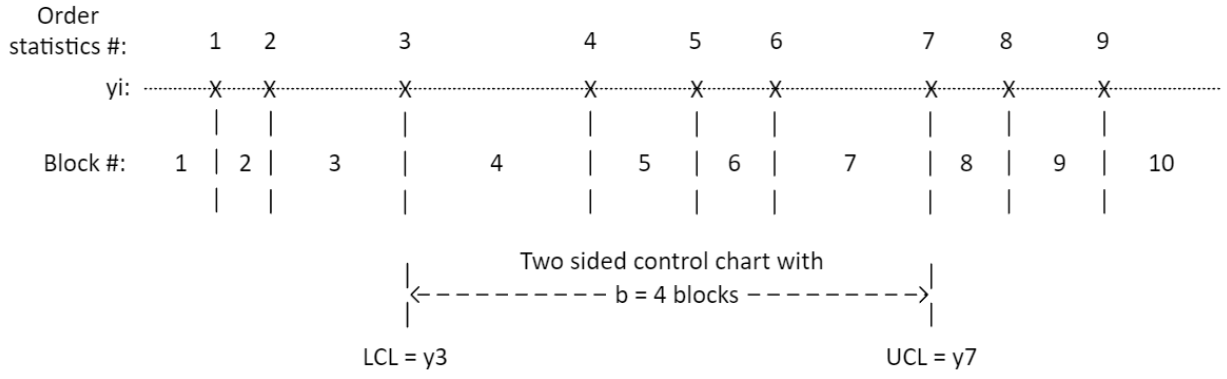


Figure 8 - Control limits from ERD

Consider the example in Figure 8. Here the order statistics is $m = 9$, which is divided by $m + 1 = 10$ statistically equivalent blocks. The chart is composed of limits centered around the mean of b = 4 blocks. Since $y_{(k)}$ and $y_{(k+b)}$ are random variables, P is also a random variable. Due to the theory explained by Mosteller and Rourke (1973), it follows that the probability P of a point falling within any set of b blocks has the expected value of $E[P] = \frac{b}{(m+1)}$. For the example in Figure 8 this would mean that the probability of a point falling in the block centered around the mean of the process is $E[P] = \frac{4}{(9+1)} = 0.4$. This, in turn, means that the probability of a point falling outside of the blocks is equal to $1 - E[P] = 0.6$.

3.3.2 Phase II charts

The Phase II applications of control charting are statistically more complex. Here it is assumed that the process is in control. With this, it is meant that the processes Phase I control charts have been evaluated and that significant sources of special cause variation have been removed. The two primary charts used for this phase are the cumulative sum (CUSUM) and exponentially weighted moving average (EWMA) control charts. The goal of Phase II charting is monitoring the in-control process en spotting slight changes in variation or process mean. One of the key differences is the application of probability models. For Phase II charting applications, normality is assumed for the data. The performance of, for example, an Individuals chart when the data is even moderately non-normal distributed decreases significantly. This means that the computed control limits might be entirely inappropriate for Phase II monitoring (Montgomery, 2009). To combat this, one can transform the variable to a new form that is approximately normally distributed or fit another type of distribution to the data.

CUSUM CHART:

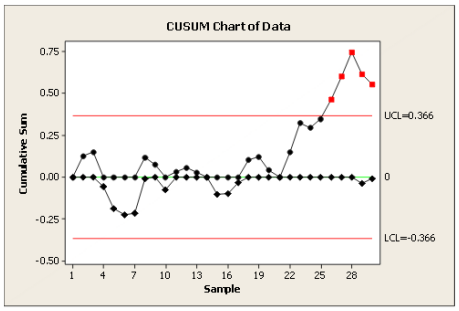


Figure 9 - CUSUM chart

Where the Shewhart control charts excel at detecting large deviations in average (1,5 Sigma and larger), it is not very good at detecting small process changes. If the mean of the process has a slight shift, it is still plotted as in control for a Shewhart averages chart. The solution proposed for this is the CUSUM chart. This chart plots the deviation of a range of samples compared to a set target value. This means that the CUSUM chart can detect small shifts in process performance. If the process is in control, it is expected that a random walk around μ_0, that is the target value of the process, is observed. If the process starts to deviate from this target value, a run on either side of the CUSUM chart will be seen, indicating that a process shift has occurred. The control chart is formed by plotting the value $C_i = \sum_{j=1}^{i}(\bar{x}_j - \mu_0)$, where $\bar{x}_j$ is the average of sample j against the sample number i. The most common form of the CUSUM, the Tabular CUSUM, has one-sided upper and lower CUSUMS. They are calculated by $C_i^+ = \max[0, x_i - (\mu_0 + K) + C_{i-1}^+]$ & $C_i^- = \max[0, (\mu_0 - K) - x_i + C_{i-1}^-]$. This results in two lines that collect deviations above μ_0 until the obtained value becomes negative and thus resets itself to 0. The value K is called the slack value and is chosen between the target μ_0 and the out-of-control value of μ_1 that is of interest for quick detection (Montgomery, 2009). This value works as a scaling factor and prevents the chart from going out of control too quickly. Figure 9 displays a CUSUM chart where a run on the positive side is occurring. As can be seen, it has broken the control limit with multiple points, and thus it is safe to assume that a shift in process performance has occurred.

EWMA Chart:

Like the CUSUM chart, the EWMA chart also takes advantage of the sequential accumulating nature of the data arising in a typical SPC environment and is known to be efficient in detecting more minor shifts (Chakraborti & Graham, 2019). The benefit of the EWMA is that it is very insensitive to the normality assumption. This is because it is a weighted average of all past and current observations, making it an ideal chart for individual observations. The EWMA is computed following the formulas in Table 3.

weighted average (z_i)	UCL	CL	LCL
$z_i = \lambda x_i + (1-\lambda) z_{i-1}$	$UCL = \mu_0 + L\sigma\sqrt{\frac{\lambda}{(2-\lambda)}[1-(1-\lambda)^{2i}]}$	μ_0	$LCL = \mu_0 - L\sigma\sqrt{\frac{\lambda}{(2-\lambda)}[1-(1-\lambda)^{2i}]}$

Table 3 - Formulas of the EWMA chart

The weighted average (z_i) is plotted against sample i and calculated by multiplying the current observation x_i with the scaling factor λ and adding the previous weighted average with the inverse of the scaling factor. Commonly the scaling factor is chosen between $0.05 \leq \lambda \leq 0.25$, where a smaller lambda is chosen to detect more minor shifts in the process. Here it is seen why the EWMA is insensitive to the normality assumption. The current observation x_i only accounts for a small part of the new weighted average, which means that previous observations are heavily represented in the formula.

The control limits are calculated by taking the process mean (or set point) μ_0 and adding or subtracting the formula for the limits. Here the factor L is the width of the control limits, which is usually set as 3, and sigma is the standard deviation of the model. The factor $[1-(1-\lambda)^{2i}]$ approaches unity for large i, and thus eventually, the formula converges to $UCL/LCL = \mu_0 \pm L\sigma\sqrt{\frac{\lambda}{(2-\lambda)}}$.

3.4 REQUIREMENTS FOR SUCCESSFUL IMPLEMENTATION

In this section, the implementation of Stochastic Process Control is discussed. In Subsection 3.4.1, literature focussed on SPC implementation is discussed. In Subsection 3.4.2, other methodologies that use SPC are discussed.

3.4.1 Implementation of SPC

According to Noskievicova et al. (2012), SPC should be built as 'the problem-solving' process with the following sub-processes: "Out-of-control signal revelation – Root cause identification – corrective or improvement action acceptance – verification of action.". Noskievicova et al. (2012) recognize four phases that should be walked through for an appropriate application of SPC. They are starting with a preparatory phase. It is focused on understanding the process, defining the controlled quality characteristics, and performing a Measurement System Analysis (MSA). Furthermore, defining intervals and subgroups size. From there, the process should be evaluated on its statistical stability and capability and determined if it is indeed stable enough or if further research is required. Finally is the implementation and transfer of ownership to Operators, and Quality managers.

Coleman et al. (2001) recognize SPC as a dynamic process that should follow Deming's PDCA (plan, do check, act) cycle. This is also incorporated into its provided framework, which starts with defining the points of measurement, calculating statistical limits, selecting charts, making charts, and evaluating charts. Constantly reviewing the framework is deemed necessary for effective implementation. Next to that, it should have endorsement by senior management, and the ownership of the charts should be kept in the hands of the creator of the charts themselves. Keeping the ownership at the creator of the chart is something that Coleman et al. (2001) differentiate from other theories. Most theories hand over ownership of the charts to the Process Engineers or Operators that are responsible for the process, not the expert on SPC. Furthermore, his approach focuses mainly on the quality of the control chart. Not much is mentioned about integration within the organization itself.

Does et al. (1997) have an approach focused on the implementation's methodological and organizational aspects. They recognized that the risks of implementing SPC are more often due to organizational and

social factors than the creation of control charts and mathematical modeling. They created an approach that tackled most risks found when implementing SPC. Starting off, they made a four-Phase Implementation roadmap for the organizational side, focusing on top-down implementation with the ultimate goal of ownership at the operator level. They proposed an organizational structure (Figure 10) that should be used to achieve the goal of top-down implementation.

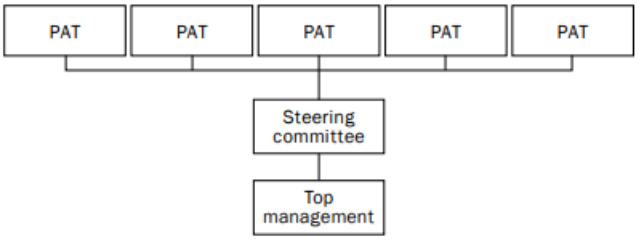


Figure 10 - Organizational structure for SPC implementation (Does et al. 1997)

The first Phase Is creating awareness in the organization. The goal is that all staff have a general idea of what SPC is and what the benefits can be for the organization. During this phase, a Steering Committee is formed that will interview all departments to get an idea of projects that can be used for the pilot phase.

The second phase starts with several pilot projects. These projects are performed by PATs (Process Action Teams). These PATS follow the ten-step method proposed by Does et al.(1997) and are guided by the steering committee. The process is called an operational SPC point when the ten steps have successfully been executed.

The third phase focuses on integral implementation in production. In this phase, several PATs are installed under the steering committee. A company should identify its weakest-performing processes and assign PATs to these. After completing the ten-step approach, another operational SPC point is achieved. All critical process steps of the production line should be covered by these PATs and evaluated. Another critical factor here is an SPC coordinator. The SPC coordinator should become familiar with all the ins and outs of SPC and servers as a question beacon to the PATs and as a trainer of SPC methods if needed.

The fourth and final Phase Is 'setting the stage for Total Quality Management.' Here the PATs are dismissed and transformed into Process Improvement Teams. They are tasked to keep the process in control, tackle upcoming problems and search for new opportunities for continuous improvement. In this phase, the production process ought to be in control, and the application of SPC should be broadened to other parts of the company. Think of the purchasing department, warehousing, or product development. Furthermore, the company should press its suppliers to adopt SPC within their production processes. Total quality can only be achieved if all suppliers and departments apply SPC to their processes.

In this methodology, top management has given commitment and control to the steering committee. The steering committee has an essential role within the organization as the controlling and initiating entity. Does et al. (1997) proposed that the manager of operations should be the committee chair, accompanied by the managers for purchasing, maintenance, quality, and development. Furthermore, the SPC coordinator or experts should also be part of the steering committee.

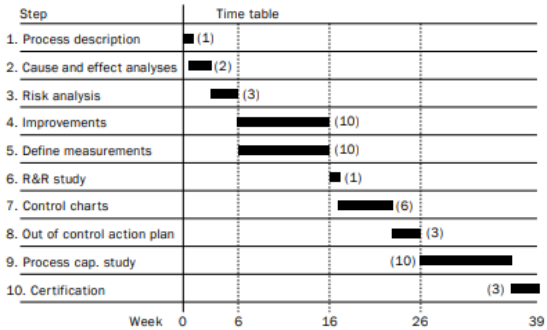


Figure 11 - The ten-step method (Does et al. 1997)

The PATs should consist of two to five operators, their supervisor (in Abbott's case, the Front-Line Leader), a Process Engineer, the Maintenance Engineer (in Abbott's case, the Mechanical Excellence Engineer), and an SPC expert (also the Process Engineer in Abbott's case).

The ten-step approach proposed by Does is visualized in Figure 11.

The methodology is a structured approach that can be followed in almost every situation, and that can be standardized across the organization. This way of working integrates top management with operators, which aligns interests and motivation for implementing SPC on an organizational level.

Another critical point is the creation of Out of Control Action Plans (OCAP) to define a way Operators should handle whenever a process is out of statistical bounds. The OCAP should be a living document; it should be changed whenever new deviations in variation get recognized due to normal variation (e.g., a new supplier of base products that require different production settings).

Anotony et al. (2003) provide a literature review on implementing SPC, highlighting a few crucial aspects. First of all, the importance of SPC and variability reduction should be translated organization-wide, not only to the management and stakeholders. This is the first step to a successful implementation. From then on, a training program focusing on all company levels should create sufficient understanding and knowledge of statistics and SPC. They approach it like a LEAN methodology, where the entire organization adopts a working method.

In conclusion, the essential elements for a successful implementation that can be recognized can be split into two categories. Of course, the data, charts, and statistics should be valid. If they are not valid, the implementation is based on a faulty model, which will surely be a disaster. This is something widely recognized in literature, and a lot of research and models exist for the creation and choosing of the right charts. However, the more interesting side is the organization and methodological requirements mentioned in the papers of Antony et al. (2003) and Does et al. (1997). This is not widely recognized, and very limited literature is available on this topic. The available literature, however, agrees that it should be a top-down, organization-wide initiative. Everyone should be on board and have a basic understanding of how to integrate PMC. Another important aspect is securing the obtained knowledge in an OCAP and constantly reviewing the SPC models to reevaluate.

3.4.2 Other approaches to implementing SPC

As stated above, limited research is available in the literature focussing on the implementation of SPC specific. The approaches that are provided above provide a specific framework for SPC implementation. However, companies might resist these frameworks due to the lack of literature and use in practice. To combat this we also explore more general approaches used to implement SPC within an organization. One of these models is the Six Sigma approach.

Motorola introduced the Six Sigma methodology in the late 1980s. Six Sigma aims to achieve a rate of defects of 3.4 defects/million opportunities. To achieve this, two methodologies are proposed, one for the implementation process and one for the development of new products or services. The methodology for implementation is the DMAIC (Define, Measure, Analyze, Improve, Control), and the methodology for developing new products is the DFSS (Design For Six Sigma). This Six Sigma approach is widely used by Abbott, and almost all projects are approached through the DMAIC approach. For Six Sigma projects,

seven Quality Control tools are generally recognized. The seven tools are; Flowcharts, Fishbone diagrams, Checklists, Pareto charts, Scatter plots, Histograms, and the Control Chart.

The tools are used to examine the production process, identify the key issues, and control the fluctuations in product quality. Control Charts (mainly Shewhart charts) are often part of the Control phase of the DMAIC (see, e.g., Mason 2000, Gambhire et al. 2015). However, this does not align with the literature found earlier looking at the application of control charts during Phase I and II. Control charts used within Six Sigma have Phase I and II charting elements. It resembles Phase I charting because the goal is to *improve* the production process on *one specific aspect* by looking at the variability of the process. The actual application of the charts resembles Phase II charting. Control charts are used to evaluate and monitor the changes made to a process and to watch whether a process is in control and if the changes made had the desired impact. This is also one of its significant flaws. Where an approach focussed on SPC implementation makes a clear distinction between the use and application of Phase I and Phase II charting, the distinction between them is absent in the DMAIC. DMAIC projects work through a project charter, a sheet specifying the project's goal, how the project will be tackled, and the estimation of the resources needed and who the process owners are. After every step of the DMAIC structure, a gate review follows. This is a moment where all team members get together and evaluate the results of the previous phase. At this moment, they also decide whether to continue with the project or not. The last gate, the control gate, is the final check of whether the project has had its desired effect on the organization. During this phase of the DMAIC, control charts and capability studies are mainly used because they provide statistical proof of the changes' impact.

3.5 CONCLUSIONS ON LITERATURE REVIEW

The literature available on statistical process control (SPC) is quite extensive. A lot of information is available on the statistics behind control charts and the different types and variations on charts. Within the literature, there is some discussion on the use of probability distributions and the goal of SPC. One of the most important takeaways is the difference between Phase I and Phase II charting. The statistical part is something that (in general) is done right, while the implementation of the charting methods is often overlooked. Where literature on charting is quite extensive, the literature on implementing SPC within an organization is scarce.

For this research, we first determine the critical process parameters . From there on, we evaluate the historical data and determine what Phase of charting the parameter is in. This also means that we decide whether to fit a distribution to the data or not. After that, decisions on how to form subgroups and what is measured for each process parameter are made. From here on, we determine the best type of control chart for the parameters, and decide wether to apply sensitizing rules. Finally, we review the organizational structure, and a method on how SPC should be implemented at the filler of the ARTH line is proposed.

4. EVALUATING PROCESS PARAMETERS

This research aims to develop a Process Monitoring and Control tool to improve the stability of the filling machine of the ARTH line and quality of the product, to increase insight on the shop floor, and to prevent unsafe situations regarding the quality and safety of the products. To achieve this objective, we draft a long list of process parameters in Section 4.1 that should be evaluated. Section 4.2 elaborates on how data is collected and screened. From there, we perform a Phase I studyin Section 4.3, where the long list of parameters is analyzed, and the critical process parameters are selected. In Section 4.4, the type of control chart and our calculations of the control limits are elaborated for the process parameters. This chapter aims to identify the critical process parameters that directly relate to the product's quality and safety, and that require permanent monitoring to improve the performance of the ARTH filler and to increase insight on the shop floor.

4.1 SELECTING PROCESS PARAMETERS

In this section, the criteria of Abbott that should be taken into account when selecting the process parameters for monitoring are described. Furthermore, a long list of process parameters is created that aligns with the criteria and could be a fit for PMC.

First of all, the demands and wishes of the product's end users are determined. As noted in our problem statement:

There is insufficient insight on the shop floor on the performance of the ARTH filler.

This research's core objective is to increase the insight on the shop floor of the ARTH filler. After discussion with the Front Line Leaders, Operators, and Process Engineers, the following criteria for the PMC tool are formed:

1) It should be easy to use and understand.
2) Only parameters that show or have shown special cause variation should be monitored.
3) The focus should lie on improving quality and safety.
4) There should not be excessive warning signals on the PMC chart that do not significantly impact the production process.

Criterion 1 is important for Abbott because of several reasons. First of all, the goal is that Operators will engage with the tool and use it to further broaden their knowledge of the performance of the ARTH filler. Almost all Operators lack statistical training and do not have the proper background to understand complex statistical tools, charts, or methods easily. Next to the statistical knowledge limitation, the dashboard is built into PI Processbook, a tool that Process Engineers use almost exclusively. Most other stakeholders have little to no knowledge of PI Processbook. This is, of course, something that they can learn, but for this study, where most stakeholders are not familiar with the program, an easy-to-understand and use model is preferred.

Criterion 2 builds on criterion 1. In an ideal situation, all important process parameters to the line should be monitored. However, there are, on the one hand, physical limitations, where the screens present at the filler are not big enough to monitor 20 different types of charts for an acceptable time interval. And on the other hand, front-line leaders and Operators have expressed that monitoring parameters daily that have not shown special cause variation over a significant amount of time will increase the risk that the tool itself will not be used.

The Process Engineers suggest criterion 3. The tool should help reduce and prevent unsafe situations regarding the quality and safety of the products. This will indirectly influence the operational performance of the line. However, the focus should lie on improving the stability and quality of the machine.

Criterion 4 is that the chart should not display out-of-control signals too often. If a chart is too sensitive, it poses a risk that alarms will not get followed up and that the chart in itself will be dismissed.

Through several meetings with Process Engineers, Mechanical Excellence Engineers, and Front-Line Leaders, a long list of parameters is devised that should be evaluated. From this long list, parameters that fit the above criteria are selected. The long list of parameters is provided in Appendix IV.

19 out of the 20 parameters on the long list in Appendix IV come from the Batch Work Order of the ARTH filler. Almost all parameters selected are monitoring values that directly relate to the product's quality and safety. The only parameter that does not fall in this category is the 108030_CRASH_CNT001. This is a sensor that monitors the bottle infeed at the RQT machine. This sensor is placed because there have previously been various problems with bottles not falling correctly in place when entering the machine. This has caused various stops of the filler. The parameter is interesting to monitor because there are two different types of 500ml bottles. One is produced in Zwolle, and the other in Germunde, Germany. These bottles have slightly different specifications, and the Mechanical Excellence Engineer wants to monitor the number of bottles that do not fall into place in relation to 100k bottles produced.

Of these 20 parameters, six are marked bold. These parameters are critical during production and fall under two categories. Four parameters fall under the first category; all these variables have something to do with hydrogen peroxide, which is an essential ingredient needed for the proper sterilization of bottles. If one of these four parameters is outside of specification, a sterile product cannot be ensured, and the product must be discarded.

The other two critical parameters are related to the compressed air flow, which is essential to maintain the pressures needed to ensure sterility.

The 108030_CRASH_CNT001 parameter and the 108040_FIQ098_PV parameter are marked as problematic through meetings with the Mechanical Excellence Engineer and the Process Engineer. They are known to cause problems for the line and thus are also deemed critical for evaluation.

4.2 DATA COLLECTION

Before the actual data is analyzed, it is important to elaborate on the decisions made regarding the gathering and filtering of the data. This is important to create a homogenous data set from which the control limits and control charts can be created. The filtering of data is discussed in Subsection 4.2.1. Furthermore, the sampling interval is discussed in Subsection 4.2.2.

4.2.1 Data filtering

To better understand the importance of data filtering and subgrouping for the parameters of the ARTH filler, the different production steps of the filler first need to be looked at. As noted earlier, the filler is operated via a SCADA system. This system is connected to various Programmable Logic Controllers (PLCs), which are connected to the filler's motors, valves, sensors, et cetera. Let us assume that the line is not in production. Every machine is turned off, and Abbott wants to start the production of bottles. Before this can be done, the filler needs to finish several intermediate steps. The filler needs to be

cleaned, the pressure needs to build up, temperatures must be reached, and the machine needs to be sterile. A 'roadmap' of steps has been programmed into the SCADA system for this. Every step is either a check or a command for one or multiple sensors, motors, valves, et cetera, that either sets it in the correct stance for production or checks if the right values are reached for production. The ARTH fillers step chain sequences consist of 76 different steps. Of these 76, only two are important when the line is producing. These are steps 212 and step 213. Step 212 is when the machine is sterile but is in standby mode. This means that all variables needed to ensure a sterile work environment are maintained, but the variables needed during production are turned off. The sprayer of H2O2 for the outside of the bottles is, for example, turned off since there are no bottles present ready for spraying. Step 213 is the production step. This means there are no errors, everything is working correctly, and the line is producing bottles. The other 74 steps are related to the machine's start-up, cleaning, and shutdown.

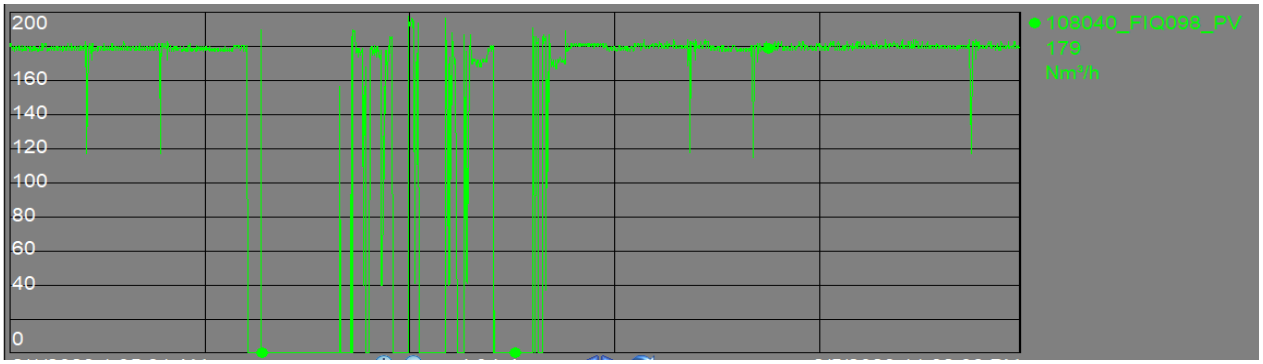


Figure 12 - FIQ098 no filter

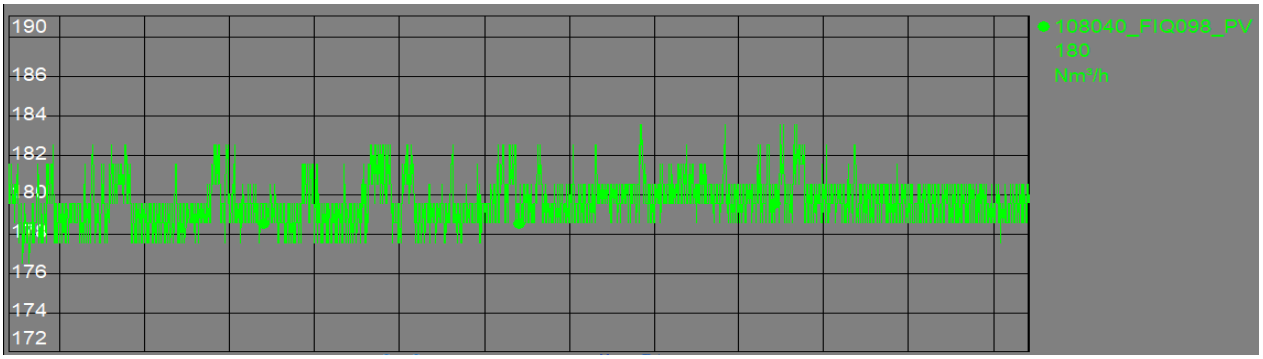


Figure 13 - FIQ098 filtered

This brings us to Process Monitoring and Control. The machine has very different values during each step in the step chain sequence. Figure 12 displays the unfiltered data of the compressed air flow to the bottles. This means that all of the measurements during the different production steps are plotted. Figure 13 displays the same parameter but now only during steps 212 and 213. During steps 212 and 213, the parameter moves between 176.5 +/- and 183.5 +/-, where the unfiltered data ranges between 0 and +/- 200. If unfiltered data were to be used for the control charts, the control limits would be widely inflated and not represent the proper control zones for the parameter. Appendix V displays the selected steps for each process parameter on the long list. Monitoring during production is, for now, the most interesting. In the future, one might decide to monitor the entire step chain, with different control limits

for each production step. However, due to technical limitations, we decidednot to do this. More on this is elaborated in Section 5.3.2.

The bottle size should also be considered for the filters. The long list has seven parameters with different set points during production for different bottle sizes. The distinction is made between the 500 mL bottle (bottle code = 3) and the 1000mL & 1500mL bottles (bottle codes 1 and 2, respectively). The other exception is the CRASH_CNT001 parameter that only monitors the 500 mL bottles. This is because the 1000- and 1500-mL bottles do not have problems falling into the placement cup at the entrance for the RQT. The parameters that need to be filtered on bottle size are also visible in Appendix V.

4.2.2 Sampling interval

The data is sampled using a time-based approach, as introduced in Section 2.2.2. Two years of data have been collected for each process parameter with 1-minute intervals between each new value. Two years of data are chosen in consultation with the Process Engineers. Two years of data give us sufficient data to spot long-lasting trends that might not be visible when evaluating a shorter period. The one-minute-based sampling is chosen because it is a sufficiently accurate representation of the process parameters' performance while maintaining a relatively high computing speed when performing calculations. A shorter time interval between samples gives a more accurate representation of reality but significantly increases the computing time for analysis and data gathering. Longer intervals pose the risk of missing out-of-control signals within the sample period. One minute is deemed appropriate by Process Engineers to spot fluctuations in temperature and pressure sensors.

4.3 PHASE I STUDY

In this section, we perform a Phase I analysis for the process parameters selected in Section 4.1. The goal of a Phase I study is to analyze historical data and estimate the unknown characteristics of parameters by iterative statistical calculations. This is done by plotting run charts and data set evaluation. Through evaluation, special cause variation is identified and either rejected or accepted in the data set for further calculation. This is repeated until all sources of special cause variation are accepted or rejected. From there, a decision can be made for control charting and control limits. In subsection 4.3.1. the filtering and grouping of the data is discussed. Moreover, the performance of the process parameters is evaluated in subsection 4.3.2.

4.3.1 Grouping and filtering data

The data for the process parameters are filtered on bottle type and step chain values. This results in a raw data set ready for Phase I data analysis. The goal of a Phase I study is to analyze past data and estimate the unknown parameters by iterative statistical calculations. The data analysis is started by plotting a run chart of the 2 years of data for each process parameter. This is the first step in Phase I analysis, where large instances of special cause variation are spotted relatively easily. From there, the principle of rational subgrouping is applied to obtain a data set that can be used for further estimation of process capability and control limits. After establishing the control limits, they are evaluated, and any out-of-control data points indicated by the control limits are investigated. From there, the decision is made to either reject the sources of special cause variation from the data set and recalculate the control limit or to keep the data as normal cause variation.

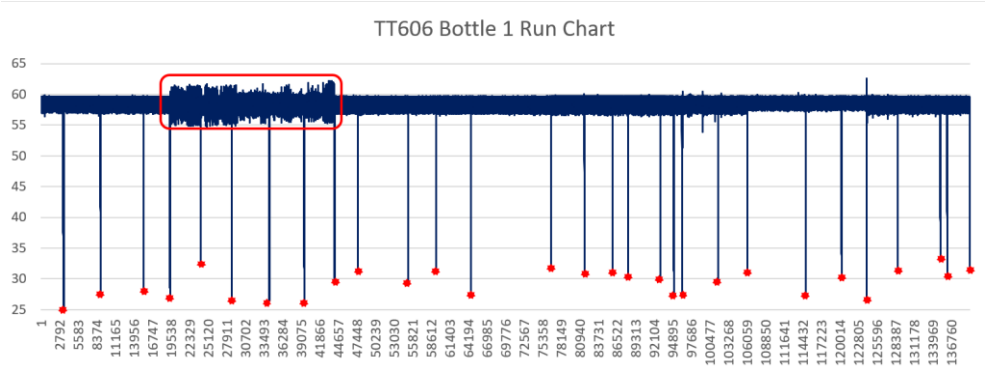


Figure 14 - Run chart TT606 Bottle 1

Figure 14 displays the run chart of TT606 for bottle 1 (1000 mL). TT606 measures the air temperature, which is used to preheat the bottle before spraying it with H2O2. Within the chart, various things stand out. First of all, a 20-day period is seen within the sample where the temperature variation is increased. The variation is only seen during that period and seems to be resolved. This might be due to actions of the Process Engineer or e.g. a replaced machine part. This period is marked as special cause variation and discarded from the data set for further analysis. Furthermore, various drops in temperature can be seen during the sampling period. These drops are significantly larger than the 'normal' temperature variation present within the data set; thus, the root cause of these drops is investigated.

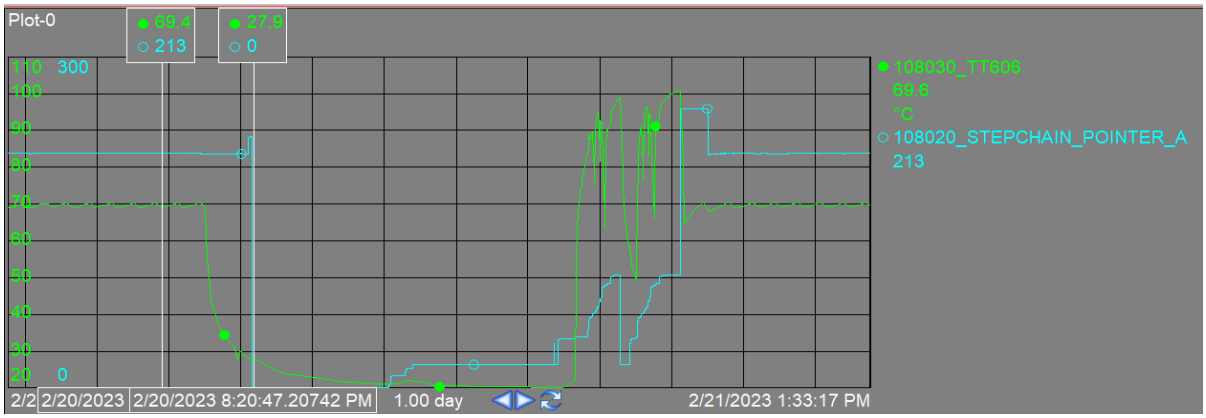


Figure 15 - TT606 temperature drops

Figure 15 displays the run chart of TT606 (green) in addition to the step_chain_pointer_a (blue), which displays the production step of the machine over time. The step_chain_pointer changes from 213, the production step, to 0, which means that the machine is off. Notice that the step chain pointer is still at 213 when the temperature is already dropping off. During a discussion with the Process Engineer, the conclusion was made that there is a delay in the step chain pointer compared to the temperature sensor. This means that every time production is stopped, the temperature drop-off period is registered as if the machine is still producing while the line, in reality, has already stopped. This behavior is also seen for other process parameters and should be filtered out from the data sets. If this delay in the step chain is not filtered out, the control limits for the control charts will be largely inflated and not accurately represent reality.

Other forms of variability that can be seen in the data are step-changes in machine performance (Figure 16) and macro trends (Figure 17), where a slight downtrend over the last two years can be seen. The downtrend in Figure 17 is something that has not been resolved just yet, so we cannot reject the trend from the data set (since it is continuous), and thus the special cause variation is accepted in the data set for further calculations. The step-change seen in Figure 16 is identified as an anomaly caused by a change in setpoint or replacement of a defective part. After discussion with the Process Engineer, the data is marked as special cause variation and thus removed from the data set.

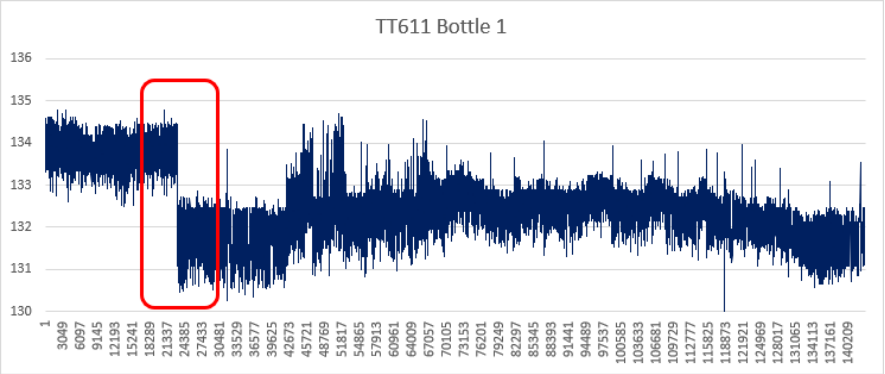


Figure 16 - TT611 Bottle 1 step-change

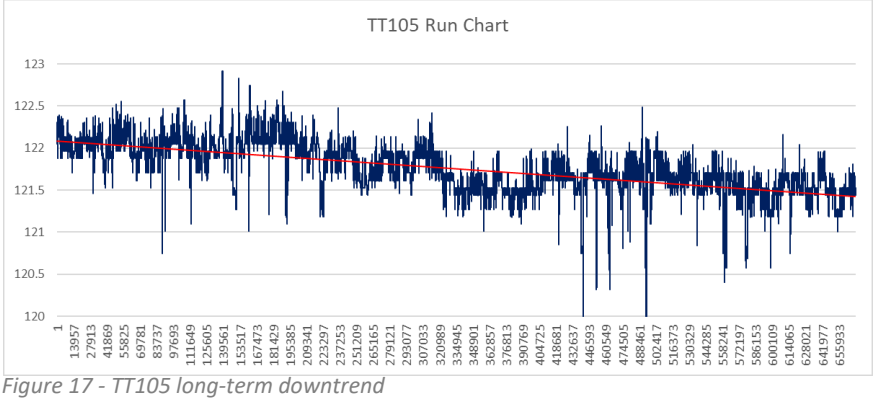


Figure 17 - TT105 long-term downtrend

This process is done for all process parameters. Started by plotting a run chart of the parameter over two years and marking special cause variations. After that, researching the special cause variation and, with the Process Engineer, the decision is made to either reject or accept the variation within the data set. Now the data set is 'clean,' and best represents the machine's performance, from which further calculations can be done.

4.3.2 Performance of process parameters.

After filtering and subgrouping, the data sets for the process parameters are now best representing the parameters' actual behavior. Within this subsection, the performance of the process parameters is quantified. First, the decisions made regarding normality and capability and the use of other descriptive statistics are elaborated. Afterward, the process parameters are evaluated on how well they can produce within the specification limits provided by Abbott. Finally, the most critical parameters within this research are selected.

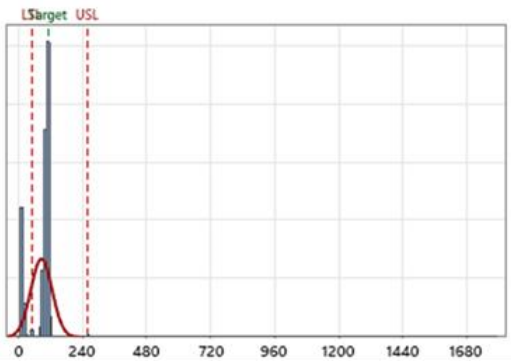


Figure 18 - PIT082 normality fit unfiltered

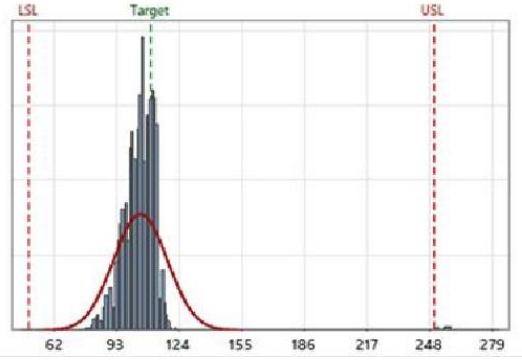


Figure 19 - PIT082 normality fit filtered

A common way of assessing the performance of a production system is by analyzing its capability. The capability of a process is a measure that quantifies how well a process can produce within its specification limits. One of the requirements for a capability study is that the data used is normally distributed. If this is not the case, one can use transformations on the data set to reach a normal state or by fitting another distribution to the data set. For Abbott's

19 process parameters, two normality tests have been applied (Anderson-Darling test & Skewness-Kurtosis test) in Minitab, which none of the process parameters have passed. This is because, even for the filtered data sets, there is still too much noise and special cause variation present within the dataset. Figure 18 displays the unfiltered dataset of PIT082. Two clear distributions can be seen within the data. One is caused by the step chain delay, present for almost all process parameters, and the other is the machine's actual performance. Figure 19 shows PIT082 filtered data set. Also, here, the normality test is not passed. As can be seen, various data points still lie far outside of the normality graph. These values have not been rejected in the initial data filtering and thus are not labeled and removed as special cause variation.

Since the capability cannot be used to assess the performance of process parameters, a combination of other descriptive statistics is used. By combining these statistics with the run charts and histograms, a good indication of the process performance can be achieved.

				Initial data set			**After Phase I filtering**		
Process Parameter	Bottle (1,2,3)	Setpoint	Specification limits	Process mean	Standard deviation	PPM (DPMO)	Process mean	Standard deviation	PPM (DPMO)
FIQ523	1, 2, 3	8 m3/h	*5-10 m3/h*	7.14	1.41	9931	7.32	1.25	0
FIQ524	1, 2, 3	8 m3/h	*5-10 m3/h*	6.94	0.56	5462	6.97	0.22	182
FIQ933	1, 2, 3	850 m3/h	*800-890 m3/h*	843.67	83.13	14171	850.49	6.70	260
FIQ096_PV	1, 2	175 ml/min	*167-194 ml/min*	174.99	3.09	1298	175.02	0.78	697
	3	125 ml/min	*122-130 ml/ min*	125.14	2.15	5860	125.01	0.21	12
FIQ097_PV	1, 2, 3	44 ml/min	*43 – 69 ml/min*	44.00	0.05	0			
FIQ098_PV	1, 2	180 m3/h	*164-194 m3/h*	180.03	6.14	13140			
	3	180 m3/h	*175-185 m3/h*	179.72	2.12	8032			
FIQ099_PV	1, 2, 3	12 m3/h	*5-12 m3/h*	9.59	0.61	0			
TT606	1,2	60 °C	*55-65 °C*	58.23	2.41	9058	58.39	0.91	0
	3	70 °C	*65-75 °C*	69.39	2.92	9241	69.66	0.40	191
TT607	1, 2, 3	83 °C	*67-88 °C*	82.975	0.50	13	82.99	0.38	0
TT608	1,2	60 °C	*57-67*	59.79	2.96	20938	60.06	0.61	11417
	3	71 °C	*68-78*	70.71	3.18	9301	71.00	0.66	183
TT609	1, 2, 3	129 °C	*123-134 °C*	128.36	5.22	9211	128.82	0.63	32
TT610	1, 2, 3	134 °C	*130 – 142 °C*	133.96	0.11	19			
TT611	1, 2	134 °C	*127-139*	132.17	0.75	89			
	3	134 °C	*127-139*	133.94	0.23	43			
TT105	1, 2, 3	121 °C	*110-125 °C*	121.75	0.28	0			
TT106	1, 2, 3	121 °C	*110-125 °C*	119.44	0.43	0			
PIT082	1, 2, 3	110 Mbar	*50-260 mBar*	85.03	39.74	222367	104.98	13.26	5270
108020-PIC081	1, 2, 3	100 Pa	*6-150 Pa*	115.66	22.18	0			
108030-PIC081	1, 2, 3	100 Pa	*6-150 Pa*	107.91	22.09	0			
DT097	1, 2, 3	35%	*34.5-36%*	35.340	0.009	4			
CRASH-CNT001	3	n.a.	*n.a.*	n.a.	n.a.	n.a.			

Table 4 - Performance of process parameters

Table 4 displays the performance of the process parameters of the production line. The bottle code, setpoint, and specification limits are given on the left. These values are derived from the machine setpoints of Abbott. In the middle, the mean, standard deviation, and DPMO (Defects per Million Opportunities) are given for the baseline performance of the data before the Phase I screening. The same descriptive statistics are given, on the right, after Phase I screening. Note that not all parameters have values after the Phase I screening. This is either because the parameter is in control and no significant sources of special cause variation have been identified or because the sensor is drastically out of control, even after the Phase I filtering. This resulted in no notable differences in descriptive statistics and, thus, is not included in the table. For the evaluation, the process mean is looked at in relation to the setpoint of the parameter, the standard deviation of the parameter, and how that relates to the DPMO and the specification limits. For example, 108020-PIC081 has a mean of 115.66 and a standard deviation of 22.18; however, no defects per million opportunities are registered. This observation is interesting since the mean is approximately 1.5 standard deviations from its specification limit. This would suggest that quite a few of the observations should be out of control but are not observed. This further strengthens that there is a lot of special cause variation present within the dataset and that the process might follow a non-normal distribution. The observed standard deviation is primarily inflated by anomalies within the data set, which are either process-specific or special cause variations.

A small standard deviation with a high DPMO count could indicate that the specification limits set by Abbott are too small or that there are various sources of special cause variation present.

The green parameters within Table 5 are the in-control parameters. These parameters show little to no special cause variation and have been very stable over the past two years. See, for example, Figure 20, which plots two years of unfiltered data for DT097. As can be seen, this process has been very stable over time, varying around 35.2-35.4. The same applies to the other green parameters. In the ideal scenario, these parameters are monitored by PMC charts. However, for now, these parameters do not meet the criteria identified in Section 4.1, and thus the decision is made to exclude them for monitoring purposes. The green parameters would be ready for Phase II monitoring.

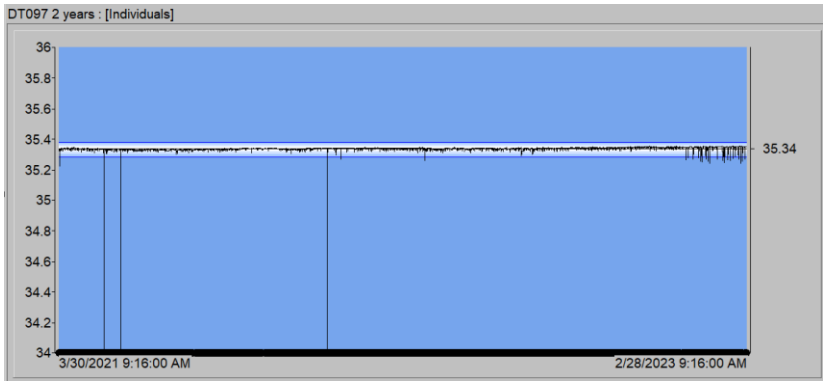


Figure 21 - DT097 2-year data

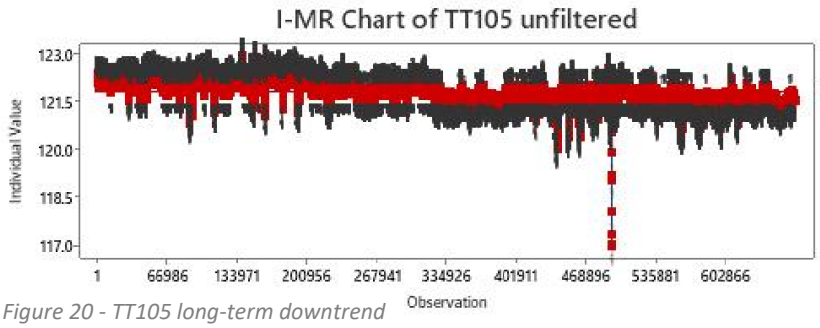


Figure 20 - TT105 long-term downtrend

The orange parameters show some special cause variation, but these are not deemed critical after filtering and subgrouping the data. Most variation present within the data is due to step chain delays or the parameters showing some form of long-term linearity. See, for example, Figure 21, which displays the long-term downtrend over time of TT105.

This in itself is not deemed critical since it is far from reaching its specification limit of 110. However, in combination with the uptrend shown by TT106, it is an interesting finding that the Process Engineerg should research.

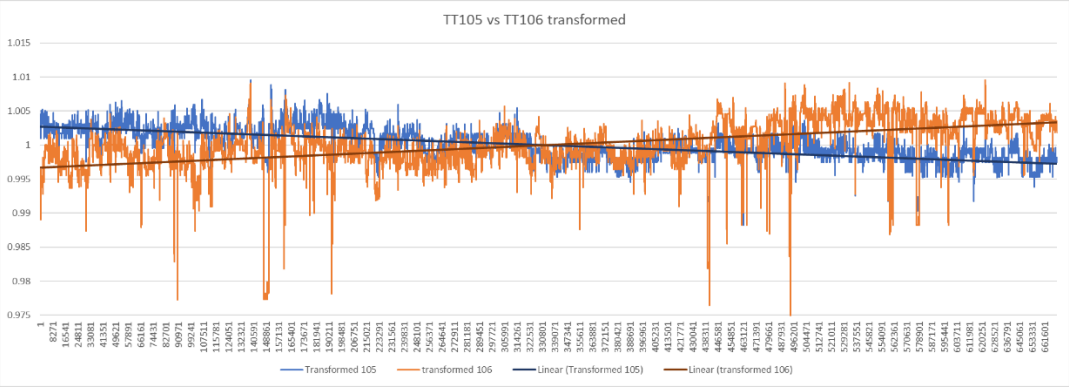


Figure 22 - TT105 vs TT106 transformed over 2 years

In Figure 22, the transformed values of TT105 are plotted against the transformed values of TT106. The transformation was done by dividing all data points of the parameters by their mean over the two years to get an average value of 1 for each parameter. This allows us to overlap both parameters and show their deviations from one, or its mean value, over time. As can be seen, the trendlines of both TT105 and TT106 reach the mean value of 1 at approximately the same time at the halfway point of the data set (1y). This could indicate some correlation between the two values and could be due to wear, for example, in a heat exchanger.

In general, orange parameters would be interesting to monitor further; however, they are not deemed critical enough in relation to the red parameters. This means that, for now, they do not qualify for daily monitoring on the shop floor. The red parameters are the critical parameters after the Phase I analysis. They either show a lot of special cause variations like TT607 (Figure 23), 108020_PIC081 (Figure 24), or 108030PIC081 (Figure 25).

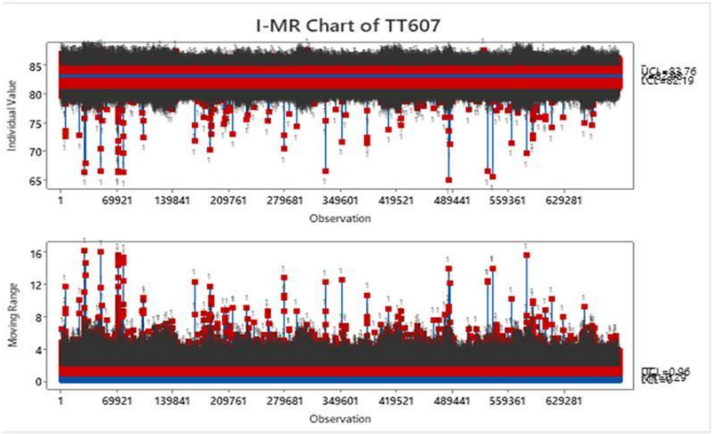


Figure 23 - TT607 special cause variation

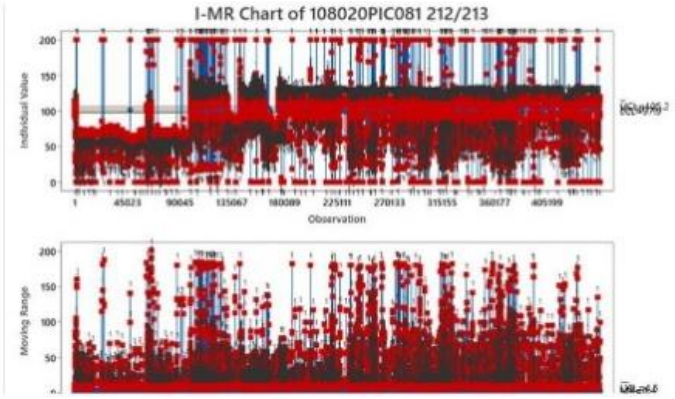


Figure 24 - 108020PIC081 special cause variation

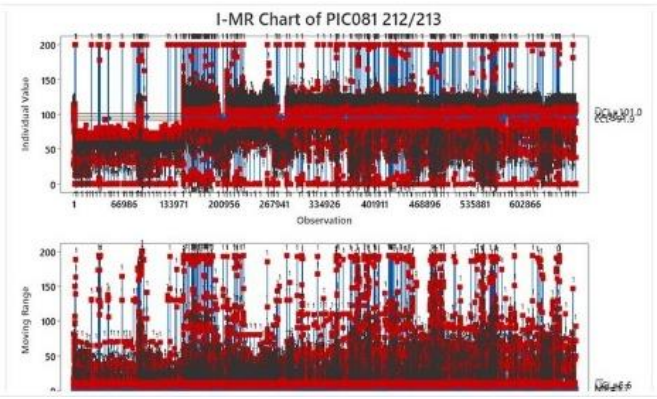


Figure 25 - 108030PIC081 special cause variation

The other reds are FIQ098 and FIQ933, which go out of their specification limits relatively often and where the specification limits are deemed critical for production. FIQ098 is especially known to go out of spec often and causes many stops at the line. Over the last year, there have been 3161 instances within the data set of 1-minute samples where FIQ098 has exceeded its specification limits during production. It is hard to quantify how much this has impacted the line's production since it represents the parameter's value at a specific moment in time. This can be a coincidence where the parameter was out of specs for a couple of seconds, or it can be for a couple of minutes, which does impact production significantly. Taking the production speed of the line, which is 6600/bottles per hour, or 1,83 bottles per second, the minimum amount of bottles lost due to FIQ098 being out of spec is 3161 * 1.83 = 5795 bottles. This is assuming that the parameter was only out of spec for 1 second when taking the snapshot value. If 30 seconds is taken as an average time, which is more realistic when looking at the data (there are quite a few instances where the parameter is out of spec for a few minutes after each other), a value of 173823 bottles of production capacity lost over a year is obtained due to this parameter being out of spec. This does not even account for the instances where the parameter has caused the machine to go unsterile, which would mean that several hours are needed to clean the machine to get it operational again. This is, of course, a rough estimate, but it does press the significance of the issue at hand.

Lastly, there is TT609. This parameter is relatively in control but is showing the same long-term downtrend as TT105. However, TT609 is closely approaching its lower specification limit. This increases the importance of monitoring the variable drastically.

In this analysis, the CRASH_CNT001 parameter is not taken into account. The Mechanical Excellence Engineer nominated the variable for process monitoring and control because it is a relatively new ongoing problem for the line. Since November 11th, 2022, a sensor (CRASH_CNT001) has been placed at the entrance of the RQT that monitors the number of crashes of the 500mL bottle. This sensor registers every time the bottle is not properly in place at a specific time. To understand how often this sensor is triggering, the time interval between sensor activations cannot be looked at. This is because the line is not always running. Sometimes the line is stopped due to other problems, or because cleaning is needed, other times the machine is running a 1000 or 1500mL bottle for which the bottle infeed is not a problem. This means that the time interval between sensor activations cannot be taken as an appropriate monitoring method. From a meeting with the Mechanical Excellence Engineer, the decision was made to track the number of activations of CRASH_CNT001 / 100.000 500 mL bottles produced. This gives a relatively accurate representation of the state of the system. This rules out times between production and only monitors when the system is showing more or fewer infeed problems.

The approach does have its limitations. The program used within Abbott, PI Processbook, cannot perform complex transformations or calculations of the data. Since the goal is to monitor the Crash/100.000 bottles, a link needs to be made between the date of the crash and the number of type 3 bottles produced in that period. In PI Processbook, this is not possible, and thus the parameter can not be monitored within the dashboard. In the Phase I study, the run chart of the CRAHS_CNT001 has been plotted since the 11th of November. This is done in Excel by manually linking the dates of crash counts with the number of bottles produced. The chart produced can be seen in Figure 26.

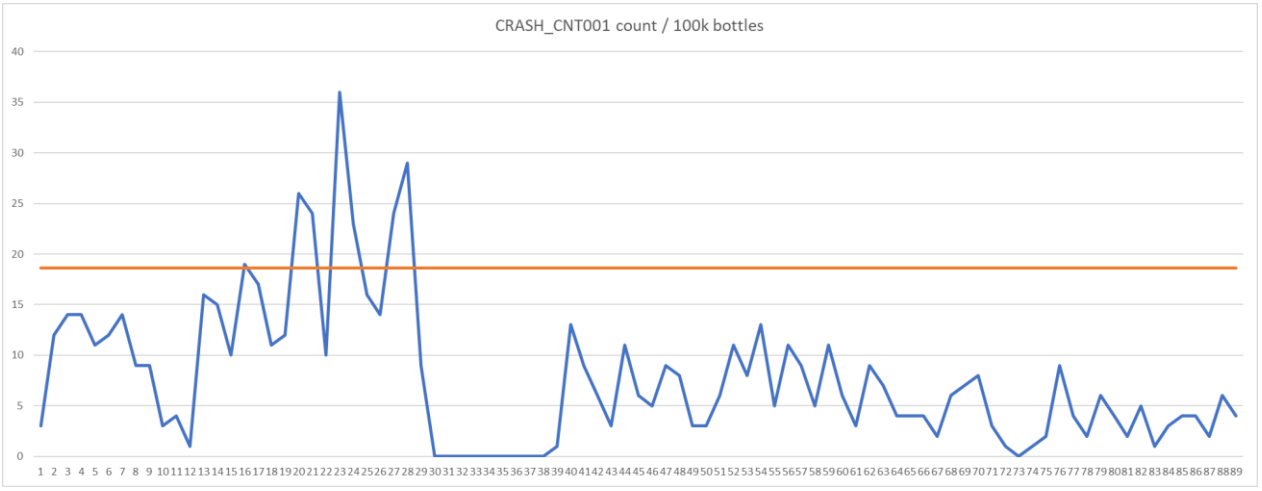


Figure 26 - CRASH_CNT001 Control chart

In discussion with the Process Engineer and Mechanical Excellence Engineer, the decision was made to exclude the parameter for monitoring on the shop floor. The proposal of manual plotting at the line or through an Excel dashboard was rejected due to the relative complexity and the need for yet another system and work instruction.

4.4 SELECTING CONTROL CHARTS AND CALCULATING LIMITS

In Section 4.3, the performance of the process parameters is analyzed, and the filtering and subgrouping are applied to the data set. From here on, control limits can be calculated for the control charts.

Recall that for a Phase I study, Shewhart control charts are the most effective way of monitoring the process. For Shewhart charts, a distinction is made between continuous and variable data. All the parameters in this study are continuous. This means that the charts that can be used are limited to the XbarR, Individuals, XbarS and EWMA, and CUSUM charts. Due to the nature of the sampling used in this study, rational subgrouping is only possible. After that, each measurement is set as its own subgroup where n = 1.

To determine the control limits, the results of the Phase I filtered observations is used as the baseline data. This data is used with an Empirical Reference Distribution (ERD) to set the control limits for the parameters. The decision to use the ERD for the control chart is due to several reasons. As stated in Section 4.3, the data is non-normal and still contains quite some special cause variation within the data set. This means that a proper fit of a probability model is complex and not in line with the wishes of Abbott. Furthermore, a simplified version of the ERD is already used by Process Engineers to calculate control limits for other charts, so it is a known procedure for them that can easily be validated. The Individuals chart is another valid phase I monitoring option, as verified in Section 3.2.1. However, using the Individuals chart results in many out-of-control signals for each parameter conflicting with criteria 4 from Section 4.1. Abbott prefers a chart that filters out major sources of special cause variation from which research cycles can be started to improve the process. Recall that the goal is to increase insight at the shopfloor and that Operators can easily understand the charts. Therefore the decision is made to construct control charts using the ERD approach.

This ERD approach as introduced in Section 3.3.1 is applied to the data, where an in-control state is selected from the initial data set. TT608 for bottle three is taken as an example of this approach. Figure 28 displays the raw data of TT608 for bottle three, which corresponds to approximately 320 days (461k 1m samples) of non-stop production (Steps 212 and 213). Figure 27 is a sample taken from this data set where the process is identified as in control, which is approximately a week of production (10k 1m samples). Now recall the study in Subsection 3.2.1., where Wheeler (2009) validates the use of 3 sigma

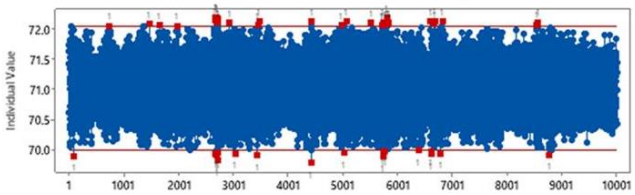


Figure 28 - TT608 in control

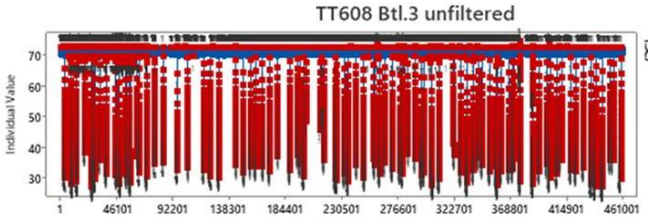


Figure 27 - TT608 unfiltered

limits. In this approach, 98% of all data points fall within the three-sigma limits for various distributions. Moreover, he deems three sigmas sufficient for filtering out the probable noise for Phase I applications. Three sigma limits correspond with a probability of 0.9973 that a data point will fall within the control limits.

This study uses the three-sigma probability as a fixed probability within the ERD, to construct the control limits. The number of blocks b that is needed for this probability is $b = P * (m + 1)$. Since this study uses two-sided control limits for the process parameters, a total of $(m + 1) - b$ blocks fall outside of the control limits, which correspond to $0.5 * (m + 1) - b$ blocks on each side. So the control limits are defined as $LCL = y_{(0.5*((m+1)-b))}$ and $UCL = y_{(m-(0.5*((m+1)-b)))}$.

Within this in-control sample, there are $m = 10000$ data points, and thus $m + 1 = 10001$ statistically equivalent blocks. Recall that the formula for determining the number of blocks for the control limits is: $b = P * (m + 1)$. For P, the probability of a three-sigma in control probability of a normal distribution is used which is 0,9973. This means that $b = 0{,}9973 * 10001) = 9974$. The control limits are then calculated by $LCL = y_{(0.5*((m+1)-b))} = y_{(0.5*((10001)-9974))} = y_{(13,501)}$ and $UCL = y_{(m-(0.5*((m+1)-b)))} = y_{(10.000-(0{,}5*((10.000+1)-9974)))} = y_{(9986,49)}$.

In Table 5, the observations of the in-control data set are ranked from small to large. Furthermore, the smallest observation is labeled as observation $y_{(1)}$. From the calculations of the control limits, $LCL = y_{(13,501)} \approx y_{(14)}$ and $UCL = y_{(9986,49)} \approx y_{(9986)}$ is obtained, which corresponds to $LCL = 69{,}97$ and $UCL = 72{,}08$ respectively.

The mean of the parameters from the in-control observation is set as the Center Line in the control chart.

Observation Yi	Temperature °c	# Blocks
1	69,64	1
2	69,71	2
3	69,73	3
...	...	4
13	69,96	...
14	69,97	13
15	69,99	14
...	...	15
9985	72,07	16
9986	72,08	...
9987	72,11	9985
...	...	9986
9998	72,19	9987
9999	72,20	9988
10.000	72,23	...
		9998
		9999
		10.000
		10.001

Table 5 - TT608 Bottle 3 Control limits

This process is repeated for almost all process parameters and filter configurations, the control limits for these parameters can be found in Table 6. Note that some exceptions are made regarding the setpoint and calculation for the control limits.

An example of this is FIQ098. If the ERD approach had been used, the control limits would be wider than the specification limits for the parameter. The choice is made to rely more heavily on the voice of the customer and thus set the specification limits as control limits instead of listening to the voice of the process, which indicates wider control limits. This is done to prevent confusion for Operators and is in line with Abbott's wishes regarding the selection and visualization of process parameters, as noted in Subsection 4.1

Other parameters for which exceptions have been made are the following:

- FIQ523: The control limits are set as integers since the parameter also behaves like one. For the in-control data set, the parameter moves between 5 and 9 (out of control, it has step-changes to 10 and 11)
- FIQ524: The same applies here. The control limits are also rounded to an integer.
- FIQ097: The same also applies here. Due to the nature of compression and exception settings or the machine behavior, the control limits are set as integers.

Process Parameter	**Bottle (1,2,3)**	**Setpoint**	**Specification limits**	**LCL**	**CL**	**UCL**
FIQ523	1, 2, 3	8 m3/h	*5-10 m3/h*	5	7.2	9
FIQ524	1, 2, 3	8 m3/h	*5-10 m3/h*	5	7	8
FIQ933	1, 2, 3	850 m3/h	*800-890 m3/h*	838	850	862
FIQ096_PV	1, 2	175 ml/min	*167-194 ml/min*	172	175	183
	3	125 ml/min	*122-130 ml/ min*	125	125.01	130
FIQ097_PV	1, 2, 3	44 ml/min	*43 – 69 ml/min*	43	44	45
FIQ098_PV	1, 2	180 m3/h	*164-194 m3/h*	164	180	194
	3	180 m3/h	*175-185 m3/h*	175	180	185
FIQ099_PV	1, 2, 3	12 m3/h	*5-12 m3/h*	8.9	9.5	10.1
TT606	1,2	60 °C	*55-65 °C*	55.67	58.54	61.21
	3	70 °C	*65-75 °C*	68.5	69.67	70.85
TT607	1, 2, 3	83 °C	*67-88 °C*	79.95	82.97	85.63
TT608	1,2	60 °C	*57-67*	58	60	61.9
	3	71 °C	*68-78*	69.97	71	72.08
TT609	1, 2, 3	129 °C	*123-134 °C*	126.57	129.04	129.56
TT610	1, 2, 3	134 °C	*130 – 142 °C*	133.63	133.96	134.43
TT611	1, 2	134 °C	*127-139*	130.7	131.84	132.53
	3	134 °C	*127-139*	132.94	133.94	134.61
TT105	1, 2, 3	121 °C	*110-125 °C*	120.64	121.75	122.57
TT106	1, 2, 3	121 °C	*110-125 °C*	118.15	119.94	120.4
PIT082	1, 2, 3	110 Mbar	*50-260 mBar*	78.84	104.17	119.21
108020-PIC081	1, 2, 3	100 Pa	*6-150 Pa*	91.2	115.65	118.57
108030-PIC081	1, 2, 3	100 Pa	*6-150 Pa*	78.61	107.9	113.83
DT097	1, 2, 3	35%	*34.5-36%*	35.38	35.34	35.35

Table 6 - Control limits for process parameters

4.5 CONCLUSION ON CONTROL PARAMETERS

In this chapter, the process parameters are evaluated, and the control chart that best fits the wishes of Abbott for monitoring the critical parameters is determined. In this analysis, eight parameters are marked as ready for Phase II monitoring. These parameters show long-term in-control behavior and are best further monitored using more complex charts and fitting distributions to the data. Eleven parameters are marked as out of control, of which six are deemed critical. The six critical parameters are nominated for daily on-the-line monitoring through individuals control charts with control limits derived from the ERD. The remaining five parameters should be further investigated by the Process Engineers or could be monitored weekly.

5. APPLICATION OF PROCESS MONITORING AND CONTROL

In this chapter, the choices made regarding the design of the dashboards is elaborated in Section 5.1. Next, how the dashboards are implemented at the ARTH line is discussed in Section 5.2. In Section 5.3. the practical and methodological improvements that can be made at Abbott Zwolle regarding the further use of PMC within the organization is elaborated.

5.1 DASHBOARD DESIGN

In Subsection 5.1.1., the dashboard designed for Abbott's Morning meeting and for Abbott's operators is discussed. In Subsection 5.1.2., the limitations of these dashboards are discussed.

5.1.1 Dashboards for the filler and morning meeting.

In the analysis, six sensors are identified that are deemed critical and for which daily monitoring would be a significant benefit. Recall that this research aims to increase insight on the shop floor. In this section, the choices made regarding the dashboards, time intervals, and integration methods is elaborated.

To visualize the six critical process parameters, two Process Monitoring and Control dashboards have been created in PI Processbook. These dashboards are displayed during the morning meeting and on a monitor that is located next to the filler. The dashboard contains 6 Individuals charts that display the critical parameters from Section 4.3. The dashboard displays the measurements of the process parameters over a 5-day period, filtered on steps 212 and 213.

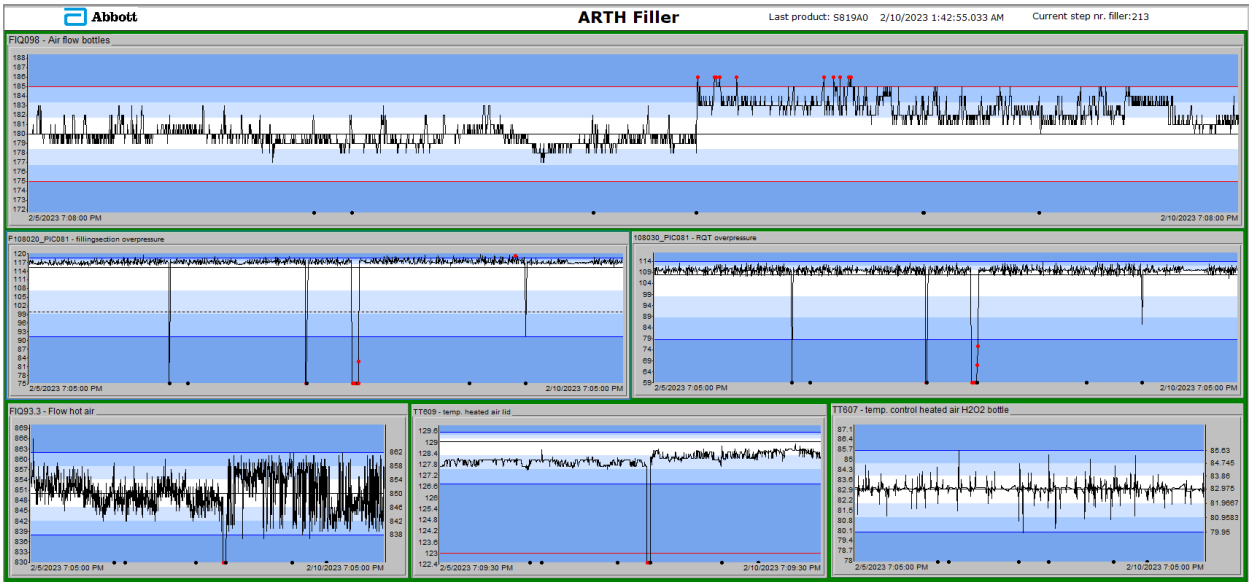


Figure 29 - Morning meeting dashboard

The 5-day period is chosen as the time frame because it is a relatively small time frame that is detailed enough to spot minor sources of variation whilst being long enough to spot step-changes. An additional benefit of the five days is that the team who just got back from their 4-day leave can see the performance of the parameters during their 4-day absence in relation to their last working day before their leave. During the morning meeting, the dashboard displayed in Figure 29 is looked at and discussed. Here out-of-control signals are analyzed, and other weird patterns that are present in the data

are discussed. Note that some out-of-control signals can be seen in de charts. These again can be explained by the step chain delay discussed in Section 4.3.1.

To further increase the insight of operators, another dashboard is made for a screen next to the filling section of the machine (Figure 30). Here Operators can look at the real-time performance of the machine. Again, the six most critical parameters are visualized, but the real-time parameters of the Batch Work Order are also displayed. The benefit of this is that operators, on the one hand, have all parameters in a logical sequence on one screen. This makes it easier for them to note the values for the hourly Batch Work Order check and likely reduces mistakes. Moreover, it is an incentive to hourly check the Individuals' charts of the six critical parameters.

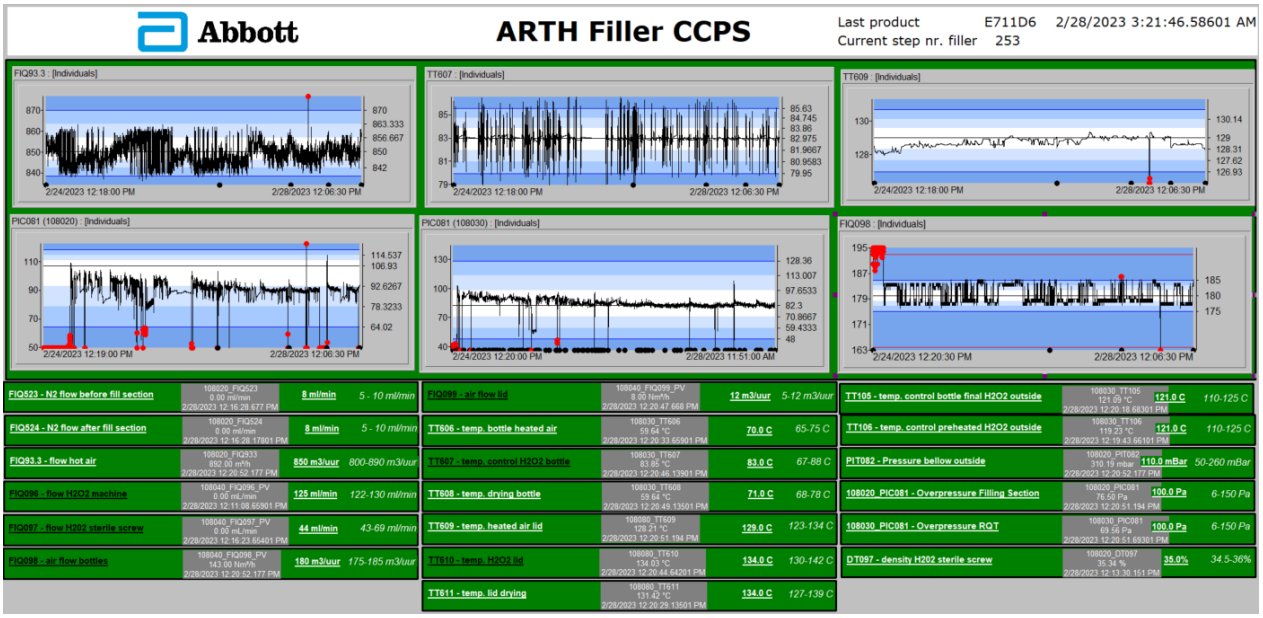


Figure 30 - Dashboard next to the filler

During the two-week period in which these dashboards were introduced, several comments were made layout-wise and content-wise. At the end of the two weeks, Operators, and morning meeting members were enthusiastic about discussing the parameters and saw the dashboard as an added value.

5.1.2 Limitations of Dashboard Design

Although Operators, and other stakeholders are generally positive, some limitations of the dashboards in this research are discussed. The dashboards increase the current insight at the shop floor; however, there is room for further improvement.

During this research, two factors were identified that were limiting the useability of the dashboards. The first category is PI Processbook. The program is part of the OsiSoft system. However, it is a legacy program. The latest version was created in 2015 and has not received any updates since 2020. Since the beginning of this year, the program will no longer receive security updates and patches. OsiSoft has retired the system in favor of PI Vision, a modern version of PI Processbook that allows the user to plot and display data collected in the PI server. However, within Abbott, this migration has not taken place. During this research, the first initiative was started to use another program, SEEQ, instead of PI Processbook, which has additional functionalities.

Limitations that are encountered in this research regarding the implementation and use of PI Processbook are the following:

- Slow processing time: Plotting data and making changes to charts would take several minutes before the new screen was loaded.
- Slow start-up time: Starting up the screen at the filler could take up to 10 minutes
- Data visualization:
    - Labeling axes or enlarging text in charts is not possible
    - Formatting and display options are minimal (e.g., color coding a parameter red when outside of specification)
    - Visualizing data breaks is not possible (In this case, plotting steps 212 and 213. This is displayed as a continuous graph during the time frame selected. However, it might be the case that during those five days, the machine was offline 2 of them. This is not possible to visualize within the chart and can lead to much confusion)
    - Control limits for the three bottle type are possible but quite complex; a new table must be created within the OSIsoft data structure, where the data tag, bottle code, and control limits must be specified. From there, a control chart can be constructed where the limits refer to the internal table from which it retrieves the current control limit for the type of bottle that is in production.
- It only runs as a desktop application
- Calculation:
    - Calculations of any sort are *very* limited within the program (It is possible to write a VBA macro that would run within the PI Processbook application. However, this was very slow and would give many errors.)
    - Dynamic or optimal run charts are not possible due to the lack of calculation possibilities
    - The Excel plug-in function would also take a very long time for data to load. (For some parameters, the maximum query length could be approx seven days, retrieving 2y of data would thus take a long time)

The second category is the validation of PI Data tags. As stated earlier, Abbott Zwolle has approximately 100,000 PI data entry points for its site. However, of these 100k points, only approximately 300 are validated. For the application, this is quite disadvantageous. It means the data points displayed in any PI application can not be used for official purposes like validating a batch. Especially during the implementation phase, this is something that was a significant limitation. This is because the parameters displayed in Figure 30, for example, can not officially be used to fill in a Batch Work Order. This is quite weird and was found out quite late in the study. Recall that Abbott's Process Engineers use the tags to optimize and correct the process settings, but the same data can not be used for hourly batch checks and or approvals.

The unvalidated tags might also be the root cause of the step-change delay encountered with the STEPCHAIN_POINTER. Another limitation of not validating the PI data points is that the ExDev and Compdev settings might not be correct. Currently, the values of the Exdev and Compdev for new parameters are copied from similar existing parameters. For example, a flow gauge will likely receive the same Exdev and Compdev settings as another already monitored flow gauge. This research identified 4 parameters (out of 19) that had bad Exdev and Compdev settings. The Exdev and Compdev settings for these parameters were more sensitively calibrated than the sensor itself could measure. This resulted in

a lot of ‘grass’ within the data, where the PI system registered fluctuations where it should not have done so. There are a few adverse side effects that result from this. First of all, the control chart becomes less clear to interpret. There is much noise on the chart, which makes it harder to spot special cause variation. Second of all, an excess of data points is stored on the PI server. This data does not tell us anything but is registered as an event. This also means that if calculations need to be made for that parameter or if a chart needs to be plotted, it takes quite some time for the program to process all events. This is something that was encountered a lot during this study. Moreover, it is not good for statistical computations. Where the process, in reality, might have a mode of, for example, 2, with bad Exdev and Compdev settings, these could then be registered as 1.5 or 2.5. In the data, this would be represented by two different distributions where it actually might only be one.

5.2 PMC AT THE ARTH LINE

The implementation of PMC at the production line started with the introduction of PMC to the Front Line Leaders. Through various meetings, the benefits of PMC were explained if needed, and their criteria for the PMC dashboards were discussed. In these meetings, several Operators were selected from the production teams to ask for further input and to be involved with the program's creation and implementation. This approach was chosen over training the entire team for several reasons. Most importantly, not all the Operators were enthusiastic about the new tool. Most lacked the statistical knowledge and interest in IT systems to learn about yet another program. Second of all, there would be a clear distinction within the production team who would be the internal “PMC expert.” For all stakeholders involved, it would be easier if one or two Operators of the team were the point of contact regarding PMC-related questions or activities. This approach is an early step toward the process action teams (PATs) that is discussed in Section 3.4.1. These Operators were explained the basics of PMC, what they should look for, and how they could interact with the charts.

Every morning the Operators are responsible for discussing the charts with the stakeholders of the morning meeting. During this moment, the chart is pulled up to the screen, and sources of special cause variation are identified and discussed. The most important trigger for a discussion is an out-of-control signal indicated by the red marker. For the charts, it was decided not to include additional run rules. This is because the parameters were selected for their variability. Applying additional run rules will only trigger extra alarms, which would clutter the chart whilst not adding sufficient benefits for the stakeholders. The charts are all still out of control, and by adding run rules, the number of out-of-control triggers would be too large.

The daily evaluation of the selected process parameters functions as a training tool for Operators to familiarize themselves with PMC. It serves as a pilot project for the line and is something that can be indefinitely monitored. If a parameter is brought into control, a reevaluation of parameters should happen, and the most variable parameters should be selected. This creates a standard moment each day where PMC is discussed, and the most critical parameters for quality and safety are evaluated.

The PMC screen next to the filler is present and can be used, however, the unvalidated sensors limit its usefulness and intended application. If Abbott were to validate these parameters, it would be a great added value for Operators and Process Engineers. An hourly evaluation of the critical parameters could help prevent problems on the line, such as the FIQ098 discussed earlier.

5.3 IMPROVING PMC

This section discusses possible improvements regarding the use and implementation of PMC within Abbott Zwolle. Starting with methodological improvements in subsection 5.3.1., after which some practical improvements are discussed in subsection 5.3.2.

5.3.1 Methodological improvements

This section discusses the application of PMC and how Abbott can go from Phase I charting to Phase II applications. During this research, the lack of a common approach for widespread PMC integration was lacking. At the company, the DMAIC is a commonly used approach. However, the fit with PMC integration is less evident in comparison to standard DMAIC projects. This section introduces a step-wise approach that Abbott can follow to get a process from an out-of-control state to Phase II charting applications in a DMAIC format.

The methodology of Does et al. (1997) is the cornerstone of this approach. It is analyzed on how it fits within Abbott as a company and how the methodology could help them reach a new phase of process monitoring and control.

The methodology is broken down into a few parts. First of all, Does et al. (1997) divide the implementation of PMC into four levels (in their paper, Phases, but for clarity, this study uses Levels). These serve as a ranking and indication of the level of readiness of the PMC application within an organization.

- Level 1: Awareness
- Level 2: Pilot projects
- Level 3: Integral implementation in production
- Level 4: Total quality

Note that these Levels relate to the state of implementation company-wide. A clear distinction should be made between the Phase I and Phase II applications since these relate to the state of the charting applications and the level of control reached for the parameters.

Abbott Zwolle would currently rank between Levels 2 and 3. Abbott has a few pilot projects underway, and several people have extensive knowledge of stochastic process control. However, some key elements noted by Does (see also Section 3.4.1) are missing within Abbott. For Level 1, all boxes are ticked, there is a general awareness of PMC and its goals within Abbott, and a steering committee exists.

For the second level, the approach should be to introduce PATs within the company, and pilot projects should be started and executed using the 10-step method. Within Abbott Zwolle, several pilots have been started. However, these projects generally followed the DMAIC approach. This is a Lean Six Sigma approach where any project is broken up into a Define, Measure, Analyze, Implement, and Control Phase. Recall Section 3.4.2. where control charting in the DMAIC structure is reviewed. Here control charting was mainly used in the control phase.

The third level is integral implementation in production. This is something that Abbott is currently working towards. A PMC project has been completed at the powder department, and PMC is still actively used to monitor a part of the line. Furthermore, at the CPA department, PMC is used to control the effectiveness of CIPs. Operators use PMC charts to determine whether or not another round of cleaning is needed. And finally, this project at the ARTH filler aims to increase the use of PMC in production.

Abbott's goals for the coming year are to review the current charts, eliminate and update where needed, and introduce control charting on all of the liquid production lines. For this, a comprehensive DMAIC process approach is introduced in which the 10-step method of Does et al. (1997) is integrated. Abbott widely uses the DMAIC and thus it has the benefit that the methodology is known to the stakeholders. Furthermore, the company employs Operational Excellence project managers. They are trained in the application of the DMAIC and how it should be applied in project work. By proposing a new methodology for Abbott incorporating the best of both, it is hoped that the detailed process cycle can be followed to bring any process under control.

Figure 31 displays the DMAIC process in which the 10-step approach is integrated. Below, the different steps and goals for each phase are described.

Figure 31 - 10 step method in the DMAIC

The Define phase corresponds with the start-up of a PMC project. During this phase, Steerco or management might ask for PMC integration on one of the liquid lines. During this phase, the aim is to identify or validate the improvement opportunity that is presented. Furthermore, the Process Action Team is formed, and a project charter is made. The define phase serves as the preparation phase for the PMC assignment. The goal should be pretty broad since it is still unknown what and if processes are out of control and require action.

Key actions Define phase:

- Identifying and validating the improvement opportunity
- Forming a PAT
- Creating a project charter
- Outlining the scope

The key objective of the Measure Phase Is to document the existing processes and establish a performance baseline. In the DMAIC, common activities during this phase are Y = f(x) analysis (input, process, output analysis), FMEA (failure mode and effects analysis), and plotting baseline data.

Key actions Measure phase:

- Step 1: Process description > Dividing the process into steps of one distinct transformation. The goal is to obtain a process description form with the different process steps and names, see, for example, Figure 4.
- Step 2: Cause and Effects analysis > This is also a descriptive action. Key problems of the line and the possible causes should be listed here. In this study, FIQ098 might be an example of the cause, where the effect is the downtime of the filler.
- Step 3: Risk analysis: During this step, the relative importance of each cause-and-effect relationship is calculated. For example, how often it occurs, what is the severity of the causes, et cetera. This ranks the out-of-control states of all processes and makes it easier to select the most pressing issues at hand.

The analyze phase aims to verify that improvement is focused on causes rather than symptoms. In this phase, different improvements are proposed, and measurable experiments are designed. For a PMC project, this should be an iterative phase, where solutions are proposed, measurements are designed, and reliability is tested. After this phase, Phase I control charts are created to spot sources of special cause variation. After monitoring these charts, an in-control state or out-of-control state can be identified. If the process is out of control, one should return to the analyze phase, where new improvements and measurements are designed that can again be tested in a control chart. When a state of control is reached, where all root causes for deviations within a key parameter have been eliminated, a distribution can be fitted to the data, leaving the iterative Phase I and Analyze loop and continuing to Phase II charting. It is essential to document how and why proposed solutions should affect the root cause issue. By documenting this, knowledge of the process and its behavior can be stored, which will be helpful in step 8, where an OCAP is generated.

Key actions of the Analyze phase:

- Step 4: Improvements > Generating possible improvements for the identified cause and effect relationships. The goal is to obtain a list of improvements for the most pressing issues at hand.
- Step 5: Define measurements > Select data for analysis and parameters for process control. Defining the measurements plan if applicable (how often and what should an operator measure? What data should be collected that is not presently available?)
- Step 6: Repeatability and reproducibility study (R&R study) > Determine the systematic error and variation of the measurements. Repeatability is defined as the variability present in the measurement device itself (a sensor that shows variation when the process is stable), and reproducibility is the variation that is present between different measurement devices. This step is also not always applicable. In some cases, only one measurement device is used, or only one operator performs the action. In these cases, the measurements still need to be verified (e.g., calibrating the sensor or reviewing the operator's measurement actions.)

The first Improve phase can be seen as an intermediate solution. In this phase, Shewhart charts are used to monitor the process parameters. At this time, the process parameter is not in control. It is expected that a PAT will bounce between the analyze and Phase I improve phase multiple times, where solutions are proposed, and the results are monitored and evaluated using control charts. After removing all sources of special cause variation, one can continue from the Phase I improve phase and take the next step in process control.

Key Actions Improve Phase I:

- Step 7: Control charts > The Process Action Teams apply control charting to gain insight into the characteristics of parameters that can be used to control the process. The control charting should help detect out-of-control situations. The application of control charting follows a multi-step approach. Starting with preliminary control limits calculated from the raw dataset. This results in widely inflated limits. From there, these limits are used to identify out-of-control situations that should be investigated. After investigation, these points can either be accepted within the data set or rejected. After this step, the control limits should be recalculated, and new out-of-control points should be investigated. Based on the knowledge obtained through the analysis of out-of-control situations, the team can decide to return to Step 4 (analyze phase) and search for new possible improvements.

The Improve Phase II activities can start when a state of control has been reached through the Improve Phase I and Analyze loop. Here it is important to fit a distribution to the data. The fitting of distributions is needed for the more complex control charts that should be applied in Phase II charting. This is a statistically more complex step where some data might need transformations to fit in a distribution. Within Abbott, statistical knowledge is present to do those transformations. However, the end user (operators) will need additional training or instruction on how to interpret the control charts signals. Again by operating in a process action team and going through the previous steps in this cycle, the Operators in the PAT should have a sufficient basic understanding of PMC.

Key Actions Improve Phase II:

- Fitting distributions to sample data of in control parameters
- Step 7: Control charts > Create more complex and sensitive control charts focussed on spotting out-of-control situations and small process shifts. Ideal charts for this are the CUSUM or EWMA charts. Other options are the optimal run chart and the dynamic control chart.
- Step 8: Create an OCAP (Out of Control Action plan) for the process parameters. All the findings in the analyze, Phase I and Phase II Improve phase, come together here. Specific out-of-control signals or combinations of out-of-control signals for the process parameters are documented, and an action plan is defined. The creation of the OCAP is only useful when the problem has already once been resolved. The OCAP has no true purpose for this study since the selected process parameters have not reached the appropiate level of control.

Control is the final phase of the DMAIC project. The goal of this phase is to establish monitoring processes and procedures that will ensure the long-term success of the PMC project. This is done by quantifying the results of the improvements made and updating standard work documentation and procedures.

Key activities Control phase:

- Step 9: Capability study on the process parameters. Determine the capability of a process and decide whether additional improvements need to be made. With the process's capability and a good distribution fit to the data set, the number of out-of-spec points can be predicted and used as a benchmark for the parameter.
- Step 10: Certification. In this final step, the activities of the PAT are evaluated by the steering committee. An internal audit will be held where the work of the PAT is evaluated, and the activities on the shop floor are checked. This is a final check to ensure Operators know how to work with the SPC charts and if all processes are correctly being documented.
- Creation of the Process Improvement Team (PIT): It consists of the Process Action Team members and focuses on improving the process. The process is in control and behaves predictably, but improvements can be made to reach new targets and strive for continuous improvement.

By following this step-by-step guide, any process can theoretically be brought into control. By combining the 10-step method of Does et al. (1997) and placing it in the DMAIC structure, a framework is proposed, focussing on SPC improvement using a well-known methodology within Abbott. There is quite some overlap between the frameworks, and that makes it quite a good fit.

5.3.2 Practical improvements

Other than methodological improvements, some practical improvements should be made to reach level 3 of control charting.

First of all, the application used for PMC should be changed to another program. As stated in Section 5.1.2., there are quite some limitations to the program PI Processbook. A program like SEEQ (for which a pilot project has been started) tackles many of these problems. SEEQ is a web-based application that can be linked to the PI system. It connects to the system without moving or copying the data. This means that it uses real-time data as it is stored in PI. And thus, it does not differ from something like PI Processbook, which is currently used. The benefit of SEEQ is that it can be used for a broader range of

purposes than PI Processbook. One of the significant benefits is that people can collaborate in real time on the project since it is web-based. Furthermore, it has new features like pattern recognition, machine learning, and complex calculations while also providing basic features like trending, monitoring, and creating alerts. An example of this is the 'profile search' feature which marks similar patterns in the data compared to the selection of data that is made. This makes it easier to clean data. Where this study struggled significantly with problems due to the step chain delay, SEEQ could have filtered out the data by marking and cleaning similar events within the data set. Figure 32 displays a dynamic control chart where the control limits are calculated over the past performance of the parameter. As can be seen, the setpoint of the parameter changes and the control limits move with the changes. Another benefit is that one can monitor the entire step chain compared to this study, where only steps 212 and 213 are monitored. This also means that periods of no production are visible, which the dashboards in this study are lacking.

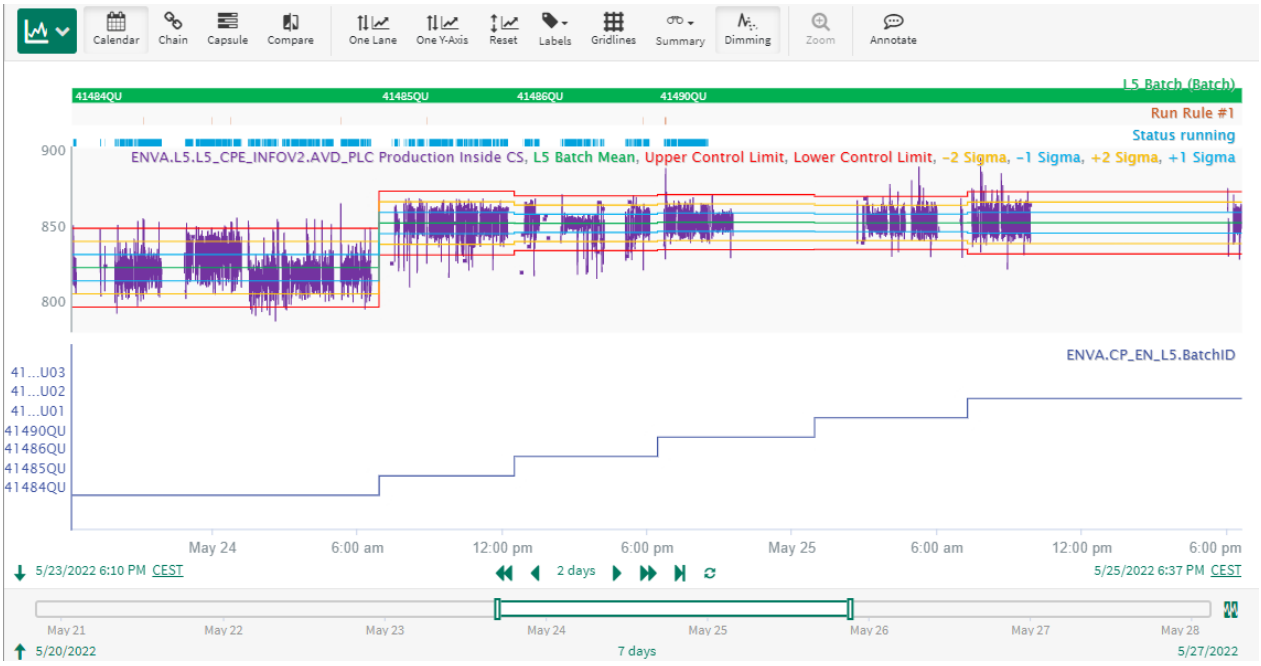


Figure 32 - Dynamic control chart

The program is also better suited for more complex charts like dynamic EWMA or autoregression charts. This is especially beneficial for the Phase II charting applications where a process is already in Control, and minor deviations should be monitored. Complex charts with more calculations are used in Phase II charting, which a program like PI Processbook only partially supports.

Next to a new application for control charting, the validation of process parameters should be a standard procedure before any PMC project is started. By validating the sensors that are to be monitored, the data will be more accurate, and the use of a program like SEEQ can be used optimally. In this research, the final dashboard could not be used as input for process verification, limiting interaction with Operators on the shop floor. Furthermore, the validation of sensors might also remove the step chain delay that can be seen within the data of this study, which will also benefit SPC applications.

6. CONCLUSIONS AND RECOMMENDATIONS

In this chapter, the conclusions of this research and recommendations for Abbott are given. In section 6.1 the conclusions are drawn. Section 6.2 provides the recommendations.

6.1 CONCLUSIONS

The current tools available to Operators at Abbott Zwolle provide limited insight into the production process, leading to a reactive approach to arising problems. As a result, there is insufficient understanding of the performance of the processes within the ARTH filler on the shop floor. The core problem of this research is thus defined as the following:

There is insufficient insight on the shop floor on the performance of the ARTH filler

To address this issue, Abbott aims to explore the potential of Process Monitoring and Control to enable Operators to review the production process, identify potential issues, and implement preventive measures to mitigate problems before they occur. The objective of this research is defined as the following:

To design, implement and evaluate Process Monitoring and Control for Abbott Zwolle's filler of the Aseptic Ready to Hang line.

To solve the core problem, this research was started by analyzing the current situation at Abbott Zwolle. From there, literature on the application of PMC was reviewed, looking into the statistical side of charting and the methodological side of implementation. After this, the critical process parameters for the ARTH filler were identified, and a phase I study was performed. From there, a selection of parameters was chosen for implementation on the shop floor.

In the Phase I analysis of the process parameter of the ARTH filler, 8 parameters were identified as in-control, which would be ready for Phase II monitoring. 11 other parameters were marked as out-of-control. From these 11 parameters, 6 were ranked as critical. These are critical because they directly influence the sterility of the filler and show a lot of special cause variation. The 6 critical parameters were selected for daily stochastic monitoring through discussion with the Process Engineers. Due to the nature of the data of these parameters, and the lack of normality for the data set, the individuals chart is the only option. Through an empirical reference distribution, control limits for the process parameters were determined to have an out-of-control probability similar to a normally distributed three-sigma control chart.

The critical parameters are visualized on two dashboards; one made explicitly for the morning meeting where the relevant stakeholders of the ARTH line get together and the other as a screen available for Operators next to the filler itself. Next to the dashboards, the systems used by Abbott are evaluated, and suggestions for further improvements on the methodology and practical application of PMC are made.

In conclusion, through the implementation and evaluation of PMC for the filler at the ARTH line, this research enables real-time monitoring of critical process parameters and increases insight into the processes of the ARTH filler. Operators are able to identify and address problems before they result in significant defects or production downtime. Furthermore, the use of PMC within Abbott is critically evaluated, and recommendations are given to help them excel in their strive to become a world-class producer.

6.2 RECOMMENDATIONS

Based on the findings of this research, the following recommendations are given to Abbott Zwolle:

First, before a Process Monitoring and Control project starts, the sensors of interest should be validated. By validating the sensors, Abbott can ensure that the data is a correct representation of reality, reduce processing speeds and prevent errors like the step chain pointer delay.

Second, Abbott should consider moving their PMC activities to a new IT system like SEEQ. The PI Processbook system is very outdated, and security might become a risk. Furthermore, the system is very rudimental for the current day and age, where data visualization is being replaced with machine learning, prediction, and complex analysis. If Abbott wants to position itself better for the future, where data plays a crucial role in decision-making processes, the move to a new IT system is essential.

Third, introducing PMC on a new production line should start with easy-to-use and understandable charts. Most stakeholders are untrained in statistics and should get familiar with the basics before moving on to more complex forms of process control. A good way of doing this is by reviewing parameters of interest in a Shewhart-type format daily.

Fourth, testing the proposed methodology of following the 10-step method of Does in the DMAIC structure. Hopefully, this fits Abbott's traditional project approach while focusing on the crucial aspects relevant to PMC integration.

Fifth, the in-control parameters should be reviewed in a Phase II study. A probability distribution should be fitted to the data set, and an OCAP should be created for these parameters.

Sixth, the out-of-control parameters that are not deemed critical in this study should be reviewed by a Process Action Team and be brought further into control. Due to capacity constraints, the focus should first lie on weekly monitoring of out-of-control signals, and when more time is available, the DMAIC-10-step approach should be applied.

Seventh, the 6 critical marked parameters should be further reviewed and brought into control. Start with creating a process action team and involving Operators with the project.

Eighth, Abbott should consider hiring a specific PMC specialist. By having a single expert within the organization, someone has time available to train Process Action Team members, answer specific questions, serve as an internal auditor for PMC charts and projects, and as a project lead for complex PMC applications in Phase II charting.

7. BIBLIOGRAPHY

AggreGate. (n.d.). Supervisory control for oil and gas transportation. Retrieved from https://aggregate.digital/products/scada-hmi.html

Antony, J., & Taner, T. (2003). A conceptual framework for the effective implementation of statistical process control. Business Process Management Journal, 9(4), 473-489. doi:10.1108/14637150310484526.

Atalay, M., Testik, M. C., Duran, S., & Weiß, C. (2019). Guidelines for automating Phase I of control charts by considering effects on Phase-II performance of individuals control chart. Quality Engineering, 32, 1-21. doi: 10.1080/08982112.2019.1641208.

Coleman, S. Y., Arunakumar, G., Foldvary, F., & Feltham, R. (2001). SPC as a tool for creating a successful business measurement framework. Journal of Applied Statistics, 28(3-4), 325-334. doi:10.1080/02664760120034063.

Does, R. J. M. M., Schippers, W. A. J., & Trip, A. (1997). A framework for implementation of statistical process control. International Journal of Quality Science, 2, 181-198. Retrieved from https://dare.uva.nl/search?identifier=1ce41e8c-e477-4f29-92da-242aaaff446e

Gambhire, G., Dhake, R., & Bhangale, P. (2015). Reduction in Defects of Car Body Panel Using 7 QC Tools Approach. doi: 10.13140/RG.2.1.1613.9926.

Inez M. Zwetsloot & William H. Woodall. (2021). A Review of Some Sampling and Aggregation Strategies for Basic Statistical Process Monitoring. Journal of Quality Technology, 53(1), 1-16. doi: 10.1080/00224065.2019.1611354.

Khakifirooz, M., Tercero, G. V., & Woodall, W. (2021). The role of the normal distribution in statistical process monitoring. Quality Engineering, 33, 1-14. doi: 10.1080/08982112.2021.1909731.

Mason, Y. (2000). Interpretive features of a T2 chart in multivariate SPC. Quality Progress, 33(4), 84-90.

Montgomery, D.C. (2009). Introduction to Statistical Quality Control. 6th Edition, John Wiley & Sons Inc., Hoboken.

Mosteller, F., & Rourke, R. E. K. (1973). Sturdy statistics: Nonparametrics and order statistics. Addison-Wesley Pub.

Noskievičová, D., & Kucharczyk, R. (2012). Effective application of statistical process control (SPC) on the lengthwise tonsure rolled plates process. Metalurgija, 51(1), 137-140. https://www.scopus.com/inward/record.uri?eid=2-s2.0-80053474457&partnerID=40&md5=2b1fcfd0c21fc6451c9533122660c17c

Chakraborti, S., & Graham, M. A. (2019). Nonparametric (distribution-free) control charts: An updated overview and some results. Quality Engineering. https://doi.org/10.1080/08982112.2018.1549330

Shewhart, W. A. (1931). Economic control of quality of manufactured product. ASQ Quality Press.

Shewhart, W. A. (1939). Statistical method from the viewpoint of quality control. Graduate School of the Department of Agriculture. (Republished in 1986 by Dover Publications, Inc., Mineola, NY.) doi: 10.2307/2983634

Western Electric. (1956). Statistical Quality Control Handbook. Western Electric Corporation, Indianapolis, IN.

Wheeler, D.J. (2010). The Right and Wrong Ways of Computing Limits. Quality Digest Daily, Manuscript No. 205.

Wheeler, D.J. (2015). Probability limits. Quality Digest Daily, Manuscript No. 297.

Wheeler, D.J. (2017). Don't We Need Good Measurements? Quality Digest, Manuscript No. 307.

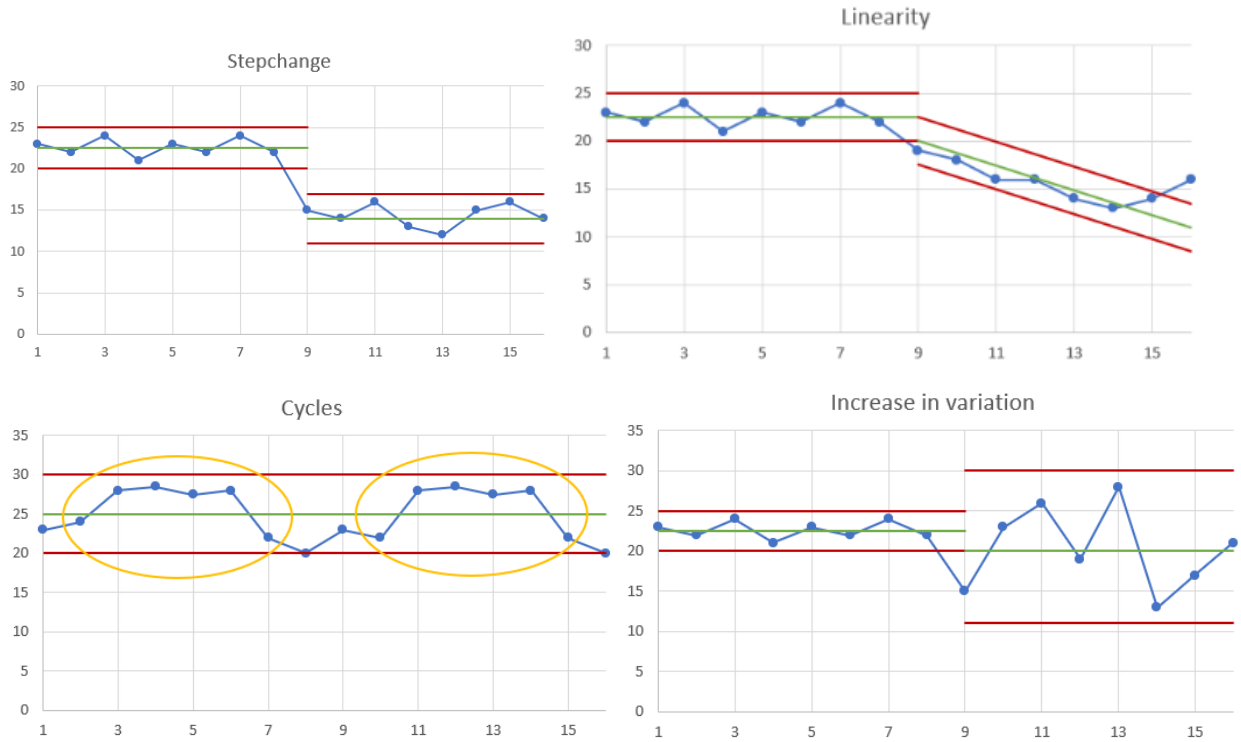
Wheeler, D.J. (2022). How Can a Control Chart Work Without a Distribution? Quality Digest, Manuscript No. 398.

Willemain, T. R., & Runger, G. C. (1996). Designing Control Charts Using an Empirical Reference Distribution. Journal of Quality Technology, 28(1), 31–38.

Woodall, W.H. (2000). Controversies and Contradictions in Statistical Process Control. Journal of Quality Technology, 32(4), 341-350.

8. APPENDICES

8.1 APPENDIX I: TYPES OF SPECIAL CAUSE VARIATION



8.2 APPENDIX II: CONTROL CHART CONSTANTS

Tables of Constants for Control charts

Table 8B Variable Data — ref : AIAG manual for SPC

	Median Charts				Charts for Individuals			
	Chart for Medians	Chart for Ranges (R)			Chart for Individuals	Chart for Moving Range (R)		
	Control Limits Factor	Divisors to Estimate σ_x	Factors for Control Limits		Control Limits Factor	Divisors to Estimate σ_x	Factors for Control Limits	
Subgroup size	$\tilde{\tilde{A}}_2$	d_2	D3	D4	E_2	d_2	D_3	D_4
2	1.880	1.128	-	3.267	2.660	1.128	-	3.267
3	1.187	1.693	-	2.574	1.772	1.693	-	2.574
4	0.796	2.059	-	2.282	1.457	2.059	-	2.282
5	0.691	2.326	-	2.114	1.290	2.326	-	2.114
6	0.548	2.534	-	2.004	1.184	2.534	-	2.004
7	0.508	2.704	0.076	1.924	1.109	2.704	0.076	1.924
8	0.433	2.847	0.136	1.864	1.054	2.847	0.136	1.864
9	0.412	2.970	0.184	1.816	1.010	2.970	0.184	1.816
10	0.362	3.078	0.223	1.777	0.975	3.078	0.223	1.777

	Centerline	Control Limits	
Median Charts	$CL_{\tilde{x}} = \tilde{\tilde{X}}$	$UCL_{\tilde{x}} = \tilde{\tilde{X}} + \tilde{\tilde{A}}_2\bar{R}$	$LCL_{\tilde{x}} = \tilde{\tilde{X}} - \tilde{\tilde{A}}_2\bar{R}$
	$CL_R = \bar{R}$	$UCL_R = D_4\bar{R}$	$LCL_R = D_3\bar{R}$
Charts for Individuals	$CL_X = \bar{X}$	$UCL_X = \bar{X} + E_2\bar{R}$	$LCL_X = \bar{X} - E_2\bar{R}$
	$CL_R = \bar{R}$	$UCL_R = D_4\bar{R}$	$LCL_R = D_3\bar{R}$

8.3 APPENDIX III: COMPUTATIONAL METHODS FOR CONTROL CHART STATISTICS

Summary of Right and Wrong Ways to Compute Limits for Average Charts

	Statistic Used for Limits	Lower Average Limit	Upper Average Limit	Result for Average Chart	Signals Between Subgroups	Signals Within Subgroups	Summary
(1)	Average Range	45.02	52.31	6 of 6 Out	Robust	Robust	DEFAULT METHOD
(2)	Average Std. Dev.	44.87	52.46	5 of 6 Out	Robust	Robust	DEFAULT METHOD
(3)	Median Range	46.02	51.32	6 of 6 Out	Robust	Robust	ALTERNATE METHOD
(4)	Median Std. Dev.	45.76	51.58	6 of 6 Out	Robust	Robust	ALTERNATE METHOD
(5)	Pooled Variance	44.16	53.17	None Out	Robust	**More Inflated Than (1) or (2)**	ALMOST RIGHT
(6)	Global Std. Dev. (X)	40.61	55.19	None Out	**Not Robust**	**Not Robust**	**WRONG**
(7)	Global Std. Dev. (Avg.)	35.50	61.83	None Out	**Not Robust**	**Not Robust**	**VERY WRONG**

Study of Wheeler (2010) on the computation of the statistics used for control limits

8.4 APPENDIX IV: LONG LIST OF PARAMETERS

Long list of parameters

Data tag	**Description**	**Units**
Nitrogen flow		
108020_FIQ523	ARTH Filler - N2 flow before fill section	m^3/h
108020_FIQ524	ARTH Filler - N2 flow after fill section	m^3/h
Hot airflow		
108020_FIQ933	ARTH Filler - flow hot air	m^3/h
Peroxide flow		
108040_FIQ096_PV	**ARTH Filler - flow H2O2 machine**	**mL/min**
108040_FIQ097_PV	**ARTH Filler - flow H202 sterile screw**	**mL/min**
Compressed air flow		
108040_FIQ098_PV	**ARTH Filler - air flow bottles**	**m^3/h**
108040_FIQ099_PV	**ARTH Filler - air flow lid**	**m^3/h**
Bottle sterilization		
108030_TT606	temp. bottle heated air	°C
108030_TT607	**temp. control heated air H2O2 bottle**	**°C**
108030_TT608	temp. drying bottle	°C
Seal sterilization		
108080_TT609	temp. heated air lid	°C
108080_TT610	**temp. H2O2 lid**	**°C**
108080_TT611	temp. lid drying	°C
RQT-sterilisation		
108030_TT105	temp. control bottle final H2O2 outside	°C
108030_TT106	temp. control preheated H2O2 outside	°C
Overpressures		
108020_PIT082	ARTH Filler - Pressure bellow outside	mBar
108020_PIC081	ARTH Filler - Overpressure Filling Section	Pa
108030_PIC081	RQT - Overpressure 1	Pa
Peroxide concentration		
108020_DT097	ARTH Filler - density H202 sterile screw	%
Bottle infeed RQT		
108030_CRASH__CNT001	ARTH filler – RQT first crash detected for 500mL bottles	integer

8.5 APPENDIX V: FILTERS FOR PROCESS PARAMETERS

Filters for process parameters

Process Parameter	**Stepchain filter**	**Bottle size filter**
FIQ523 – N2 flow before fill section	Steps 212 and 213	-
FIQ524 – N2 flow after fill section	Step 213	-
FIQ933 – hot air flow	Steps 212 and 213	-
FIQ096_PV – H2O2 flow machine	**Step 213**	**Bottle 3 and Bottle 1/2**
FIQ097_PV – H2O2 flow sterile screw	**Steps 212 and 213**	**-**
FIQ098_PV – air flow bottles	**Steps 212 and 213**	**Bottle 3 and Bottle 1/2**
FIQ099_PV – air flow lid	**Steps 212 and 213**	
TT606 - temp. Bottle heated air	Steps 212 and 213	Bottle 3 and Bottle 1/2
TT607 – temp. Control heated air H202 bottle	**Step 213**	**-**
TT608 – temp. Drying bottle	Steps 212 and 213	Bottle 3 and Bottle 1/2
TT609 – temp. Heated air lid	Steps 212 and 213	-
TT610 – temp. H2O2 lid	Steps 212 and 213	**-**
TT611 – temp. Lid drying	Steps 212 and 213	Bottle 3 and Bottle 1/2
TT105 – temp. Control bottle final H2O2	Steps 212 and 213	-
TT106 – temp. Control preheated H2O2	Steps 212 and 213	-
PIT082 – Pressure bellow outside	Step 213	-
PIC081 – Overpressure filling section	Step 213	-
PIC081 – RQT overpressure	Steps 212 and 213	-
DT097 – density H2O2 sterile screw	Steps 212 and 213	-
CRASH__CNT001 – RQT infeed first crash	-	Bottle 3