Batch cycle time reduction analysis in a small vaccine development facility

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ABSTRACT

Batch cycle time is an important component of a vaccine development company. In a mature economy, pharmaceutical manufacturing companies aren't coming up with new and novel ideas but being first to market and making sure that store shelves are stocked are the most important strategies for success. If a company has long batch cycle times this could delay them getting product to market and risk an increase in backorders.

This research involves exploring sources of batch cycle time challenges at Trivax, a startup vaccine development company that, interestingly, enough started operations a couple of years before the Covid-19 pandemic. The study will analyze their data for vaccine production units and individual vaccines to identify the cause of the longer batch cycle days occurring in some of their production lines. It will also evaluate the effect of implementation of mitigation strategies the batch cycle days.

Data was collected using the Tableau software program. Averages of batch cycle days were collected for vaccine production units for a series of months over two years. Further breaking down the data collecting to five individual vaccines within the lowest percent change vaccine unit from the year 2020 to 2021.

The data collected shows that the vaccine units all have higher than theoretical batch cycle days and even with the implementation of mitigation strategies, continue to be high. Trivax identified two areas of focus for further research and have started that research to try and uncover the issues behind the high number of batch cycle days.

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The author wishes to first and foremost thank my husband Tristen. Without you, I wouldn't have been able to accomplish this dream and keep all things moving forward, the kids, the house, and the farm. Thank you for all your support, love, and encouragement, even when I thought about giving up because of life circumstances. I would also like to thank my son Corbin. You have given me the ability to keep going despite trials and make you proud of the accomplishments that you are able to achieve if you keep going and never give up. I love you to the moon and back buddy! Thank you to Cayden, for being my special surprise blessing that I didn't know I needed and that I had no idea my life was missing until you showed up. It was a challenge to be your second mommy and finish this degree but I'm so happy that you were here for this journey. I would also like to thank Dr. V (Vincent Amanor-Boadu). You have been a great source of knowledge and wisdom and I have enjoyed working with you to accomplish my dream. Your positivity and encouragement are greatly appreciated in a hectic life to get to the finish line. Last but certainly not least, to God above. You have thrown some unexpected blessings into our path over the course of this program work and have also kept us going with encouragement and understanding that this is all in your plan. I hope that I can use this new knowledge to your glory.

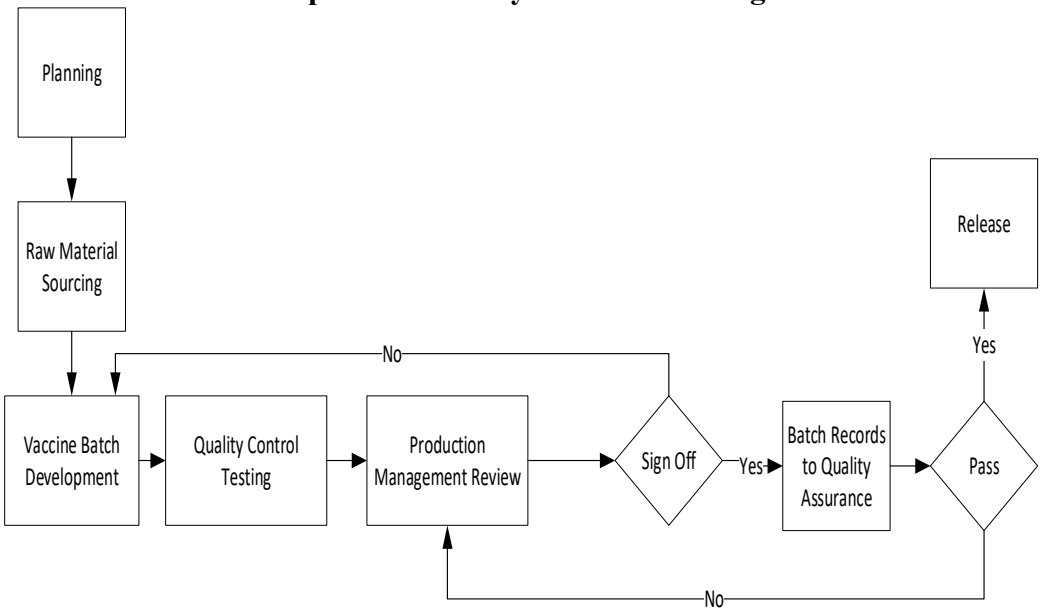
CHAPTER I: INTRODUCTION

One of the greatest improvements that a vaccine development company like Trivax can make is to decrease the batch cycle times for operations. Development organizations are faced with the need to optimize the way they function to achieve the best possible performance within necessary constraints (Han, 2011). Vaccine development is a mature market and being the first to market and maintaining efficient stock is forefront in determining who remains number one in the industry. With some very well-established competitors in its market, Trivax needs to differentiate itself by overcoming one of the major challenges facing the industry: batch cycle time. There are formulas put into place to determine the number of days that are acceptable for each vaccine batch cycle time and these are tracked. Data is tracked to ensure that all cycle times are appropriate for getting vaccine batches into serials and products out the door to the customers.

One way that development companies improve performance is to evaluate and monitor batch cycle time. Cycle time is defined as the time it takes to complete a manufacturing operation on one or more units, (vaccines or components) from start to finish. In the industry, vaccines play an important role in the manufacturing of biologics. To ensure quality and safety, each vaccine batch has specified development/production protocols consisting of specific activities with defined durations. Employees involved in the development/production process are expected to follow the specified protocols for each vaccine batch. A major requirement for quality control is that employees record their specific activities to the batch development/production at each step in the process as well as a time stamp of when their contribution stage started and finished. The sum of the time at each stage of the process is the cycle time. The recorded cycle time is compared against

acceptable cycle times for the specific vaccine that is being developed. Deviations outside defined tolerances become causes for concern and demand corrective actions. These actions begin with understanding the sources of the deviations and how they may be ameliorated. The responsibility of evaluating cycle times for each batch rests with Quality Assurance (QA).

Figure 1.1: Vaccine Development Batch Cycle from Planning to Release



This process starts with the generation of a unique process number by planning and the verification by sourcing that all the components are available to make that new vaccine. Once it has been determined that the raw ingredients are available, then production prints off a batch record for the process and the vaccine development process can begin. During this process, the vaccine is made and manipulated in the lab to achieve the best potential that can be achieved. After the development/production period, the batch record that has

been concurrently documented in during the entire process, is then signed off by production and goes to the production management review team for a review and sign off. During this sign off time, QC has also been given test samples that are tested by various tests and results are sent to Quality Assurance (QA). After production management has signed off on the record, the record can then go to QA where it will get final review and married up with the corresponding QC results and then released. Once the record is signed off and the vaccine is released, the batch cycle time is then stopped. If there is a blank, an error, or a deviation found at the production review stage or the QA stage, then the batch record returns to production as indicated in Figure 1.1, for further corrections, clarifications, or justifications. This process of returning to production, increases the number of batch cycle days.

In a vaccine development company, quality assurance (QA), plays a vital role in making sure that products are produced to specifications and are made following the batch record steps that have been laid out. At the conclusion of vaccine development/production, the batch records are sent to QA to be reviewed and evaluated to ensure all requirements and governances have been followed and the antigen material has been made correctly. QA is crucial in making sure that the company is on track for meeting the on-time batch cycle times. QA monitors batch cycle times and helps to provide suggestions and resources to help keep those batch cycle times as close to expected as possible.

There are formulas used to determine the number of days that are acceptable or theoretical for each vaccine batch cycle time and these are all tracked. QA can then use these data to ensure that all cycle times are appropriate for getting vaccine batches out the door to the customers.

1.1 Research Question

The vaccine development industry is highly competitive and fast paced. To sustain competitive advantage, companies have to control their batch cycle times. The problem this research seeks to address is to develop a solution to the significant deviations from expected cycle times for the batches produced by the small company Trivax. The company develops vaccines. Longer than expected cycle times in the antigen production process creates a bullwhip effect in the product manufacturing process. The bullwhip effect (also known as the Forrester effect) is defined as the demand distortion that travels upstream in the supply chain from the retailer through to the wholesaler and manufacturer due to the variance of orders which may be larger than that of sales. This adversely affects customer satisfaction, which has the potential of adversely affecting the company's competitiveness. This research, therefore, seeks to address the causes of the deviations from expected batch production cycle times and identify solutions to addressing the deviations. The quality imperative cannot be compromised in the process of address the batch cycle time deviations.

1.2 Research Objectives

The overall objective of this research is to discover the primary causes of deviations from specified cycle times along the batch production process in the vaccine development industry and find ways to reduce the batch cycle time without compromising quality. The specific objectives are as follows:

1. Provide a complete description of the vaccine development batch record cycle process for the case company along with the time at each stage for a select vaccine over a recent historical period.
2. Identify the key steps of the batch cycle that could be the bottleneck for the process and what could specifically be done at those steps.
3. Identify the percent change in development/production units from one year to the next in batch cycle times to identify if strategies implemented are playing a key role in reduction of cycle times.
4. Determine the lowest percent change in a production unit and further analyze individual vaccines within that development/production unis to get a better understanding of the potential sources of the bottleneck to batch cycle times improvement.

1.3 Thesis Outline

The thesis is laid out as follows. The first chapter has presented a background to the problem, defined by the research question and determined the objectives that the thesis seeks to achieve. Chapter 2 presents the literature review encompassing antigen production protocols and their cycle times. It will also review the literature on solutions to cycle time from various industries, including the auto racing industry and the airline industry. Chapter 3 will present the theoretical foundations of the research and describe the data and methods used for the analyses. Chapter 4 focuses on the discussion of the results and implications. Chapter 5 summarizes the study, provides the study's conclusions emanating from the

analyses, and the recommendations for implementing the study's solutions as well as suggestions for future research.

CHAPTER II: LITERATURE REVIEW

This chapter presents a review of the relevant literature on cycle time. It is organized into four subsections. Subsection 2.1 presents a review of alternative definitions of batch cycle time across various industries. The purpose is to provide a connection of the concept across the survey industries in the literature and show that its meaning is consistent across industries. Section 2.2 presents the antigen batch cycle as it is known to exist at the case manufacturing site. Section 2.3 discusses how Trivax can reduce batch cycle time and Section 2.4 shows the reasons why a reduced batch cycle time is desired.

2.1 Batch Cycle Time in Industries

Batch cycle time can best be defined as the time it takes to complete a task or group of tasks from start to finish. It is a measure of the duration of the tasks in the production process (MRP Easy 2020). Organizations are interested in measuring cycle time because it provides insight into better scheduling plans and improving operational efficiency. Various industries, including the auto industry, airplane networks, steel manufacturing and bakeries, use cycle time. Major procurement organizations, such as the Defense Department, also focus on acquisition cycle times to improve their efficiencies (Tate 2016). However, the specific steps in the processes included in cycle time differ across industries. For example, in the computer manufacturing industry, cycle times for the manufacture of various components are measured to identify bottlenecks prior to the assemblage (Demeester 1996)

Automobile manufacturing uses several batch cycles and requires many employees and machines to be working together. BASF conducted a study to find out what they could

do to shorten their batch cycle time between batch strike-ups by 59 percent. They used several analytical tools, including Lean Assessment, Lead Leader Training, Site Steering Team, 5S and Visual Management in the study. Their initial assessment began with mapping process flows using Kaizen. This identified locations of gaps in their processes. The information provided various pathways to reducing cycle time in their processes. The company performed 56 Kaizen events with 174 employees participating. Through Kaizen events and assessment tools, they were able to reduce their cycle time by 53% and saved the company hundreds of thousands of dollars in the process (Online 2021).

There are two key factors that impact airline profitability: The first is the cycle time, which is defined in the airline industry as the operational capacity to turn an aircraft around quickly (Grittell 2001). The other is the design of its flight network to minimize the time it takes for planes to go from one airport to another and return to their original airport (Nero 1999). The design of a flight network for an airline is critically important as it determines a large portion of an airlines cost (Barnhart 2004). A common flight network in the industry is referred to as the hub-and-spoke (HS) strategy, which is defined by Rosenberger et al. (Rosenburger 2002) as a flight network with a large percentage of the flight segments into or out of a small subset of stations called hubs. This Hub-and-spoke strategy can cause major issues in the batch cycle time of a plane. If the hub is too congested and people miss flights, if there is a problem with the plane at the first hub and passengers miss the flight at the second hub, if the second hub is experiencing poor weather conditions that require them to cancel the second hub, there are all kinds of factors that play into this flight network strategy. Most recognize that the hub-and-spoke flight design is not positively related to performance and usually does not have a positive effect on cycle time. Another strategy is

the point to point (PP) network. Southwest Airlines uses this strategy for their flights, and they have a positive performance for cycle times. In this strategy passengers are routed from point of origin to destination with no stop in between. Southwest has been able to reduce their cycle time by focusing on the PP network by taking out the variable factors of the HS strategy.

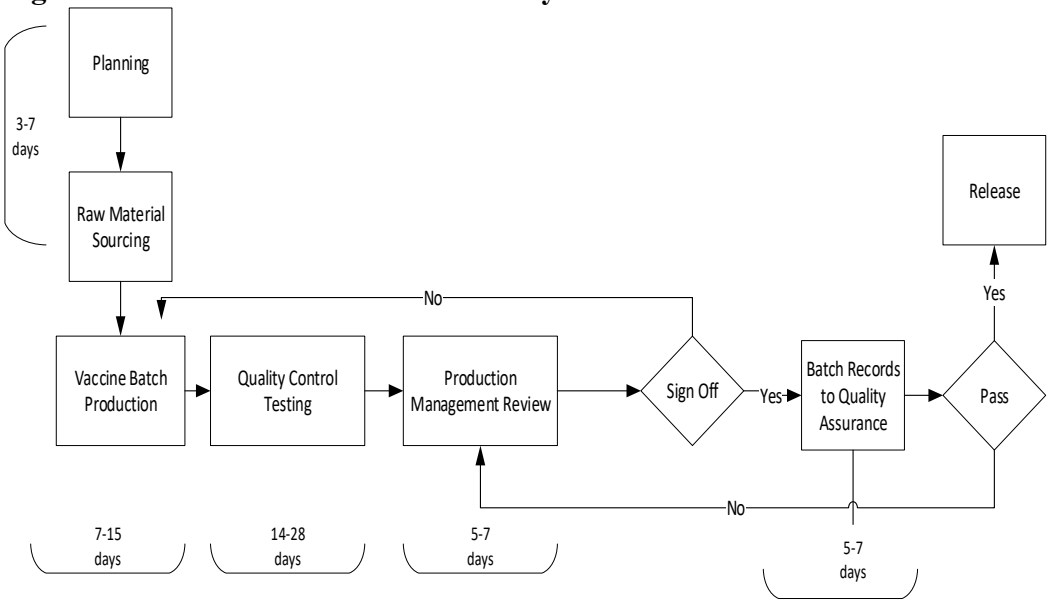
The second batch cycle time in the airline industry is the aircraft turnaround process after a flight has landed. The success or failure of the aircraft turnaround process can make or break an airlines reputation for both reliability and profitability. The importance of speed as a competitive weapon helps to show that cycle time is a significant key to success (Hult 2002). Reducing the amount of time that it takes to get an airplane cleaned and ready for the next flight will determine how many flights you can have in a day and how many flights each plane can take in a week. It is important to maximize the number of trips a plane can have in a week without jeopardizing the safety and integrity of the plane. Cycle time is also important in the NASCAR racing industry. When the cars come into the pits at NASCAR, they have so much time to get tires changed and fueled before they need to be back out on the track. If the pit crew is slow or something happens during the changing of the tires to delay the car, then the car runs the risk of not making it back out to the track to continue the race. Seconds can make the difference is whether a car wins or loses a race and those seconds can be attributed to the time spent in the pit. Racers and their teams spend time and effort on the study of how to cut down that time spent in the pit and how to reduce that cycle time. Every second spent in the pit is time that is not being used on the track to win the race. Just like it is important to the race car driver to get back on the track, it is important for the vaccine development company to reduce the batch cycle time to be

the first to market or maintain their products in the market to make their company profitable and number one in the industry.

2.2 Vaccine Development Production Batch Cycle

The Trivax company produces vaccines in batches. Therefore, it measures its vaccine production cycle time on a batch basis. The vaccine production batch cycle may differ across companies and vaccines. Batch cycles will have different steps and different organizations of steps as well as different times that are typical for each step. Figure 2.1 shows the theoretical vaccine batch cycle time for Trivax.

Figure 2.1: Theoretical Vaccine Batch Cycle Time



As Figure 2.1 shows, planning and sourcing are the first two stops on the course of the batch record. During the planning stage, the planners determine what the need is and what vaccine should be produced at what time. They are the ones that schedule the

vaccines on the calendar that everybody in the plant can then follow. Sourcing makes sure that the raw ingredients/materials that will be needed for the processes are available and that animals are available for necessary testing, prior to manufacturing of a vaccine. The planning and sourcing portion of the process should take between three to seven days and will occur prior to batch production. The vaccine batch production can be a little more varied, based on the biological being produced, but is typically between seven and fifteen days. Production prints the batch records; operators execute the steps in the batch record to make the necessary solutions/medias and mix the necessary ingredients to make the vaccine and the process concludes with the vaccine being stored until further manufacturing can occur. Production then sends samples of the new vaccine to QC and sends the completed batch record to production review. After production, QC samples are submitted and those tests are fourteen to twenty-eight days, depending on the type of test needing to be performed. While testing is being done by the QC department, production management review can be taking place and should take no more than five to seven days for batch records to be reviewed and corrections to be made by production. Quality Assurance (QA) should then be handed the batch record to review in five to seven days and also get corrections. With corrections and reviews being done, QA can marry the batch record and the QC results together at the end of the fourteen to twenty-eight days and release the batch. When this release is final, that ends the batch cycle time. For a theoretical batch, the batch cycle time should be between 34 and 54 days.

2.3 Reducing Batch Cycle Time

Cycle time reduction is one of the most important keys to successful production today. More and more, customers are demanding that manufacturers respond quickly to their demands and wants, delivering perfect quality products on time (Patel 2014). Demand is making it even more important for companies to focus on their batch cycle time. Finding ways to reduce batch cycle time is more important than ever. With the market being saturated with vaccines, Trivax has to stand apart from the other companies and batch cycle time can be what makes them successful on the market first with vaccines.

There are many ways that companies try to reduce batch cycle time. Several methods have been reviewed to help with this reduction including adding labor, adding in overtime for labor already employed, reducing wasted time, reducing the number of process steps, fine tuning, and reducing non-value added operations. An additional way to reduce batch cycle time is to perform tasks in parallel. In the Figure 2.1, production review and QC testing can be done in parallel so that when both are completed, both can be sent to QA to be reviewed and released together. By doing these tasks in parallel by two different departments, the number of days is being utilized by two different tasks and therefore not adding additional days to the process. Overall employee involvement might also help with reduction of cycle times. When the employees are engaged and actively looking at making improvements to the process to make it better, they have a more vested interested in the process and therefore take more pride in the process. If they are the ones working at the core of the problem, they are more likely to have better ideas of how to get things done more efficiently. Other initiatives to reduce batch cycle time are lean manufacturing and supply chain management. Lean manufacturing is defined as radically redesigning

information flow and material flow processes with dramatically shorter cycle times, lower costs, minimum inventory and usually perfect performance on delivery. Supply chain management is defined as the implementing of supply chain planning, execution, and event-level alert systems (Patel 2014). When demand is up the supply chain can be ready to meet that demand quickly and efficiently.

There is an ERP computer system that is used by Trivax to track the number of allowed cycle days for each vaccine batch produced. If the fixed number of days in the ERP is entered incorrectly from the start, then the number of overall batch cycle days or the number of days past due will ultimately be jeopardized as always being an unattainable number for the quality assurance (QA) group. If the fixed days were to be corrected in the ERP using a formula to make the numbers more aligned across the board, then maybe the batch cycle times would be reduced. This formula will be discussed in the methods section as well as the method for changing the computer system days.

In the manufacturing case company, the cycle time reduction can begin to occur in a couple of different areas of the batch cycle. Many of the key areas of the value stream cycle are fixed and defined, however; there are a couple of areas where improvements could be explored and days could be trimmed from the overall batch cycle time. Those areas are the production management review and the quality assurance review processes. Reducing the number of days that the batch record sits in those two areas of the chain would greatly reduce the overall batch cycle times and therefore get vaccine released for further processing in a more reasonable and timely manner. Determining why batch records are sitting in those areas and why those two sections of the value stream are acting as a bottleneck will be the key to answering the thesis problem.

2.4 Advantages of Reduced Batch Cycle Time

There are many benefits to a company when batch cycle times are reduced. Some of those advantages include being more responsive to changing customer demands, quicker time to market with new products, quicker feedback for process development and process improvement processes, improved employee productivity, and reduction in non-productive process control measurements.

CHAPTER III: DATA, THEORY AND METHODS

3.1 Introduction

In this chapter, an overview of the collection process for the data and the methods used to analyze the data will be presented. The theory guiding this analysis and the link to economics and management will also be presented. Data were collected over a two-year time span and a couple of different computer processes have been used to analyze the data.

3.2 Theory

The Trivax company produces vaccines in batches. Therefore, it measures its vaccine production cycle time on a batch basis. The vaccine production batch cycle may differ across companies and vaccines. Batch cycles will have different steps and different organizations of steps as well as different times that are typical for each step. Figure 3.1 shows the theoretical vaccine batch cycle time for Trivax.

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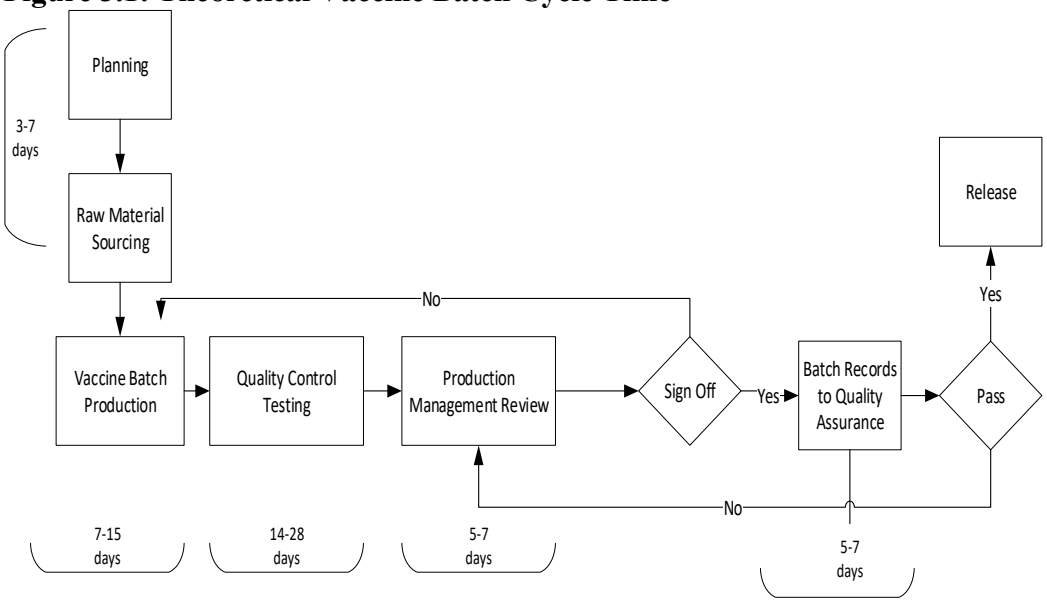

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There are many benefits to a company when batch cycle times are reduced. Some of those advantages include being more responsive to changing customer demands, quicker time to market with new products, quicker feedback for process development and process improvement processes, improved employee productivity, and reduction in non-productive process control measurements. Vaccine development companies need to have efficient and effective ways of getting products out to customers in a timely manner. Being the first to market or the maintaining stock on the shelves in stores is at the top of a manufacturer's priority list. Batch cycle times are important to manufacturing companies to make sure that products stay on the market. The focus of this research is to see where the bottlenecks are

in a batch cycle process for case company and then to come up with some ideas for further research on how to reduce batch cycle time.

Companies recognize that consistent and disciplined application of lean manufacturing strategies with the emphasis on waste elimination and process streamlining can lead to business excellence (Mejabi 2003) and thus to reduction of batch cycle time. Strategies such as Kaizen and the implementation of value stream mapping (VSM) help organizations visualize the wasted time in the batch cycle and the future possibility of reducing that over all time. Using these tools along with computer software, we can create a clear picture and provide management with a system that allows a simple flow of the batch cycle to reduce time and cost and keep customers satisfied.

3.5 Data

This batch cycle day data comes from four vaccine production units and five vaccines within one of those units, at the Trivax vaccine development company. The data will cover average batch cycle times for May-December of 2020 and May-December of 2021.

3.6 Methods

For this study, the company utilized a computer program called Tableau to pull data for average number of batch cycle days for both vaccine production units as well as individual vaccines. Trivax also utilized an ERP system that they use to keep track of their development production inventory and product batch cycle inspection lot days. Strategies

such as the implementation and development of a value stream map were also used to focus on the problem areas and determine the breakdown in the batch cycle.

There are four vaccine production units that were tracked for May-December 2020 and May-December 2021. The average yearly batch cycle days for May-December 2020 were recorded and compared to the average number of days for May-December 2021. They also took the vaccine production unit with the lowest percent change in batch cycle days for those time periods and randomly chose five vaccines to further breakdown by the same time frame and analyze.

The study identified seven key steps in the batch cycle for the case development company. By identifying the number of theoretical days for each of the seven steps and then the actual number of days, the company was able to analyze the data and come up with ways to reduce the batch cycle days and make plans for further research.

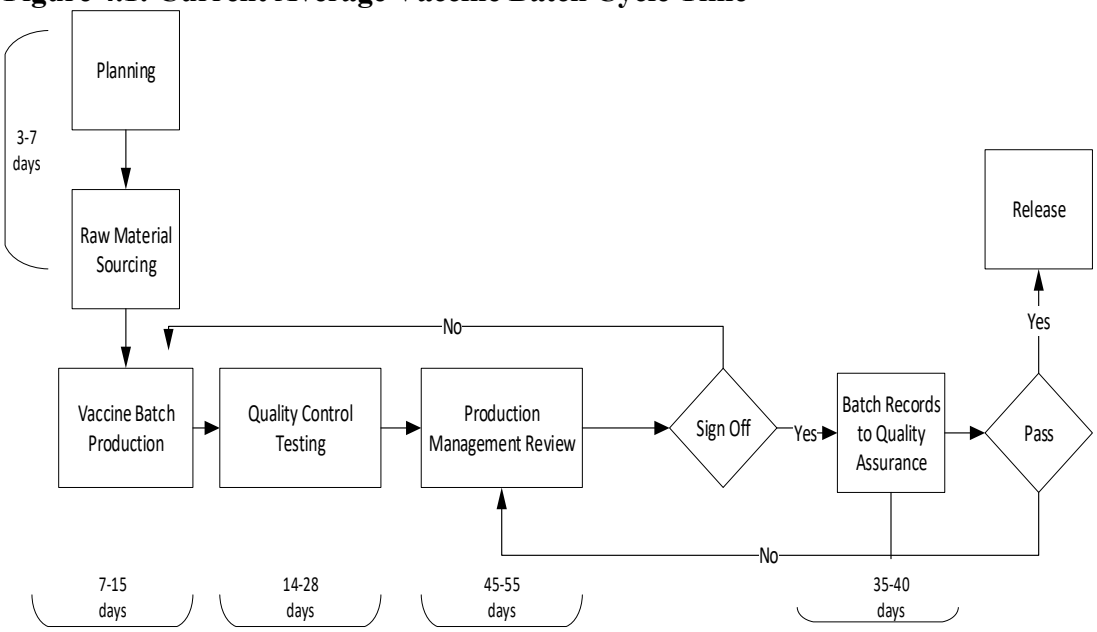
CHAPTER IV: ANALYSIS AND DISCUSSION

We present data from a selection of vaccine production units to provide case examples of the problem that this research is focusing on. Next, we take the lowest percent change unit and look at a selection of their vaccine production batch cycles. This chapter is divided into three parts. The first will describe the value stream map and the analysis of the number of days for each step in the process. The second part will discuss the vaccine production units batch cycle times and what has been done so far to help reduce those days as of the end of 2021. The final part discusses the cycle times for the selected vaccines in the production unit B.

4.1 Value Stream Map Development

The current value stream map is show in Figure 4.1. This figure has been presented before but this time it shows the current range of number of days for each of the seven steps (areas) in the batch cycle. Several of the steps in the batch cycle are more fixed and permanent. Planning and raw material sourcing are still at three to seven days for batch cycle currently. The batch cycle time for vaccine batch production is still going to vary from seven to fifteen days depending on the biological being made. Each biological is going to have different conditions and processes that are going to lead to variability in the number of days that it takes to process. Quality control is going to remain fixed at fourteen to twenty-eight days due to the testing involved and the government requirements for that testing.

Figure 4.1: Current Average Vaccine Batch Cycle Time



The two major areas of concern have been identified as the production management review and the batch record review by quality assurance (QA). These two areas of the value stream can be significant variable in the duration of their activities because of the numerous factors that influence their ability to turn things around, most importantly the people aspect. These are the two areas that are heavily people dependent on many different aspects. People are needed to review the documents, and these documents can be as few as 50 pages in length or as long as 500 pages. They have to be reviewed carefully and errors identified and corrected. The reviewers and those making corrections are different. Therefore, depending on how many errors the reviewers find, they have to send the documents back to the appropriate individuals to make the corrections. Once corrections are completed, they return them for a confirmation that they have been done. The number of reviewers and those addressing errors in documents and the synchronization of their processes can introduce significant variability and uncertainty in the time it takes to complete the review step in the process. The problem is exacerbated by the fact that

reviewers have the responsibility of finding and tracking down the individuals responsible for making the corrections.

Uncertainty in QA is similar to that in production review, as people are still needed to review these large number of different sized records and get the corrections done that are required to make the batch records correct and accurate for release.

Given the relative certainty associated with the other areas in the batch cycle, any management of the batch cycle time need to focus on production management review and quality assurance. Any reduction in time in these two areas would produce the highest marginal benefit to the cycle time reduction strategy.

4.2 Analysis of Vaccine Production Units

Trivax started collecting data in 2020 for batch cycle times. They monitored batch cycle times for four vaccine production units within the company. Each vaccine production unit produces unique vaccines requiring different production skills, and hence, technical production staff. Starting in May 2021, Trivax started implementing new strategies to decrease batch cycle time across its production system. Trivax started communicating the tracking of the average number of monthly batch cycle days for each of the four production units in May of 2021 with the start of a new project. The project was to implement new techniques to bring down the batch cycle times and ensure that the average numbers were less than those of 2020. Each month the numbers were ran for each vaccine unit in Tableau and compared to the 2020 value.

In May 2021, the company implemented an escalation process to make sure that management was made aware of corrections needing to be completed in their individual

vaccine production unit. If those corrections were not completed in three days, then an email was sent to Associate Directors over those production units to bring awareness to the urgency of getting corrections and problems on batch records fixed and completed. The company monitored that change for the month of May and those results were reported in June. In June, the company decided to implement correction stations.

It became apparent that the physical organization of production could be contributing to the cycle time challenge. Manufacturing was split between two buildings and corrections can be difficult to get from those two buildings if operators are not working in that building where the record is residing. Production was also running three shifts. The correction stations aimed to minimize the need for operators and scientists moving between buildings to find each other to make corrections. Correction stations should reduce the burden on reviewers searching and tracking down those needed to make corrections. The correction assignments could then be completed during the appropriate staff person's shifts.

The analyses established May through December 2020 as the reference benchmark for batch cycle times. Table 4.1 shows the estimated average batch cycle duration (in days) for all vaccine production in four randomly selected production units. The table shows that the average batch cycle time ranged from 159 days for Unit D in 2020. For 2021, the range had improved, from 68 days to 136 days. However, while the reduction in batch cycle times occurred in three of the four units, Unit B experienced an increase of about 22% in its batch cycle time. Unit B had the lowest average cycle time in 2020 but was the third highest in 2021.

While the strategies implemented to reduce batch cycle time seem to have worked, there is some curiosity about what happened in Unit B.

Table 4.1: Average Batch Cycle Days for Vaccine Production Units between May and December for 2020 and 2021

Production Unit	2020 Average	2021 Average	Percent Difference Between 2020 and 2021
Unit A	90	68	24%
Unit B	78	95	-22%
Unit C	132	91	31%
Unit D	159	136	14%

Trivax still was not satisfied with the number of days, but they were improving overall, but the company wanted to implement one more thing. Up to this point in 2021, quality assurance had an office area in one of the two production buildings. Were they missing an opportunity to help production proactively before mistakes were made and to help get corrections done faster if we had quality assurance employees in both buildings? In October, two members of the quality assurance group moved over to the second production manufacturing building to be quality assurance in the office area of the scientist and managers for three of the production units. Now all four production units had QA in their office area to ask questions and get corrections. Trivax believed this to be a win and a great strategy for moving forward. Trivax continued to monitor the averages for the months to follow in 2021.

In investigating the data, it was discovered that one of the four vaccine production units seemed to have a lower percent change, and this made them curious as to what was going on with this vaccine development/production unit. The company decided to go a little deeper into that unit and take a look at five individual vaccines produced by the vaccine unit based on the 2020 and 2021 comparisons. The hypothesis is that understanding the vaccine

development profile in the production unit could shed some light on the performance outcomes.

4.3 Analysis of Five Vaccines from Production Unit B

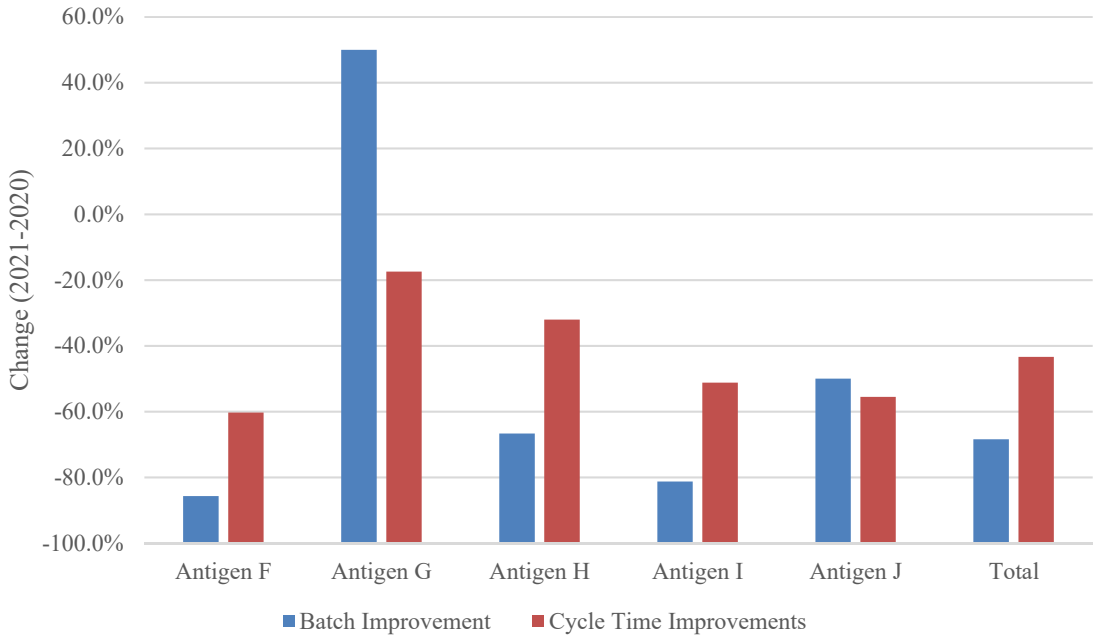
From Table 4.1, the worst performing production unit was Unit B. Trivax randomly selected five vaccines that were produced by the production unit for further analyses of their performance. Table 4.2 presents the average batch cycle time and number of batches for Unit B's randomly selected vaccines for the two time periods. It shows that the total number of batches produced in 2020 was 38 compared to 12 in 2021. Across the five vaccines, the average number of batches produced in 2020 was eight compared to two in 2021. This is equivalent to nearly 70% reduction in the total number of batches produced. Although the biology of the different antigens differs, i.e., they require different durations to grow, the average batch time for growing the same vaccine should not change between periods. Therefore, any change in batch cycle time is attributed to the activities occurring after the vaccine production stage. Assuming a fixed number of reviewers and QA specialists, then it is plausible to assume that increasing batches will increase workload and increase cycle time per batch in post-vaccine production stage.

Table 4.2: Average Batch Cycle Time and Number of Batches Produced by Unit B in 2020 and 2021

Unit B	2020			2021		
	Average Batch Cycle Time	Batches per Year	Total Production Days	Average Batch Cycle Time	Batches per Year	Total Production Days
Vaccine F	68	7	476	27	1	27
Vaccine G	86	2	172	71	3	213
Vaccine H	128	9	1152	87	3	261
Vaccine I	127	16	2032	62	3	186
Vaccine J	126	4	504	56	2	112
Total		38	4336		12	799
Average	107	8	813	61	2	145

Table 4.2 shows that the average batch cycle time across the five vaccines in 2020 was 107 days, with a range from 68 to 127 days. This contrasts with an average of 61 days in 2021, ranging from 27 days to 87 days. The changes in the number of batches and cycle time between 2020 and 2021 for the five vaccines are summarize in Figure 4.2. The figure shows that the total number of batches declined by 68% and cycle time also declined on average by 43%. Similarly, there was about 85% reduction in the number of batches of Vaccine F produced, and its average cycle time declined by 60.1%.

Figure 4.2: Changes in Number of Batches Produced and Cycle Time per Batch (2021-2020)



The figure shows a relationship between cycle time and number of batches. We try to determine the extent to which the number of batches produced, then, influences the cycle time. Assuming the average of the time ranges in Figure 4.1 are applied to all vaccines from planning and raw material sourcing to vaccine production (front end), then the average time from planning to the end of vaccine production is 16 days. This would suggest that the difference in average cycle time when not accounting for the front-end time is all due to product management and review and QA. This is because while vaccine production is constrained by production capacity, there seems to be no such constraint recognized for production management and review and QA. The results for regressing the difference between average cycle time and number of batches for 2020 and 2021 are presented in Table 4.3. The results show that prior to the implementation of the improvement strategies i.e., in 2020), decreasing the number of batches by one reduced

average batch cycle time by about 10.68 days ($p < 0.022$). However, after the improvements, a unit reduction in the number of batches reduced average batch cycle time by nearly 25 days ($p < 0.000$). The intercept is not calculated because it is assumed that no batches imply no production, which implies cycle time is zero.

Table 4.3: Regression Results for Average and Average Balance Batch Cycle Time on Number of Batches (2020 and 2021)

Period of Analysis	Coeff.	S.E.	t	P>t	[95% CI]	
					Lower Bound	Upper Bound
Average Batch Cycle Time (2020)						
Number of Batches (2020)	10.68	2.95	3.62	0.022	2.50	18.86
Average Batch Cycle Time (2021)						
Number of Batches (2021)	24.97	1.70	14.71	0.000	20.25	29.68
Balance of Cycle Time (2020)						
Number of Batches (2020)	9.18	2.52	3.64	0.022	2.18	16.19
Balance of Cycle Time (2021)						
Number of Batches (2021)	18.97	1.74	10.88	0.000	14.13	23.81

The interesting result is using the balance of batch cycle time as the regressor. The balance of cycle time is the difference between the average cycle time for each vaccine and the assumed constant average time required from planning to vaccine production, which was estimated to be about 16 days. The results when the balance of cycle time is used are respectively 9.18 days ($p < 0.022$) and 18.97 days ($p < 0.000$). Therefore, taking out the front-end produces a higher impact in 2021 than in 2020, i.e., -24.03% versus -14.02%.

The foregoing results also indicate, for their corollaries, that increasing the number of batches would increase the average batch cycle time with the improvement strategies more than the 2020 situation before the improvement strategies were implemented. For

example, increasing the number of batches by a unit in 2021 would increase the average batch cycle time by about 19 days if balance of cycle time is used as the regressor and by nearly 25 days if average cycle time is used as the regressor. This means that it is not the number of batches per se that increases the batch cycle time. Rather, it is the number of people available to review and conduct QA tasks on the increased number of batches. If the number of staff working in the back end of the cycle are increased in tandem to the number of batches, then the problem will go away. The challenge facing management, then, is balancing the cost of longer batch cycle times against the payroll cost of increasing headcount in production management review and QA.

CHAPTER V: SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

This final chapter presents the summary of the results from the analyses conducted in this research and its major conclusions. It also presents the recommendations that may be made as a result of the results. The chapter is organized in three sections. The first presents the summary of the thesis. Section 5.2 presents the major conclusions from the study and their insights. Section 5.3 presents the recommendations for using the results to improve performance. It also identified further work that needs to be done to attain the desired performance outcomes.

5.1 Summary

In summary, research was undertaken to better understand batch cycle times and how they relate to the case manufacturing company. To first analyze the cycle times, a value stream map had to be drawn to show all the different steps of the process and truly understand the path and where the bottlenecks could be coming from. Then data was taken from Tableau and analyzed for a series of months in 2020 and 2021 to compare four vaccine production units and determine the percent change for those two-year time periods and if a series of suggested implementations were successful in driving down the batch cycle times. The lowest percent change vaccine production unit was then chosen, and the company decided to dive deeper to the vaccine level. Trivax randomly selected five vaccines from Unit B and further analyzed for the same time, the percent change. With it being a small sample set, we could have randomly chosen another five for the unit B, as the five we chose showed us that they had fewer batches of those vaccines produced in 2021 as compared to 2020.

In the analysis of Unit B, our hypothesis was proven that the difference in average cycle time when not accounting for the front-end time is all due to product management and review and QA review. Table 4.3 showed regression results, and the results when the balance of cycle time is used are respectively 9.18 days ($p < 0.022$) and 18.97 days ($p < 0.000$). Therefore, taking out the Front end produces a higher impact in 2021 than in 2020, i.e., -24.03% versus -14.02%. This means that it is not the number of batches per se that increases the batch cycle time. Rather, it is the number of people available to review and conduct QA on the increased number of batches. If the number of staff working in the back- end of the cycle are increased in tandem to the number of batches, then the problem will go away.

5.2 Conclusions

After all the analysis of the data from the vaccine units and vaccines, Trivax needed to calculate the theoretical batch cycle days for the vaccines that were used for the data analysis so we could better tell what the actual target was for each of those vaccines. Having this data would provide them with a better understanding of how many days it should be taking for each of the vaccines versus what it is taking on average. The calculated theoretical batch cycle days are presented in Table 5.1. The table shows that it is expected that the time it takes for all activities to be completed is independent of the vaccines with the exception of the production time. Production time is also based on the biology of the vaccine and cannot be improved as long as the growth systems used in their production remain unchanged. The data in Table 5.1 indicated that production time also accounts for an average of about 20% total batch cycle time. This implies that there is an opportunity to improve 80% of the time because those days are completely physical and can be manipulated to enhance batch cycle time improvement.

Table 5.1: Theoretical Days for Each Activity in the Batch Cycle for Five Vaccines in Unit B

		Vaccines				
		F	G	H	I	J
Batch Cycle Steps	Planning	3	3	3	3	3
	Sourcing	5	5	5	5	5
	Production	7	10	10	8	9
	QC Testing	14	14	14	14	14
	Prod. Review	5	5	5	5	5
	QA Review	5	5	5	5	5
	Release	1	1	1	1	1
Theoretical Total		40	43	43	41	42

For these five vaccines, the theoretical total is less than the average number of batch cycle days that have been reported for the vaccine units. The theoretical is the best-case scenario for each of the vaccines and might not be able to be achieved, but the actual should be closer to the theoretical to make the process more efficient. The bottleneck seems to be the production review and the QA review, and these are the variables that can be changed. So now as a company they need to figure out why these two areas are adding days to the batch cycle time overall and what can be done to reduce the number of days the batch records sit with each of these two steps before being released for further manufacturing.

5.3 Recommendations

The company will start this further research by talking with the reviewers in each of the areas and area management and finding out what they believe are the reasons that batch records get stuck in their designated areas and then try to determine what can be done to fix those issues.

Trivax is also running three shifts of production and only one shift of both the production review and QA review. If they think of this in terms of lanes on a highway and

they are going from three lanes of traffic down to one, the company can ensure that there is going to be a traffic jam at the point where the three highways meet. If one of the bottlenecks is getting corrections completed by someone on an off shift, then maybe they need reviewers on that off shift to ensure that those corrections get completed. These issues need to be examined deeper in further research for this project. Maybe they don't need to go so far as to suggest three shifts for each of those areas but at least swing shifts so that someone for those reviewing departments is there for at least an hour or so of each of the three shifts to answer questions that operators might have or get corrections done in a timely manner.

After analyzing the individual vaccines, Trivax went to their production management computer system and decided to look at it and see if there was anything that they could do to make the batch cycle times decrease from the electronic standpoint. These data are shown in Table 5.2.

Upon looking at results from the vaccine production units, Trivax realized that some of the numbers in the Tableau computer program they were not correct for cycle days for various material numbers. An investigation into why these numbers were incorrect was then initiated. Tableau pulls its information from their manufacturing production inventory system. Those numbers have to remain accurate or the numbers that they get in Tableau for analyzing will be inaccurate. The company was able to pull a list of 1,984 material numbers and group them into 4 buckets. These buckets were then analyzed to see what the inventory system was using as its set theoretical batch cycle days for each of the material numbers. For the vaccine bucket, there were a total of 216 material numbers to comb through. They analyzed what the system said versus what the longest testing time was

based on the quality standard for each material. They were then able to come up with a calculation to determine what the system should theoretically say each material number should have for batch cycle days. They could then compare this to what the system is currently reading as the number of batch cycle days and determine what percentage of the numbers are correct in the system. Table 5.2 shows the calculated days that they were able to implement to come up with a more accurate theoretical batch cycle time for each material number.

Table 5.2: Recalculated Theoretical Batch Cycle Days Based on Longest Testing

Test	Days
No Testing/Batch Record Review Only	28
Mycoplasma Longest Test- 28 day	49
Sterility Longest Test- 14 days	35
Animal A Safety-7 days	28
Animal B Safety-7 days	28
Inactivation Test- 21 days	42
Animal C safety- 21 days	42
Animal potency-52 day	73
Animal potency- 35 days	56
Animal Test-42 days	63
Animal Testing-49 days	70
Testing-32 days	53

Out of 216 vaccine numbers in the system, 144 are accurate when compared to the theoretical number set in the manufacturing system. Thus, 67% are correct and 33% are inaccurate. These 33% can be adjusted in the system to add batch cycle days. By adding days and having a more accurate batch cycle time, Trivax is not reporting those material numbers as past due every time that material is made. That will add value overall to the project for trying to reduce batch cycle days as this is all being based on the number of days the batches are being processed beyond theoretical.

By looking at these numbers, Trivax was then able to see how many of their current materials have an accurate theoretical batch cycle day length in the manufacturing system and how many will always be longer than theoretical because the system is set incorrectly. By eliminating days wrong in the system, Trivax can ensure that they are focusing on the right area of the cycle chain to make our corrections and reduce batch cycle days.

Going with the above table will also make the entire system more streamlined and all materials with a certain testing will automatically be assigned the correct days in the future and they can hopefully eliminate the confusion and discrepancies uncovered in this research. The updates to this manufacturing inventory system are being adjusted and the benefits are yet to be determined. Further research would need to be done on this area of the thesis to see if this adjusting of 33% of the vaccines makes a difference in the overall outcome of the batch cycle time reduction process.

There is further research to be done on this project. The company would like to look at the other vaccine production units and possibly other vaccines within those units to see if the statistics stay true in other areas of the company like they did in unit B. They would also like to explore the adjusted work schedules for the production review staff and the QA staff and see if that makes a difference in the reduction of batch cycle times. Analyzing the data for the other units might bring more areas for research and further investigation. Trivax has been able to narrow down the focus to the key areas that need to improve to drive down the batch cycle times and gain a more efficient system moving forward. With the implementation of the new days in the computer system and the new strategies at the reviewing stages, the hope would be to decrease the number of batch cycle

days to a more reasonable number as to make the total number of days from planning to release more in line with theoretical expectations and ensure that Trivax stays at the top of the market and keeps product on the shelf.

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