Stochastic Capacity Modeling to Support Demand/Capacity Gap Planning

by

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Abstract

Capacity strategy has established methods of dealing with uncertainty in future demand. This project advances the concept of capacity strategy under conditions of uncertainty in cases where capacity is the primary source of uncertainty.

Novartis Vaccines, one of five divisions of Novartis AG, produces nearly two dozen vaccines which are offered in syringes, vials, multi or single pack, and multi or single dose and delivered in language-specific packaging to countries all over the world. Bexsero is a new product in 2013. As demand for Bexsero and other products increases over the next ten years, the production lines used to package them will need to accommodate more and more volume.

Capacity planning compares capacity gaps between future demand and current estimated capacity. Because of recurring shortfalls in production relative to planned capacity, current estimates of capacity are not trusted for long-term planning. Understanding how international product demand will be allocated to each production line and what drives current capacity limitations will help Novartis Vaccines prioritize investment to optimally develop this capacity over time.

Thus, the purpose of this model is to establish baseline capacity estimates using historical data and allow for the simulation of new production scenarios in order to demonstrate the impact of production policy on mean and variance of capacity over a specified time horizon. Incorporating simulated results produces a mean and standard deviation of capacity we are likely to see.

Long-term demand was assessed, capacity versus peak demand views were created, and production scenarios were simulated on a single line/product/format basis over the time horizon to determine expected capacity. Recommendations were made for each of the pre-filled syringe, multi-format, and vial format lines and these results were used to shape an overall packaging capacity development plan.

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Introduction

1.1 Context and Thesis Summary

In any manufacturing organization, understanding what the current capacity is to produce various products is essential. The question, how much can we make is so closely related to the question, how much can we sell. Unfortunately process variability, equipment variability, and strategic product variability can all complicate the answers to these questions and capacity uncertainty can become a significant source for distrust and conflict between manufacturing and short and long-term supply planning functions. Novartis Vaccines' packaging area is a prime example. In this context, research was performed to develop a method of explaining and quantifying the uncertainty in a manufacturing system and to propose how the output of this method can be used to develop a capacity strategy, extending the existing concepts of uncertainty hedging in capacity strategy models.

1.2 Problem Statement

The purpose of this research was to create a capacity development strategy for Novartis Vaccines and to enable the on-going yearly refinement of that strategy by developing a stochastic capacity model to support demand/capacity gap planning. The methodology can be considered a proposal for how to create capacity strategies for production systems where there is high-product mix or process variability. Under the conditions mentioned above which lead to significant uncertainty in capacity, there is no currently proposed method of performing long-term capacity development

1.3 Hypothesis and Research Questions

The hypothesis of this research was as follows:

Monte Carlo simulation can be an effective method to model capacity uncertainty for use in strategic capacity planning and the results can form the basis for implementation and change.

The goals of this project were to provide answers to the following questions:

- What is our current capacity and why is it different from what we estimate?

- Communicate insights from the analysis with recommendations to address capacity constraints

- Shape an overall packaging strategy with specific recommendations to address business issues over the long-term planning period

Upon achieving these goals, this research hoped to answer the following research questions: Is it possible to develop a capacity development strategy which takes into account uncertainty in current capacity limitations; how does treatment of capacity uncertainty fit into the capacity strategy framework and models laid out by Rosenfield and Beckman?

1.4   Research Methods

Historical data was gathered together from numerous forward looking and historical sources to explain why we see the capacities we do nowadays. Using the historical data, uncertainty in the system including variability in effective rates, cleaning, clearance, and setup times, quality, and batch delivery rates is used to simulate production over a specified time horizon. Simulated results produce a mean and standard deviation of capacity we are likely to see.

1.5   Thesis Chapter Summary

Background

This chapter provides the industry and company context for this project. Strategic factors affecting growth in the vaccine industry are discussed, the history and structure of Novartis Vaccines are

introduced and historical shortages in the vaccine industry are discussed as a motivation for a project to develop a capacity strategy that both conserves capital while ensuring supply. Finally, the packaging area at Novartis Vaccines is introduced and the changeability of existing capacity estimates is compared.

Literature Review

This chapter explores the various approaches to capacity strategy found in academic literature and in industry documentation. It describes existing methodology for capacity strategy that hedges uncertainty in demand. Lastly, this chapter provides an overview of the use of Monte Carlo simulation in manufacturing.

The Novartis Packaging Production Simulation Model

This chapter similarly describes the process and results of the Packaging Production Simulation which was developed to help Novartis Vaccines understand the expected range of capacity for each production line. Design requirements and decisions in development of the model are discussed and validation of the model is summarized.

Packaging Area Capacity Development

This chapter details the initial implementation of the model at Novartis Vaccines. The process of Demand/Supply Gap Analysis is described and the decision to focus initial efforts on development of a capacity plan for multi and single pack syringe packaging is justified. Next, this chapter discusses the performance, utilization, and expansion levers for capacity development and describes an example scenario simulation performed to develop a plan for multi-pack syringe. Lastly, this section presents the

key recommendations for implementation of the capacity strategy and the practical space considerations required to formalize the plan.

Conclusions

The final chapter discusses the merits of the simulation and proposed capacity strategy methodology as it is currently implemented and explores future development opportunities for the model. In addition, opportunities for future initiatives are recommended which would smooth demand and enable efficient utilization of current and future capacity.

2 Background

This chapter outlines the strategic landscape of the vaccine manufacturing industry and the historical threat of vaccine shortage, introduces the Novartis Vaccines packaging area and describes the problem of variability in capacity estimation and how this affects the ability to plan for long-term demand.

2.1 Industry Overview

The vaccine industry is undergoing significant consolidation. 35 years ago, there were 14 key companies in the vaccine industry. Now, only five main players dominate 80% of the market. Consolidation and attrition have been caused by sparse profitability conditions in the industry. Low profitability results from a combination of high costs of research, development, production, and liability combined with strong buyer power from public tender system.

These trends are likely to continue in the future with budget constraints and pressure on the cost of health care. However, demand volumes growing and shortages have occurred, especially with influenza vaccination [1] [2]. But while pediatric vaccines are relatively predictable, the production and distribution of influenza vaccines has several complications [3]. First, influenza vaccines are seasonal and companies race to produce vaccines between the date that the strain combination is declared and the date at which countries will vaccinate their populations. This means a short production season with significant competition based on time. Additionally, commoditization puts the power to buyers who regulate custom requirements or request customizations (format, artwork). Moreover, the pressure to produce high volumes in order to capitalize on this yearly spike in demand puts strain on the capacity of the vaccine manufacturer. Finally, because influenza vaccination is highly visible to the public, any

shortfall will have immediate implications on good will towards the vaccine manufacturer. Thus, the products are quite important despite their low profitability.

Because this industry profitability has far-reaching impact on vaccine research and development investment, it is of vital importance that capital expenditure in capacity development is made intelligently in order to both conserve capital and minimize the risk of shortage. This project considers the case of Novartis Vaccines' packaging capacity strategy development and draws conclusions which may have uses both within the vaccine industry and elsewhere.

2.2   Novartis Vaccines

Novartis International AG is the world's second largest pharmaceutical company by sales with $57.9B in 2013 [4]. The company is based in Basel, Switzerland and holds a pipeline of over 200 new products. Novartis International AG currently has six divisions: Pharmaceuticals,

History	Novartis Vaccines is one of five divisions of Novartis AG. It was acquired from Chiron in 2006.
Products	There are nearly two dozen vaccines which are offered in syringes, vials, multi or single pack, and multi or single dose and delivered in language-specific packaging to countries all over the world
Planning	Planning for production occurs on multiple time horizons because of poor schedule adherence to accomodate shortages and rush orders.
Outlook	Bexsero is a new product in 2013. As demand for Bexsero and other products increases over the next ten years, the production lines used to package them will need to accommodate more and more volume.

Vaccines, Generics, Consumer Health, Eye Care, and Research and Development [5]. Of these,

Pharmaceuticals represents the lion's share of net sales, accounting for 55.6% ($32.2M) in 2013.

Novartis Vaccines and Diagnostics, by contrast, represents a much smaller share of the net sales ($2.0M in 2013 / 3.4% of net sales) but grew sales volumes by 7% in 2013 versus the flat performance (0% change) from Pharmaceuticals.

Novartis Vaccines and Diagnostics was formed in 2006 after Novartis AG acquired Chiron. Chiron then included three main areas: biopharmaceuticals, vaccines, and blood testing [6] and was in the midst of recovery from a production license suspension in 2004 which caused a shortfall in influenza production volumes by half relative to demand that year [6].

Since acquisition, Novartis Vaccines and Diagnostics has grown to employ 6,122 employees in 30 countries and produces 20 marketed products with over 15 products in clinical development. Novartis Vaccines is headquartered in Cambridge, MA, but most production takes place at sites in Italy, Germany, the United Kingdom, and Holly Springs, North Carolina [7]. Sales increases in 2013 were driven by increased volumes of Menveo, seasonal influenza, and pre-pandemic sales [4].

2.3   Other Historical Vaccine Shortages

Shortfalls in vaccine production are a major problem to which the US has taken a risk-management approach. While the shortage in 2004 of Influenza vaccine was caused by an unexpected bacterial contamination at one producer (Chiron), there have also been five other significant shortages between 2000 and 2005 in childhood vaccines. Shortages occurred across a range of childhood vaccines including, Td, DTaP, PCV, MMR, Varicella, and Influenza. These shortages have been caused by decisions by manufacturers to temporarily decrease or cease production or by unexpected demand. Of these six shortfalls in vaccine production, three can be attributed to decreased production at Wyeth, two to
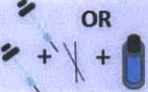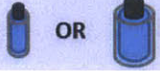
voluntary renovations at Merck, and only one to the bacterial contamination at Chiron [8]. In order to mitigate shortfalls in vaccine production for reasons of unexpected disruption, the CDC established a strategic reserve of childhood vaccines in 1982 which is meant to hold a six-month supply of vaccines recommended for children. There have been 12 withdrawals from this stockpile over the course of its history.

2.4   Packaging at Novartis Vaccines

The packaging area consists of seven specialized machines to package syringes and vials in multi or single package formats or single or multi-dose. Lines are qualified only for specific products. This qualification is not equal and some lines are useful for many more products than others.

For the Northern Hemisphere Flu season, (manufacturing demand peak), C10, C18, C6, C14, and C16 take on demand.

Table 1 Novartis Vaccines Packaging Area

	Packaging Line	PACKAGING FORMAT		Single/ Multi PACK	Single/ Multi DOSE	Validated Products
PRE-FILLED SYRINGE	C10	10 Pre-Filled Syringes / Box, 1 Ds / PFS		MULTI / BLISTER	SINGLE	FLU PRODUCTS MENINGITIS PRODUCTS PEDIATRICS & SPECIALTY PRODUCTS
	C18	10 Pre-Filled Syringes / Box, 1 Ds / PFS		MULTI / MONO-MATERIAL	SINGLE	LIMITED FLU PRODUCTS LIMITED MENINGITIS PRODUCTS
	C6	1 Pre-Filled Syringe (PFS) / Box, 1 Ds / PFS		SINGLE	SINGLE	FLU PRODUCTS MENINGITIS PRODUCTS PEDIATRICS & SPECIALTY PRODUCTS
MULTI	C14	Kit 1 Pre-Filled Syringe 1 PFS w/ Needle	OR	SINGLE	SINGLE	FLU PRODUCTS MENINGITIS PRODUCTS PEDIATRICS & SPECIALTY PRODUCTS
VIAL	C13	10 Vials / Box, 5 or 10 Ds/Box		MULTI	SINGLE / MULTI	LIMITED MENINGITIS PRODUCTS LIMITED PEDIATRICS & SPECIALTY PRODUCTS
	C15	2 Vials / Box, 1Ds/2Vials		SINGLE	SINGLE	LIMITED MENINGITIS PRODUCTS LIMITED PEDIATRICS & SPECIALTY PRODUCTS
	C16	1 Vial / Box, 10 Ds / Vial	OR	SINGLE	SINGLE / MULTI	LIMITED FLU PRODUCTS LIMITED PEDIATRICS & SPECIALTY PRODUCTS

2.5   Variability in Packaging Capacity Estimation

There are three capacity estimates generated on an ongoing basis by the packaging area in Rosia. These include the Packaging Site Capacity Review Operational Capacity, the Packaging Plan Assumptions, and the Packaging Site Rolling Average. Over the past several years, there has been significant variation across these estimates as well as within each estimate from year to year. Below, these estimates have been graphed for the C10 (Multi-pack syringe) line:
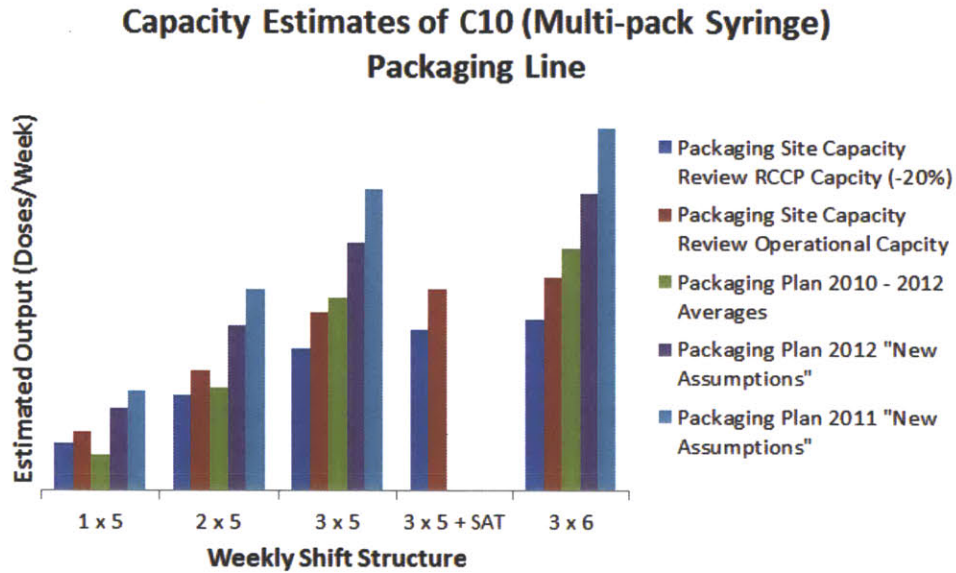
Figure 1 Historical Capacity Estimates for Multi-pack Syringe

The variation in capacity estimation is clear and given this degree of uncertainty in capacity, it is

certainly understandable that the functions at Novartis responsible for production planning or customer

relationships would have a justifiable degree of skepticism and frustration. In this context, the natural

reaction is to err on the side of conservatism in production planning. The currently used capacity

estimate is the Packaging Site Capacity Review Operational Capacity (the red bar above). The Packaging

Site Capacity Review RCCP Capacity (dark blue above) represents a flat 20% reduction from this estimate

and these values are currently used for production planning.

2.6 Capacity Planning at Novartis Vaccines

At Novartis Vaccines, capacity development planning is conducted by the Manufacturing Strategy Group

on an as-needed basis. The process of capacity development planning at Novartis Vaccines compares

capacity gaps between future demand and current estimated capacity on a yearly basis for annual

products. There is also a boundary condition for flu supply is that the filling and packaging operation for an entire season must be accomplished in a specific number of weeks.

Long-term capacity is the name for the capacity estimate used for long term planning over the next 2 to 10 years. This model maintained by the tech ops strategy group is meant to be based on operational capacity maintained by the global capacity management group. Planning for the 10 year horizon is based on an operational capacity with 3 x 6 shift assumption adjusted for the expected change in equipment performance over the long-term horizon. Capacity analysis is conducted assuming 80% of the long-term capacity is available to meet demand [9]. However, because of recurring shortfalls in production relative to planned capacity, current estimates of capacity are not trusted for long-term planning.
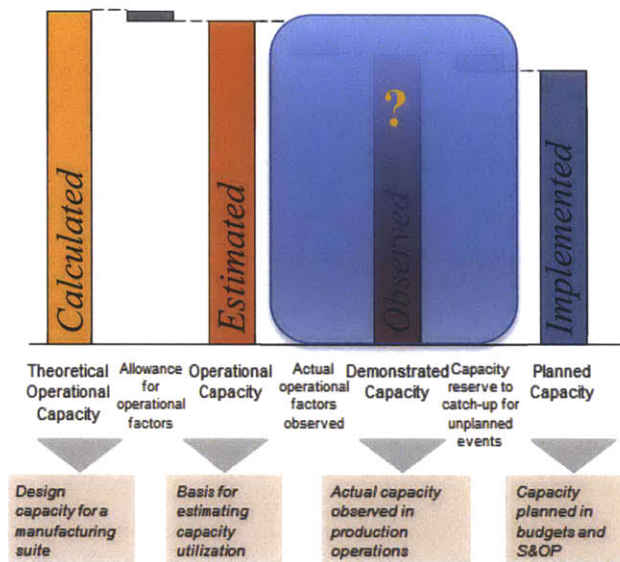
Figure 2 Capacity Estimation Relationships

The process for estimating long-term demand is less defined for the capacity planning process. Long-term demand is estimated on a yearly basis by the four Global Product Teams (Flu, Pediatrics, Meningitis, and Travel). To understand demand on specific equipment for which we can estimate or observe capacity, it is necessary to break down product forecasts into demand for the particular formats that define production allocation. In the past, estimate ratios have been extrapolated forward from current volume breakdowns. This yields a single estimate for demand for each capacity unit. While a Baseline and Upside demand are provided for many long-term product forecasts, there has not yet been any attempt to measure or track the accuracy of the format allocation process for long-term product demand. Understanding how international demand will be allocated to each production line and what drives current capacity limitations will help Novartis Vaccines prioritize investment to optimally develop this capacity over time.

3   Literature Review

3.1   Capacity Strategy

The body of knowledge and thought around capacity strategy helps companies cope with the complexity

involved with demand variability and long-term industry and competitive trends, new product

introductions, long capacity installation times, multiple product lines, staffing constraints, and limited

physical space and capital. Strategy development hinges on answering the following questions [10]:

- What is the forecasted demand in the time horizon of development planning?

- How much capacity should the company have to cover expected demand? What reserve
  capacity does the company wish to use to buffer against unexpected demand?

- In what increments and intervals should the company add capacity?

- What type of capacity should the company add? Human resources? Process and information
  technology? Facilities? Can the company extract more output from existing resources?

- Where in the value chain should capacity be added?

Beckman and Rosenfield outline a comprehensive seven step process for creating a capacity strategy,

citing examples from Intel, which includes five key qualitative and quantitative models designed to

facilitate capacity decisions. The stages included in the capacity strategy process include:

1. Understand the Business Strategy and Competitive Environment
2. Develop a Demand Forecast
3. Identify Capacity Expansion Alternatives
4. Apply Relevant Models to Develop a Capacity Strategy
   a. Lead, lag, or stay even: Timing of Expansion
   b. Competitive gaming: Timing and Size
   c. Economies of Scale and Return on Investment: Size and timing
   d. Hedging to cover demand fluctuations: Size
   e. Hedging to cover demand growth: Size
   f. Dynamic Decision Trees: Increment size, timing, and type
5. Assess Implications for Flexibility and Balance

6. Develop an Implementation Plan
7. Implement, Assess and Measure Results

In contrast to the lead model which increases capacity ahead of anticipated demand and a lag model, which waits until demand has been fully demonstrated, a stay-even (also sometimes referred to as a match or tracking policy) originally described by Hayes and Wheelright [11], is a moderate model which seeks to build capacity according to long-term forecast, balancing the need to minimize cost by maximizing utilization with the need to prevent shortfall.
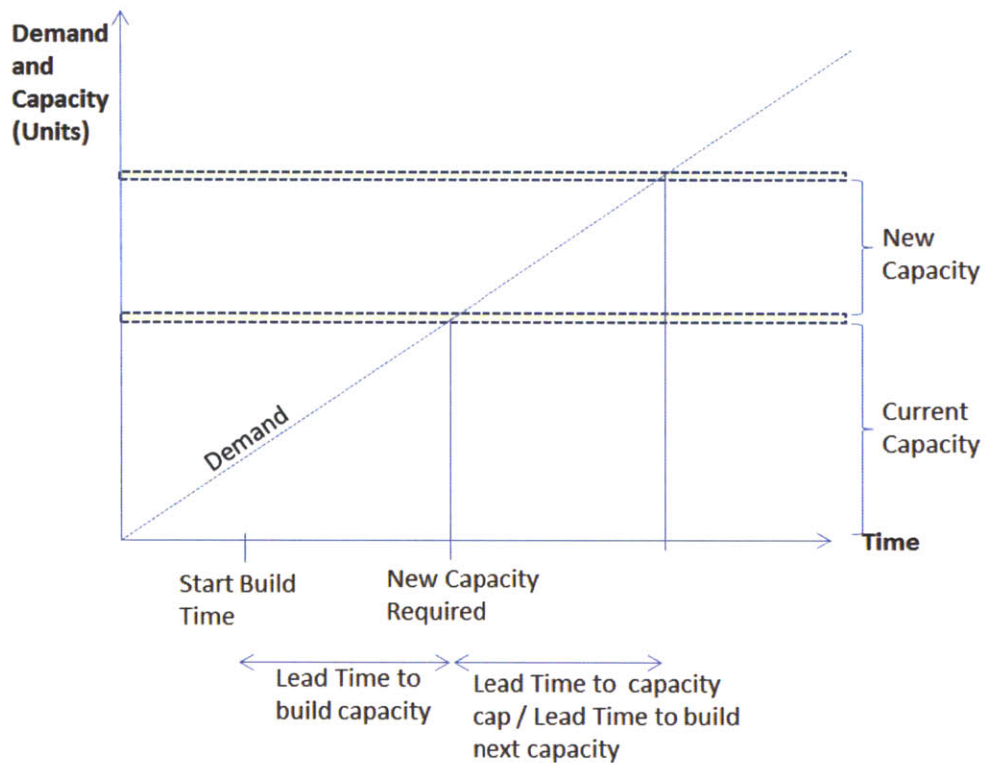

Figure 3 Capacity Expansion under Deterministic Conditions [Adapted from Beckman and Rosenfield 2008]

Other methods proposed for sophisticated capacity planning utilize scenario-based stochastic programming models. Eppen et al. 1989, Swaminathan 2001, and Karabuk and Wu 2002 provide examples of this methodology. Eppen et al. models the strategic capacity development of a car

manufacturer and proposes a stochastic programming solution that prescribes facility selection decisions corresponding to demand scenarios [12]. Swaminathan uses deterministic demand and models capacity expansion as well as inventory management decisions to compare the total cost (including holding, capacity purchase, inventory, unit purchase, and cycle stock cost) of solutions comprised of purchase periods [13]. Karabuk and Wu describe a two-phase multi-stage dynamic programming model which incorporates scenario demand uncertainty and allows decisions about capacity expansion and configuration to be made both at the start of the year and in reaction (by marketing or manufacturing managers) to materializing demand [14]. While this model incorporates well the uncertainty due to materializing demand and capacity and allows for short and long-term capacity decisions, the model also relies on numerous assumptions which would be very difficult to quantify (eg. The "bias each product manager has about the supply source quality and performance).

In addition to the popular stochastic programming approach discussed above, others have used deterministic approximations to avoid the complexities of a nonlinear stochastic formulation. Bitran and Yanesse propose a deterministic approximation to the stochastic production models in order to extend the bounds on feasible number of periods and cost structures [15]. Paraskevopoulos and Karakitsos propose another deterministic approach which seeks optimal capacity expansion and utilization plans based on demand uncertainty and minimizes the sensitivity of profitability to this uncertainty to prescribe a tradeoff between the optimally profitable performance and the less risky robust performance [16]. Yet, both of these solutions still appear to be restricted in implementation by industry and in this context, it makes sense to contrast these solutions to those proposed in industry.

In contrast to the academically proposed solutions discussed above, some off-the-shelf solutions exist to perform strategic capacity assessment for the pharmaceutical industry. Bio-G (Bioproduction Group) is

a quantitative biotech process modeling company providing a real-time modeling system that inputs data from dynamic SQL production databases to assess capacity against estimated demand. The product's granularity is based on a calculated estimate of days per batch for each product and incorporates changeovers between products. In order to compare demand and capacity, an "occupancy" chart is provided which is equivalent to utilization of the line.
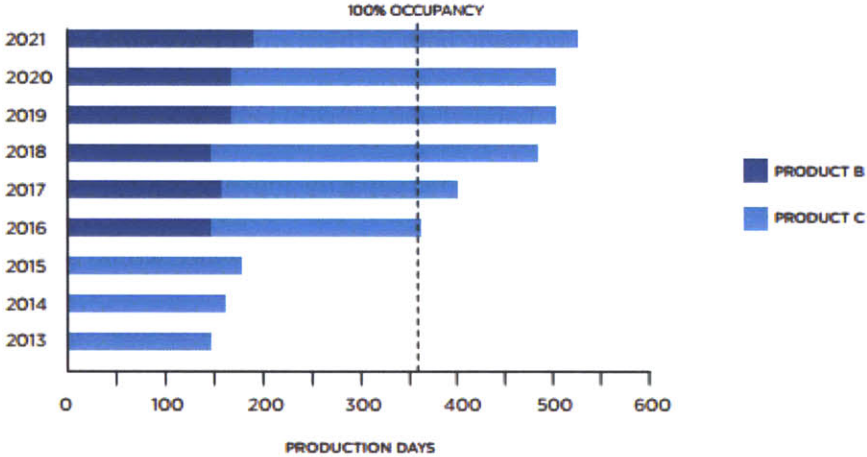
Figure 4 Bio-G Occupancy Analysis Example

While Bio-G's software can provide a sound example of capacity strategy formulation, the underlying capacity calculation is focused on formulation variables (titres, tank size, etc.) and focuses treatment of variability on batch yield and risk of uncertain demand. By contrast, Novartis Vaccines packaging area has recorded consistently high yields and sees significant variation in packaging or area-specific production process variables [17].

The Bioproduction Group makes the argument that while much research has been devoted to accurately predicting demand, there is still a need for "integrated supply-demand models that incorporate uncertainty in raw material supply and manufacturing capacity [17]. Zhang and Johnston discuss the significant variability in production processes which cause difficulty in measuring capacity in

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biopharmaceutical plant operations, "One of the key issues with variability in operating times is that changes to one or more manufacturing unit operations may have unexpected changes in the performance of other (untouched) areas of the plant. A unit operation requiring additional cleaning, for example, may exhaust existing CIP/SIP capability, reducing the total capacity of the facility. These unforeseen bottlenecks are common in almost all biopharmaceutical processing plants" [18]. The cartoon in Figure 5 illustrates their observation of this concept in the pharmaceutical industry. This project aims to advance the body of knowledge in this area.
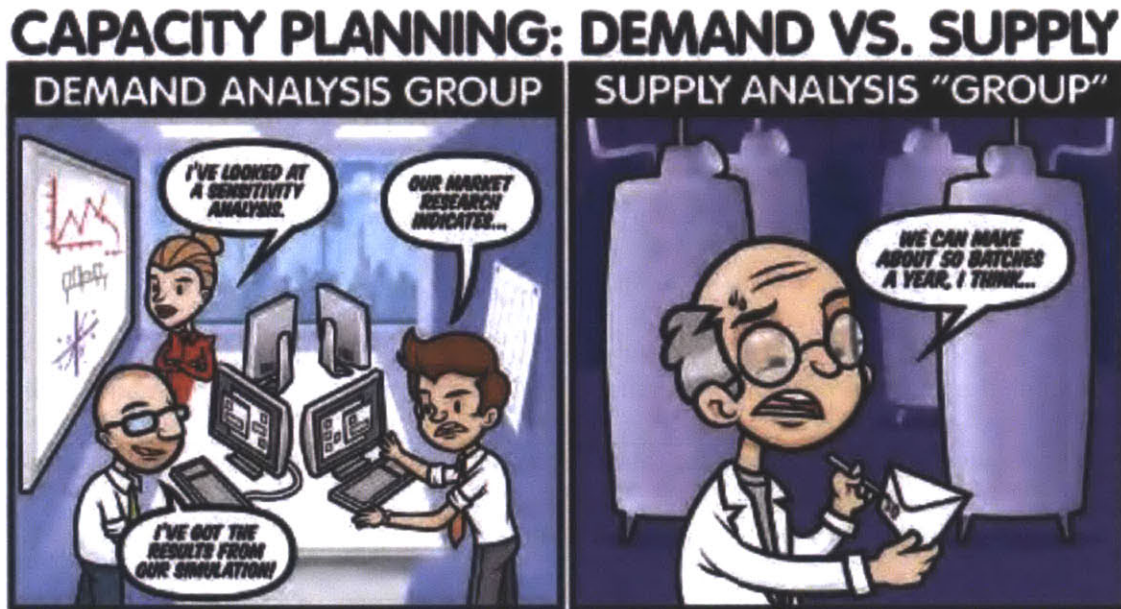
Figure 5 Bio-G Capacity Planning Cartoon

This project laid out the roadmap for Novartis to follow this staged process for capacity strategy proposed by Rosenfield and Beckman. Development work in this project is focused on overcoming a major hurdle in this implementation: quantifying capacity and capacity variability through simulation. An adapted version of the hedging model is described which can incorporate capacity uncertainty in long-term capacity planning.

3.1.1 Hedging Methods for Capacity Strategy Under Demand Uncertainty

Because the primary question in this project is how to incorporate uncertainty in capacity into the capacity planning process, it is useful to examine the ways in which uncertainty in demand is handled before we proceed to quantify capacity uncertainty through simulation.

Under the most basic models for capacity strategy, the basic premise is to start investment in capacity one lead time before it is projected to be required to meet demand. However, if there is uncertainty as to what the future demand will be, this coordination becomes difficult as less future demand requires less additional capacity investment and may require less lead time. By contrast, more future demand may mean a company must move sooner to add (or subtract) more new capacity.

Beckman and Rosenfield recommend three models for hedging uncertainty in demand, drawing upon the established methodologies for inventory management.

The first model, the Short-Term Demand Fluctuations Model is formulated to allow a manufacturer to select a service level that is appropriate for their business conditions. A company may choose to meet the average demand, peak demand, or to meet demand some certain percentage of the time based on the probabilistic distribution of future demand.

The second model, the Long-Term Growth Expectation Model is proposed in order to integrate two forms of uncertainty: long-term demand uncertainty and capacity development lead time uncertainty. It is based on the standard equation for standard deviation for demand during lead time used in inventory management (Safety stock and reorder period policies) and incorporates two sources of variation, demand and lead time [19]:

$$M = L\mu_x \qquad S = \sqrt{L\sigma_x^2 + \mu_X^2 s_L^2}$$

For a demand with mean, μ_x, and standard deviation, σ_x, and a lead time with mean L and standard deviation, s_L, the above equations are the mean and standard deviation of the demand during lead time. By extension, the formulation for the standard deviation in the demand *growth* during the lead time is:

$$\sigma_{gL} = \sqrt{E(L)\,\sigma_g^2 + E(g)^2\sigma_L^2}$$

Where E(L) = expected lead time

σ_L= standard deviation of lead time

E(g) = expected growth in demand

σ_g= standard deviation of growth

This standard deviation for the demand growth during the lead time can then be used to calculate the amount of capacity required by plugging into the previously discussed formulation for demand fluctuations [10]:

$$Required\ Capacity\ Increase = \mu_{Demand\ growth\ over\ the\ lead\ time} + (z \times \sigma_{gL})$$

Finally, the Dynamic Decision-Making Methods (single and multi-stage) are intended to account for probabilistic scenarios where there are multiple options, the economic value of which is calculable, for multiple outcome scenarios. The selection of an option is then made for the option whose expected return is highest:

Expected Return (Option 1)

$$= \sum_{i=1}^{m} (Return\ for\ Option\ 1\ and\ outcome\ i\ \times probability\ of\ outcome\ i)$$

This structure is then expanded for multi-stage by rolling up the returns for each option by selecting the best option at each successive stage starting at the last decision and working backwards towards the first.

For capacity planning at Novartis, the Long-Term Growth Expectation Model and Dynamic Decision-making Method are recommended. The Long-Term Growth Expectations Model was adapted in order to develop a capacity development process that would fit well with the joint pressures of cost and availability and which would be able to take into account the uncertainty in capacity seen at Novartis Vaccines. The model described in this paper, the Packaging Production Simulation Model was developed to determine capacity under various production scenarios and the Dynamic Decision-Making Method proposed would allow Novartis to prioritize multiple satisfactory options.

3.2   Monte Carlo Simulation and Simulation in Manufacturing

While strategic capacity planning is generally done using static mathematical analysis or through a scenario based approach to demand uncertainty, this type of analysis become burdensome if the number of possible scenarios increases [20]. Business processes are often dynamic and interrelated and a static analysis often does not provide enough confidence for basing strategic decisions. Simulation can provide more insights into the real system behavior [21]. In essence, simulation is the creation of a model which can approximate a real-world system over time by accurately representing characteristics of that system's behavior [22]. Simulations are used to understand the outcomes of alternative courses

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of action and are useful where experimentation with the real system may not be possible, either because the real system is unavailable or because experimentation would be difficult and/or expensive.

The principal behind Monte Carlo simulation is that we sometimes may be able to measure the behavior (mean and variance of system coefficients) of individual features of the real-world system but are not able to access the full system in order to document its performance or to understand the cumulative impact of subsystem variability on the variability of system output. By simulating the system's performance many times while randomly sampling from the subsystem input distributions, it is possible to create a distribution for the full system output which accurately represents the overall variability given the possibility of rare events in each subsystem variable.

IBM Software describes the process and justification for Monte Carlo simulation in their white paper, "Better Decision Making under Uncertain Conditions using Monte Carlo Simulation". IBM points out that there are three methods that are most commonly used to address uncertainty:

- Point Estimation: Uses the most likely value for the uncertain variable
- Range Estimation: Sets three scenarios: a best, worst, and most likely case
- What-if Scenarios: Explore the effect of things you can control from among the best, worst, and most likely case.

Instead of sampling from historical outcomes to determine a *most likely* outcome, a Monte Carlo simulation models fundamental system functionality and defines probability distributions for inputs to the system. This allows for a greater range of inputs since distributions can be modified or shifted at will to capture the effect of a project. Finally, the Better Decision Making whitepaper presents example use cases for stochastic analysis ranging from financial risk modeling and investment appraisal, to business and strategic planning, sales forecasting, and pricing [23].

Kumar and Bhat support the idea that business processes can be modeled using Monte Carlo Simulation though they also mention the challenge of extensive data analysis and skilled knowledge to infer from historic data. They define a Monte Carlo model for capacity planning at a call center and provide a deeper discussion of a three step system for architecting Monte Carlo simulations. The first step proposed is to model the business process; the second task is to allocate resources to activities; the third step is to schedule the customer arrival in the process [21]. In the Novartis Packaging Production Simulation Model, a similar architecture is used with the "Batch Simulator" modeling the business process (production) and incorporating uncertainty, and the Line Simulator taking on the task of resource allocation and scheduling. In this project however, the answer sought was not the binary success or failure at meeting demand, but a projection of expected maximum capacity under a particular scenario. Thus, instead of the customer arrival discussed by Kumar and Bhat, sufficient demand is provided by the Line Simulator to keep the line busy.

A relevant example from the pharmaceutical industry was documented by John Souza, who used Monte Carlo simulation to determine plant capacity and variability of Caprolactam[1] production at AlliedSignal in 1997 [24]. Souza cited the project motivations as follows:

- Accurate capacity and variability determination
- Enable better business planning
- Optimize resource allocation

In building his simulation to meet these goals, Souza designed a model to incorporate variability information of relevant factors such as plant temperature and to include plant policy factors like

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[1] Caprolactam is a component of the nylon polymer used to produce many textile, industrial, and specialty nylon products.

preventative maintenance. The output generated by Souza is presented as a probability distribution and was intended to be used to weigh the impact of proposed performance projects individually or collectively on system performance. Comparing the output of various combinations of proposals ("Production Scenarios"), Souza evaluates hypothetical scenarios to select the best for implementation.

In the Novartis Packaging Production Model, a similar structure is used with inputs including plant downtime, line speed, set up time, overhead time, etc., and the output probability distribution of scenario capacity is used to generate a preliminary capacity development plan for Novartis Vaccines. Because the system is very challenging to understand analytically, the simulation serves to make the underlying system dynamics and variability visible and palpable, and these features contributed to the endorsement given to the model by the head of the packaging area for use in long-term capacity planning.

4 The Novartis Packaging Production Simulation Model

4.1 Model Requirements

At Novartis, there are several significant challenges that make implementation of the established Capacity Strategy methods difficult. While some Global Product Teams provide both a "Baseline" and "Upside" demand forecast, not all do this and prior to this effort, there was no established process for creating probabilistic distributions for long-term packaging demand. Moreover, as discussed previously, there is significant uncertainty with regards to what the capacity of the packaging area is to produce in various formats. Moreover, production policies which affect the plant's capacity are expected to be implemented in the future as additional capacity is required. The unknown impact of these changes adds further uncertainty to the capacity estimation. Thus, for this project, it was necessary to develop a model of packaging capacity which would:

a. Adapt the existing hedging methods for capacity strategy under demand uncertainty to incorporate uncertainty about current capacity

b. Simulate future projects and policy changes to enable resource planning and project prioritization by evaluating mean and variance of capacity(similar to Souza)

c. Dynamically gather model parameters from existing data sources while leaving open the possibility that data sources will be replaced in the future

d. Ensure ongoing usefulness by employing common systems that enable knowledge transfer

This project proposes using the stochastic capacity distribution generated as an output of this model in order to eventually be used in the following adapted version of the demand uncertainty capacity strategy method:
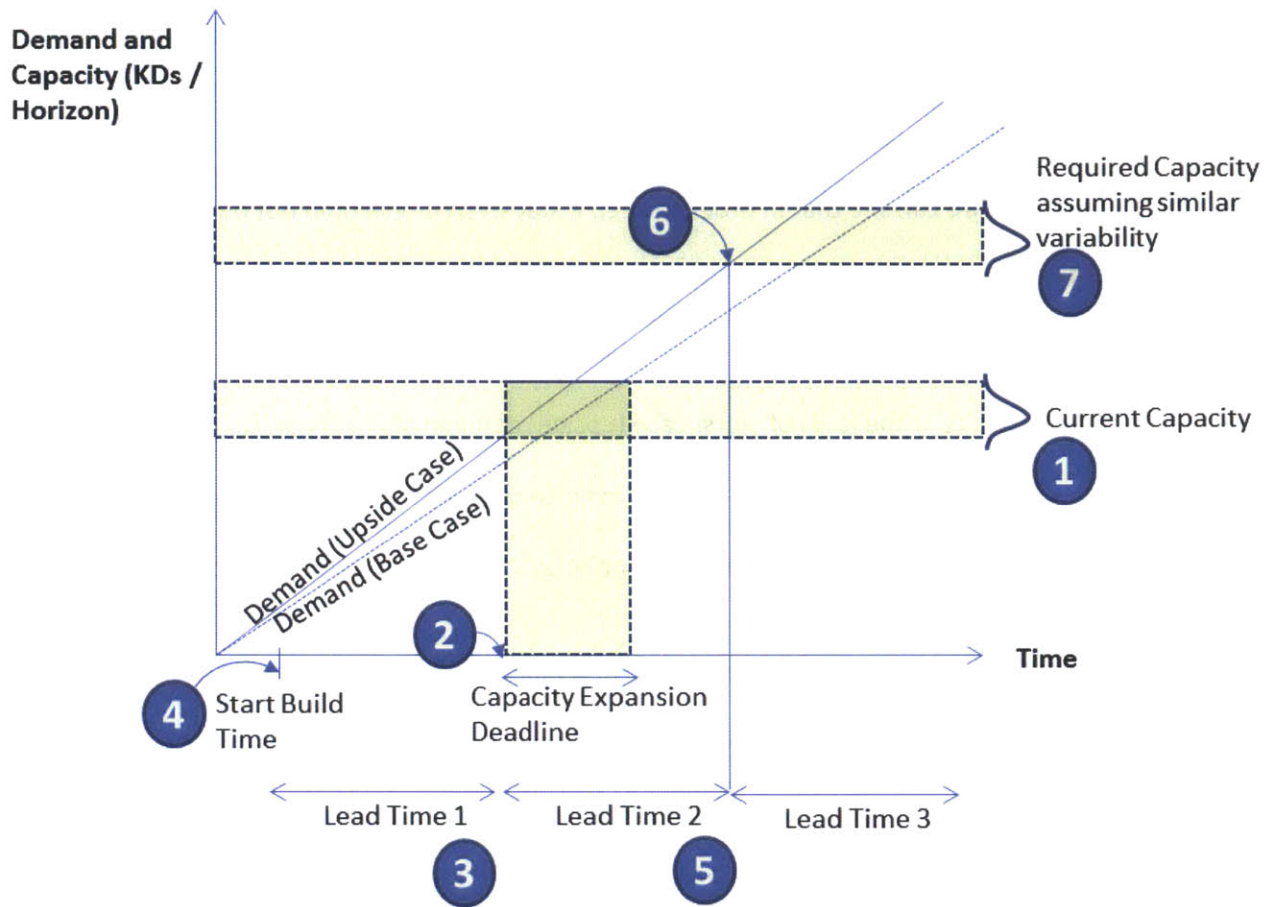
Figure 6 Long-term Capacity Requirements Hedging for Uncertain Capacity and Demand

The goal of the proposed uncertainty hedging model is to decide both the time at which to start building new capacity as well as the required amount of new capacity. Both are affected by uncertainty in current capacity levels.

Given a distribution or range we can expect for current capacity (1), it is reasonable to deduce that there is a worst case capacity which a growing demand line would pass soonest. Conversely, there is a best case (from a capacity shortfall perspective) point in time where we would see a high capacity and low demand. Between this range of time is our Capacity Expansion Deadline. At the time of this deadline,

additional capacity is required to have been completed (2). In order to find the time at which we should

start building this new capacity, we back up one lead time (3) from the worst case deadline point and

call this our Start Build Time (4).

Extrapolating forward, we can see that in order to keep a stay-even model (and not build extra capacity

before we need to), we should keep a continuous cycle of capacity building. At a point, one lead time in

the future from the capacity deadline, there is the next deadline (5). Thus, to keep the cycle, we should

build to place our capacity at the level of worst case (upside) demand at that time (6). Assuming that

the expanded capacity will also have a distribution similar to current capacity, we should consider the

required capacity distribution to have its worst case point at a level sufficient to meet demand (7).

Thus, the size of the capacity required in this case now depends on the time at which it was determined

that new capacity would be required as shown above. This proposed method determines a build date

and quantity for capacity expansion which accounts for variability or uncertainty with regards to

Capacity.

4.2   Limitations of the Data and Assumptions

The project draws on data from the following input data sources:

- Packaging Area Plan (for shift information and non-production activities)
- Packaging Line Records (for batches produced on each day and individual batch run-times and setup of batches)
- SAP Exports (to validate batches and quantities that are delivered)
- The Formati Validatte Velocita Macchina and SOP
- GPT and RFC Demand Forecasts and expert opinions

However, production performance data (Packaging Line Records) currently available has been gathered

manually and significant problems with inaccurate or unrecorded data have been documented. Plans

are currently in place to implement automated batch data gathering systems, but these were not

available for use in this project. Additionally, dates corresponding to batch production recorded in SAP do not correspond to the same dates in the Packaging Line Records (in end date or duration of production) and batch output disagreement has been seen between these two sources. Process engineers believe that these deviations occur because the staff entering the received data may forget to record an element of a batch recording and may "save up batches" to be entered at once. The cause of these mistakes may be that staff are not properly trained or lack understanding for what the data will be used for.

There is similar disagreement between the line rates recorded as the maximum qualified rates in the Formati Validatte Velocita Macchina and the Standard Operating Procedures (SOP) and further disagreement with the Packaging Line Record recorded line speed as calculated by dividing yield by production duration. Deviations in this area are believed to be caused by unrecorded stoppage time from temporary line malfunction or from environmental excursion which must be investigated and corrected before packaging can resume.

Finally, there is also disagreement between the activity planned on the lines (recorded in the Packaging Area Plan) even for the most recent, morning-of-production plans and the activity recorded on the lines in the Packaging Line Record. The causes of these deviations are the subject of ongoing study in the Packaging Area but may result from upstream shortage of material (packaging or filled vaccine syringes or vials), shortage of qualified staff (because staff must be told to come in at least one month ahead of production), changing prioritization of specific lots due to economics and dynamic customer relations, or technical malfunction on a line, among other sources.

Reconciling the differences mentioned above and creating a data processing system that could be used on an ongoing basis were both key goals for this project and thus, the following steps were taken:

Spreadsheet data sources were kept in the format they were provided from the source staff member closest to collection. Because data sources are acceptable as they currently stand, the model's owner should be able to request that the most recent version of the data source be provided in order to update the system results on an ongoing basis. A single data integration database of batches parses all data sources to consolidate all information about the packaging area activity over all time periods available into one place. This database performs the reconciliation by giving authority to the Packaging Line Record for batch data, the Packaging Area Plan for line maintenance and non-production activity time and staffing, and the SAP Export (Warehouse record) for the final batch yields produced and delivered. This assignment of authority represents several assumptions about accuracy which have been verified with the packaging area operations manager. This database also takes the role of filtering out (by declaring invalid) batches for which there are missing fields of data. Figure 7 shows the impact of this filtering and categorization into specific product/line pairings. The derived variable probability distribution inputs (discussed later) can be assumed to have more strength with larger numbers of available batches to draw from.
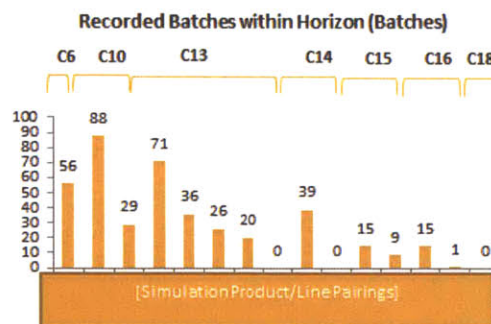

Figure 7 2012 Validated Batches (Fully Recorded Production Data)

A secondary benefit of the Batch Analysis record consolidator is that the enumeration of the fields it collects represents the data that would be required from the automated system to be implemented in the future. Once the system is implemented, links to the data in the current Batch Analysis database may be replaced by links to an export of accurate updated data from the automated line monitoring system.

The batch data discussed above represents all of the data that was available for this project. Lower level production line data such as individual machine rates or batch stoppage time was not available and thus, full line rate distributions are assumed to represent the aggregate effect of all lower-level activity. Similarly, causes of downtime on the line were not readily available in statistically significant quantities and therefore time which was staffed but for which no line production is recorded is assumed to represent the aggregate effect of all underlying causes (maintenance, clinical trial activity, cleaning, etc.). This assumption is also dependent on an assumption that recorded line staffing is accurate and that staff recorded as having worked an hour for one line are not re-assigned to another line during the day. Though it was not possible to quantify the degree to which this "staff reassignment" takes place, it was possible to verify reports of these incidences by showing a line that has recorded more batch hours than staffed hours. In all cases, the existing data was used for this analysis and plans were discussed which highlight the need for automated data gathering systems which would eliminate the need for many of these assumptions.

4.3 Design Decisions

The Packaging Production Simulation Model is an Excel-based Monte Carlo based simulation of a packaging line's activities and output over a specified time horizon. A Monte Carlo simulation is a simulation that uses repeated random sampling to obtain numerical results. In this case, key factors that affect capacity such as running rate, setup time, and overhead rate have significant amounts of uncertainty due to variability in process and handling of deviations.
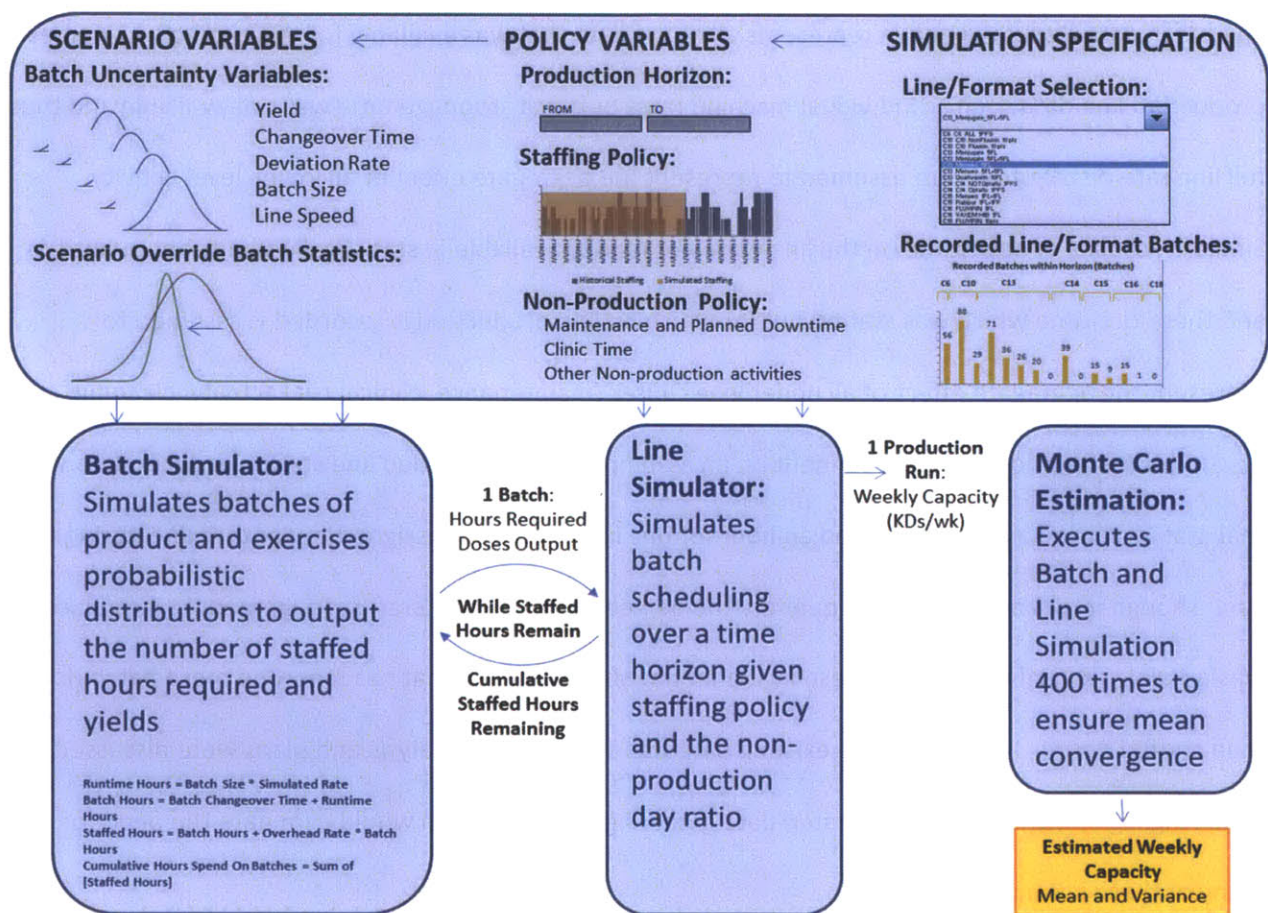

Figure 8 Packaging Capacity Simulation Block Diagram

The model begins with Production Scenario Specification via the model Dashboard. The user specifies the time horizon and packaging line/product/format they would like to simulate. These inputs help the

model identify the specific group of similar batches from 2012 and 2013 from which to generate baseline uncertainty variables.

Gaussian distributions are assumed for several inputs and ratios are derived for others. Baseline values generated may be accepted on the model dashboard or overridden by the user in order to test the impact of changes to production policy or improvement projects. These uncertainty variables are inputs to the batch simulator. The batch simulator simulates many batches, sampling from the uncertain scenario variables to generate batch output and the amount of staffed time required on the line to produce that batch. These batches are then assigned to time on the line by the Line simulator. The Line Simulator keeps track of all hours on the line and staffs the line according to the specified policy variable inputs. Ultimately, the Line Simulator decides how many of the Batch Simulator's batches actually get produced during the simulated time horizon. This output number of doses produced represents a single data-point for the Monte Carlo Estimation. The whole production horizon is run four hundred times to generate a single output mean and variance for the simulation.

4.3.1 Batch Simulator

The Batch Simulator generates individual batches based on probabilistic inputs for batch size, line speed, changeover time, yield and deviation/success rate using an inverse normal function (Batch Size is used as an example):

$$Batch\ Size = MAX(NORM.INV(RAND(), \mu_{Batch\ Size}, \sigma_{Batch\ Size}), MinimumBatchSize)$$

After sampling from the Batch Size (Boxes) and Batch Rate(Boxes/Hour), a value of Runtime Hours is generated representing the amount of time required to produce that batch size at that rate. The

distribution for Batch Changeover Time (Hours) is then sampled to generate the number of hours required for that batch:

$$Batch\ Hours = RunTime\ Hourse + Changeover\ Time$$

An overhead time scalar is then applied which represents the average amount of overhead time required per recorded batch hour on the packaging line under simulation:

$$Staffed\ Hours = Batch\ Hours \times Overhead\ Burden\ Rate$$

Finally, a batch success rate and batch yield rate are applied to generate the number of output doses:

$$If(RAND() < BatchSuccessRate, Batch\ Size \times Batch\ Yield, 0)$$

Thus, the outputs used by the Batch Simulator are the batch yield and the amount of staffed hours used to produce that batch. The Batch Simulator will generate enough batches to fill the staffed time scheduled for production based on the staffing policy input from the Line Simulator.

4.3.2 Line Simulator

The Line Simulator incorporates staffing policy inputs and maintenance to manage availability of the line. A day is first classified as eligible or ineligible based on the weekly daily staffing policy. Production is then assigned or not assigned depending on the probability that a day will be required for planned maintenance, cleaning, or clinical trials. Once the day is assigned, the number of hours of staffing is tabulated for that day. Then the Batch Simulator results are referenced to determine which batch would be in production on that day depending on the cumulative number of staffed hours required to produce batches:

Line Simulator: Simulates Staffing and Batches over the Horizon					
WEEKS 1–53	DATE	SEASON CLASSIFICATION	PRODUCTION	STAFFED HOURS	BATCH IN PRODUCTION
1	1-Jan	WEEKEND		0.0	
1	2-Jan	ELIGIBLE	PRODUCTION	21.0	1
1	3-Jan	ELIGIBLE	PRODUCTION	21.0	1
1	4-Jan	ELIGIBLE	PRODUCTION	21.0	2
1	5-Jan	ELIGIBLE	PRODUCTION	21.0	2
1	6-Jan	ELIGIBLE	PRODUCTION	21.0	2
1	7-Jan	ELIGIBLE	PRODUCTION	21.0	3
2	8-Jan	WEEKEND		0.0	
2	9-Jan	ELIGIBLE	PRODUCTION	21.0	3
2	10-Jan	ELIGIBLE	PRODUCTION	21.0	4
2	11-Jan	ELIGIBLE	PRODUCTION	21.0	4
2	12-Jan	ELIGIBLE	PRODUCTION	21.0	5
2	13-Jan	ELIGIBLE	PRODUCTION	21.0	5
2	14-Jan	ELIGIBLE	PRODUCTION	21.0	6
3	15-Jan	WEEKEND		0.0	
3	16-Jan	ELIGIBLE	PRODUCTION	21.0	6
3	17-Jan	ELIGIBLE	PRODUCTION	21.0	6
3	18-Jan	ELIGIBLE	PRODUCTION	21.0	7
3	19-Jan	ELIGIBLE	PRODUCTION	21.0	7
3	20-Jan	ELIGIBLE	PRODUCTION	21.0	9
3	21-Jan	ELIGIBLE	PRODUCTION	21.0	10
4	22-Jan	WEEKEND		0.0	
4	23-Jan	ELIGIBLE	PRODUCTION	21.0	10
4	24-Jan	ELIGIBLE	PRODUCTION	21.0	12
4	25-Jan	ELIGIBLE	PRODUCTION	21.0	12
4	26-Jan	ELIGIBLE	PRODUCTION	21.0	13

Figure 9 Line Simulator Example

The total amount of product produced in the specified time horizon is divided by the number of weeks included in that horizon to produce a weekly capacity result in Kilodoses per Week.

4.3.3 Monte Carlo Estimation

Finally, the Monte Carlo Estimation Macro runs the Line Simulator four hundred times in order to fully exercise the variability distributions. The following figure shows the structure of these trials which run T weeks in duration (specified by the user) and have an average and standard deviation of weekly production, $\bar{x}_j, \sigma_j$:

Time Horizon (T Weeks of Production)

	WEEK 1	$\cdots$	WEEK t	$\cdots$	WEEK T	$\bar{x}_j, \bar{\sigma}_j$
TRIAL 1 TRIAL 2	$x_{j,t}$ $\cdots$				$\cdots$ $x_{1,T}$	$\bar{x}_1, \bar{\sigma}_1$
$\vdots$						
TRIAL j		$x_{j,t}$ Doses Produced on Week t for Trial j				
$\vdots$						
TRIAL 400	$x_{400,1}$ $\cdots$				$\cdots$ $x_{400,T}$	$\bar{x}_{400}, \bar{\sigma}_{400}$

(left axis label: Simulation Runs)

Figure 10 Monte Carlo Simulation Trial Structure

The resulting sample mean and sample standard deviation pairs ($\bar{x}_j, \bar{\sigma}_j$ pairs) have a mean which

represents the expected range capacity we can expect to see given the underlying variability of the

component variables. Tracking statistics of $\bar{x}_j$ and $\bar{\sigma}_j$ for each of the 400 trials can yield further insights:
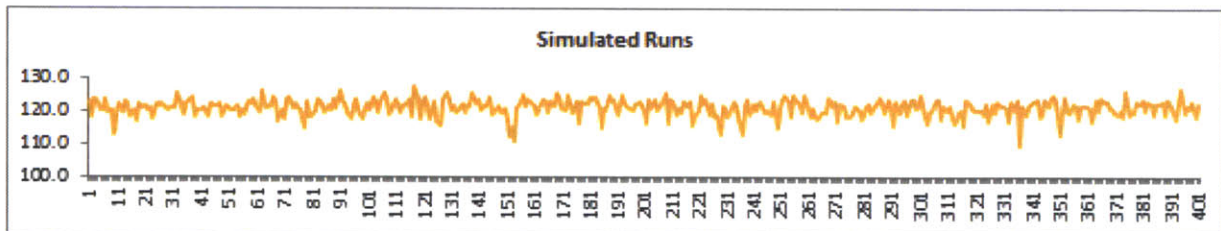

Figure 11 Simulated Sample Mean Weekly Capacity

Taking a running average of the values for $\bar{x}_j$ as the simulation proceeds through the trials, it is possible

to observe convergence. The Simulated Capacity result at each point j, is calculated by:
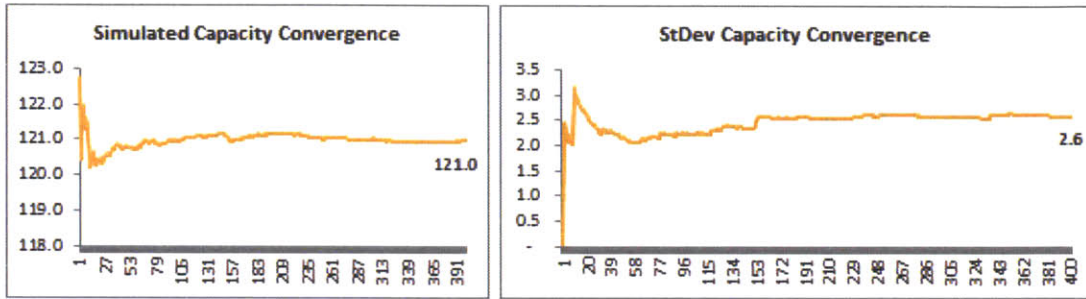
$$y_j = \frac{\sum_1^j \bar{x}_j}{j}$$

Figure 12 Convergence of the Simulation

The Simulated Capacity runs can be shown to converge with the following equation for the variance of

$\bar{y}_j$:

$$Var\ y_N = Var\left(\frac{\sum_1^N \bar{x}_j}{N}\right)$$

$$Var\ y_N = \frac{1}{N^2}Var\left(\sum_1^N \bar{x}_j\right)$$

$$Var\ y_N = \frac{1}{N}Var\left(\bar{x}_j\right)$$

Thus, because capacity and standard deviation values are observed to converge reasonably well after

400 runs, an N value of 400 is sufficient for estimation via simulation.

4.4   Model Inputs

The Packaging Production Simulation Model includes three types of input:

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- Simulation Scenario Specification

- Baseline Production Activity Variables

- User Overrides of Production Activity Variables

4.4.1 Simulation Scenario Specification

The Simulation Scenario Specification inputs ask the user for inputs that specify the group of historical batches from which to derive baseline variables. These batches are determined by specifying a time horizon and the line and packaging format to single out for simulation. These specifications are entered by the user on the dashboard as shown below:

Figure 13 Dashboard Input for Simulation Scenario Specification
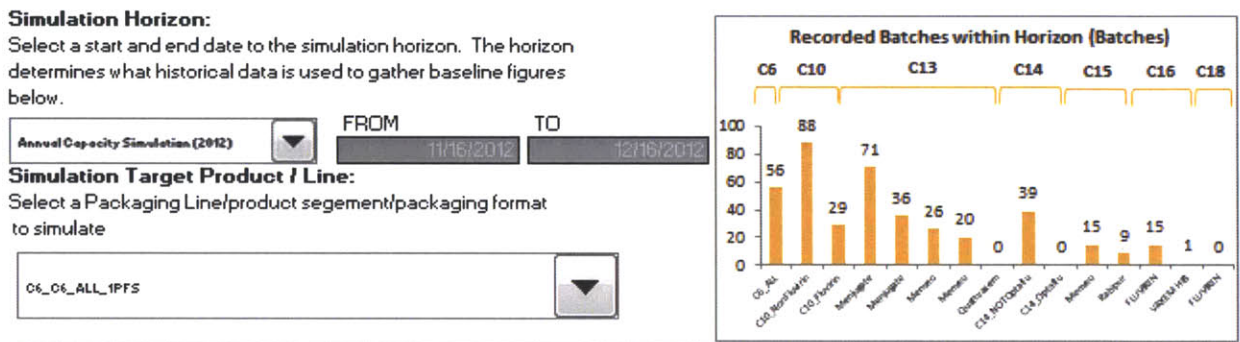
The graph at the right, shows the number of batches available for a specific grouping in the time horizon specified. The model automatically filters for batches which include complete information. Three options are allowed for specifying the time horizon of batches. These include, the Northern Hemisphere Flu Season, Annual, or a Manual start and end date:

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Figure 14 Dashboard Input for Simulation Scenario Specification - Close View

Once the model has identified the batches to include, Baseline Production Activity Variables are generated from the data sources.

4.4.2   Baseline Production Activity Variables and User Overrides

The following section of the dashboard is used to display the generated baseline production activity variables and to allow user overrides of these variables:

Core Simulation Inputs

Baseline historical values are gathered from various sources including Supply Chain Plans, Process Engineering Line Records, SAP Exports, and Standard Operating Policy. New production scenarios can be simulated by overriding baseline values with new values in the *RIGHT* column below:
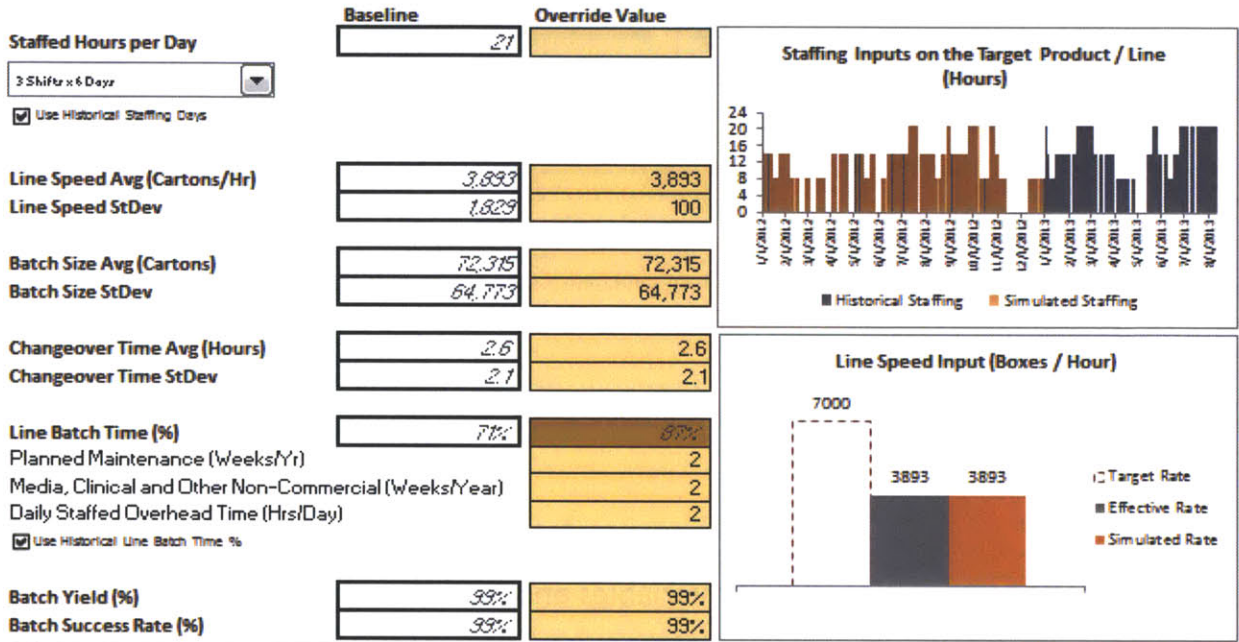
	Baseline	Override Value
Staffed Hours per Day	21	
3 Shifts x 6 Days		
☑ Use Historical Staffing Days		
Line Speed Avg (Cartons/Hr)	3,893	3,893
Line Speed StDev	1,829	100
Batch Size Avg (Cartons)	72,315	72,315
Batch Size StDev	64,773	64,773
Changeover Time Avg (Hours)	2.6	2.6
Changeover Time StDev	2.1	2.1
Line Batch Time (%)	71%	87%
Planned Maintenance (Weeks/Yr)		2
Media, Clinical and Other Non-Commercial (Weeks/Year)		2
Daily Staffed Overhead Time (Hrs/Day)		2
☑ Use Historical Line Batch Time %		
Batch Yield (%)	99%	99%
Batch Success Rate (%)	99%	99%

Staffing Inputs on the Target Product / Line (Hours)

■ Historical Staffing   ■ Simulated Staffing

Line Speed Input (Boxes / Hour)

7000

3893   3893

▢ Target Rate
■ Effective Rate
■ Simulated Rate

Figure 15 Production Scenario Baseline and Overrides

4.5   Outputs

The Packaging Model Simulation's primary output is a value of Capacity and a 95% Confidence interval around that Capacity which is represents the two standard deviation range from the mean for the production scenario under simulation. Output is presented alongside a historical recorded output figure, which is an amount of output from batches that fit the format specifications extrapolated out to the full loading of the line. The latest Rough Cut Capacity Planning estimate for the format and line specified for the production scenario is also presented for a comparison reference.

Additionally, the simulation dashboard also provides an estimated Overall Equipment Effectiveness metric for the production scenario specified.
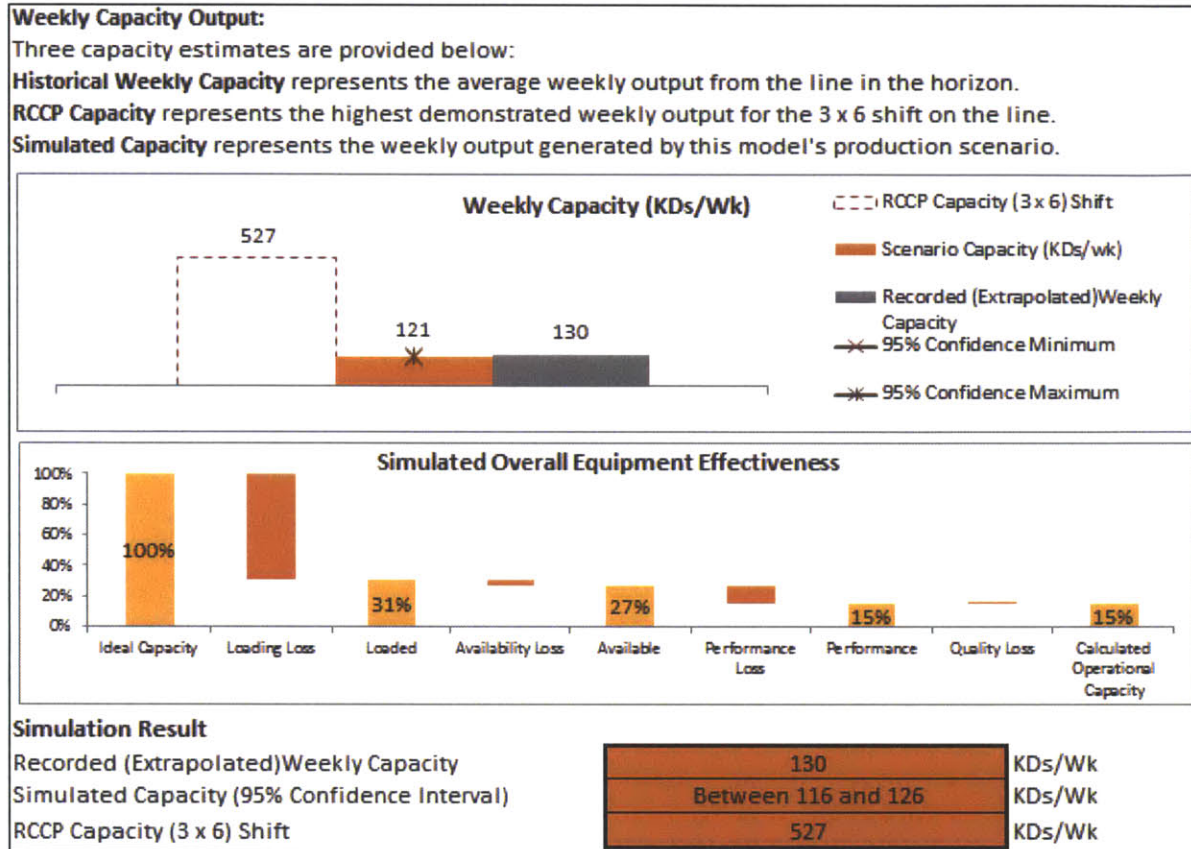

Figure 16 Sample Packaging Simulation Model Output

4.6 Validation of the Model

The output of the Packaging Model Simulation were validated at the baseline values which represent the recorded production policies of the past year. Thus, for the validation of each line, the historical staffing, distributions for line speed, batch size, changeover time, overhead time, batch yield, and success rate were used and the output Scenario Capacity was compared to the Recorded (Extrapolated) Weekly Capacity. Figure 16 shows a comparison for one of the packaging lines.

Lines which had a significant pool of valid batches from which to draw historical baseline inputs matched very well versus historical results. Other production line/format pairs which did not have enough recorded batches or where inaccuracy was suspected with regards to dose unit recording did not validate well. However, because this validation process showed strong validation for lines with good input, the underlying mechanics of the model were validated. As more data becomes available in the future, the model baseline inputs can be updated for each line to obtain a valid baseline from which to simulate. While the process of updating inputs was discussed, the actual task of future updating was outside the scope of this work.

5 Packaging Area Capacity Development

5.1 Capacity / Demand Analysis

5.1.1 Packaging-Allocated Demand Forecasts

In order to understand the demand outlook that each of the packaging lines would need to accommodate, a long-term packaging demand forecast was created. The current demand forecast process is carried out by the Global Product Teams which include value chain management and marketing representation and input. Each year, these teams are asked to create demand forecasts for each product within their product category. These product forecasts and historical packaging format preferences were used as the basis for packaging format allocations. Initial forecasts produced were modified and approved by each Global Product Teams to accommodate best knowledge of packaging format preferences. The following example shows an example forecast approved by the Flu Global Product Team for Flu demand:
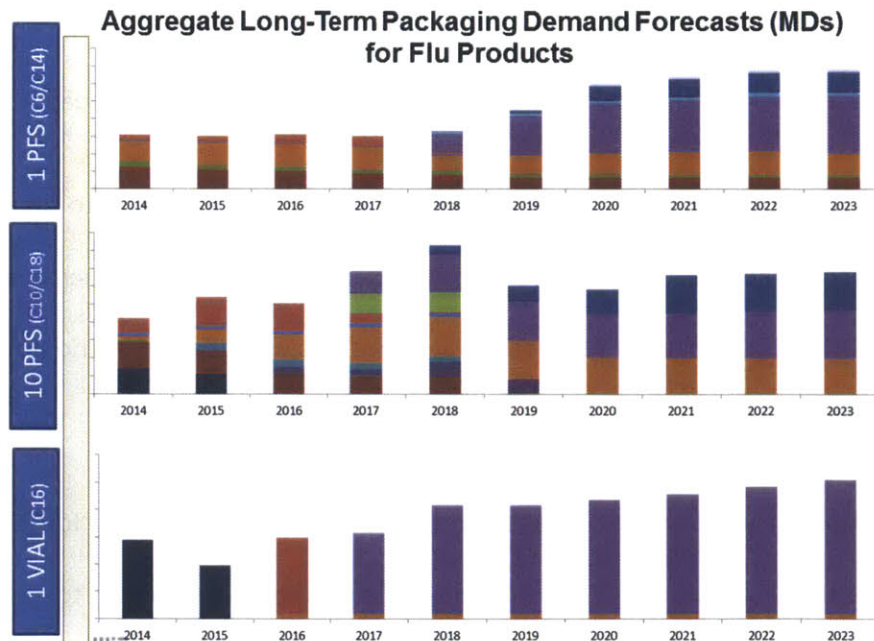

Figure 17 Long-term demand for Flu Products

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5.1.2 Identifying Capacity / Demand Gaps

After formulating long-term demand forecasts, capacity / demand gaps were identified by comparing demand to current maximum capacity estimates under maximal staffing for each year of the ten-year horizon to identify when demand for a packaging format would exceed current capacity . In this process, the existing capacity estimates generated by the Packaging area were used because they would add credibility to the analysis conclusions at this preliminary stage.

Relevant time horizons for production were considered such that capacity to produce for Northern Hemisphere Flu Vaccine demand was restricted to the nine-week window allowed for this seasonal product. Other products which have demand throughout the year were given production windows of 52 weeks. Additionally, because some packaging formats are produced on the same production lines, it is possible to transfer capacity between the two formats. Thus, for this group (single-pack syringe and KIT) capacity for two machine lines and demand for both formats were grouped together to determine potential shortfall for the lines themselves rather than for the packaging format specifically.

Other factors were also considered at this stage including known future changes to capacity and access to contract manufacturing capacity; in the case of probabilistic future capacity (such as an uncertain technology transfer), supply certainty was desired and thus, the worst case scenario (technology transfer failure with upside demand coming in) was used for analysis.

After performing this analysis, syringe packaging formats were identified as areas for long-term concern: multi-pack syringe and single-pack / KIT both faced significant shortfall in the mid to long-term. Therefore, these packaging formats were highlighted for capacity strategy analysis in order to determine

a plan for developing this capacity over time.

Capacity offered by C10 (10PFS blister pack) does not meet future 10PFS demand (Luer-Lock with Needles) for Non-North American NH Flu Products
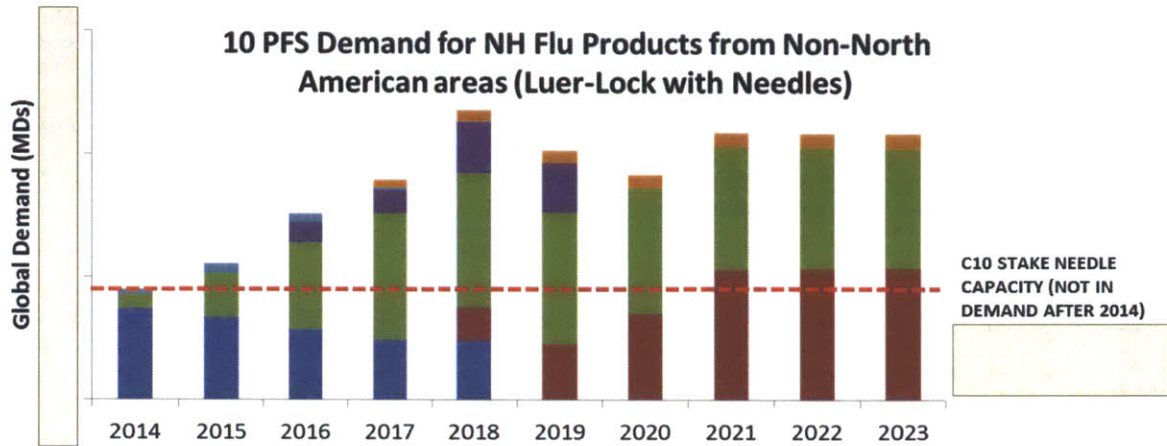

Figure 18 Capacity / Demand Gap Example for the Multipack Syringe Packaging Format

5.2 Production Scenarios

5.2.1 Capacity Lever Rationale and Feasibility

Beckman and Rosenfield also contribute discussion of the levers for capacity expansion and existing

capacity utilization improvement [10]:

- Human Resources Training and Flexibility
- Process and Information Technology Investment
- Facilities Investment
- Suppliers and Subcontractors
- Quality Improvement
- Process Optimization

This project considered capacity levers in the following way which classifies a method as a Performance

Lever, a Utilization Lever, or an Expansion Lever as follows:

Table 2 Capacity Levers Used for this Project

	Capacity Lever	Rationale	Feasibility
PERFORMANCE LEVERS	**Delay Differentiation** by removing the need for country differentiation where possible	Increase Batch Sizing, Demand Aggregation	Initial study for QR code packaging art was proposed by Andrew Kewson. Other methods of referring to country-specific digital content are possible. Regulatory approvals would be required.
	Batch Sizing Optimization (through Minimum Order Quantity)	Increase Utilization and Reduce Changeover Time Impact	Our batch sizes come from aseptic batches and market demand. We can increase capacity up to aseptic capacity for vials if countries can be persuaded to accept higher MOQ.
	Reduce Cancellations of Planned Production	Improve estimates used to smooth planning	Data is available to identify the primary drivers of Cancellations. Further analysis may show easy wins.
UTILIZATION LEVERS	**Cross –Qualify Products** to Increase Flexibility and Balance the Load	Load Balancing	C13 is taking on the bulk of Bexsero demand which is currently only qualified for C14. Others might be shifted from C14. Could any demand shift to 1 vial? C18 is currently only qualified for US products.
	Optimal Product Allocation	Improve Utilization through Load Balancing and Rates	Demand for multi-pack syringes comes largely from Public tenders where administrators hold lots of inventory and must minimize space. Is multi-dose vial an option?
	Increase Line Loading/Staffing	Increase Utilization	3 x 5 shift is feasible on an ongoing basis. Training/negotiation will be required for 3 x 6.
EXPANSION LEVERS	**Upgrade Existing Lines**	Increase Throughput	Both C10 and C18 are operating with rates comparable to their maximum machine rates but others may be possible to upgrade.
	Purchase New Lines	Increase Capacity	Yes, purchasing a new line is possible though a building expansion may be required. The new lines could be either Dividella 10pfs (7.5M Euros est), KIT (8M Euros est), and/or 10vials (4.5M Euros est).
	Outsource Packaging / Utilizing other resources	Increase Capacity	Holly Springs capacity is incorporated for multipack syringes. Ankleshwar has capacity only for vials on the non-US/non-EU markets. Outsourcing should come only after staffing increases at NVD plants.

A Performance Lever was a lever which strove to increase the yield at a constant utilization level. A Utilization Lever was classified as a lever which increased utilization of existing equipment. An Expansion Lever was classified as a lever which increases the baseline capacity available by adding additional resources. Each lever was discussed with the packaging area to understand the feasibility of such an option.

Capacity levers for this project were prioritized on the basis of implementation difficulty followed by perceived cost. This prioritization scheme was not viewed as an optimal solution, but would follow the feasibility ordering of the levers to execute, as perceived by packaging operations staff. Thus, utilization levers, which rely solely on internal policy changes which incrementally change existing processes were given top priority; performance levers, which rely on more substantial changes across departments or at

the customer; Expansion levers, which are the most costly in the short-term, were given lowest priority to be utilized if other levers had been exhausted. The methodology of simulating scenario capacity does not depend on having a consistent or optimal project prioritization scheme although it would certainly benefit from one. Instead, as previously mentioned, the simulation model allows for experimentation to show the impact of potential projects and proposals.

5.2.2 Syringe Packaging Scenarios: 10PFS Northern Hemisphere Flu Example

Below, it is possible to see an example of how the output of the Packaging Production Simulation Model were used to simulate the nine-week capacity of a single production line under multiple production scenarios. A brief description of the inputs used for this process is included below as an example.

1. DISCONTINUE C10: This scenario represents the impact of the known future reduction in capacity due to obsolescence of the existing production capability caused by coming regulation. Because the current production line cannot be used, capacity goes to zero. This scenario did not use the Simulation Model.

2. CROSS-QUALIFY + RETROFIT C18 WITH LUER-LOCK NEEDLE CAPABILITY: A new line not currently in use for these products is capable of meeting some demand if the line is retrofitted and the production process is validated. These steps were deemed feasible by the Packaging area. Historical staffing levels and batches on C18 were used to generate baseline mean and standard deviation values.

3. REDUCE OVERHEAD TIME AND MOVE TO 3x5 SHIFT: Under this scenario, two changes were made. Instead of using historical staffing of C18, a three shift per day, five days per week policy is instituted resulting in significantly more staffed hours available. Additionally, a project is

instituted to reduce overhead time such that a larger percentage of staffed hours on this line are used for production rather than overhead. 5% of time is used as an overhead ratio goal here.

4. MOVE TO 3x6 SHIFT AND INCREASE BATCH SIZE BY 50%: Under this scenario, a sixth day of three shifts (an additional 21 hours) is added to the production policy and batch sizes are increased to 120% of the mean batch size for current demand on C18.

5. INCREASE BATCH SIZE TO 120% OF CURRENT C10 BATCHES: Projects that could support this type of shift include removing packaging differentiation such that batches of similar products designated for different countries may be produced together or changes to the Minimum Order Quantity set out for vaccine tenders. In this and the previous scenario, the variation of batch size was kept constant to show no change in the variability of demand.

6. NEW LINE LUER-LOCK (C19) ADDED TO C18 CAPABILITY: In this scenario, all previously discussed projects have been implemented on C18 and a new line similar to C18 is installed as a capacity increase. This type of installation would need to be timed according to the previously discussed capacity strategy methodology in order to be available in time to meet production goals. In this case, installation was recommended as soon as possible given 2014 forecasted demand.

The sixth scenario represented below shows enough capacity to pass the 80% of demand service level desired for the nine-week production horizon. Additional demand for multi-pack syringe packaging from Northern Hemisphere Flu Season will be met later in the season rather than via Build-to-Stock.

Utilizing OEE Performance Levers and Utilization Levers, C18 cannot meet forecast Rosia demand alone. A new Luer-lock line is required for mid-term demand (Expansion Lever).
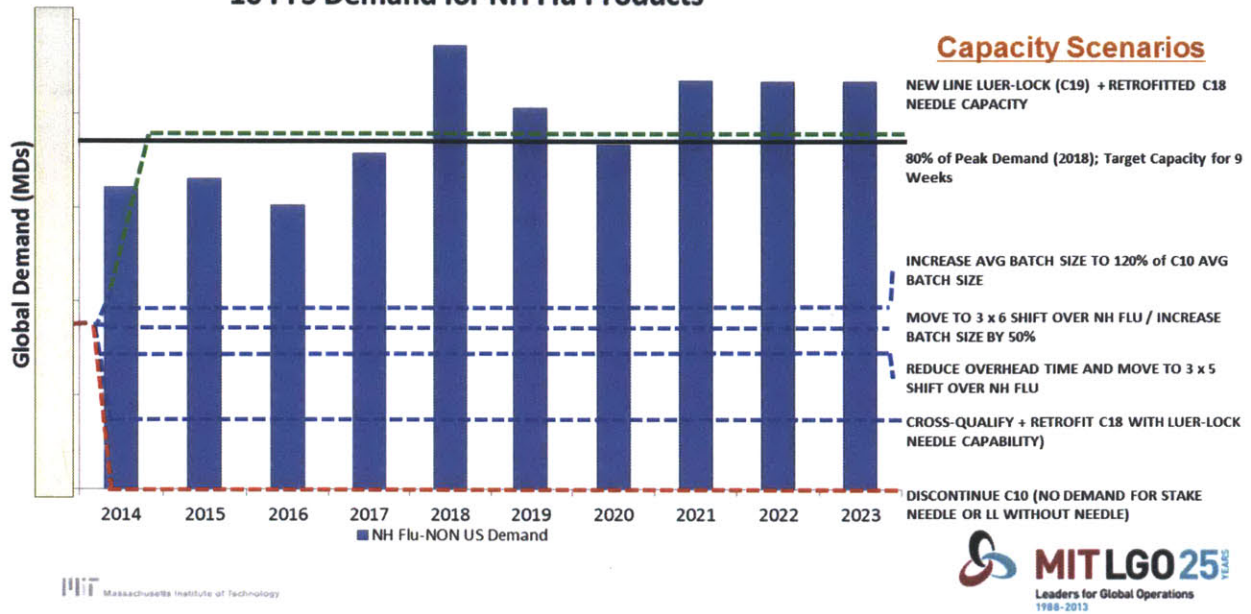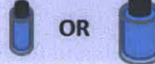
10 PFS Demand for NH Flu Products

Figure 19 Capacity Scenarios Superimposed on the Long-term Demand for Multipack Syringe Format

5.3   Key Recommendations

Based on analyses conducted similarly to the example discussed above for multi-pack syringe packaging, specific recommendations were generated to develop capacity for single syringe and KIT packaging. Per the results of the Capacity/Demand Analysis and Packaging Capacity Simulations, the following key recommendations were made to develop packaging capacity to meet long-term demand:

Table 3 Recommendations for Packaging Strategy Implementation

	Packaging Line	PACKAGING FORMAT		RECOMMENDATION
PRE-FILLED SYRINGE	C10	10 Pre-Filled Syringes / Box, 1 Ds / PFS		To meet long-range 10PFS demand :
	C18	10 Pre-Filled Syringes / Box, 1 Ds / PFS		-Products currently qualified only on C10 must be qualified on C18 (*Currently only Limited Flu Products and Bexsero*), OEE improvements are required. -A new line (C19) must be purchased with Luer-Lock + Needles capability -Batch Size increase options should be evaluated as valuable capacity levers
MULTI	C6	1 Pre-Filled Syringe (PFS) / Box, 1 Ds / PFS		To meet long-range 1PFS demand:
	C14	Kit 1 Pre-Filled Syringe 1 PFS w/ Needle		-Increase staffing and pursue packaging efficiency projects to improve OEE metrics for both C6 and C14. -If necessary, convert C10 to mono-PFS and employ batch size increase levers -Carefully watch long-range demand estimates in the coming 2-3 years. If high QIV and aQIV demand are realized as currently forecasted, one or two new 1PFS lines may be required. Space can be found by retiring C10 at that time.
VIAL	C13	10 Vials / Box, 5 or 10 Ds/Box		Under worst case conditions where no outsourcing relief from a 3rd Party is possible, maximal shift, multi-pack vial capacity appears just enough to match demand (with no buffer for variability).
	C15	2 Vials / Box, 1Ds/2Vials		C15 appears to have enough capacity to cover demand, even during the NH Flu peak demand period
	C16	1 Vial / Box, 10 Ds / Vial	OR	C16 appears to have enough capacity to cover demand, even during the NH Flu peak demand period

Per the results of the Capacity/Demand Analysis it is recommended that Novartis Vaccines build on this project's capacity uncertainty results, acquire recommended new machinery and focus on projects to reduce stoppage time on the key lines resulting in inconsistent and reduced throughput/capacity. Reducing uncertainty in the system would lead to a lower requirement for a time buffer for capacity expansion based on more certain estimations of current and future capacity.

As with any strategy, there are limitations to modeling and some operational factors must be accounted for afterwards. In this case, the physical space available for development is limited and so a plan was required to account for the recommended changes. The following figure shows this plan. In the near-term the proposed new multipack syringe line is recommended to replace a disused line (which used to

supply Polio ampoule dispensers). As demand for single pack syringes and KIT format increases, an expansion to Building 22 is proposed to allow for the recommended capacity expansion of that format.
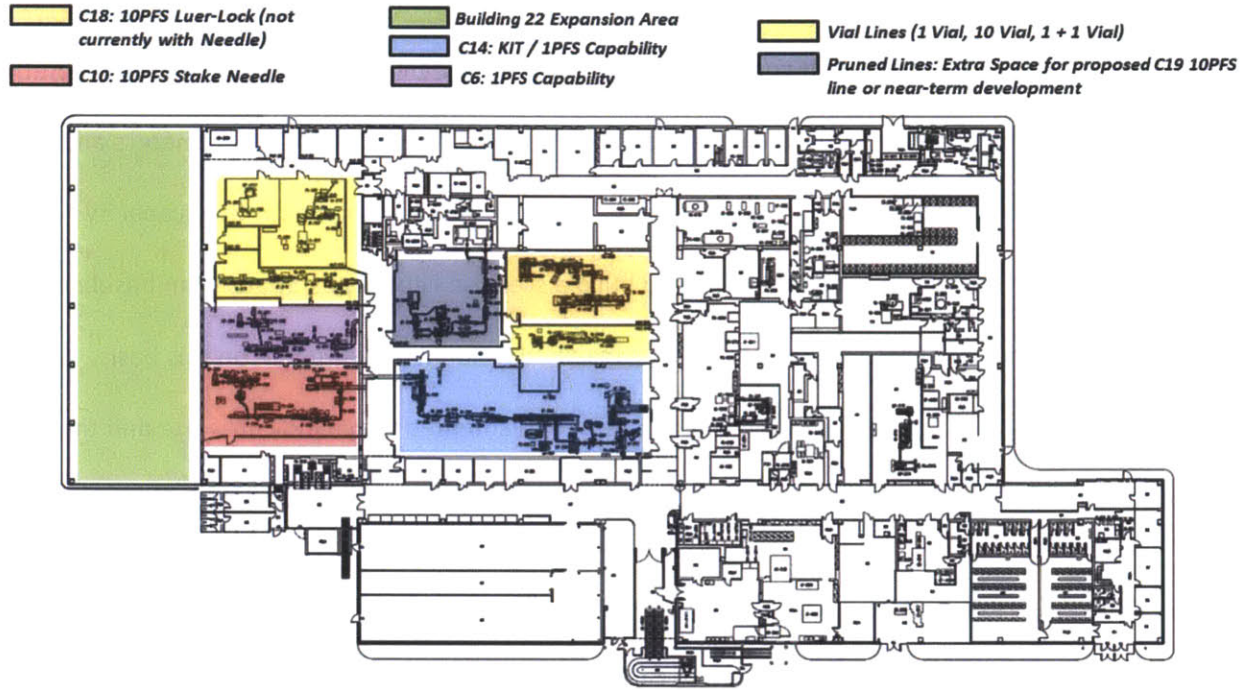

C18: 10PFS Luer-Lock (not currently with Needle)

C10: 10PFS Stake Needle

Building 22 Expansion Area

C14: KIT / 1PFS Capability

C6: 1PFS Capability

Vial Lines (1 Vial, 10 Vial, 1 + 1 Vial)

Pruned Lines: Extra Space for proposed C19 10PFS line or near-term development

Figure 20 Physical Layout of the Recommended Packaging Area Configuration

6 Conclusions & Recommendations

6.1 Review of the System

This project sets the foundation for a capacity strategy model which can account for uncertainty in capacity and production processes. It completes the initial stages of this development by implementing a capacity model which draws means and variances from historical batches for key parameters and outputs a range of expected capacity over a time horizon. An example is shown for how capacity projects and policies may be simulated together to build a scenario capacity estimate from baseline historical batches and initial recommendations for capacity development are made on this basis. An overarching capacity strategy model is described but not implemented which indicates size and timing for uncertainty-hedged capacity expansion. Key limitations preventing implementation include:

- Inadequate recorded data for batches of some line/format pairs

- Time-estimations for implementation of capacity levers was allegorical and tight coordination of capacity expansion timing would be risky

- Multiple format/line simulation is not yet possible although this is not necessarily a problem for dedicated periods such as for Northern Hemisphere Flu production season.

- While projects can be combined into many production scenarios, this model provides no aid in selecting from among viable options

However, based on the assumptions discussed in Section 4.2, the existing system does meet the goals of the project as set out by the Novartis Secondary Manufacturing Strategy Group; current capacity is estimated reliably and explanation is provided for differences with current estimation methodology. Supply/demand analysis insights were communicated and recommendations were made in order to address capacity constraints based on simulation of packaging area production scenarios. These initial

recommendations form the basis for an overall packaging strategy which includes integration of the simulation model into a broader recommended model for capacity strategy under conditions of uncertainty.

The use of Monte Carlo Simulation lead to positive changes in the packaging area at Novartis Vaccines because the packaging area was able to directly see the links to and usage of the batch data generated in their department. This transparency lead to general agreement with the model's capacity results and to buy-in for proposed budgetary priorities in capacity expansion and production policy changes to meet long-term demand. The model was used by the Secondary Manufacturing Strategy Group in development of the 2014 Strategic Plan for Novartis Vaccines Secondary Manufacturing and further development to improve and expand scope of the model is planned.

6.2 Further Development of the System

Problems with manual collection of batch data were known by packaging area operations managers from the beginning of this project. A system has been identified and installed on one line which would enable automatic collection of production line data but correlation with batches and database infrastructure has not yet been completed and this initiative had lost momentum at the beginning of this project.

As initial results of this work were presented throughout the project, momentum grew around completing this system and integrating its results with the global resource management and planning database. As part of this project, specific data structures were recommended for collection from the system to enable daily measurement of operational equipment effectiveness. Increasing the accuracy/consistency of data such as production start and end times, units of quantities produced

(doses v. cartons), staffed hours on the line, and non-production activity time logging would greatly improve the efficacy of the simulation model.

Maintenance in this area and future development of that capability constitutes the greatest opportunity and risk in ongoing use for this system. Thus, handoff of the Packaging Area Simulation Model to the Secondary Manufacturing Strategy Team focused on communicating the vision for how this system was built to allow for easy input from SAP exports once packaging line data was available in that system.

Additional ideas presented for further development of the simulation are described below. These focus on presenting a dashboard of production line activity which are thought to provide insight for comparison between products and production lines and to recognize patterns over time.
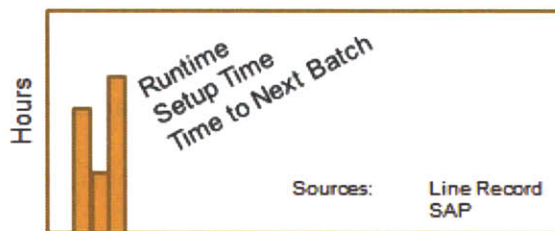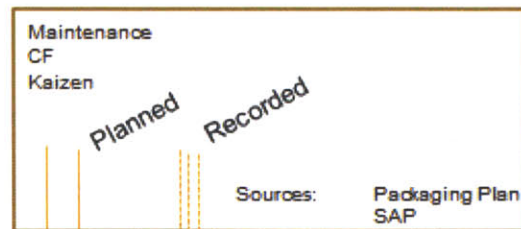

Recorded Batches
Why?: Would help to understand where most time is spent and if it varies across batches
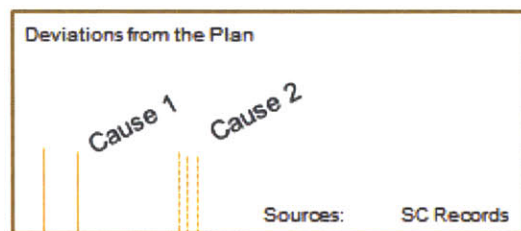
Weeks
Why?: Would help understand what causes deviations on each line and when during the year these occur
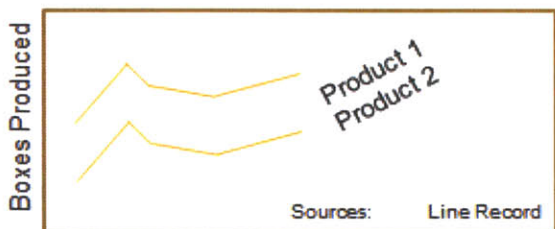
Weeks
Why?: Would help to visualize how capacity is allocated on the line and how often product switches are occurring

Days
Why?: Would help explain non-production days observed when the line is staffed and visually how often these days occur.

Figure 21 Potential Extended Features of the Packaging Capacity Model and their Rationale

6.3   Recommendations for Future Initiatives

It was further recommended that Novartis Vaccines take steps to understand the impact of upstream production planning on staffing decisions, and thus, the line's utilization. Current implementation of the simulation model smooths production by setting a consistent staffing policy over the time horizon. However, current staffing decisions are made based on upstream job availability. Under conditions of high utilization with more demand coming from customers, it is reasonable to expect that job availability for packaging would allow this smoothing to occur. However, steps can be taken to investigate the impact of having an unsmooth production schedule in terms of back-ups due to demand variability and the impact of manual last-minute re-planning by Site Supply Chain Team. Highlighting this impact could help Novartis Vaccines build momentum for demand smoothing both internally and externally and a short-term resource tracking and planning system is recommended to gather and prioritize a job queue.

Ultimately, smoothing demand for packaging facilities can be accomplished by insourcing production to stabilize peak/off-peak demand. This demand smoothing could allow Novartis Vaccines to run at a consistent staffing level and to train sufficient staff to operate at 3 x 5, 3 x 6, or 3 x 7 shifts continuously. Consistency in staffing is thought to boost learning and loyalty and may lead to its own productivity increases as a result.

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