SUPPLY CHAIN PLANNING FOR CLINICAL TRIALS

A PRACTICAL GUIDE

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Contents

Preface

Welcome to the exciting, dynamic, and complex world of clinical trial supply chain management! If you're reading this book, there is a good chance you're responsible for managing some aspect of the clinical trial supply chain or are interested in learning how to do so. Congratulations, you've made an excellent career choice. This work is deeply impactful as the decisions made by clinical supply chain planners directly impact millions of clinical trial participants around the world who need access to cutting-edge therapies. Your work contributes to extending and saving lives on a grand scale.

The top priority of this job is to ensure that every person who enters a clinical trial receives the drug they're expecting when they expect to receive it. Theoretically, producing the right amount of drug for a clinical trial should be easy. The total amount of drug required to service a clinical trial is known because the clinical protocol prescribes the number of subjects who will enroll and how much drug each subject will take over the duration of the trial. Multiply these two variables and we have our supply requirement for the trial. In a world of unlimited resources, we could simply make double or triple that amount of drug, and we'd have more than enough to supply the trial. I've seen that strategy employed in my past!

But we don't live in a world of unlimited resources. This is particularly true for the burgeoning class of pre-commercial biopharmaceutical and cell therapy companies for whom every dollar is precious. Supply chain management gives us the tools to develop an optimal supply plan that adequately supplies the trial while also minimizing the amount of money it takes to do so. Across the industry, there has been increasing recognition that effective supply chain management is a potential gold mine of savings for a company. One large-molecule drug substance batch costs anywhere between $2 and 5M, enough to fund a Phase I study (or two) on its own! Meanwhile, a 2016 study showed that drug companies waste almost half of the clinical trial supply they produce.[1] More recent data suggests that the number may be as high as a staggering 75%.[2]

Combatting this waste epidemic starts with better supply chain planning. The word planning has a specific definition in the supply chain lexicon. It is the process of optimizing the manufacture and delivery of goods by balancing supply and demand. When supply is balanced with demand, the consumer gets what they expect, when they expect it, and waste and costs are minimized throughout the supply chain. Simply put, better planning leads to better outcomes.

That's why I decided to write this book. I've worked in clinical supply chain management for over 15 years, partnering with hundreds of dedicated, talented colleagues who are committed to eradicating disease and improving lives. Many people who work in the biopharmaceutical sector have received extensive training in their area of expertise. Doctors, chemists, biologists, and pharmacologists all have degrees that underpin their day-to-day work. However, when you look at

the backgrounds of people who work in biopharmaceutical supply chain management, you'll often find a hodgepodge of degrees and backgrounds. While some people do have formal business training via business school or have past experience in logistics or a related discipline, many don't. And even amongst those with a specialized degree, their exposure to the nuances of clinical trials is often limited. This means that most people walking into a clinical supply chain role have never been trained or had exposure to a clinical trial supply chain. Even for those of us who do have formal training in business and supply chain management, we've had to relearn much of what we were taught in the classroom because the practical application differs so much from the theoretical concept in the world of clinical trials.

This is because supply chain planning for clinical trials is fundamentally different from managing a commercially available good that can be purchased at your local grocery store. The demand forecast is built on a completely unique set of assumptions. Supply planning requires an understanding of not only the manufacturing steps in the process but also the quality standards and regulatory requirements of the biopharmaceutical space. Throw in relatively short expiry periods, a heaping dose of stakeholder complexity, and enormous costs, and you've developed a recipe where newcomers to clinical trial supply chain management are often lost and must learn their job the hard way – through trial and error.

This book aims to put a stake in the ground for clinical trial supply chain planning. You've probably heard the phrase "proper planning prevents poor performance," and nowhere is that truer than for clinical trials. There are so many variables in play that can impact supply availability; it takes a trained professional to understand what to do, when to do it, how to do it, and who to work with to make sure it's all done properly.

Unfortunately, there isn't one "right" way to do this. Every biopharmaceutical company, every product, and every clinical trial is unique and has its own set of considerations and challenges. But there are a set of guiding principles and concepts that every clinical planner needs to be aware of and understand. This book attempts to lay those out in a way that's approachable for someone who is entirely new to supply chain management or to clinical trials. Please understand that the content here isn't designed to cover every possible approach, strategy, or scenario. The space is too complex and moves too fast for that, and even an encyclopedia wouldn't have enough room to contain it all. The broad strokes are here though, and a good bit of detail, too.

While this book spends a majority of its time on supply chain planning in the traditional context, there is much more to discuss than just demand and supply planning. To reach the broadest audience possible, the book is laid out in three sections:

- *Clinical Supply Chain Foundations:* Chapters 1–6 are intended for the audience who has never been formally trained in supply chain management or worked on a clinical trial before. These chapters introduce the reader to general supply chain management, clinical trial design, the pharmaceutical supply chain, how quality impacts the clinical trial supply chain, regulatory considerations, and the randomization and trial supply management technology. The intent of these chapters is not to cover every potential topic in detail but rather to provide a broad introduction of the concepts that are most relevant and important for supply chain planning.
- *Supply Chain Planning for Clinical Trials*: Chapters 7–19 comprise the majority of the text and offer a deep dive into the world of supply chain planning for clinical trials. Beginning with an overview of the objectives and elements of demand and supply planning, this section walks the reader through the supply chain planning process in a step-by-step fashion. Demand forecasting, finished product supply planning, finished product distribution planning, expiry planning, and

upstream drug substance and drug product planning are all covered in extensive detail. More advanced concepts like aggregate forecasting, attrition, SKU-switching, and low case-high case planning are also given attention. Supply chain planning in this space is about much more than just the mechanics of creating and maintaining a plan though. It's also about effectively using data to monitor and communicate supply chain performance. And effective business process design and implementation are necessary to get information to the clinical planner and to supply outputs to the stakeholders who need to act on the plan. We'll cover all of these points in this section as well. Special note should be made of Chapter 16, which takes the reader through a day in the life of a clinical planner and provides insight into what makes the job both tremendously exciting and equally challenging. Chapters 17–19 introduce nontraditional clinical trial supply chains including comparators, just-in-time supply chains, and direct-to-patient supply chains and talk about supply chain considerations holistically from both a planning perspective and an operational perspective.

- *Additional Clinical Supply Chain Considerations:* Chapters 20–23 conclude our journey by touching on other aspects of clinical trial supply chain management that influence supply chain planning specifically. Contract manufacturing and logistics are two fundamental areas of the clinical trial supply chain, and planners who are familiar with the intricacies of these spaces tend to produce better plans. It's also impossible to conclude a review of supply chain planning without touching on the tools and technology that clinical planners use to create and maintain their plans. We conclude with a review of the final step of the clinical development process, commercialization, and how to integrate the clinical and commercial supply chains within an organization.

There is also an appendix that catalogues the data elements and equations used in the supply chain planning process, and a glossary that catalogues the definition of key terms, of which there are many. Every chapter concludes with a summary of key takeaways for the reader to consider. More experienced readers may want to glance through the key takeaways first, and if they're familiar with the content, then the reader may choose to skip ahead to more advanced content.

For those readers who are grizzled veterans, you will likely find yourself disagreeing with some of what's recommended here. Good! This book also intends to provoke, and it's my sincere hope to have more discussion in the future about the merits of weeks versus months-of-supply or to challenge my assumptions on just-in-time manufacturing's relevance for clinical labeling. Our industry needs more conversation, more debate, and more transparency when it comes to supply chain planning for clinical trials. We can do better as a collective, and I want this book to push all of us toward more innovation and better performance.

Supply chain planning for clinical trials is a difficult job. It requires expertise in supply chain management and clinical trial design, analytical skills, strategic thinking, and people who can successfully collaborate across functions, cultures, and companies. This is also an incredibly fun, stimulating, and rewarding job. Our industry needs good people who are committed to this work, and people who have the fundamentals to do this work well. My sincere hope is for this book to engage those who are interested, to educate those new to the role, and to reinvigorate those who have been at this work a long time.

Thank you for reading.

-Ryan Mills

Notes

1 Lamberti M., Hsia R., Mahon C., Milligan C., Getz K. (2016). Assessing Global Clinical Supply Logistics. *Applied Clinical Trials* October/November 2016: 26–34.
2 https://lifesciences.n-side.com/blog/decrease-clinical-trial-supply-chain-waste-even-more-with-the-n-side-supply-app-refined-algorithm

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This book would not have been possible without the contributions of so many, beginning with Wiley and my first managing editor, Dr. Julia Squarr, who saw the value of creating a book on this topic. Dr. Squarr encouraged me to think broadly and to make the book as educational and accessible as possible for people who are interested in learning more about our industry and this space in particular.

I recognize the Association for Supply Chain Management (ASCM) for granting permission to reproduce their Supply Chain Operations Reference (SCOR) model in Chapter 1. The SCOR model is foundational to understanding modern supply chains and provides important context for a large amount of content that's covered in later chapters. I also recognize the International Council for Harmonisation (ICH) for allowing content from their guidelines to be reproduced in works like these.

I'm inspired every day by the people I work with, particularly my supply chain colleagues in industry. Krishna, Emily, Patty, Vipul, and Ben have taught me so much about why people matter more than anything else in the supply chain field. Their dedication, willingness to both teach and learn, and their ambition to create a world-class supply chain have provided boundless inspiration.

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Finally, and most importantly, thank you to my family, who have supported me in this journey from inception to publication. To my wife Crisel, I love you to the moon and back, and I'm so appreciative of all the time you've given me to pursue this passion project. And to my kids, Olivia and Alex, I hope this work will provide a source of inspiration that you can accomplish anything and change the world in a positive way when you set your mind to it.

1

Supply Chain Management

1.1 Supply Chain Management

The goal of this chapter is to introduce basic supply chain management principles. Before understanding the nuances of pharmaceutical supply chains, it's helpful to have a general summary of what a supply chain is, the nodes within the supply chain, and the goals of supply chain management as a discipline. The terms and concepts shared in this chapter underpin the remainder of the book, so this is an excellent starting point for those without a theoretical background in supply chain management.

A supply chain is a network of suppliers, manufacturers, and distributors that collaborate to manufacture a good/product and make it available for consumption. Supply chains are responsible for delivering the simplest items, from fresh strawberries at a farmer's market delivered by truck that morning, to the most complex items, like biopharmaceuticals that require dozens of suppliers and manufacturers. Supply chains have existed for hundreds of years, but they have taken on special importance over the last few decades. Technological advances in manufacturing combined with the advent of the internet have enabled supply chains to stretch around the world, and they can react to consumer requirements almost instantaneously. We now take it for granted that we can order an item on Amazon, and it will be delivered within hours or days.

As modern supply chains have stretched themselves further and further across suppliers and continents, they have become more vulnerable to disruption. War, natural disasters, and political–economic turmoil can all derail a supply chain from delivering on its intended promise. These risks became particularly clear during the COVID-19 pandemic and its aftermath when basic goods such as toilet paper and more advanced goods like microprocessors became scarce or weren't available at all. These shortages illustrated how important properly managed supply chains have become to both the global economy and the individual consumer.

The supply chain itself is a sequence of interconnected nodes with a manufacturer standing as the central node in the chain. Upstream of the manufacturer are a set of first-degree suppliers who provide the components needed to make the good. First-degree suppliers may have suppliers of their own – **second-degree suppliers** – who provide them with the raw materials or components they need to make their product. Like a spider web, supply chains can spiral out for several nodes before hitting basic raw materials. Downstream of the manufacturer is the consumer. In most cases, an intermediary such as a retailer, warehouse, or pharmacy will store the good. The connection between these upstream and downstream nodes is why these networks are called supply chains.

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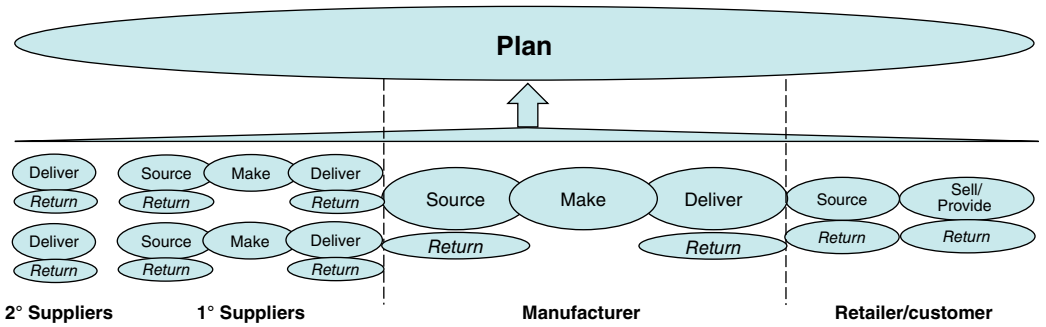

Figure 1.1 Supply Chain Operations Reference Model. *Source:* With permission of APICS[1]

The Supply Chain Operations Reference (SCOR) model that's been developed by the Association for Supply Chain Management (ASCM) provides an excellent diagram of the basic elements of a supply chain.

Figure 1.1 shows the SCOR model, which lays out the four core processes involved in supply chain management:

- *Plan*: The act of developing the supply chain strategy. Planners are responsible for determining how much material will be procured or produced, when sourcing or manufacturing activities will take place, and where goods should be distributed through the supply chain. Given the importance of developing an optimal supply chain strategy, planning is the focus of this book.
- *Source*: The act of purchasing or acquiring a good (e.g. a raw material or component) that is needed to facilitate a downstream manufacturing step. Suppliers provide these goods to downstream parties.
- *Make*: The act of producing a good that will be used in a downstream step of the supply chain or sold as the final product. Manufacturers make the components and products within the supply chain.
- *Deliver/Return*: The act of providing a good to a downstream node in the supply chain such as a manufacturer, retailer, or consumer. Return is the act of returning a good to an upstream node of the supply chain. Transportation service providers (TSPs) and couriers ship raw materials, components, and goods through the supply chain.

Supply chain management is the discipline of planning, coordinating, and executing supply chain activities. It has been recognized as a separate field from manufacturing operations since the 1980s. Following the development of computer hardware and software applications that enabled tracking sales, manufacturing, and logistics activities, it became possible to develop cohesive analyses and strategies incorporating each of the supply chain processes. Supply chain management is now a core function whose goal is to ensure sufficient supply of a product to meet consumer demand at the lowest cost possible.

To achieve this, it's not enough to just plan, source, make, deliver, and then call it a day. The supply chain does not exist in a vacuum, and the external environment around it is constantly changing and evolving. Therefore, another central tenet of effective supply chain management is to appropriately manage supply chain risk. A supply chain risk is anything that can disrupt the supply chain from delivering sufficient supply where and when it's needed. There are many categories of supply chain risk; demand risk, economic risk, environmental risk, sociopolitical risk, and ethical risks are all examples. An effective supply chain management strategy takes these risks into

account and attempts to build resilience within the supply chain. Supply chain resilience is the ability of the supply chain to withstand the realization of these risks. If a war closes access to a key market or if a natural disaster shutters a critical supplier or if a distributor is found in breach of contract, does the manufacturer have strategies in place to enable the supply chain to continue functioning?

How much, when, and where are the questions at the heart of supply chain management. To answer these, supply chains need three elements operating in harmony – teams of people to do the work, well-defined business processes that enable efficient execution, and data and technology to facilitate the flow of information: People–Process–Technology. People come first in this equation because supply chain management is the ultimate team sport. Collaboration is the secret ingredient because no actor can succeed without the partnership of their upstream and downstream partners.

A business process is a sequence of tasks designed to accomplish a specific objective and to ensure that information is generated and passed to the stakeholders who need it to act. Business processes provide structure to supply chain activities and ensure consistency across task execution. Meanwhile, technology is the great enabler of supply chain management. The internet, big data, and tailored supply chain systems have combined to put an incredible amount of data at a user's fingertips. The world's best supply chains are armed with well-trained people, well-defined business processes, and well-designed technology solutions that enable processes to run efficiently and people to make good decisions.

We will spend the remainder of this chapter elaborating on the core elements of the supply chain: plan, source, make, and deliver/return. Each section below will describe the purpose of the process; how the process is executed; strategic considerations, including how to manage risk within that process; and the stakeholders responsible for making the process happen. After reviewing each process, we will analyze how data and metrics are used to drive the supply chain and improve supply chain performance. Then, we will conclude the chapter by revisiting supply chain management within the framework of People–Process–Technology before finishing with key takeaways.

1.2 Plan

The definition of planning is "to create a detailed proposal for doing or achieving something.[2]" Planning determines activities within a supply chain that need to be executed, and it takes place at every level. With that said, there is one planning process that governs the entire end-to-end supply chain – demand and supply planning – and it is the primary focus of this book. Demand and supply planning takes a demand forecast for a good and converts that data into a supply plan for production and distribution. This process begins with demand forecast generation, where demand is defined as the quantity of a good required by a consumer of that good. The demand forecast indicates how many units of the good are required within a specified timeframe (e.g. days, weeks, months, or years). The demand forecast for the finished good is also known as independent demand because this demand is independent of any other variable than the consumer's needs. The finished good demand forecast creates a requirement for supply to meet that demand. Supply is the quantity of a finished good that a manufacturer must produce to meet demand, and the supply plan indicates how many units need to be produced or distributed to a location within a specified timeframe.

Once the supply plan has been generated, the supply needs to be allocated to each source of demand. For a commercial good, these sources may be an online store or a brick-and-mortar retail

location. In a simplified example, if the total demand for a bicycle over one year is 1000 units and that demand is projected to be spread evenly at 500 bicycles apiece between two locations, the supply plan may call for 1200 bicycles and for 600 to be sent to each location. The additional 200 units of supply is safety stock, and these extra units are intended to protect against demand uncertainty. In other words, what happens if demand does not split evenly according to the forecast, and 600 consumers (each wanting one bike of course!) show up to one store and 400 to another? Or what if demand exceeds expectations and 550 consumers show up to each store?

The finished good supply plan serves another purpose. Where the independent demand forecast creates requirements for supply, the finished good supply plan creates requirements for the components and materials needed to produce those finished goods. To continue the example above, the finished good supply plan calls for 1200 bicycles. Those 1200 bicycles will need 2400 tires, 2400 pedals, and 1200 frames. The need for 1200 frames will create further requirements for metals, and so on. The demand for components created by the finished good supply plan is known as dependent demand because it is dependent on the finished good.

Figure 1.2 shows a demand and supply planning schematic where an independent finished good demand forecast creates a requirement for finished good supply. When the finished good is manufactured, supply from each batch must be allocated to satisfy finished good demand. The finished good supply plan also creates dependent demand for the components that are needed to manufacture the finished good.

The objective of demand and supply planning is to ensure the *right product* is delivered in the *right quantity* to the *desired place* at the *desired time* for the *least amount of money* possible. Meeting these five objectives requires a combination of data, analytics, strategy, and collaboration across the organization. To generate a robust demand forecast and supply plan, it should incorporate the following elements. First, the plan should be end-to-end which means the plan should account for

- A demand forecast window that fits the product's lifecycle.
- All the finished good products that are consumed in the network.
- All critical upstream production or sourcing required to enable the manufacture and distribution of the finished good is accounted for in the plan.

Second, the supply plan should be entirely demand driven. All production and distribution decisions need to be made within the context of demand. If an external event (such as a sale) increases demand, the plan should incorporate this. If the company raises the price of a product and demand decreases, the plan should incorporate this. Similarly, dependent demand creates

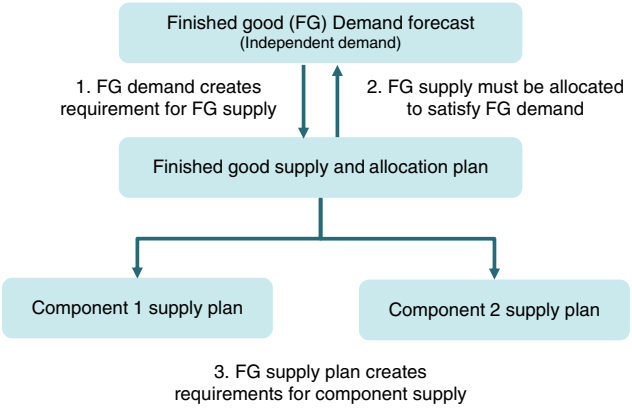

Figure 1.2 Demand and Supply Planning Schematic

requirements for components, and these requirements form the initial basis of the planning process for upstream materials. Requirements for the finished goods and their components will be modified during the planning process, but working without requirements is flying blind and a precursor to waste.

Third, the supply plan should be weeks-(or days ... or months)-of-supply (WoS) based. Weeks-(or days ... or months)-of-supply describes how much on-hand inventory is available within a specific forecast period, and it is the most accurate way to measure and communicate the inventory position of a good. If a manufacturer has 500 units in inventory, that might sound like a lot. But, if demand for that product runs at 200 units/week, that manufacturer will stock out in just three weeks. Conversely, let's assume that the same manufacturer has 50 units of another good in inventory. That doesn't sound like nearly as much as the good with 500 units, but if demand for the second product runs at an average of 1 unit/week, there's enough inventory on hand to last a whole year. Therefore, communicating in WoS – for example, "The product has seven weeks and is starting to run lean" or "The product has 18 weeks and is running long" – tells a more accurate story about the relative strength of the inventory position and what actions may need to be taken within the plan.

Building a plan that's end-to-end, demand driven, and WoS based mitigates the risk inherent to all demand forecasts and supply plans – that the plan will be wrong: more specifically, the risk that the demand forecast will be too low and not enough supply will be produced to meet actual demand, or the risk that the demand forecast will be too high and an excess of supply will be manufactured. When the forecast is too low, this can result in missed sales and lost revenue, but if the forecast is too high, then cash gets tied up in inventory and potentially wasted altogether. Here is a hard truth, the demand forecast will always – I repeat, always – be wrong in one direction or the other. While the theoretical goal is to manage the demand forecast and supply plan to a perfect balance, the reality is that the plan will need to be constantly updated and rebalanced in pursuit of that goal.

When a demand forecast and supply plan incorporates these elements, they give the organization three powerful tools for managing the supply chain – visibility, control, and flexibility. Visibility means an organization has insight to changes in demand signals and supply risks. If the plan is not end-to-end, then a risk to a key component may be missed. If the plan is not demand driven, line of sight to component requirements is lost. And if the plan is not WoS based, changes in demand will not signal a risk of under- or oversupply on the horizon. Visibility is powerful, and without it, the risk that a plan will fail to meet demand or waste money increases exponentially.

Second, if there is no visibility as to where problems may occur, there is no way to control the strategy. There is no worse feeling than the helplessness of finding a problem without an apparent reason for why that problem exists. Without a visible cause, control is lost, so visibility and control go hand in hand. To achieve visibility and control, the plan must be built at the appropriate level of detail. End-to-end planning translates to control over all aspects of the supply chain, and WoS enables better decision-making through the supply chain when events go awry.

Finally, these elements enable flexibility to respond when events don't go as planned. Flexibility has two meanings in the context of demand and supply planning – flexibility in approach and flexibility in strategy. Flexibility in approach means that the plan is tailored to meet the needs of the consumer, the product, and the supply chain. No two supply chains are alike, and the plan must be adaptable to the unique circumstances that it attempts to model. Flexibility in strategy means the plan has a variety of options embedded in it to account for the plan going wrong in either direction. If demand is high, appropriate safety stocks exist to buffer at the finished product level and at the component level. If demand is low, production and ordering can be delayed to a desirable date.

End-to-end plans, demand-driven plans, and WoS-based plans enable this strategic thought process as we will learn in Chapters 7–13.

With all of that in mind, a well-designed plan that lives in isolation is not enough. Business processes must exist to manage the plan, and there are two of these to note. The first is the demand and supply planning process itself. On a regular cadence – weekly or monthly in most cases – the plan needs to incorporate historical demand (e.g. sales) and supply (e.g. production) actuals. Then, the plan needs to incorporate any new demand or supply assumptions before it is updated for the next planning cycle. Second, the entire organization, from sales to operations to finance, needs to align around and endorse the demand and supply plan because it governs both the manufacturing operations of the company and the spend required to support that production. Sales and operations planning (S&OP) is the business process for gaining this alignment and endorsement.

The function responsible for these processes is planning. Within a planning organization, individual planners are typically assigned to a specific product or product line. For highly complex supply chains, these roles may be split into demand planning and supply planning for a single product. The planner serves as a bridge between the sales and operations organizations and must effectively collaborate with both functions to develop an optimal plan. Without this collaboration, the plan will have poor or unrealistic inputs, which then drive poor or unrealistic outputs that the company will march to – garbage in, garbage out as the saying goes. Planners must also think analytically while updating the plan and strategically to place the plan outputs into the overall context of the product. For example, if the plan calls for a surge in supply, but the company is planning to discontinue the product in six months, that plan doesn't make sense.

To summarize, planners should build demand forecasts and supply plans that are end-to-end, demand driven, and WoS based. This structure gives planners the visibility they need to control the plan and execute a flexible strategy that can respond to unforeseen events without jeopardizing product supply. The planner needs to work closely with sales, operations, finance, and product strategy to collect the proper inputs for the plan and ensure the outputs are realistic and in sync with the overall strategy.

1.3 Source

Sourcing is the act of identifying, selecting, qualifying, and engaging with external organizations for the acquisition of goods and/or services. Without raw materials and component suppliers, it's impossible for a supply chain to function. There are many attributes that separate a good supplier from a poor one, and a single supplier may be a strong fit for one manufacturer and a poor fit for another. The goal for all supplier relationships is the same though – to acquire the goods and/or services on time, in full (OTIF), at the expected quality level, and for the negotiated price.

Every supplier relationship follows a basic four-step process – identification, selection, qualification, and management. The sourcing process begins with recognizing the need for a supplier to provide a good or service. In most cases, this decision is obvious. If an outside party can provide a good cheaper than a manufacturer can make it itself, it makes sense to procure that good from that outside party. In some cases, though, it may not be immediately obvious that sourcing a good is cheaper than making it or there may be other factors to consider. In these circumstances, a make-versus-buy analysis may be required to determine whether it makes sense to insource (e.g. make it in-house) or outsource (e.g. procure from a third party) the good in question. Additional factors may include increased control over the process to manufacture it or the opportunity to leverage learnings from in-house production to other areas of the business.

Once the decision to outsource has been made, the supplier identification process will begin. This first step will often include sending out a request for information (RFI) to suppliers who have demonstrated the capability to produce the good or service in question. RFIs are intended to solicit feedback from potential suppliers across a multitude of categories such as location, company size and history, team structure, service levels, quality levels, and cost for the goods rendered. Once the field of candidates has been narrowed to three to five potential candidates, the selection process will begin.

The first step in supplier selection is to develop a request for proposal (RFP) or a request for quote (RFQ). The RFP/RFQ contains a detailed description of the goods or services required by the manufacturer, the timeline by which these goods or services should be delivered, and the expected quality standards. The RFP/RFQs are then sent to each potential supplier for response. After the responses have been collected, the team responsible for making the selection decision will evaluate the suppliers against predefined criteria. While cost is always a part of the analysis, other factors may be more important to consider. For example, if the good or service must be delivered within a narrow timeframe, project management and customer responsiveness may rank highly in the decision.

Once a decision has been made and the selected party has been notified, the contract and qualification processes will begin. If the work will be done on a one-time basis, a simple statement of work (SOW) will suffice. But, if the products will be delivered on an ongoing basis, then a master services agreement (MSA) may also be required. An MSA describes the legal framework within which the two parties – the buyer and the seller – will engage. The MSA is designed to establish ways of working and to protect both parties in case of failure to deliver on the terms of the contract.

In some cases, a supplier will also need to undergo further qualification to ensure they have the capabilities and controls in place to deliver the product or service on a consistent basis. This additional qualification may take place via an audit of the supplier, which is an official inspection of the organization. Audits are especially common in the biopharmaceutical industry because of regulatory requirements.

The final step of the supplier lifecycle is supplier management – monitoring supplier performance over time. If the supplier provides routine goods or services, this may be as simple as tracking budgeted spend. Most suppliers fall into this routine transactional category and don't require much energy or investment. However, there is another category of supplier – those that provide a particularly critical or expensive good to the buyer. For those suppliers, a more robust supplier management strategy is appropriate.

Supplier/strategic relationship management (SRM) is a holistic approach to managing critical suppliers that reframes the buyer–seller relationship from a transaction basis into a partnership basis. Managing these relationships is not just about tracking spend or performance, but also about learning the supplier's values, goals, and ways of working. When both parties understand each other, they can find areas where their objectives may coincide. Using this partnership framework can then increase the value of the relationship for both the buyer and the seller. In the biopharmaceutical industry, SRM fits as a philosophy for outsourced manufacturers who make the drug on the company's behalf. Key tenets of SRM that may be applied to this type of relationship include

- Establishment of MSA and supply agreements.
- Development and implementation of acceptable service-level metrics.
- Provision of production forecasts and negotiation of critical path activity lead times.
- Quarterly business reviews to discuss goals, expectations, and future projects.
- Use of supplier score carding to measure supplier performance.

Alongside individual supplier management, supply chain risk and resiliency must also be considered within the sourcing strategy and selection framework. There are two strategies that firms can use to reduce risk and improve resiliency within their supply chain. The first strategy is to pursue relationships with multiple suppliers who provide the same good. If two such suppliers exist, this is known as dual-sourcing, and if there are more than two suppliers for a specific good, this is known as multi-sourcing. When a firm is dual- or multi-sourced for a particularly critical good, it has an insurance policy against disaster striking one of its suppliers. Dual-sourcing makes the most sense when the suppliers are geographically spread out and belong to separate corporate entities to further reduce risk. There is a downside to pursuing multiple suppliers, though. It is expensive and resource intensive to maintain multiple relationships, particularly if the need to have more than one supplier isn't justified by the demand profile of the final product.

Another strategy firms are pursuing now more than they have in the past is onshoring. Onshoring means to bring an activity that had been outsourced to an international partner back to a domestic partner. Beginning in the 1970s and 1980s, many American and European firms pursued offshoring, particularly to China and Southeast Asia, as a strategy to save money from cheaper labor sources. Offshoring can expose a company to multiple supply chain risks, including geopolitical risks and transportation risks. During the COVID-19 pandemic, these risks were realized for innumerable organizations as COVID restrictions shut down China's ports for months at a time.

Like all supply chain processes, sourcing requires a team of people, but there is one function that owns the sourcing process – procurement. Procurement's responsibilities will vary from company to company, but they always drive the supplier selection process and almost always develop the overall sourcing strategy. Procurement owns contract negotiations, supplier agreements, and budgetary issues and usually manage supplier performance as well. With that said, procurement is not typically responsible for the technical requirements and deliverables needed from the supplier. To return to the outsourced manufacturing example, manufacturing experts need to partner with procurement to provide those technical details.

Once an engagement with a supplier has begun, delivery is the highest priority. Within the supplier, there are three roles worth mentioning. First is the team of people who are directly responsible for delivering the good. Wherever possible, this team should be identified before the work begins to properly evaluate their credentials and working style. Second, and arguably as important as the people delivering the work or good, is the project manager. The project manager can make or break an engagement with a supplier, particularly for highly complex projects such as pharmaceutical development and manufacturing. A strong project manager will set expectations, communicate in a timely fashion, and identify risks before they materialize. A weak project manager will lead to chaos, missed deadlines, and frustration. Finally, the sales/business development lead has an important role to play. They are incentivized to please their customers and can be an advocate within the supplier organization for the buying party.

1.4 Make

Simply put, manufacturing is the production of goods. And while a detailed analysis of specific manufacturing operations is beyond the scope of this book, a general summary of manufacturing resource planning (MRP II) yields lessons that are applicable to the discipline of supply chain management. MRP II encompasses the processes and inputs a plant must consider when planning production, including demand, materials, capacity, labor, and cost. This approach is known as MRP II because it improves upon materials requirements planning (MRP I). MRP I was designed

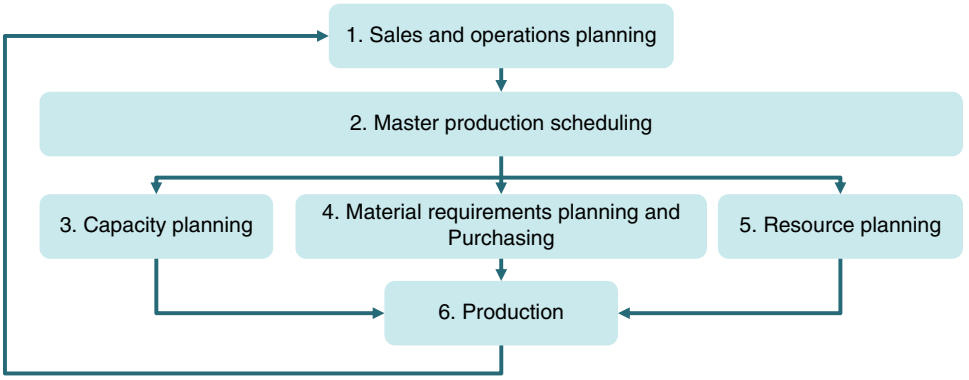

Figure 1.3 MRP II Process Flow

to ensure that sufficient materials were on hand to support scheduled manufacturing while minimizing inventory holding costs. MRP I had serious flaws in that it did not account for capacity or resource requirements. Thus, MRP II was developed to incorporate these inputs and improve plant operations.

A streamlined MRP II process flow is captured in Figure 1.3.

In Figure 1.3, there are six planning, scheduling, and manufacturing processes:

1) *Sales and Operations Planning (S&OP)*: S&OP is a business process where the sales function provides the demand forecast to the planning and operations function. Planning then reviews the forecast and develops the production plan to support that forecast. This process creates alignment across the entire company on what operations can deliver. This alignment is important because it prevents sales from overpromising and gives operations a concrete supply forecast to hit. S&OP is fundamental to successfully managing manufacturing because without it, demand variability can overwhelm operations' ability to respond and provide supply to meet that demand. S&OP principles are applicable to clinical trial supply chain management, and this will be revisited in Chapter 15 – Clinical Supply Chain Planning Processes.
2) *Master Production Scheduling (MPS)*: The master production schedule tells the plant what to produce, how much to produce, and when to produce it. The MPS ties the top-line forecast agreed to during the S&OP process to the detailed operations of the plant. Typically, the MPS is broken down into specific stockkeeping units (SKUs). The MPS takes into consideration plant capacity, component availability, and plant resources to ensure the production schedule is feasible. Due to these requirements, MPS generation is typically managed by a software or cloud-based solution known as enterprise resource planning (ERP), which is the technological backbone of many mid- and large-sized manufacturing companies.
3) *Capacity Planning*: Capacity planning assesses how many units of a good can be produced with the plant's available resources. Two variables used in capacity planning are the number of machines and the maximum utilization of those machines. The specific manufacturing process in question will dictate the analysis, but the key point is that capacity planning places a constraint, or limitation, on the amount of goods that can be produced within a particular machine or equipment train. These constraints must be considered in the development of the MPS because if they are exceeded, the plan is no longer feasible.
4) *Materials Requirements Planning (MRP) and purchasing*: MRP translates the MPS into specific component requirements that support the production schedule. MRP relies on an accurate bill

of materials (BOM) to run. A BOM lists all the required components and the quantities of each component needed to produce the final good. The BOM for each SKU must be accurate because MRP drives the component planning and purchasing process. For example, if the production schedule requires 100 finished good units and the BOM calls for two component unit parts (e.g. wheels on a bicycle), then 200 components are needed. If only 150 units are available in inventory, then a replenishment order for that SKU must be generated. The other variable MRP considers is replenishment lead time (RLT) or how long it will take a component to be received for use from the time it is ordered. If the RLT for the component in the above example is 10 weeks, then MRP will create a request to order that component 10 weeks ahead of the requirement date. Combining the BOM and RLTs enables the creation of a purchasing strategy for requisite components.

5) *Resource Planning*: Like capacity planning, resource planning considers human labor as a potential constraint to the manufacturing process. And, like MRP, resource planning creates a labor requirement for the production schedule. This enables the plant manager to appropriately allocate human resources to the schedule. If those resources are unavailable or not sufficient to meet the schedule, then the plan must be updated to account for this shortage. Planning resources is more difficult than components because human labor cannot be acquired as easily as material goods. Hiring, training, and off-boarding must all be considered in the process.
6) *Production*: Once the equipment, components, and labor are ready, manufacturing can begin. When production ends, the outputs are fed back into the demand and supply plans, and the planning cycle begins anew.

Many different manufacturing strategies exist, but the biopharmaceutical industry largely uses batch production in which a group of identical units of a particular SKU are produced. This is a different approach than job-based production, which produces an individual unit of an SKU, or flow production, which produces identical units on a continuous basis of an SKU. Batch production gives biopharma manufacturers the flexibility to scale production up or down as needed and to meet the strict regulatory requirements of the industry.

Another manufacturing strategy that biopharma companies traditionally pursue is make-to-stock (MTS) manufacturing, as opposed to make-to-order (MTO). In an MTS strategy, stockpiles of inventory are built ahead of demand to ensure sufficient inventory is available. MTS is most appropriate when the supply chain has a long lead time and/or customers require a good as soon as they have demand for it (e.g. buying fresh milk off the shelf). In an MTO strategy, units are produced only after the demand signal is received. MTO works well for supply chains that have fast lead times or for consumers who are willing to wait for a unique product (e.g. a custom laptop). Biopharmaceuticals have long lead times and consumers who need a product immediately and, therefore, MTS has traditionally been favored by the industry. As we'll see in Chapter 18, new drug modalities and approaches to supply chain management are challenging this paradigm.

There are two risks within the production floor that must be balanced. The first risk is a failure to meet the MPS. Any hiccup in operations, from an equipment issue to a component stockout to a labor shortage, may cause a delay in production. The possibility of this risk happening increases as the plant is pushed close to its capacity and room for error is reduced or removed entirely. One approach to mitigate against this failure is to add redundant capacity or additional inventory to ensure production will run smoothly even if a problem occurs. But, this strategy introduces a second risk – wasted spend on unutilized equipment, inventory, or labor. Balancing these risks