ESTABLISHING A COMMERCIALLY VIABLE SUPPLY CHAIN FOR EARLY STAGE DRUG COMPANIES

A Trout Creek Consulting white paper by
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Trout Creek Consulting, LLC
Creating Value Through Improved Decision Making and Effective Execution[SM]

CONTENTS

EXECUTIVE SUMMARY

In the current life science funding and deal environment, an early stage drug company may have to take its products well into Phase III, or even to market, to obtain an acceptable exit valuation from an acquirer, licensee, or IPO. Having a commercially viable supply chain builds credibility that reassures both late stage investors and potential acquirers and licensees. Importantly, a commercially viable supply chain provides negotiating leverage with potential acquirers and licensees by signaling "we are prepared and proceeding to market (the deal value goes up from here)." This article provides an overview of the key supply chain considerations for early stage pharmaceutical and biopharmaceutical companies, including when an early stage drug company should start creating its commercially viable supply chain.

INTRODUCTION

For most early stage[1] drug companies, securing funding, quick progression into clinical development, and achieving a financially attractive exit are the top priorities, as they have been for many years. Traditionally, supply chain planning and creation at early stage companies consisted of making material for preclinical, Phase I, and Phase II clinical trials. Any supply chain work beyond this was left to either the acquirer of the early stage company itself or the licensee of its drug product(s). However, the changing dynamics of the exit and ever increasing global healthcare cost pressures are bringing more thoughtful supply chain planning and creation, for both clinical materials and ongoing post-approval commercial sales, to the fore. Early stage drug companies with good, but not blockbuster, products may have to take these products well into Phase III or even to market to obtain an acceptable exit valuation from an acquirer, licensee, or the near dormant IPO market. Even companies with potential blockbuster products may need progress against a viable commercialization and supply chain plan as leverage to obtain the highest pre-approval exit valuation.

As many drug industry participants and observers have noted in recent years, Big Pharma/Big Biotech/Specialty Pharma are most interested in driving near term profit growth => their preferred acquisition targets are (a) late stage[2], substantially de-risked compounds and (b) companies with significant cost synergies and late stage development pipelines. Pfizer's acquisition of Wyeth, rather than acquiring much of the early stage biotech world for the same price, is an extreme example of Big Pharma pursuing cost synergies and late stage (including already commercialized) assets. Development pipeline rationalizations caused by industry mergers combined with the financially "hungry" nature of many early stage companies due to the recent recession and prolonged funding drought have increased acquirers' leverage in the early stage drug product market. Acquisitions of pre-revenue drug companies can resemble licenses with (a) upfront payments that may yield little return-on-capital for venture capitalists and (b) various milestone payments that tie venture capitalist/founder/executive payouts to the post-acquisition success of the early stage company's products. Healthcare reform pressures on drug product prices, the use of comparative effectiveness and cost/benefit analyses, an increased focus on personalized medicine targeting smaller patient populations, Big Pharma's desire to find profit growth

[1] For this article, "early stage" means prior to Phase III clinical trials.

[2] For this article, "late stage" means after Phase II clinical trials.

through sales in emerging markets, and the prospect of Big Pharma/Big Biotech having to make money in a generic/biosimilar "aftermarket" due to low NCE/NBE approvals will increase pressure on Cost of Goods Sold (COGS).

What does this mean for an early stage drug company and its supply chain? In short, it means that **early stage drug companies should prepare for exits during Phase III, post NDA/BLA filing, or post-approval once commercial sales have begun**. More specifically, this means (a) having a commercially viable drug product that will attract both late stage investors to fund development through commercialization and good exit opportunities and (b) progress against a solid commercialization and supply chain plan to take the drug product to market in the absence of a pre-approval exit. This "progress against a solid…plan" provides both leverage in discussions with potential acquirers and licensees and an increased level of confidence to investors that they will achieve a return.

WHAT ARE THE ATTRIBUTES OF A COMMERCIALLY VIABLE DRUG PRODUCT?

A commercially viable drug product has the following attributes:

- Great clinical data illustrating safety, efficacy, and a therapeutic benefit relative to other treatments (Comparative Effectiveness);
- Credible (read "good enough") clinical data and related economic analysis indicating an economic benefit relative to other treatments (Health Economics and Outcomes Research);
- Great or good regulatory strategy and package;
- Great or good market opportunity with attractive (but realistic) pricing/reimbursement and favorable competitive positioning;
- Good intellectual property;
- Commercially viable (read "good enough") supply chain exhibiting good COGS.

Notice a lot of "good." "Great" is hard to achieve and "average" doesn't cut it.

WHAT IS MEANT BY SUPPLY CHAIN?

Figure 1 provides an overview of the commercial, post-approval supply chain for a virtual drug company.

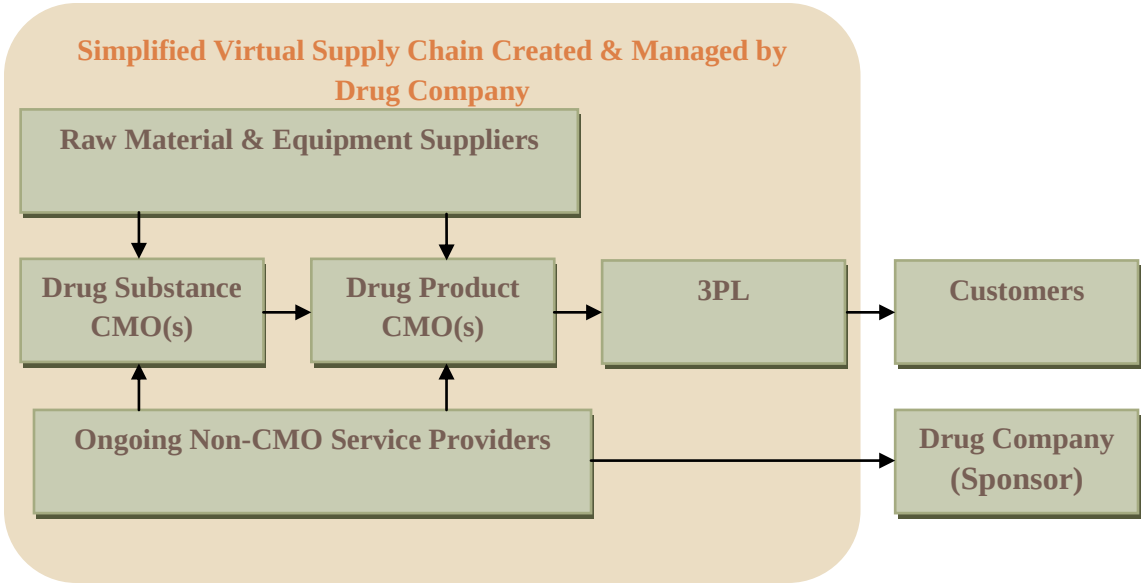


FIGURE 1 -- VIRTUAL DRUG COMPANY SUPPLY CHAIN

The major components of a supply chain include:

- **Raw Material & Equipment Suppliers.** These vendors supply starting materials, excipients, adjuvants, cell culture media, packaging components, specialized equipment, and other items used in the manufacturing process. For drug products based on existing drug substances, the drug substance may be sourced as a raw material.
- **Drug Substance CMO(s).** These Contract Manufacturing Organizations are known by a variety of acronyms, including CDMO (contract development and manufacturing organization) and CRAMS (custom research and manufacturing service). These firms manufacture the fine chemical or biologic drug substance and may be involved in both process and product development. Drug substance CMOs come in a wide variety of scales and capabilities – the supplier of small volume early stage clinical materials may not be the supplier of Phase III and

post-approval volumes. Depending on the situation, a drug company may have multiple CMOs to mitigate risk, respond to upside demand, and control costs. Complex process technology, such as a small molecule with a number of synthesis steps and/or unique chemistry, may necessitate the use of several CMOs to make the intermediates.

- **Drug Product CMO(s).** These firms are known by terms that typically reflect their functionality, including DFMP (Dosage Form Manufacturing and Packaging), Fill/Finish, contract packager, and secondary manufacturer. Drug product CMOs may be involved in both process and product development. As with drug substance CMOs, the drug product CMO supplying small volume early stage clinical materials may not be the supplier of Phase III and post-approval volumes. A drug company may need several CMOs to complete drug product manufacturing, mitigate risk, and satisfy regulatory requirements in different countries.

- **3PL.** This is a 3rd party logistics company that serves as the warehouse and shipping organization for the drug company and may also provide order-to-cash and other services. Drug product is shipped from the 3PL to customers (e.g., wholesalers, group purchasing organizations or GPOs).

- **Ongoing Non-CMO Service Providers.** This category of vendors is a catch-all for other service providers who are used in the supply of a drug product. This category includes cell banking services, 3rd party analytical testing and release services, and 3rd party cGMP auditors.

This article is focused on outsourcing rather than developing internal supply chain capabilities since outsourcing is typically the fastest and least investment-intensive option for early stage companies. However, as covered later in the Make vs. Buy discussion, there can be good reasons for a drug company to own and operate a significant portion of its supply chain. The decision of what to outsource is best decided on company-by-company and product-by-product bases.

Important: Outsourcing doesn't mean throwing the supply chain over the fence to a collection of CMOs and other suppliers to manage. Even in a highly virtual environment, the drug company still needs to manage the supply chain to (a) ensure that all suppliers are performing as required, including compliance with cGMP and Quality Agreements; (b) drive cost improvement; (c) mitigate risk; and (d) drive supply chain evolution to meet the drug company's future needs.

WHAT IS MEANT BY A "COMMERCIALLY VIABLE SUPPLY CHAIN?"

A commercially viable supply chain equals

a good enough supply chain, which equals

a supply chain that yields

the reliable, cost effective supply of in-spec product satisfying demand, cGMP, Environmental/Health/Safety standards, and other strategic business requirements.

A good enough supply chain reassures investors and provides leverage in exit discussions by declaring "we are prepared and proceeding to market (i.e., the deal value goes up from here)." In short, the early stage drug company needs a supply chain that delivers the right product, securely and under the right handling conditions, without regulatory issues, to the right place (e.g., drug distributor or other customer), at the right time, with the right economics (both capex[3] and COGS) to convince the company's investors and potential acquirers and licensees that the drug product will (a) make money if approved and (b) can be approved and marketed without fear of supply chain issues. In the context of good enough, "strategic business requirements" refers to meeting clinical and launch timelines, having the flexibility to quickly ramp manufacturing up or down depending on product adoption, minimizing direct-hire infrastructure, meeting pre-revenue spending plans, and other key objectives of the company's business plan.

Early stage companies generally have limited financial and personnel resources. A good enough supply chain is one that addresses all "must have" and some "want to have" and "nice to have" requirements relevant to the business. In the context of drug development, a good enough supply chain should take shape with the supply of Phase II clinical material, continue through the first 3-5 years of post-approval commercial product sales, and provide flexibility for future growth and continuous improvement.

[3] Capital Expenditure

Setting up a supply chain that can handle the first 3-5 years of commercial sales is necessary to allow the drug to ramp up to peak sales in order to maximize the benefits of exclusivity and patent coverage. It is not necessary for an early stage drug company to put too much effort into its supply chain beyond the first 5 years of commercial sales. If the company has a successful product, it will likely be acquired or IPO to become a stand-alone company. Either of these outcomes will impact long term supply chain strategy.

Good enough ***does not necessarily equal great or perfect*** – many companies do not need to make the added time and resource investments to achieve great or near perfect until they are cash flow generating and their business needs (e.g., product maturity, scale/scope of operations) merit this level of supply chain performance.

Good enough does mean ***de-risking*** the supply chain, where practical, via diversification of raw material suppliers and contract manufacturers. Importantly for early stage companies, a de-risked supply chain reduces the apprehension that potential acquirers and licensees may have about the viability of meeting or improving upon economic forecasts. While sole-sourcing does have benefits – fewer suppliers to qualify and manage, concentrated purchasing power, and reduced intellectual property leakage to name three – sole-sourced supply chains generally have higher risk and add cost when risk becomes reality. Diversification reduces the impact of plant fires and explosions, labor strife, quality issues, natural disasters (e.g., think the impact of floods in Thailand on the world supply of hard drives in 2011), and supplier price increases where switching barriers are high. Johnson & Johnson and Novartis have the scale to survive supply chain issues across multiple product lines; smaller companies will not fare as well when supply chain issues delay a lead compound's Phase III or launch or cause the recall of a marketed product.

A good enough supply chain reassures investors and provides leverage in exit discussions by declaring:

"We are prepared and proceeding to market…the deal value goes up from here."

WHEN SHOULD AN EARLY STAGE DRUG COMPANY START CREATING ITS COMMERCIALLY VIABLE SUPPLY CHAIN?

Supply chain is where product development, process development, and business strategy meet economic and timing reality – how the product will be supplied, when the product will be supplied, necessary supply chain capital investments, and COGS are determined here.

Before Phase I clinical materials are produced, early stage drug companies should have a first pass supply chain strategy addressing key scope items such as:

- **Economics:** What is the ballpark COGS that the supply chain must deliver? Is this COGS realistic given what is known about the product? "Realistic" before Phase II means is there a greater than 50% probability that process development combined with implementation of the supply chain strategy will deliver the COGS target?

- **Intellectual Property:** What IP should be protected and owned by the drug company during work with Contract Manufacturing organizations (CMOs) and other vendors? Which IP will be trade secret vs. patented? Is it necessary to spread manufacturing across several CMOs to reduce the amount of IP that any single CMO is exposed to?

- **Initial Supplier Selection:** In selecting CMOs for Phases I and II, should the drug company focus only on the needs for Phases I and II or, should it also consider CMOs with Phase III and post-approval manufacturing capabilities? Another aspect to Initial Supplier Selection is determining what "rights", if any, a Phase I/II supplier should have with respect to supplying raw materials and services for future clinical campaigns and commercialization.

- **Launch Strategy:** In what countries, and in what order, will the drug be launched? For example, is the strategy "US first, we'll worry about everyone else later" or "launch (for example, a biosimilar) in India first, then Europe, then the US" or something else?

- **Make vs. Buy:** Should the drug company consider manufacturing certain steps internally or should the company focus on outsourcing all of the manufacturing? There are product and company specific reasons for either approach including technology uniqueness, available 3rd party capacity, timing, breadth of the drug company's development pipeline and use of certain technology across that pipeline, nature and extent of IP, risk management, available funding, and desired return on capital.

- **Offshoring:** What is the drug company's comfort with using suppliers who are located in countries other than its own? Which parts of the supply chain require "high touch" involvement by the drug company and should be located closer to the drug company, if possible? Which parts of the supply chain have the potential for creating valuable IP or the greatest need for IP protection? In an ideal world, suppliers would be located in the same time zone and country as the drug company. This makes everything, from communication and oversight to selection of contract law, much easier. In the real world, capability (e.g., CMOs with the necessary technical talent, equipment kit, and cGMP experience), availability (e.g., where raw material is manufactured or grown if natural), cost, and locations of end-markets and licensees/alliance partners lead to

The concept of Green Chemistry is migrating into the drug industry from the commodity chemicals industry, starting with Big Pharma/Big Biotech/Big Fine Chemicals, due to concerns about chemical waste and safety. At some point in the future, early stage drug companies may want (or need) to specifically incorporate Green Chemistry into their supply chain strategies.

At present, the balance of economic (both development funding and COGS/capex), regulatory (drug/environmental), safety, technical, and timing constraints leads to the natural inclusion of some principles of Green Chemistry in process development.

offshoring. For reference, a small molecule supply chain to just supply the drug company's home country will likely stretch across several countries and, occasionally, six continents (yes - this author has experienced this).

- **Timing:** What is the timeline for clinical development, obtaining funding, obtaining an exit, and commercialization?

Note that the supply chain strategy is a living document; it will evolve as development and commercialization progress.

Once these scope items have been addressed, the "when" associated with planning and creating a good enough supply chain largely depends on whether the drug is a ***small molecule*** or ***biologic***.

Small Molecule Supply Chain

> ***"It is advisable to build process development and a supply chain revamping into...Phase II and in the run up…to Phase III. This author has seen...drug programs hit significant barriers between Phases II and III because the process used to make clinical materials for a few dozen to a few hundred patients was not commercially viable when contemplating (the number of)…Phase III patients and…post-approval patients."***

There are several flavors to small molecule drug products: new drug substance (new chemical entity or NCE) and drug product, new drug product with existing drug substance, generic drug product, and over-the-counter drug product. This article will touch on the most complicated flavor – NCE; the other flavors are typically less involved, although certain drug delivery mechanisms may add considerable complexity.

With an NCE, both the drug substance and the drug product require process development. The manufacturing steps may be common (e.g., reaction, crystallization, direct compression, tablet coating) to many small molecule drugs, but the chemistry, process technology (e.g., simulated moving bed chromatography, type of mill, type of packaging), and operating parameters are substance and product specific. While it would be great to develop the ideal process and supply chain from the start – this is not typically practical. Prior to Phase IIA completion, an early stage company may have neither enough data supporting the product nor sufficient money to justify process development of the optimized, commercially viable drug product. In this situation, there may be two stages of supply chain activity for NCEs:

- **Supply Chain Stage 1**: Quickly and inexpensively supply clinical materials for Phases I and IIA.

- **Supply Chain Stage 2**: Conduct an in-depth **Process Technology & Supply Chain Assessment** (PTSCA) of the Phase I/IIA process and product and then construct the commercially viable supply chain for Phase III and beyond based on the process development undertaken after Phase IIA.

Supply of Phase IIB clinical materials can fall into either stage.

An in-depth PTSCA will identify, prioritize, and justify process development priorities based on economic, regulatory, technical, and timing merits; determine weak points in the commercial supply chain; and recommend key supply chain initiatives.

In many cases, it is advisable to build process development and a supply chain revamping into the budget as activities that occur during Phase II and in the run up to the campaign to make Phase III clinical materials. This author has seen small molecule drug programs hit significant barriers between Phases II and III because the process used to make clinical materials for a few dozen to a few hundred patients was not commercially viable when contemplating thousands of Phase III patients and tens of thousands to millions of post-approval patients. Some of the reasons for commercial non-viability included:

- High COGS relative to the market price point of the drug product, especially for non-life threatening indications;
- High capex to supply both Phase III and post-approval volumes;
- Raw material, safety, and environmental issues with the initial process at large patient volumes (e.g., "You'll be 4x current world demand for this raw material!", "Can't build or buy enough waste processing capacity for this product!").

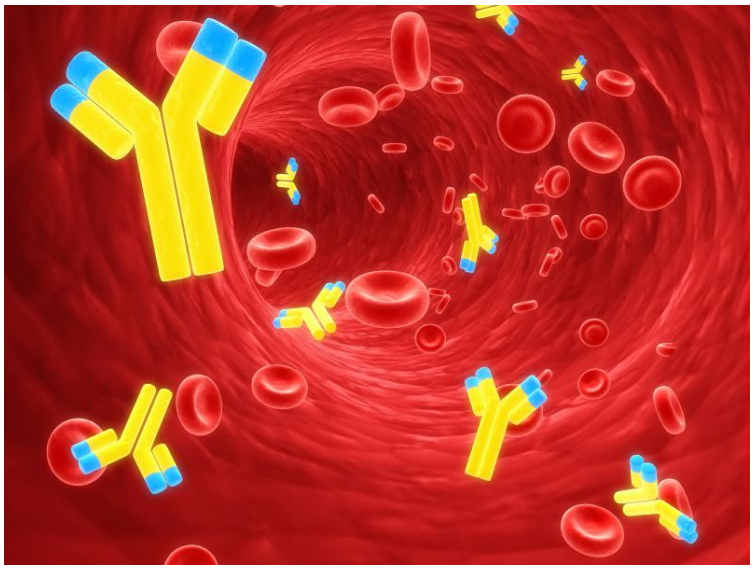
As a rule of thumb, if (a) the drug product requires an unusually high dose or has a very large expected patient population or (b) the drug substance has unusual or hazardous chemistry or more than 4-6 synthesis steps or more than 5-10 solvents, then assume additional process development will be needed once supply chain commercial viability is factored in.

From a regulatory perspective, it is more straightforward and less stressful if the clinical materials for Phases IIB and III are made using the same raw materials and process route. The Phase III manufacturing campaign can then demonstrate and confirm Quality-by-Design.

Biologic Supply Chain

Biologic drug products have several flavors too: (a) microbial or mammalian, (b) new biological entity (NBE) or biosimilar, and (c) early or later cell line optimization; i.e., the decision to develop an optimized, higher titer cell line before Phase I clinical trials or to develop an un-optimized, lower titer cell line for rapid entry into the clinic followed by development of an optimized cell line once favorable early clinical results are obtained. If a biosimilar, there may be the further complexity of launching different emerging market and EU/US versions of the biosimilar to accelerate profitability.

Volumes have been written about the similarities and differences between small molecule and biologic drugs. For the purposes of this article, it is sufficient to say that for technical and regulatory reasons, a significant amount of biologic product and process development occurs before and during Phase I. It is therefore important to have in-depth supply chain involvement in biologic products before and during Phase I to determine supply chain strategy, select suppliers, and negotiate contracts for Phase I while keeping an eye on the needs for Phase II and beyond.



DO WE HAVE THE RIGHT SUPPLY CHAIN PARTNERS?

Whether small molecule or biologic, **the process development phase after initial clinical trials have been conducted is the time to ask,** "***Are we working with the right CMO(s) and suppliers?***"

At this point, the drug company is now in a better position to justify and undertake a higher level of supply chain planning. That is, the drug company now has some data that its drug might work; therefore, it's worth a deeper look at the supply chain.

In addition, the drug company will have sufficient experience to judge (a) how well the CMOs and other suppliers do their work and (b) how they are to work with. For example, are their offerings really geared to early stage customers "as advertised" or do they focus on Big Pharma/big volumes and "fit you in" where they can? Are they really good at what they do? Can they work independently or does the drug company need to teach or ride herd on its CMOs and suppliers? Are the revised COGS and capex estimates to supply the remaining clinical trial and post-approval commercial demand, updated based on the learning from the most recent clinical campaign, acceptable? Are the drug company-CMO/supplier cultures compatible? Are these the CMOs and suppliers that the drug company wants to bet its future on and work with long term?

ABOUT SUPPLY CHAIN PARTNERS

CMOs, contract research organizations, equipment and raw material suppliers, and other vendors are not strictly partners. The early stage drug company is typically paying these suppliers in cash, not equity, for their services. Yes, these suppliers may have an opportunity cost associated with working for one client vs. another, but they are not partners in the sense that they share the losses and are uncompensated for their efforts should a drug candidate fail. At some point in clinical development and certainly post-approval, a drug company might spend millions (tens of millions post-approval!) of US dollars annually on one product with a supplier. It is important for early stage companies to think of themselves as customers looking to obtain value for their spending. As a customer, you may not always be right, but you should obtain value, service, and reliability for your spend.

Early stage companies should keep in mind that their suppliers typically operate in a rational business manner. That is, they correctly focus on the customers and customer segments that drive value creation for them; e.g., the "80/20 rule." Where practical, the early stage company should build its supply chain around suppliers who view the company as an important customer or as a member of an important customer segment. This will align cultures and work processes to drive both near and long term success.

Finally, early stage companies should remember that their suppliers are not mind readers. They may not know what the client wants, needs, or expects. The early stage company may not know this either! However, since it is the customer paying the bill, the early stage company should have the in-house or consulting resources to clearly define, communicate, and manage its supply chain. Tossing the supply chain over the fence to a collection of CMOs and other suppliers without some sort of plan, regular communication, and oversight doesn't ensure commercial viability!

SWITCHING SUPPLIERS

In the 25+ years since entering the drug industry, this author has seen CMO switches for a combination of technical, economic, strategic, and cultural fit reasons prior to NDA approval. **The key is that the Phase III and immediate launch suppliers be the same**. Interest from "commercial scale" CMOs and other suppliers generally builds from Phase II onward. Prior to Phase II/III, their interest is discounted by the probability of success, the distant timeframe to commercialization, and the smaller value of Phase I/II business. This change in interest at and beyond Phase II naturally facilitates switching suppliers at this point in development, especially if the Phase I/IIA supplier doesn't have the necessary commercial scale capabilities.

WHAT ARE THE STEPS INVOLVED IN CREATING A SUPPLY CHAIN?

A numbers of steps are involved in creating a drug product supply chain. Many factors impact the nature and timing of these steps, including small molecule vs. biologic, current clinical phase of development, NCE vs. existing drug substance, process technology, COGS target, patient population size, dosage, acute vs. chronic treatment, long lead items, etc. In general, setting up a supply chain has the following high-level steps:

- **Supply Chain Strategy Definition** to define supply chain scope items as discussed earlier, contract strategy and desired terms, raw materials and services to multi-source, required manufacturing capacity flexibility, and other supply chain objectives to support the business plan.

- **Process Development and Process Engineering** to determine raw materials, process technology, and process capacity needs. This includes assembling a Technology Package covering (a) the scale up and manufacture of the drug substance and drug product, (b) nuances and sensitivities associated with the manufacturing process, (c) Quality by Design, (d) analytical methods, and (e) specifications. This Technology Package ensures that the drug company has the manufacturing technology and can transfer manufacturing to additional CMO(s) as needed.

- **Project Management** to drive supply chain activities from clinical supply through at least the first 6 months of post-approval manufacturing. After 6 months of post-approval manufacturing, the focus of supply chain management should change from (a) creation/start up to (b) routine/continuous improvement at both the drug company and CMO(s).

- **Risk Assessment** on at least an annual basis, and more frequently if needed, to understand supply chain risks, develop risk mitigation strategies, and determine the decision criteria and timeframe to implement these risk mitigation strategies. Supply chains evolve and their risk profiles change based on internal (e.g., clinical progression, process and product development, expanded therapeutic indications) and external (e.g., natural disasters, feedstock interruptions) events. Potential acquirers and licensees find risk assessments valuable because they

reduce uncertainty; they will understand why an early stage company doesn't have the money or need (e.g., clinical development not progressed far enough) to implement all of the risk mitigation strategies.

- **Sales and Operations Planning** to forecast (a) how much product needs to be made when and delivered where, (b) when should raw materials be ordered and (c) what raw materials, work in process, and finished goods inventories are required given various scenarios for clinical supply through the first few years of post-approval sales.

- **Supplier Identification, Screening, Selection, and Contracting** for raw materials (including packaging components), equipment (if any), CMO(s), and the 3PL.

- **Technology Transfer** as additional CMOs are brought on-stream.

- **Work Process Creation** including creating standard operating procedures and other infrastructure for post-approval commercial sales. These activities can generally start after submission of the NDA, BLA, or other marketing authorization.

The key thing to remember in supply chain planning for most early stage drug companies is that ***good enough is the requirement, not great or perfect***.

The most likely outcome for a successful single-product or few-product virtual drug company is that it will be acquired before or soon after receiving marketing approval**. An early stage drug company needs a good enough supply chain that takes care of its clinical needs, will serve it well in the first 3-5 years post-approval if needed, and demonstrates a credible go-to-market capability that will comfort investors and provide leverage in negotiations with prospective acquirers or licensees.** It is important to not lock potential acquirers and licensees into suppliers who might not fit the acquirer's or licensee's strategic needs.

WHO SHOULD CREATE THE SUPPLY CHAIN?

Early stage companies can access the required skills to create a supply chain through either the use of a good, cost-effective, external consultant or by investing in an in-house supply chain function. Whichever resource is chosen, it is important to remember that the supply chain should be created and managed by an individual(s) retained to drive the interests of the drug company ***first***.

Allowing a particular CMO too much autonomy or control over the creation and management of the supply chain can create conflicts of interest between what is best for the drug company and what is best for the CMO. For example, dual sourcing for risk mitigation or to offset price increases may be difficult if the current CMO holds the procurement agreement with the supplier of a starting material.

A WORD ABOUT CONTRACTS

Somewhere during clinical development, executives at early stage drug companies will ask themselves, "***Where do we need contracts in our supply chain?"*** For a developer of biologic drug products, this question might come up in Phase I or earlier. For a developer of small molecule drug products based on existing drug substances, this question might not come up until Phase III. Catalysts for asking the question include: a supplier asking for a long term supply agreement, investor concern about commercialization planning, regulatory advice to have quality agreements, a desire for lower supplier pricing, the need to access or protect intellectual property, and the general sense that it's "the right thing to do." From a commercial and not legal perspective, early stage drug companies should enter into supply chain contracts where it is necessary to:

- Secure reliable supply of raw materials and services at an attractive and/or predictable cost on acceptable terms and conditions;
- Specify quality requirements and methods for resolving quality issues;
- Allocate liability and mitigate risk;
- Clarify roles, responsibilities, timing, and communication;
- Define ownership – who owns what intellectual property;
- Detail treatment of special situations – take or pay agreement to cover capex, meet or release pricing, acquisition of supplier or customer, etc.

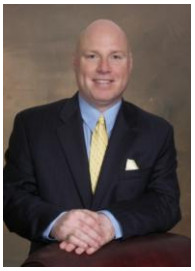
A critical and additional factor for early stage companies is that usually, the company or its products will be acquired by a larger drug company. Hence, early stage drug companies should ensure that the supply agreements they enter into with CMOs and other suppliers are:

- **Consistent** with agreements that a profit-generating operating company could live with because (a) that is who the acquirer or licensee will be and (b) that is what the early stage company might have to become, depending on the exit;
- **Transferable** to acquirers or licensees of the early stage company or its product(s);
- **Flexible** enough to allow the acquirer or licensee to exit at a reasonable point but not so flexible that the supplier can exit at a time that disrupts the business.

SOME FINAL WORDS

Creating a supply chain from scratch is usually easier than fixing one that has fundamental problems. When tackled early enough such that some level of process development and/or supplier switching are options, problematic supply chains can be identified and fixed before they create economic, reliability, quality, acquisition/licensing, and other issues. Hence, the recommendation that early stage drug companies start supply chain planning sooner and have a **Process Technology & Supply Chain Assessment** to identify problems.

About Hal Craig



Hal Craig founded Trout Creek Consulting (TCC) in 2007 on the principle that management consultants with strong problem solving and finance skills, significant operating experience, and industry knowledge will deliver superior value to clients through improved decision making and effective execution. TCC's offerings include defining Actionable Strategies, providing Deal Advisory services, and creating Life Science Supply Chains. Mr. Craig, who earned his MBA from the University of Michigan and his BSChE from the University of California at Berkeley, entered the life science industry in 1984; his experience includes drugs (biologic and small molecule) and devices. Mr. Craig is also on the Physical Sciences Investment Advisory Committee of Ben Franklin Technology Partners of Southeastern Pennsylvania. Away from TCC, Mr. Craig volunteers as an Assistant Scoutmaster with the Boy Scouts of America.

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