DEVELOPING BIOTECHNOLOGY COMPANY'S FUTURE POSITIONING STRATEGY IN PREFILLED SYRINGE MARKET

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Submitted to the MIT Sloan School of Management and the Department of Mechanical Engineering in Partial Fulfillment of the Requirements for the Degrees of

Master of Business Administration
AND
Master of Science in Mechanical Engineering

In conjunction with the Leaders for Global Operations Program at the
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Developing Biotechnology Company's Future Positioning Strategy in Prefilled Syringe Market

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ABSTRACT

The primary goal for the thesis is to develop a recommendation for Amgen's future prefilled syringe strategy related to its drug process development, supplier relationship management plan, supply and sourcing, and procurement. The goal is achieved 1) by analyzing the historic growth drivers in the market and current market trends including changes and challenges, 2) by developing an analytical tool to understand complicated market dynamics between suppliers and buyers, 3) by developing a few future scenarios on how the market will evolve based on former analyses and models and 4) by developing and finalizing a recommendation for Amgen's future strategy.

The prefilled syringe market is uniquely interesting for several reasons: 1) the prefilled syringe is an important primary drug container to both biotechnology and pharmaceutical companies, 2) there has been only one dominant supplier in the US, 3) biotech has been challenged with quality issues related to prefilled syringes and required the highest quality standards of syringe suppliers, 4) biotech's stringent quality standards and relatively low volume, compared with other big therapeutic classes such as anti-coagulants (heparins) and vaccines, can make it less attractive for the suppliers to align to biotech's needs, 5) new launch of advanced auto-injection device requires even higher prefilled syringe quality standards, and 6) the market is reshaping rapidly these days.

First, the thesis analyzes the prefilled syringe market's history, major growth drivers, key suppliers and buyers, and market dynamics featuring key players. Secondly, it turns to discuss the challenges and issues Amgen has faced with these days and the backgrounds. Thirdly, it develops recommendations regarding Amgen's decisions on single versus multi sourcing, supplier selection, and supplier relationship structures.

Lastly, it should be noted that all views, opinions, and assertions made in this thesis are those of the author alone, not of Amgen.

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The author is extremely grateful to his parents for their wisdom, support, understanding, motivation, and encouragement throughout his life. He appreciates all of their sacrifices that have provided him with such wonderful opportunities. None of this would have been achievable without their numerous sacrifices and continuous support.

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1 Introduction

1.1 Project Drivers

As the pace of new drug candidates entering market accelerates, the dynamics of drug development are changing. The growing emphasis on drug self-administration is having a major impact both on the pharmaceutical and on the biotechnology industries. The aging population and managed care initiatives are also major forces driving the growth of home healthcare, a trend that includes the self-administration of drug therapies for chronic conditions such as diabetes, arthritis and human growth hormone deficiency. This trend is creating an increased demand for drug delivery systems that are patient-friendly and cost-effective.

Prefilled syringes provide both pharmaceutical manufacturers and healthcare administrators with several advantages over traditional drug delivery systems such as vials for several reasons: the relative ease of use and fewer steps involved in using syringes, reduced risk of administering the wrong drug and wrong dose, reduction in overfill and waste, and prefilled syringe's critical role as a product differentiator in competitive markets. Consequently, prefilled syringes have been the primary container of choice for most injectable drug delivery systems.

In order to understand the importance of prefilled syringes to biotechnology companies such as Amgen, it should be noted that most of the biotechnology products have been large molecules, such as monoclonal antibodies and proteins, which all need to be delivered via injection route. The physical nature of these biotech-derived drugs requires administration by injection. Also, since prefilled syringes reduce overfill and waste, they are particularly attractive to product families that are extremely costly to manufacture. In addition, it is expected that prefilled syringes can play a role as a market differentiator for biotechnology drugs that serve markets which will become severely competitive as many so-far blockbuster drugs' patents will expire soon. In conclusion, prefilled syringes are important primary drug delivery systems for biotechnology companies from a commercial, procurement and device function perspectives.

1.2 Problem Statement

Biotechnology companies have faced with several challenges in delivering drugs in prefilled syringes to the market. In order to understand the prefilled syringe market, it is critical to note that there has been one dominant supplier in the US whereas a few suppliers compete on the market share in Europe, the largest prefilled syringe market.

While big pharmaceutical companies in Europe have had strong business in the existing prefilled syringe market - anti-coagulants (heparins) and vaccines markets, biotechnology companies have encountered two major challenges: 1) new requirements arose for prefilled syringes destined for biotech drugs in terms of stability and compatibility, and 2) limited bargaining power in a single source environment. In order for biotechnology companies to take advantage of prefilled syringe's value, it is important to analyze historical, current, and future growth drivers in the market, to keep monitoring changes in market dynamics among key stakeholders including suppliers and buyers, to analyze current and future options, and finally to develop suitable future positioning strategies in the market.

1.3 Thesis Overview

The document is organized as described below:

Chapter 1 outlines the general motivation for the thesis and provides an overview of the thesis contents.

Chapter 2 provides a brief discussion of the injectable drug delivery systems and Amgen's background, as well as a description of the prefilled syringe in the pharmaceutical and biotech industries. It also describes why the prefilled syringe is important to the company from commercial, procurement and product perspectives.

Chapter 3 presents a market analysis of the prefilled syringe industry including history, historical and future growth drivers, and key stakeholders.

Chapter 4 describes the challenges and issues that biotech companies have faced in the prefilled syringe market.

Chapter 5 presents the criteria to analyze the benefits and drawbacks of proceeding with single or multi source. It then presents recommendations on whether Amgen should single or multi source.

Chapter 6 details which suppliers are better strategic matches for Amgen by introducing attractiveness charts which are helpful for understanding inter-attractiveness between suppliers and buyers in the market.

Chapter 7 presents the criteria of deciding on vertical integration structure with the supplier. It also provides a recommendation on how the company can develop further relationships with the suppliers selected as strategic partners in Chapter 6.

Chapter 8 presents conclusions of the prefilled syringe market analysis and recommendations for Amgen's short-, mid-, and long-term strategy concepts in the market.

2 Background

2.1 Injectable Drug Delivery

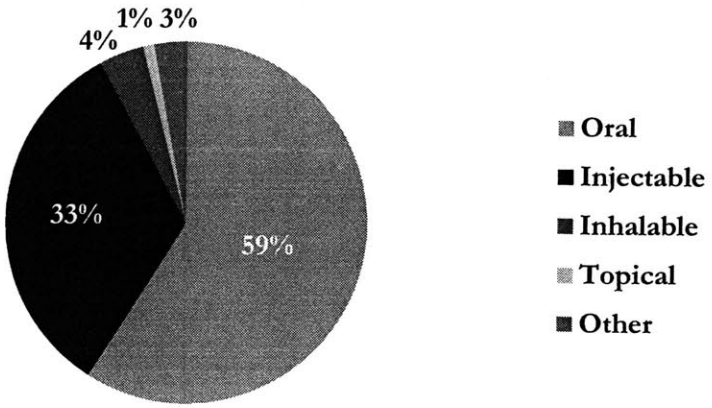

Figure 1. 2008 World Wide Drug Sales by Administration Routes[1]

As seen in Figure 1, the majority of pharmaceuticals are delivered orally and then by injection. One of the differences between these two delivery methods is that injection requires an injection device, whereas oral delivery does not.

On the one hand, the necessity of a delivery device could be viewed as an added complication for pharmaceutical product development. Whether or not involved directly in developing or manufacturing the device itself, the pharmaceutical company needs to ensure that its formulation is compatible with the delivery device, which can raise technical barriers and add cost. In the case of drug-device combinations, the pharmaceutical company is involved in the device development and must make sure that the device meets the required regulatory standards, patient's safety, ensures drug's dose accuracy, and meets market needs. From the patient's perspective, the introduction of a device into the process of taking their medicine could be seen as an additional, inconvenient step. Needle-based injection is associated with patient's pain.[2]

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[1] Raw data from Datamonitor, Others including optic, vaginal, ophthalmic, and nasal routes

[2] Guy Furness, "Introduction," in Delivering Injectables: Devices & Device Components, *ONdrugDelivery*, 2007

On the other hand, injection – intravenous, intramuscular, or subcutaneous – is a powerful delivery method. It transports the active pharmaceutical in liquid form directly into the body where it immediately begins distribution throughout the system. Compared with other delivery routes, injections expedite rapid onset, high bioavailability, and precise dosing. Furthermore, the vast majority of biopharmaceutical compounds are suitable for delivery by injection. Needle-based injection is very often the only viable option.[3]

Moreover, it should be noted that many of the innovative products have been large molecules, such as monoclonal antibodies and proteins, which all need to be delivered via the injectable route. The physical nature of these biotechnology-derived drugs means that they should be administered by injection.

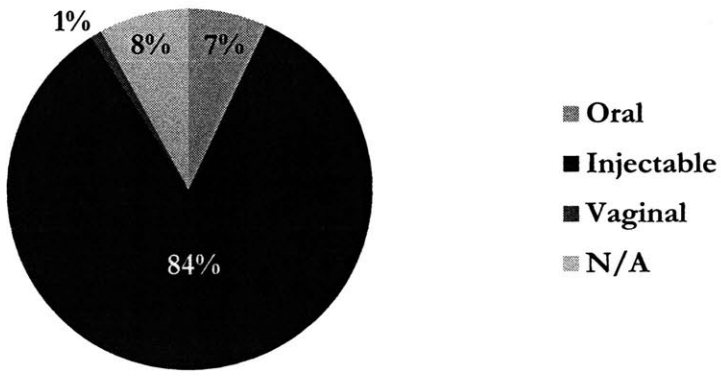

Figure 2. 2008 World Wide Biotech Drug Sales by Administration Routes[4]

As shown in Figure 2, 84% of all biotech drug sales came from injectable drugs in 2008 – this large majority is comprised of large molecule drugs. Biotech drugs which can be administered by oral and vaginal routes are all small molecules.

Therefore, injection has more advantages than disadvantages. Furthermore, to biotechnology companies, injection is the only viable option and the development of a delivery device is worthwhile for their continuous success in the market.

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[3] Guy Furness, "Introduction," in Delivering Injectables: Devices & Device Components, *ONdrugDelivery*, 2007

[4] Raw data from Datamonitor, Others including optic, vaginal, ophthalmic, and nasal routes

2.2 Prefilled Syringes

Primary drug containers for injectable drugs include vials, ampoules, cartridges, and prefilled syringes. Prefilled syringes are one of primary injectable drug containers which deliver a liquid drug inside the barrel to healthcare providers or patients. For lyophilized drugs, diluents or dual chamber prefilled syringes are used.

Most prefilled syringes in the marketplace except Japan and mentioned in this thesis are glass-barrel syringes. There are three primary needle-related prefilled syringe types as shown in Figure 3; staked-needle, luer-cone, and luer-lock.

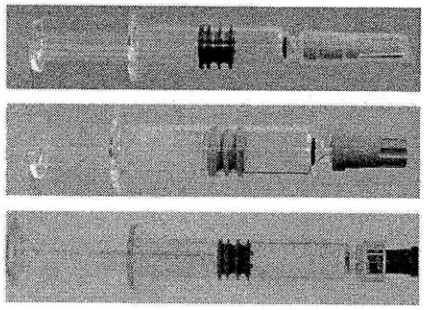

Figure 3. Three Different Needle-related Types: Staked Needle (Top), Luer-Cone (Center), and Luer-Lock (Bottom)

The drug delivery system based on prefilled syringes consists of the syringe itself, a needle shield (in the case of staked needle syringes), a tip cap (in the case of luer-cone and -lock syringes), and a rubber plunger. As the plunger is a moving part, special requirements may apply. For instance, silicone oil is commonly used to lubricate the glass inner surface/rubber plunger contact area in order to facilitate administration of drugs. For staked needle syringes, an UV curing adhesive is used for needle fixation in the glass barrel. Finally, the system itself requires a plunger rod.

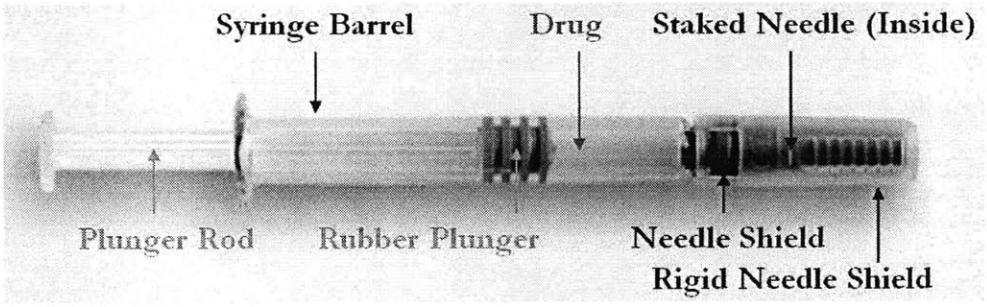

Figure 4. General Final Shape of Drug Product Delivered into Prefilled Syringes

Besides the standard components forming a drug delivery system, other accessories for syringes such as backstop and manual or automatic needle guard could be combined with the syringe system. Backstop functions as a finger flange extender, offering better handling of the syringe during injection and eliminating inadvertent rubber plunger removal (see Figure 5). Needle guard is assembled with a syringe to prevent accidental needle stick injuries to the healthcare provider after performing an injection by locking away the needle after the injection and hence eliminating the risk for unintended needle stick. Users have to manually activate manual needle guard system after use while automatic needle guard is passively engaged after use (see Figure 6).

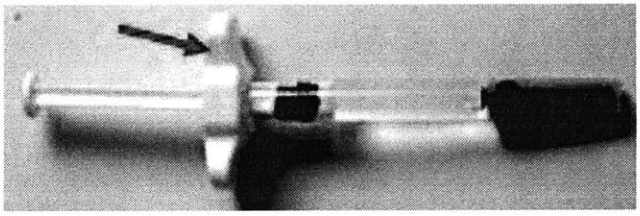

Figure 5. Backstop

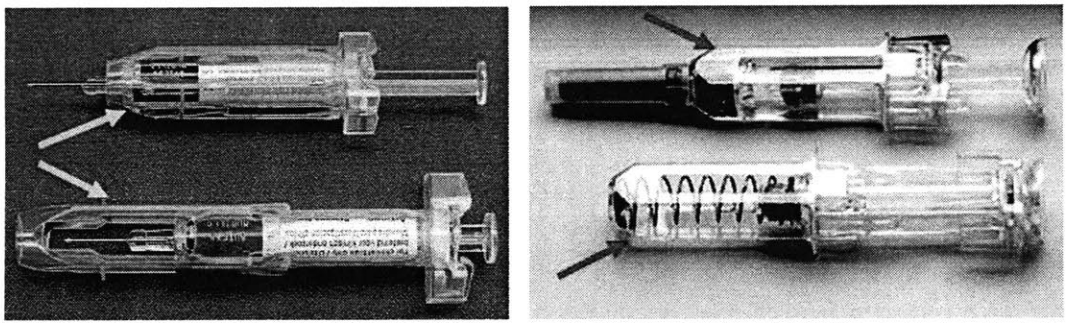

Figure 6. Manual (Left) and Automatic (Right) Needle Guards (Top before use, Bottom after use)

Prefilled syringes are supplied to pharmaceutical customers in two different versions: bulk syringes or pre-sterilized. For bulk syringes, various processes such as syringe-barrel washing, siliconization of the barrel and, if applicable, the needle (to lubricate the surfaces for easier administration and to prevent the non-specific binding of the formulation with the device), and sterilization have to be carried out after syringe manufacturing but before drug filling. These are done either by pharmaceutical companies or contract fillers. Pre-sterilized prefilled syringes including the barrel and other components are ready to be filled upon delivery. Currently, over half of the global prefilled syringe market is pre-sterilized.

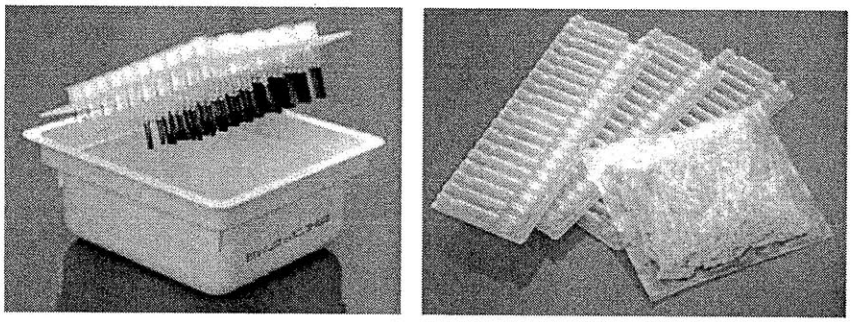

Figure 7. Pre-sterilized (Left) and Bulk syringes (Right)

2.3 Amgen Inc.

2.3.1 Company Background

Amgen, Inc. is a leader in the biotechnology industry with more than 25 years of experience applying a science-based approach to drug development. After it was founded in 1980, Amgen pioneered the use of recombinant DNA and molecular biology to develop biologically derived therapeutic products. The company introduced the biotechnology industry's first blockbusters, EPOGEN® (Epoetin alfa) approved in 1989 and NEUPOGEN® (Filgrastim) approved in 1991, which have since improved the lives of hundreds of thousands of patients. The company currently has eight products on the market that provide supportive cancer care and treat a variety of conditions from anemia to rheumatoid arthritis and other autoimmune diseases.[5]

Amgen is headquartered in Thousand Oaks, CA and has approximately 17,200 staff worldwide. As of December 31, 2009, worldwide product sales were $14.4 billion, net income was $4.6 billion, and the company invested $2.9 billion in research and development. Amgen has facilities around the world and operates manufacturing sites in California, Colorado, Rhode Island, and Puerto Rico.[6]

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[5] Amgen 2009 Fact Sheet
[6] Amgen 2009 Annual Report

2.3.2 Amgen's Injectable Drugs and Delivery Systems

This section discusses the importance of prefilled syringes for Amgen's drug delivery systems. In order to understand the importance, it should be noted how many of Amgen drugs are injectable and, further, how many of its injectable drugs are being delivered in prefilled syringes or combined with auto-injectors, in which the aseptically filled syringes are assembled.

2.3.2.1 Amgen's Drug Products

Currently, Amgen markets primarily recombinant protein therapeutics in supportive cancer care, nephrology and inflammation. Among Amgen's total eight drug product, its principal products are: Aranesp® (darbepoetin alfa) and EPOGEN® (Epoetin alfa) which are erythropoietic-stimulating agents (ESAs) that stimulate the production of red blood cells; Neulasta® (pegfilgrastim), a pegylated protein, based on the Filgrastim molecule, and NEUPOGEN® (Filgrastim), a recombinant-methionyl human granulocyte colony-stimulating factor (G-CSF), both of which selectively stimulate the production of neutrophils (a type of white blood cell that helps the body fight infection), and Enbrel® (etanercept), an inhibitor of tumor necrosis factor (TNF), a substance that plays a role in the body's response to inflammatory diseases. Amgen's principal products represented 93%, 94% and 95% of their sales in 2009, 2008 and 2007, respectively as shown in Figure 8. Amgen's other marketed products include Sensipar®/Mimpara® (cinacalcet), a small molecule calcimimetic that lowers serum calcium levels, Vectibix® (panitumumab), a fully human monoclonal antibody that binds specifically to the epidermal growth factor receptor (EGFr), and Nplate® (romiplostim), a thrombopoietin (TPO) receptor agonist that mimics endogenous TPO, the primary driver of platelet production.[7]

[7] Amgen 2009 Annual Report

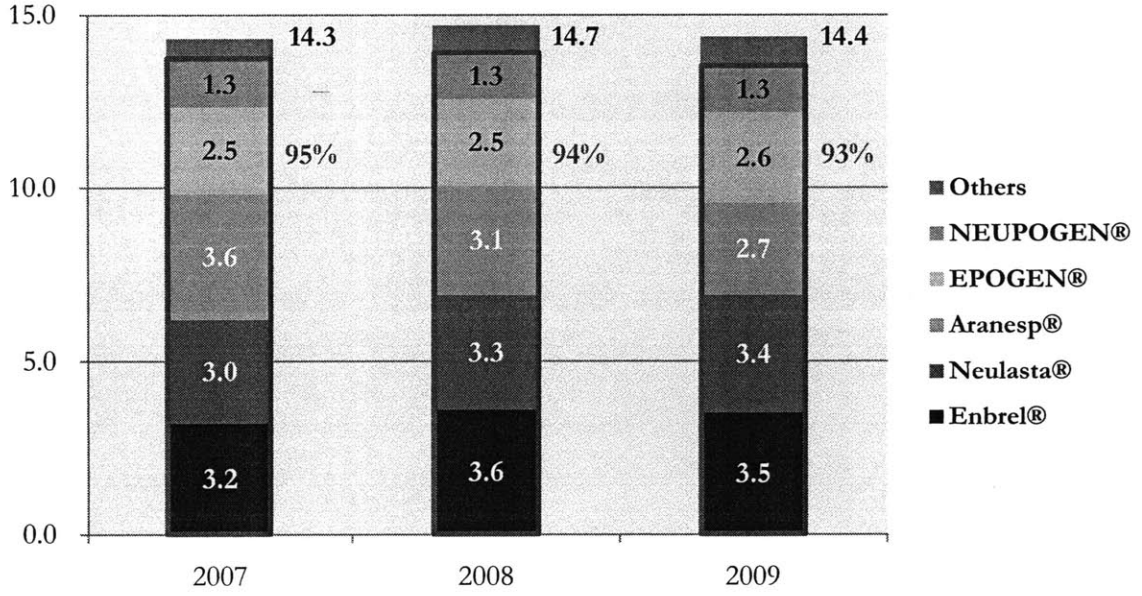

Figure 8. Amgen's Worldwide Product Sales (in billion USD)[8]

2.3.2.2 Amgen's Injectable Drugs

It is also important to note that among Amgen's total eight drug products, seven drugs are injectable. As shown in Table 1, Amgen's injectable drug container or delivery systems include vials, prefilled syringes, and auto-injectors. It is notable that auto-injector is another type of prefilled syringe. As seen in Figure 8 and Table 1, Amgen's five principal products are all injectable and four of them are being delivered in prefilled syringes. Hence, prefilled syringes are important drug delivery systems for Amgen.

In its 2009 Annual report, in addition, Amgen mentioned: "Amgen expects Prolia™ (Denosumab) approval in 2010 in the United States, Europe, and other regions, a fully human monoclonal antibody that specifically targets a ligand known as RANKL (that binds to a receptor known as RANK) which is an essential regulator of osteoclasts. Amgen announced in January, 2010 that Amgen had submitted the information the U.S. Food and Drug Administration (FDA) requested in the Complete Response letter for Prolia™ in the treatment of postmenopausal osteoporosis—an important step on the way to approval.

[8] Amgen 2009 Annual Report

Prolia™ was included in *TIME*'s list of Top 10 Medical Breakthroughs of 2009."[9] It is notable that Prolia™ (Denosumab) will be also delivered in prefilled syringes.

Table 1. Amgen's 7 Injectable Drugs

Product	Type		Container/Delivery System		
			Vial	Prefilled Syringe	Auto-Injector
Nplate®	SC[1]	Lyo[3]	O[4]	-	-
Aranesp®	SC, IV[2]	Liquid	O	O	O (SureClick™ in EU)
EPOGEN®	SC, IV	Liquid	O	-	-
Enbrel®	SC	Lyo	O (with a diluent syringe)	-	-
		Liquid	-	O	O (SureClick™ in US)
Neulasta®	SC	Liquid	-	O	-
NEUPOGEN®	SC	Liquid	O	O	-
Vectibix®	IV	Liquid	O	-	-

[1] Subcutaneous Injection
[2] Intravenous Injection
[3] Lyophilized Powder
[4] The symbol 'O' means the drugs is delivered in the delivery container/system.

[9] Amgen 2009 Annual Report

3 Prefilled Syringe Market Analysis

Since the introduction of prefilled syringe to the market, it has been successfully adopted as an innovative drug container and delivery system to anti-coagulants (heparins) and vaccines markets as well as the biotech market. Thanks to historic growth drivers including the introduction of pre-sterilized format of prefilled syringe and strong growth of traditional mass markets, the prefilled syringe market has grown significantly. This chapter analyzes the prefilled syringe market including its history, growth drivers, and suppliers and buyers in the value chain (see Figure 12).

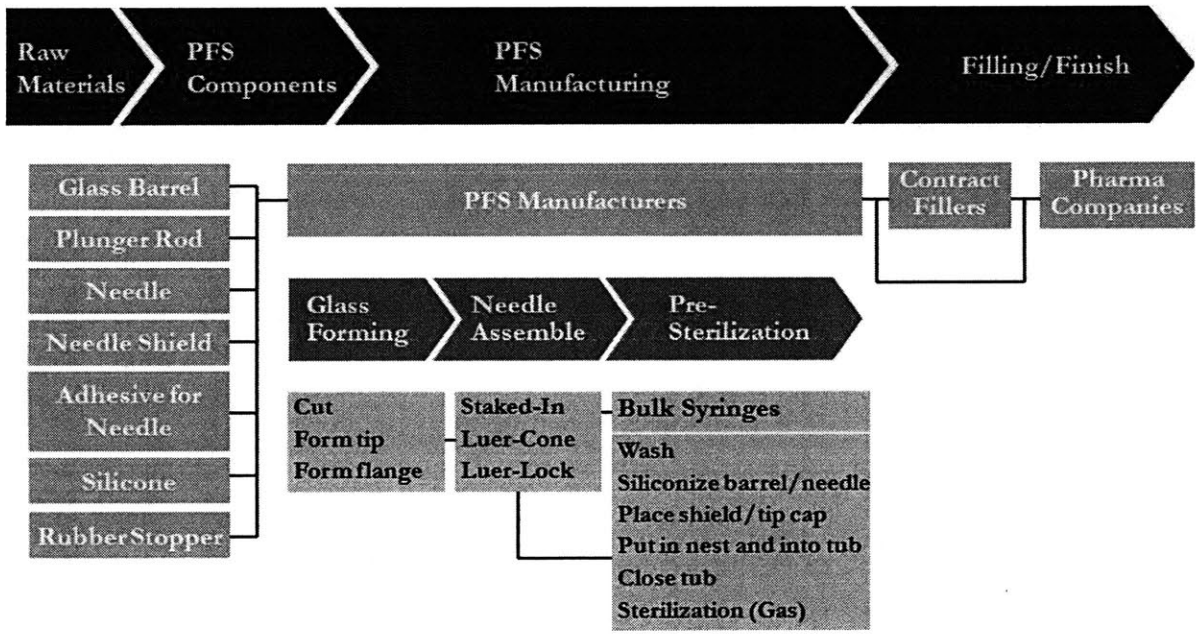

Figure 9. Prefilled Syringe Market Value Chain

3.1 History of Prefilled Syringe Market

Introduction of Prefilled Syringes[10]

Over 30 years ago, it was difficult to promote and market prefilled syringes. Single- and multi-dose vials and ampoules were the standard and the prefilled syringe was a virtually unknown product, used only for a narrow range of therapeutic classes and seen as relatively insignificantly niche market product.

The origins of the prefilled syringe's rise as a preferred container date back to early 1980s in Europe, when pharmaceutical companies successfully introduced the prefilled syringes as the drug delivery system into growing markets such as anti-coagulants (heparins) and vaccines with the innovation. As those therapeutic classes showed strong organic growth over the years, so did the numbers of prefilled syringes used.

Among the main heparin marketers were Sanofi and Rhone Poulenc-Rorer (both now Sanofi-Aventis), Pharmacia (now Pfizer), and Roche. Examples of large vaccine manufacturers were Institut Merieux (now Sanofi-Pasteur), SmithKline (now GlaxoSmithKline) and Behringwerke (now Novartis Vaccines).

After new indications for those first therapeutic classes were launched, heparins were brought into the US and grew substantially year after year. Those growing numbers made it attractive for prefilled syringe manufacturers to invest into and optimize their production. Further, machine makers were motivated to explore opportunities to improve the processing of prefilled syringes, enhancing productivity and cost efficiency. This virtuous cycle raised the profile and affordability of the prefilled syringe and awareness of the products in marketplace.

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[10] Thomas Schoenknecht, "Trends and Requirements on Prefillable Syringes: Past, Present and Future Developments," in Prefilled Syringes: The Trend for Growth Strengthens, *ONdrugDelivery*, 2006, p. 4

Introduction of Pre-sterilized Prefilled Syringes[11]

During the 1980s, an increasing number of pharmaceutical companies began filling prefilled syringes in-house. In the early days, however, prefilled syringe manufacturers supplied bulk syringes only. Hence, pharmaceutical companies had to wash, silicone, and sterilize the syringes before filling, these processes generally requiring high capital investment. To new pharmaceutical or biotechnology companies which didn't want to invest too much money to these processes, there was only one option, to depend on contract fillers who can do these processes instead of them. In order to make prefilled syringes accessible to a wider range of pharmaceutical customers, pre-siliconized and pre-sterilized syringes were developed. So, new concepts of prefilled syringe were presented with washed and siliconized syringes in a sterilized tub and ready to be filled.

With a combination of pre-sterilized format's advantages and market needs, pre-sterilized prefilled syringes has been growing substantially; many new pharmaceutical companies entered the market with pre-sterilized prefilled syringe and even leading big pharmaceutical companies who used bulk syringes turned their interests to this new syringe format.

The US market with a shorter history of prefilled syringes was particularly keen on the advantages which the pre-sterilized format gave. Currently, the US prefilled syringe market is exclusively 100% a pre-sterilized market.

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[11] Thomas Schoenknecht, "Trends and Requirements on Prefillable Syringes: Past, Present and Future Developments," in Prefilled Syringes: The Trend for Growth Strengthens, *ONdrugDelivery*, 2006, p. 4

3.2 Growth Drivers of Prefilled Syringe Market

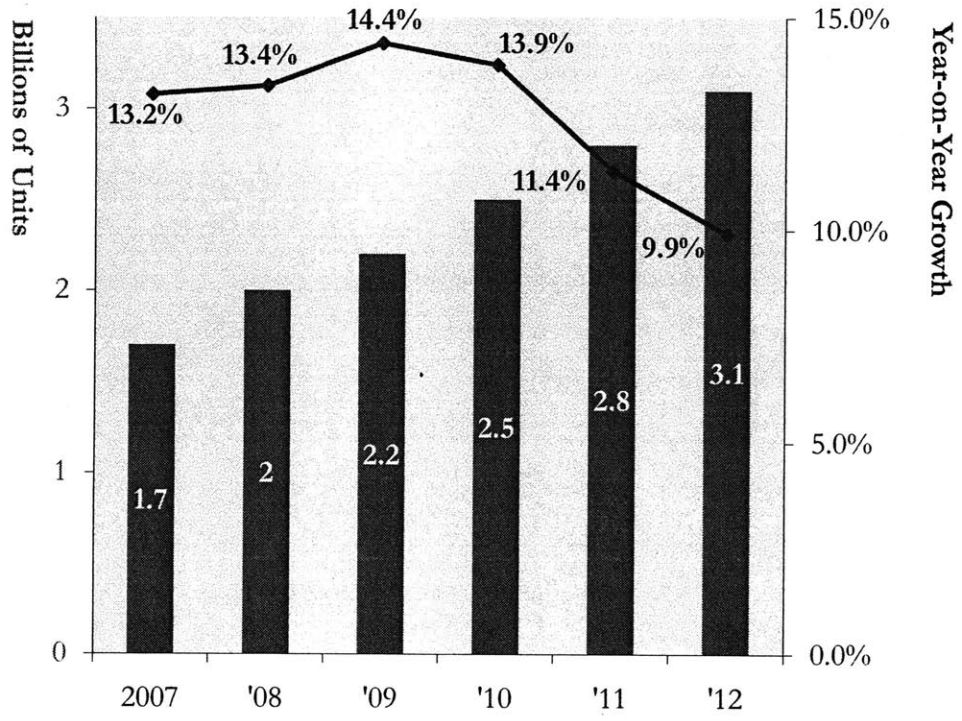

Figure 10. Historic Demand and Future Forecast of Worldwide Prefilled Syringe Market[12]

The prefilled syringe market has grown significantly and is expected to grow further in the future. Currently worldwide demand of prefilled syringes is in the range of 2 to 2.5 billion units per year with more than double-digit annual growth rates. As prefilled syringes have advantages as a drug delivery system over others such as vials and ampoules, more pharmaceutical companies have chosen prefilled syringes as a drug delivery system for their drug products based on customer satisfaction, safety, productivity, and efficiency. Now, it is critical to find what have been historical growth drivers of the prefilled syringe market and what will be future growth drivers.

[12] Greystone Associates, "*Prefilled Syringes: Drugs, Devices, and Disease Therapeutics*," May 2009

Strong Growth of Anti-Coagulants (Heparins) and Vaccines Markets

Needless to say, the origins of the prefilled syringe's rise as the preferred container were in the extremely successful market introduction of syringes as the drug delivery unit for anti-coagulants (heparins) and vaccines markets. As these two therapeutic markets account for more than 80% of worldwide prefilled syringes demand, historical and future growths of prefilled syringe market depend highly on the two markets' growths.

The anti-coagulants (heparins) market has been the biggest therapeutic area for prefilled syringes demand. In the heparins market, Sanofi-Aventis' Lovenox® (enoxaparin sodium), low molecular weight heparin for treatment and prevention of deep vein thrombosis and acute coronary syndromes, has been a dominant market leader with more than 90% of total prescriptions in the area; the net sales of Lovenox® in 2009 recorded € 3,043 million. [13] In 2009 3rd-Qtr report, moreover, Sanofi-Aventis mentioned that the 3rd-Qtr net sales of Lovenox® rose by 13.7% to € 747 million and that, over the nine months to end September, net sales of the product advanced by 9.1% to € 2,289 million. [14]

Vaccines market has been the second largest therapeutic area. It is important to note that the market has grown at more than 8% of annual growth rate and is expected to grow further for the future.[15] On Oct 31, 2009, Sanofi-Aventis' CEO Chris Viehbacher told German newspaper Frankfurter Allgemeine Zeitung that the company plans to increase its vaccines business. "We want to double it in the next five years," he said. "Its share in group sales will increase as a result from 10-11 percent to 15-16 percent." Viehbacher added that Sanofi's expansion plan was one of the reasons it bought an India-based company, which has new vaccines for diseases such as cholera in the pipeline.[16]

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[13] Sanofi-Aventis 2009 Annual Report
[14] Sanofi-Aventis 2009 3rd-Qtr Report
[15] Greystone Associates, "*Prefilled Syringes: Drugs, Devices, and Disease Therapeutics*," May 2009
[16] "Sanofi wants to double vaccine business," Routers, Frankfurt, 31 October 2009

Continuing rise in number of biotech drugs reaching the market

Both the number of products in development and marketed products from biotechnology industry has grown significantly. New treatments for diseases and chronic conditions have been developed especially in the areas of anemia, multiple sclerosis, oncology, and rheumatoid arthritis. In addition, many of the innovative products have been large molecules, such as monoclonal antibodies and proteins, which all need to be delivered via the injectable route. The physical nature of these biotechnology-derived drugs means that they are administered by injection.

The trend towards home health care and self-injection

In the past, a healthcare worker or physician would administer the injection. Today, however, an increasing number of drugs are being self-administered by the patient, and the packaging of a drug in a prefilled syringe as against a vial reduces the number of steps for the patient and therefore the risk of dosing errors. This procedural simplification equally applies to health care workers too. With prefilled syringes, many injectable drugs can be easily self-administered by the patient at home and accessed through physicians, community pharmacists, or mail-order pharmacies, which may present an opportunity to provide additional value.[17] Furthermore, as more therapies and drugs need to be taken for longer durations, the necessity of home health care and self-injection increases.

The relative ease of use, and few steps involved in prefilled syringes compared with using vials and ampoules

Data from Frost and Sullivan, a global market-research firm, demonstrate the importance of product presentation to physicians and patients. Three of the top five factors influencing a physician's choice of a drug-delivery type — ease of use by patients (16%), convenience (11%), and comfort (9%) — are affected by the presentation of the product. Physicians also commonly view patient satisfaction (14%) and a minimum of side effects (9%) as important factors in their choice of drug-delivery methods. When selecting a drug-delivery device for their patients, 46% of physicians take into account whether it easily enables self-administration.[18] Patients who have a choice between drug-

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[17] Mathias Romacker, "Injectable Drug Delivery – How far have we come and where are we going?," *American Pharmaceutical Review*, March 2009, p. 34

[18] Frost and Sullivan, "US Drug Delivery: Usage Patterns, Preferences and Opportunities in the US—Physicians'

delivery devices also judge the ease of self-administration (37%) and whether the product has been recommended by the physician (24%).[19] Prefilled syringes also present economic advantages for pharmaceutical companies who are marketing injectable therapeutics. Because the devices meet customer demands for increased safety and convenience, companies often are rewarded with premium pricing for prefilled syringes compared with vials.[20]

In order to capture the prefilled syringes' values in marketplace, for example, Teva Pharmaceuticals (Petach Tikva, Israel) changed the lyophilized vial presentation of Copaxone (glatiramer acetate) into a stable liquid offered in a prefilled syringe in 2002. Before reformulation, market share of Copaxone was declining. Yet, the new presentation achieved rapid acceptance in the market; 64% of its patients switched to the prefilled syringe version within the first three months of availability. The remainder switched within six months of the new product's launch. The Copaxone prefilled syringe had measurable advantages for patients on chronic therapy for multiple sclerosis, particularly the amount of time required for self-administration.[21] The average time a patient spent preparing for a Copaxone injection was reduced from the 235 seconds it took to reconstitute the product and draw it into a syringe to 38 seconds with a prefilled syringe. Consequently, the reformulated version saved a typical patient more than 20 hours over the course of a year. For Teva, increased patient convenience was rewarded with premium pricing, compared with the original formulation. In 2002, the premium started at 5% and rose to 48.6% by 2005.[22]

Reduction in overfill and waste compared with vials

Moreover, prefilled syringes help increase the saleable yield of active pharmaceutical ingredient (API). Filling API in prefilled syringes enables the required dose to be delivered precisely. Consequently, only trace amounts of API remain in the needle of the prefilled syringe after injection. In contrast, single-

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Perspective," Vol. 2, 2008

[19] Frost and Sullivan, "US Drug Delivery: Usage Patterns, Preferences and Opportunities in the US—The Patient's Perspective," Vol. 1, 2008

[20] Michael Borlet, "Financial Model for Converting from a Vial to a Pre-filled Syringe," *The Universe of Pre-Filled Syringes and Injection Devices*, presented at PDA, San Diego, CA, 2008

[21] Tom Polen, "Enhanced Packaging and Reformulations Give New Life to Biologics," *BioPharm International*, Vol.19, Issue 10, 2006, p. 60–66

[22] Tom Polen, "Enhanced Packaging and Reformulations Give New Life to Biologics," *BioPharm International*, Vol.19, Issue 10, 2006, p. 60–66

or multi-use vials require overfilling the API to ensure that an accurate dose is pulled into the syringe each time.[23] Not only do prefilled syringes offer better dose precision and reduce the risk of administering wrong dose compared with vials, but also they provide pharmaceutical companies with potential economic advantages. As rising numbers of high-cost drugs, such as biotechnology-derived drugs, have reached the market, moreover, it becomes more important to reduce or eliminate overfill and other sources of waste.

Increased Pressure on the branded products differentiation

In the past, some drugs showed sterling performances and became mega blockbusters as they were unique in their fields and indications. However, new product launches often occur into existing standards of care while launched products are already or will be facing fierce competition in the marketplace when patents will expire and generic and biosimilar competition loom on the horizon. Of course, if a drug can compete on safety and efficacy, marketing and promotional activities will tailor messages around those, then drug delivery may play a second tier role. For the pharmaceutical industry, however, there is now a competitive pressure within a therapeutic area. Hence, pharmaceutical companies use life-cycle management tools to protect the branded product when it loses its exclusivity. Declining productivity in pharmaceutical research and rising costs are shifting attention towards life-cycle management of established product portfolios. As many drugs move into the mature age of their life cycles, the presentation and delivery of a drug may play a major role as a differentiator for market success.[24] Currently, drug delivery systems play a pivotal role in strategies aimed at differentiation from competition.

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[23] Raul Soikes, "Moving from Vial to Prefilled Syringe: A Project Manager's Perspective," *Pharmaceutical Technology*, September 2009

[24] Mathias Romacker, "Injectable Drug Delivery – How far have we come and where are we going?," *American Pharmaceutical Review*, March 2009, p. 34

3.3 Prefilled Syringe Suppliers & Buyers

In order to analyze the prefilled syringe market further, it is critical to analyze suppliers and buyers in the value chain. This supplier and buyer analysis will be mentioned again later in Chapters 5 and 6 to develop a recommendation on balancing two factors.

3.3.1 Prefilled Syringe Suppliers

Prefilled syringe manufacturers basically manufacture and supply non-sterilized bulk syringes or pre-sterilized syringes to contract fillers or pharmaceutical companies. There have been several suppliers in the market. During my project, I analyzed five important prefilled syringe suppliers by conducting personal and phone interviews with Amgen staff and supplier representatives. It should be noted that this supplier analysis is mainly about glass prefilled syringe market.
Traditionally, prefilled syringe products have been packaged in glass syringes because the industry has decades of experience with this material as compared to plastic which are relatively new. Although innovative plastic syringes are overcoming its disadvantages and surpassing the advantages of glass, plastic syringes have recently been launched to the market and the new technology has not been commercialized in US yet as a drug storage and injection platform. The impact of the plastic syringes to the market will be analyzed later in more details. In this thesis, in addition, I will refer to each supplier as Supplier A to E to maintain confidentiality.

It is very critical to note that there has been one dominant prefilled syringe supplier in the market; 'Supplier A'. Supplier A is a multinational with a long history of supplying syringes. Supplier A has been a leading innovator in prefilled syringe market in terms of capacity, technology, and quality levels. Supplier B is the second largest prefilled syringe supplier both in pre-sterilized and in bulk syringes markets. Supplier B is an internationally leading manufacturer of high-quality specialty products made of glass and plastic for the global pharmaceutical & life science industry. Pre-sterilized syringes are one of its most important areas of business. Supplier B has more than 20% market share in total glass prefilled syringe market and, especially, approximately 40% market share in bulk syringes market.

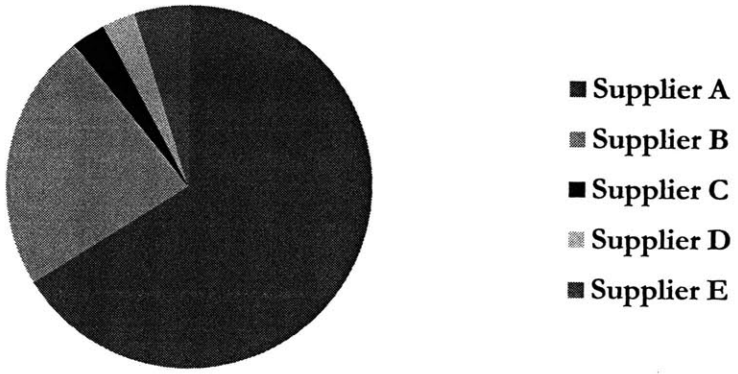

Figure 11. Market Share of Glass Prefilled Syringe Suppliers in Total Market

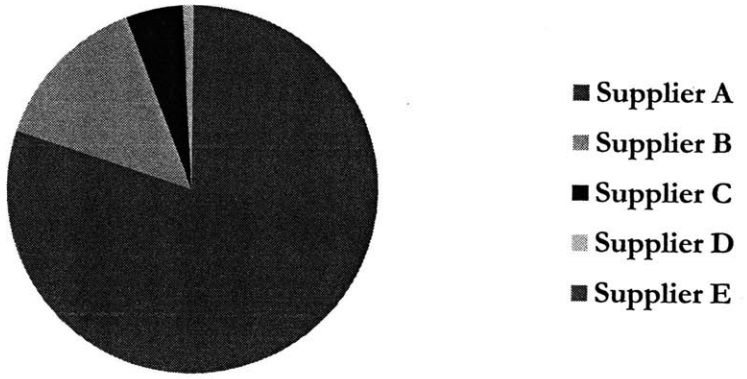

Figure 12. Market Share of Glass Prefilled Syringe Suppliers in Pre-sterilized Market: Pre-sterilized market represents approximately 60% of total market

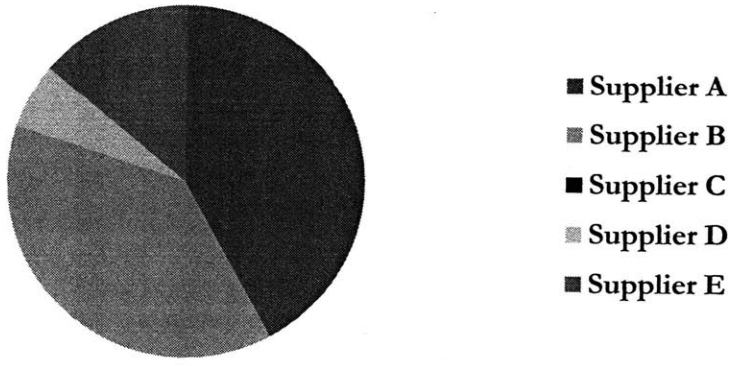

Figure 13. Market Share of Glass Prefilled Syringe Suppliers in Bulk Market[25]

[25] In Figure 14, 15, and 16, data labels are intentionally excluded for confidential issues

Table 2. Suppliers Strengths and Weaknesses Analysis[26]

	Strengths	Weaknesses
A	: Manufactures prefilled syringes globally : Highest volume capacity with economies of scale : Knows market very well and has largest market share : Has built Strong relationships with pharmaceutical companies : Has been an innovator in the market	: Has been challenged to leverage strong prefilled syringe business to other drug delivery devices : Has been under attack from competitors : Changes slowly when challenged by low volume requests
B	: Profitable and financially solid : Has been successful in other therapeutic areas such as vaccines and heparins : Has strong product development teams : High volume capacity; the second largest supplier : Has strong glass-tubing business : Has good customer base in EU; significant volume of syringe business in EU : Has a business in Asia : Strong in bulk syringes market	: Has committed to reach-easy target markets such as vaccines and heparins : Relatively weak track records in biotech pre-sterilized market : Small syringe business outside EU : Relatively narrow customer base : Cost is not as low as Supplier A : Not as innovative as Supplier A in terms of quality perspective
C	: Big company; glass producer with vertical integration from glass melting to tubing : Has manufacturing facilities in EU and US : Rated very high for technical capability	: Historically inconsistent communications about capability or commitment in the syringe market
D	: Has been focusing on the biotech market : Views itself as a real partner with its customers : Well managed privately-owned company : Strong in glass-manufacturing business; manufactures and sells glass forming and tubing machines; has high tolerance control capability for glass prefilled syringes : Strong in vial, cartridges, and ampoules businesses	: Relatively smaller business : Technically very capable but needs guidance on addressing high quality segment of biotech market : Low volume capacity
E	: Supplies vials, ampoules, and other delivery systems for injectable drugs	: Relatively newer to the market segment and need more time/development to be viable; has been only one year in pre-sterilized market : Has only one manufacturing facility in EU : Limited volume capacity

[26] This analysis is based on internal and external interviews during the project, so it may be subjective

3.3.2 Prefilled Syringe Buyers

Prefilled syringes buyers are contract fillers or pharmaceutical/biotechnology companies who fill injectable drugs into prefilled syringes and deliver those to distributors or customers including healthcare providers and patients. Some buyers, of course, wash and siliconize barrels or needles and sterilize those before filling in case they are supplied bulk syringes.

There are several therapeutic areas in which pharmaceutical and biotechnology companies use prefilled syringes for their injectable drug delivery systems. The group of therapeutic areas can be divided into three large areas: 1) high-end biotech, including Erythropoietic-Stimulating Agents (ESAs), Hematopoietics, Multiple Sclerosis (MS), Osteoarthritis, Rheumatoid Arthritis (RA), Hepatitis C, and DNA Vaccines, 2) vaccines, and 3) Anti-Coagulants (Heparins).

As mentioned earlier, vaccines and heparins areas are two largest areas for prefilled syringes demand, accounting for more than 80% of total worldwide prefilled syringes consumption. There have been consolidations on the buyer side. Currently, the three largest prefilled syringe buyers are Sanofi, GSK, and Pfizer. These three buyers represent two thirds of total prefilled syringe consumption, all of which have strong businesses both in vaccines and in heparins markets.

In summary, although prefilled syringe has become an important drug delivery system for biotech companies, most big suppliers and buyers have their main business in mass standard-quality markets. The thesis will turn to challenges and issues which biotech companies have faced in the chapter.

4 Biotech's Challenges/Issues in Prefilled Syringe Market

The biggest challenge of biotechnology companies in the prefilled syringe market is that the quality requirements are among the highest in the industry while consumption is a minor portion of the market. This makes it less attractive for prefilled syringe suppliers to align to the biotech's needs. Although biotechnology companies have made big efforts to elevate the entire bar of quality standards in the market, suppliers sometimes hesitate to follow because they also have other buyers in larger markets with lower or currently acceptable quality requirements.

4.1 High Prefilled Syringe Quality Standards

Since adopting glass prefilled syringes for its injectable drugs, biotech has been challenged with quality issues: cosmetic defects, silicone sensitivity, tungsten residuals, glass breakage and more. Most modern biopharmaceuticals are proteins/peptides, which are biopolymers with unique chemical, physical, and rheological properties. However, these molecules are sensitive to heat, light, surface agitation, and chemical contaminants. Among the causes for chemical and physical instability are leachables in container closure systems.[27] Interactions of leached contaminants with therapeutic proteins can result in aggregation, particulate formation, and loss of native protein tertiary structures.[28] Even a small fraction of aggregated proteins could reduce biological activity and enhance immunogenicity.[29] Minute concentrations of metals, plasticizers, and other packaging materials can deactivate or denature therapeutic proteins/peptides. Container closure integrity is a regulatory requirement to protect the potency, efficacy, and safety/sterility of therapeutics. In glass-based syringe systems, a range of material comes in immediate contact with the active ingredients: silicone oil, tungsten, closure, rubber stopper, glass, adhesive (for staked needle syringes), and the needle.[30]

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[27] Leonardo Allain and Qingxi Wang, "Impact of package leachables on the stability of pharmaceutical products," *American Pharmaceutical Review*, May/June 2007, Vol.10, No.4

[28] Ingrid Markovic, "Evaluation of Safety and Quality Impact of Extractable and Leachable Substances in Therapeutic Biologic Protein Products: a Risk-based Perspective," *Expert Opinion on Drug Safety*, 2007, Vol.6, No.5

[29] Amy S. Rosenberg, "Effects of Protein Aggregates, an Immunologic Perspective," *The AAPS Journal*, 2006, Vol.8, No.3

[30] Arno Fries, "Drug Delivery of Sensitive Biopharmaceuticals with Prefilled Syringes," *Drug Delivery Technology*, May 2009, p. 22-27

4.1.1 Silicone Sensitivity

Many biopharmaceuticals may be sensitive to silicone oil, a material commonly used to lubricate rubber plunger movement in glass barrel in order to facilitate administration of drugs. The silicone oil, which is used in most glass and plastic syringes, can cause issues with drug stability. Recently, some prefilled syringe manufacturers have started baking the silicone oil onto the syringe barrel to limit the amount of free silicone oil that is available, thus decreasing the potential for interaction with the drug product.[31] However, this technology is limited to use only for luer types of syringes, not for staked-needle syringes as the adhesive to attached needles cannot withstand heat sterilization. Others have developed barrier films to aid in lubricating the components, while protecting the drug product from contaminants that could potentially be leached from the elastomeric plunger which, in a syringe, is in constant contact with the product. Despite such efforts of prefilled syringe manufacturers, silicone sensitivity and controlling the amount of it is still one of the biggest quality issues of prefilled syringes.

4.1.2 Tungsten Residuals

Biotech drugs can also degrade when exposed to the tungsten residuals – the leftover traces of metal that remain after the glass-forming process. Tungsten pins typically form the nozzle end of the syringe during the glass-syringe formation process. Upon cooling, a needle is staked in with adhesive to make a glass prefilled syringe with a staked needle.[32] Many biotechnology companies are finding that tungsten extractables can cause aggregation in the protein formulations; reports describe tungsten-based particulate matter that leached into and interacted with the protein drug product.[33] Hence, biotechnology companies have been carefully using staked-needle glass syringes where tungsten tools were used in the fabrication of the glass because the process leaves a small amount of tungsten that reacts with their drug products.

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[31] Bernie Lahendro, "The Next Generation of Prefillable Syringes: Specialised Plastics Lead the Way," in Prefilled Syringes: Device Suppliers Meeting Pharmaceutical Standards, *ONdrugDelivery*, September 2007, p. 6-8

[32] Douglas Stout and Vinod Vilivalam, "Plastic Prefilled Syringes: A Better Fit for Autoinjector Systems," in Injectable Drug Delivery, *Pharmaceutical Technology*, November 2009

[33] Jared S. Bee, Stephanie A. Nelson, Erwin Freund, John F. Carpenter, and Theodore W. Randolph, "Precipitation of a Monoclonal Antibody by Soluble Tungsten," *Journal of Pharmaceutical Sciences*, 2009, Vol.98, Issue 9, p. 3290-3301

4.1.3 Higher quality standards required for devices

These days, new devices are being introduced to patients for better safety, more user convenience, and higher user satisfaction. In general, for those improvements, the complexity of device development has been increased and the devices have required higher quality standards.

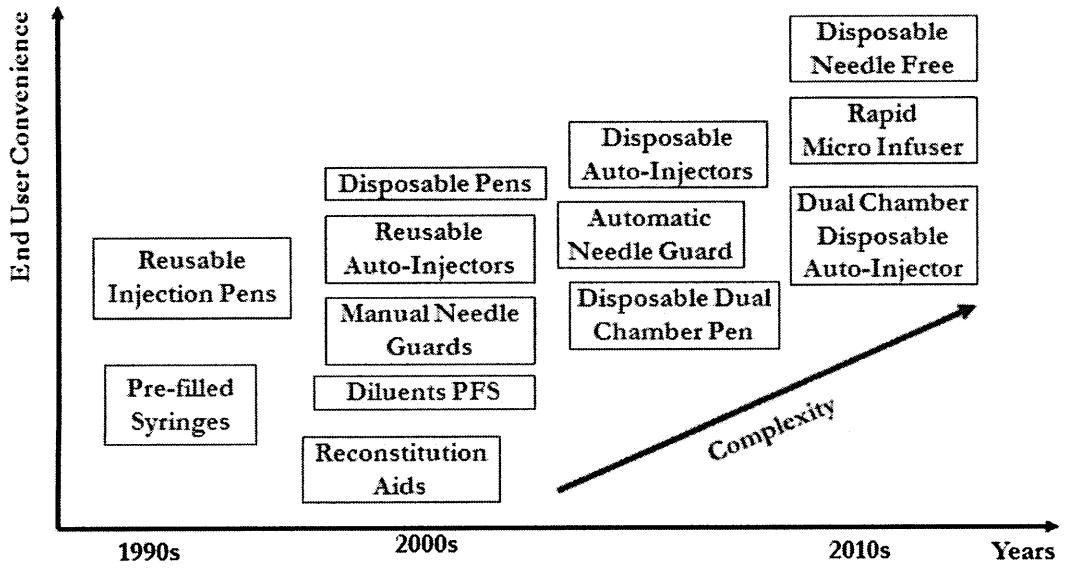

Figure 14. More Advanced Devices Have Been Launched with Complexity of Drug Product Development Increased[34]

As mentioned earlier, such new innovative devices can play a major role as a differentiator for market success especially when new products launch into an existing fiercely competitive marketplace, when an existing drug's patent is close to expiration, and when potential generics/biosimilar competition is expected. As seen in Figure 18, we can hypothesize that the higher quality standards are required for the prefilled syringes assembled into auto-injectors than for manually-working prefilled syringes.

[34] Mathias Romacker, "Development and Commercialization of a Pre-Filled Product," Management Forum Conference in London, May 2007

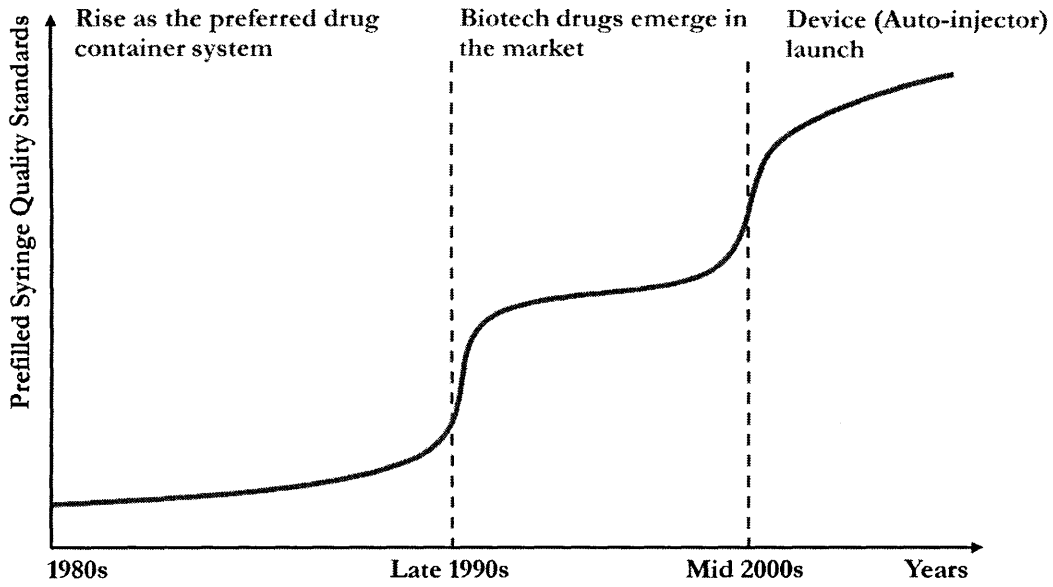

Figure 15. Prefilled Syringe Quality Standards Become Higher as Device Launching

Unevenly Distributed Silicone Oil

Unevenly distributed silicone oil may become an issue for all disposable and reusable auto-injectors. For instance, most auto-injectors work mechanically on a spring: when a patient presses a button, the spring, which has been compressed initially, starts to decompress and push a plunger rod of the prefilled syringe, injecting drugs to patient through needle. Recent studies have shown that silicone oil, which is used to increase lubricity in syringe systems, may be distributed unevenly, thus leaving certain areas of the prefilled syringe surface with insufficient lubrication.[35] The inconsistent silicone-oil coating can significantly affect the plunger-travel and glide forces in auto-injectors. In 2006, commercial lots of a drug product delivered by an auto-injector that contained a glass prefilled syringe were recalled in several European countries because of problems with slow or incomplete delivery of the drug.[36] Uneven silicone coating may increase break loose forces and cause failures such as incomplete injections. When patients inject a drug manually in such a case, it is unlikely that the subtle differences would even be notable to the syringe users.

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[35] Bruce Eu et al., Poster Presented at AAPS National Biotechnology Conference, Toronto, June 2008

[36] MHRA, Class 2 Drug Alert, Medicines Recall, Reference MDR 03-10/06, Neulasta SureClick Injection Device (London, Oct. 4, 2006)

Limitation on Glass-based Syringe: Dimensional Variability and Breakage

"Limitations on glass auto-injectors' performance may also begin with their material of construction. Glass is a formed product that must be heated. Mandrels form glass syringes' overall length, nose or tip, and flanges. This process can create dimensional variability. During manual operation, a glass syringe's variability usually is mitigated by the human user. However, dimensional tolerances may vary so much that an auto-injector system may be subject to failures such as incomplete injections."[37]

Glass also creates the possibility of breakage, which is a safety concern. Upon activation, the system's spring places all of its pressure on the syringe's glass flange. The flange, a weak point of a syringe, is fracturing if subjected to enough force. In auto-injectors, a strong spring is required to overcome system variability. Viscous drugs require more pressure for a complete injection. This pressure can lead to barrel breakage. A change in the place where pressure is applied, or registered, can greatly affect the safety of the delivery system.[38]

4.1.4 Impact of Quality Issues on Product Sales

Such quality issues may result in significantly adverse effects for the sales of drug products especially in such an industry that significantly values patient safety and is highly regulated. If new medical data or product quality issues suggest an unacceptable safety risk or previously unidentified side-effects, the company may withdraw some or all affected product — either voluntarily or by regulatory mandate — in certain therapeutic areas, or completely recall a product presentation from the market for some period or permanently. Biotechnology companies may experience the same or other problems in the future resulting in broader product recalls or adverse event trends, which may adversely affect the sales of their products.[39]

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[37] Douglas Stout and Vinod Vilivalam, "Plastic Prefilled Syringes: A Better Fit for Autoinjector Systems," in Injectable Drug Delivery, *Pharmaceutical Technology*, November 2009

[38] Douglas Stout and Vinod Vilivalam, "Plastic Prefilled Syringes: A Better Fit for Autoinjector Systems," in Injectable Drug Delivery, *Pharmaceutical Technology*, November 2009

[39] Amgen 2009 Annual Report

4.2 Small Consumption of Prefilled Syringes

Although 2 to 2.5 billion units of prefilled syringes are being supplied to the market, biotech market accounts for approximately 10% of total market demands. Amgen currently consumes tens of millions units per year for its four injectable drugs: Aranesp®, Enbrel®, NEUPOGEN®, and Neulasta®. Hence, it is important for biotech companies to understand each supplier's interest and future strategy related to prioritizing target between biotech and high volume markets or to making balance between two markets.

4.3 Single Sourcing Problem

Rapidly evolving high quality requirements have made biotech companies depend highly and solely on the leading quality innovator, the dominant prefilled syringe supplier, Supplier A. The supplier had relatively higher quality capability to meet biotech's high quality requirements than any other suppliers, making it easier for biotech companies to save efforts including time and money to achieve regulatory agencies' permissions. Since then, biotech companies have encountered single sourcing problems with dominant supplier's limited incentive to invest rapidly in biotech's needs especially when the dominant supplier has strong and stable business in other therapeutic markets which require relatively moderate quality standards with high volume. Single sourcing may also cause problems in risk management, so decision on single- or multi-souring will be examined carefully later in this thesis.

4.4 Changes in Supply Side

To prefilled syringe suppliers, anti-coagulants and vaccines markets have been and will be the markets which provide the suppliers with stable sales and also require moderate quality standards. On the other hand, the biotech market has been and is expected to continuously grow for the future and may offer higher price for prefilled syringes qualified for its sensitive biotech drugs with the market's relatively lower price sensitivity. In the prefilled syringe market, we can hypothesize that, to prefilled syringe suppliers, market value and volume of each therapeutic market are in inverse proportion. For example, high volume market such as anti-coagulants has a lower market value while biotech market has higher market value but lower volume. In addition, the business with biotech market can also provide the suppliers with opportunities to elevate their quality expectation to the next level and to be locked in the niche market.

To each prefilled syringe supplier, consequently, it is important to make a strategic decision on which market/buyer it should focus on or how to make a balance among different markets/buyers. Based on the phone interviews with supplier representatives, most suppliers agree that the biotech market is likely to be important to suppliers' future business. Some of them are considering strengthening their positions in the biotech market, and one of them appears to be highly keen on the biotech market instead of high volume markets where other suppliers have already had strong businesses. More interestingly, most of them agree that bargaining power in the market is shifting from supplier to buyer side because there has been more competition on the supplier side.

Competition in supply side between one dominant player and other suppliers

It has been noticed that competition between the dominant supplier and other suppliers in glass prefilled syringes market has become a threat. Even though the dominant supplier has improved their capabilities to offer highest -quality prefilled syringes, other suppliers have introduced better-quality prefilled syringes into the market to target sensitive drug products market including biopharmaceuticals. For example, Supplier B offers, for sensitive biopharmaceuticals and similarly demanding drugs, new advanced quality systems as a completely new quality of glass products with which it sets new standards of dimensional and cosmetic precision. The key to this is a unique system

of advanced forming processes and inspection procedures for injection vials, syringes, cartridges and ampoules. It also developed new innovative process which fixes the silicone oil deposition to the glass by thermal processes (not for syringes with needles affixed). Through this technology, it can produce prefilled syringes which offer ideal conditions for the stability of particularly sensitive ingredients such as proteins and peptides.[40] Supplier C presented a new innovative syringe product at the company's symposium in Germany, in December 2009. The company commented, "We have developed a new and highly innovative syringe system for the special needs of highly sensitive drugs. Its unique design offers improved drug stability and a gentle application." "Our new product enables the drug not to be in contact with the needle or the adhesive during storage, which prevents sensitive drugs from interacting with the adhesive or the metal of the needle" explained a Product Manager of the company.[41]

Introduction of plastic (COP, Cyclic Olefin Polymers) prefilled syringes[42]

"Glass prefilled syringes have been extensively used for packaging and delivering drugs and biologics because the pharmaceutical industry has decades of experience with this material. Although not yet reaching the adoption level of glass syringes, plastic syringe systems continue to gain strong acceptance from pharmaceutical makers because of recent improvements in their design, composition and manufacture. Plastic syringes, which first came onto the market in the early 1990s, were historically made from polypropylene, which does not have the clarity of glass. In addition, another main issue with plastic syringes has been that they are more permeable to oxygen than glass syringes. Chemical changes caused by oxygen can compromise therapeutic activity. Glass is sufficiently clear, and provides a high barrier to moisture and oxygen that can damage a therapeutic. As mentioned earlier, however, there are quality-related issues with glass syringes that may be disadvantageous for drug formulations such as interactions with silicone oil causing protein aggregation. In an attempt to address these unmet market needs, plastics makers developed a new class of thermo elastic polymers: Cyclic Olefin Polymers (COP) that are as clear as glass but are lighter and less prone to breakage. These resins are also more resistant than polypropylene to water

[40] Supplier B 2009 Annual Report
[41] Supplier C Press Release, Dec 2009
[42] Paragraphs from Bernie Lahendro, "The Next Generation of Ready-to-use Prefillable Syringes: First in Silicone-free Solutions," in Prefilled syringes: The Container of Choice for Today's Injectables, *ONdrugDelivery*, 2008, p.24-26

transmission, which lengthens the shelf life of the drugs they contain."

The attractive physical and chemical properties that COP resin can provide is mentioned in *ONdrugDelivery*'s recent issue like followings:[43]

- "High heat resistance: the material is autoclavable
- Excellent low-temperature characteristics including tolerance of freeze drying and liquid-nitrogen exposures
- Excellent drainability: offers a non-wettable surface with low surface energy and a contact angle of 80°, compared to 7° for glass
- High break-resistance and transparency
- Low extractables and solvent resistance
- Wide pH range, from 2 to 12 and
- Easy, safe, environmentally friendly disposal"

Recently, Supplier Z has introduced the COP-based plastic prefilled syringe system. This will be the market's first silicone-oil-free, tungsten-free, ready-to-use prefilled syringe system that can mitigate the risks associated with glass syringes. Supplier Z does not have business in glass prefilled syringe manufacturing but has had strong business in the market of syringe or other injectable drug delivery systems closure components, such as rubber plunger, needle shields, tip cap, and other safety/administration systems for lyophilized drug reconstitution, mixing, and transfer. Biotech companies are likely to consider switching to the COP-based plastic syringes. Because this new technology has not yet been commercialized in the US market and does not have enough volume capacity, however, the companies also hesitate to make immediate decisions. Detailed analysis of the COP-based plastic prefilled syringe's attractiveness to biotechnology companies will be conducted later in this thesis.

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[43] Paragraphs from Bernie Lahendro, "The Next Generation of Ready-to-use Prefillable Syringes: First in Silicone-free Solutions," in Prefilled syringes: The Container of Choice for Today's Injectables, *ONdrugDelivery*, 2008, p.24-26

Suppliers' Capacity Expansions

Based on the research during the project, all prefilled syringe supplier capacity is expected to increase by double-digit percentages, which outstrips the demand growth. Supplier A and C will open new prefilled syringe plants in Hungary and in US respectively. Suppliers B and E have plans to increase their capacities. In addition, Supplier Z, as mentioned earlier, will start plastic prefilled syringe production, and Sanofi and a new supplier partnered to launch a new glass prefilled syringe with integrated automatic accidental needle stick prevention feature in the future.

Until Chapter 4, the thesis thoroughly analyzed the prefilled syringe market and discussed biotech companies' (including Amgen's) challenges along with current changes and issues in the market. Based on previous analyses and discussions, now, it will turn to discuss three important subjects regarding Amgen's potential future positioning strategy in the prefilled syringe market: single or multi sourcing, strategic partner selection among suppliers, and supplier relationship structuring.

5 Single or Multi Sourcing Decision

Determining the number of suppliers is one of the key issues of supplier management. Theoretically, single and multi sourcing approaches have their own advantages and drawbacks, as listed in the table below.

Table 2. Advantages and Drawbacks of Multi-Sourcing Approach[44]

Pros of Multi-Sourcing Approach	Cons of Multi-Sourcing Approach
• Competition motivates suppliers to improve and be more responsive, and provides the buyer with financial leverage in pricing negotiations • Reduces the impact of supplier failure • Increases the flexibility to change technologies as the life cycle evolves and allows more ready experimentation with alternative technologies	• Increases the complexity of vendor relationships, spare parts, and service contract management • Requires duplicate engineering and development efforts to integrate two vendor's technologies • Vendors have less trust and loyalty, making influence over and access to them more difficult • Makes ramp-up of new facilities, transfer of production among facilities, and operations logistics more complicated • Can reduce learning curve effects, if there are multiple technologies to learn and volume is shared among them • Can increase training and equipment maintenance costs

As firms started to adopt new manufacturing strategies and technologies such as just-in-time (JIT) manufacturing, lean manufacturing or Kanban in 1980s, many companies have streamlined their supplier base following the examples of the Japanese manufacturing firms. Some firms adopted single sourcing or turned to deal with a limited number of main suppliers in order to build stronger and longer-term relationships with suppliers and to reduce the fixed costs that are incurred by multiple

[44] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 220

vendor relationships. Examples of such practices are numerous: Xerox reduced its supplier base from 5000 to 400 from 1981 to 85 and reduced its lead times from 52 to 18 weeks, as well as its product costs by almost 10% a year. AlliedSignal reduced its supplier base from 10,000 in 1992 to fewer than 2,000 in 1997, and the estimated savings in 1993 were $28 million.[45]

However, single-sourcing also happened to be very risky. For example, Ericsson learned painful lessons in the danger of consolidating supply to a single sourcing when the only chips supplier Philips suffered a fire in its plant of Albuquerque in Mar 2000. Philips' site became unable to produce the computer chips that Ericsson needed to produce mobile handsets. The damages were very brutal to Ericsson; it reported that the fire contributed to a loss of $1.8 billion in 2000 and lost almost 4% of market share.[46] Since 9/11, firms have become more aware than ever of the risks that can be caused by single-sourcing approach, and the approach has been revisited.

As described by Beckman and Rosenfield in *Operations Strategy: Competing in the 21st Century*, firms base their decision about whether to single or multi source on the following factors:

- Uniqueness of sourced item,
- Viability and reliability of suppliers,
- Stability of the technology associated with the item being sourced,
- Proportion of the buyer's purchase to the total business of the supplier,
- Branding implications of sourcing decision, and
- Competitiveness of the market.[47]

This chapter will discuss these major factors as they apply to Amgen's decision to single or multi source.

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[45] Sophie Pochard, "Managing Risks of Supply-Chain Disruptions: Dual Sourcing as a Real Option" (2003)
[46] Sophie Pochard, "Managing Risks of Supply-Chain Disruptions: Dual Sourcing as a Real Option" (2003)
[47] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 220

5.1 Uniqueness of sourced item

This factor is founded upon whether the sourced item is so unique or differentiated that it can only be produced by a single source. It is true that the dominant supplier, Supplier A, has for now a higher quality capability than any other potential suppliers. Assuming the quality of prefilled syringe is one of the most important criteria to Amgen, it can be said that Amgen should have a single prefilled syringe source to maintain high quality standards. However, a prefilled syringe is not a unique item itself. In addition, as mentioned earlier, some potential suppliers have already had strong businesses in other therapeutic areas and made big efforts on elevating their quality capability especially to meet biopharmaceutical's needs. Even though it is expected that it will take a time for other suppliers to meet Amgen's high quality standards, Amgen has dealt with and overcome many quality-related issues; as a result Amgen can work closely with other potential suppliers to meet biotech's needs. Along with those efforts, Amgen has hired world top-class experts in prefilled syringe industry including suppliers in order to have knowledge and expertise in the industry, regarding quality, manufacturing process, business dynamics, and so on, and to build stronger relationship both with the dominant supplier and with potential suppliers by learning supplier's perspectives.

5.2 Viability and reliability of suppliers

Having a supplier go out of business is not a high probability event, but disruptions such as labor strikes, fires, and floods at suppliers happen with some frequency, and performance lapses even more frequently. Supplier A is financially healthy and it is highly likely to be in business for the foreseeable future. However relying on single-source can be risky because there may be risk of natural disaster, labor strife, and so on. Along with Ericsson's example mentioned earlier, Vacuum cleaner manufacturer Oreck's manufacturing facility in Long Beach, Mississippi, was shut down for 10 days when Hurricane Katrina hit, and flash devices for internet appliance products were in short supply when manufacturers underestimated demand and were unable to meet the customer's requirements.[48]

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[48] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 221

5.3 Stability of the technology associated with the item being sourced

When a firm's competitiveness relies on using the most current process, information, or product technologies, and it procures that technology from a supplier outside the firm, the stability of the technology dictates whether or not it should use more than one supplier. If the technology is stable, then barring motivators to do otherwise, it can source from a single supplier. This assumes that if the technology changes or evolves, it does so at a rate with which the supplier can keep pace. On the other hand, if technology is changing rapidly, the capabilities of the single source could possibly be overtaken by another supplier. Having multiple sources in such a case increases the likelihood that the newest technology is available from a current supplier.[49] It is expected that the dominant prefilled syringe supplier currently has leading-edge technology, but other potential suppliers may try to overtake it.

Overall, the technology of glass prefilled syringes is likely to become stable as competition in supplier side becomes severe. On the other hand, the introduction of COP-based plastic prefilled syringes may require Amgen to explore the newer technology. My analysis suggests that the technology in prefilled syringe market is neither stable nor changing rapidly to make a big impact on the decision to single or multi source. Instead, Amgen can learn from aircraft manufacturers' strategies on aircraft engine supplier management as described below.

General Electric, Pratt & Whitney, and Rolls Royce all make aircraft engines. Even though the technology of aircraft engine industry is stable such that Boeing and Airbus can easily source engines from a single supplier, they design their new aircraft with flexibility to handle an engine from any one of these manufacturers. They do so partly because their customers, the airlines, like to have choices, but also because they want to keep all these suppliers in business. Each aircraft program Boeing and Airbus undertake is large, and they generally contract with more than one engine manufacturer on these programs. Without competition, the aircraft manufacturers figure, they cannot be assured that there will be pressure to invest in the development of the latest engine technologies. Aircraft

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[49] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 221

manufacturers multisource not only to have access to the latest technologies but also to encourage their suppliers to invent those new technologies.[50]

In other words, if Amgen can succeed on elevating the quality of prefilled syringe suppliers, Amgen can easily source prefilled syringes for its new or existing drugs from multi suppliers with higher bargaining power and can keep all approved suppliers in business.

5.4 Proportion of the buyer's purchase to the total business of the supplier

This fourth factor is the most important one related to Amgen's decision to single or multi source. Because the amount of business Amgen does with the dominant supplier represents a very small part of that supplier's business, the supplier may hold a relative position of power that makes single sourcing risky. The supplier is likely to view the business as less important than that from other customers that procure larger quantities, such as pharmaceutical companies who have stable business in vaccines and heparins, and to be less responsive to Amgen's requests. In this case, multiple sources can both mitigate risks and provide a lever in the relationship. If the dominant supplier thinks that it can gain more volume, or risks losing the work it has because other potential suppliers are providing better service, then it may be more motivated to perform. In general the negotiation power of the customer goes up with the number of suppliers from which it sources a particular item.

5.5 Branding implications of sourcing decision

Sometimes the item being sourced is a key branding mechanism of the product or service ultimately being marketed: computer marketing, for example, is often based on the microprocessor and uses the "Intel Inside" slogan. In both the pharmaceutical and biotech industries, the prefilled syringe itself is not likely to be significant to a drug's branding.

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[50] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 221

5.6 Competitiveness of market

Competitiveness tends to reduce the uniqueness of products, but in general increases the performance of suppliers across the board. As emphasized earlier, prefilled syringe suppliers are strongly competing with one another. While the dominant supplier tries to defend its market share by differentiating and augmenting its products, other suppliers have also developed innovative product and process technology to attract buyers. Most existing suppliers have capacity expansion plan at various locations, and even new players are moving into the market with new innovative materials such as COP-based plastic. Assuming that the market for prefilled syringes will be highly competitive soon, multiple suppliers are likely to compete for business from the sourcing company, offering incentives on cost and delivery or performance improvement over time. In such situations, the use of multiple sources may increase Amgen's negotiation power and drive vendor performance improvements. Ultimately, the task for Amgen is to balance the performance of suppliers with the difficulty of coordinating additional suppliers.

5.7 Conclusion

In conclusion on Amgen's single or multi sourcing decision, Amgen should develop multi-sourcing strategies on prefilled syringe supplier management. The following figure shows the current situation of Amgen with respect to where it is located between single and multi sourcing decisions for prefilled syringes.

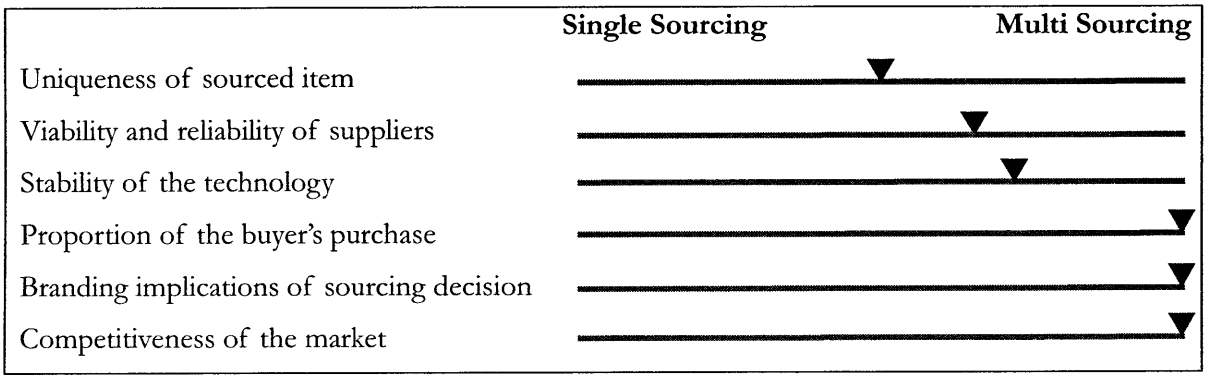


Figure 16. Amgen's Single or Multi Sourcing Decision Analysis

However, Amgen should also keep in mind that obtaining alternate sourcing of prefilled syringe may be very resource intensive and time consuming work. The dominant supplier's quality capacity is still the highest among all suppliers, and its prefilled syringes are specifically cited in Amgen's drug application with regulatory agencies. It is also notable that the switching cost to new or additional suppliers is also very high for multiple drugs and requires additional time. Furthermore, switching to multi sourcing may cause the previous single source supplier to hike prices as procured quantities may be reduced.

In its 2009 annual report, Amgen mentioned the following risk of single sourcing:[51]
"We rely on single-source unaffiliated third-party suppliers for certain raw materials, medical devices and components necessary for the formulation, fill and finish of our products. Certain of these raw materials, medical devices and components are the proprietary products of these unaffiliated third-party suppliers and are specifically cited in our drug application with regulatory agencies so that they

[51] Amgen 2009 Annual Report

must be obtained from that specific sole source and could not be obtained from another supplier unless and until the regulatory agency approved such supplier."

"Among the reasons we may be unable to obtain these raw materials, medical devices and components include:

- Regulatory requirements or action by regulatory agencies or others
- Adverse financial or other strategic developments at or affecting the supplier
- Unexpected demand for or shortage of raw materials, medical devices or components
- Labor disputes or shortages, including the effects of a pandemic flu outbreak or otherwise
- Failure to comply with our quality standards which results in quality and product failures, product contamination and/or recall

These events could adversely affect our ability to satisfy demand for our products, which could adversely affect our product sales and operating results materially."

Hence, Amgen should not only as a mid-term strategy work closely with other potential suppliers to mitigate risks and to leverage Amgen's power in supplier relationships, but also as a short-term strategy maintain a better relationship with the dominant supplier to secure stable prefilled syringe supplies until the regulatory agency approves other suppliers.

6 Buyer-Supplier Attractiveness Analysis

One of the main objectives of this project is to identify which prefilled syringe supplier is willing to be a strategic partner of Amgen by responding to Amgen's needs. In order to answer the question, it is critical to note that the prefilled syringe market has complicated dynamics featuring four major groups:

- Large pharmaceutical buyers
- Biotechnology buyers
- One dominant supplier
- Other potential suppliers

Each group has different capacities, capabilities, and requirements. In addition, attractiveness between each buyer and each supplier is too complicated to see at a glance.
Hence, I have developed 'Attractiveness Chart' to help better understand the inter-attractiveness between the four major groups.

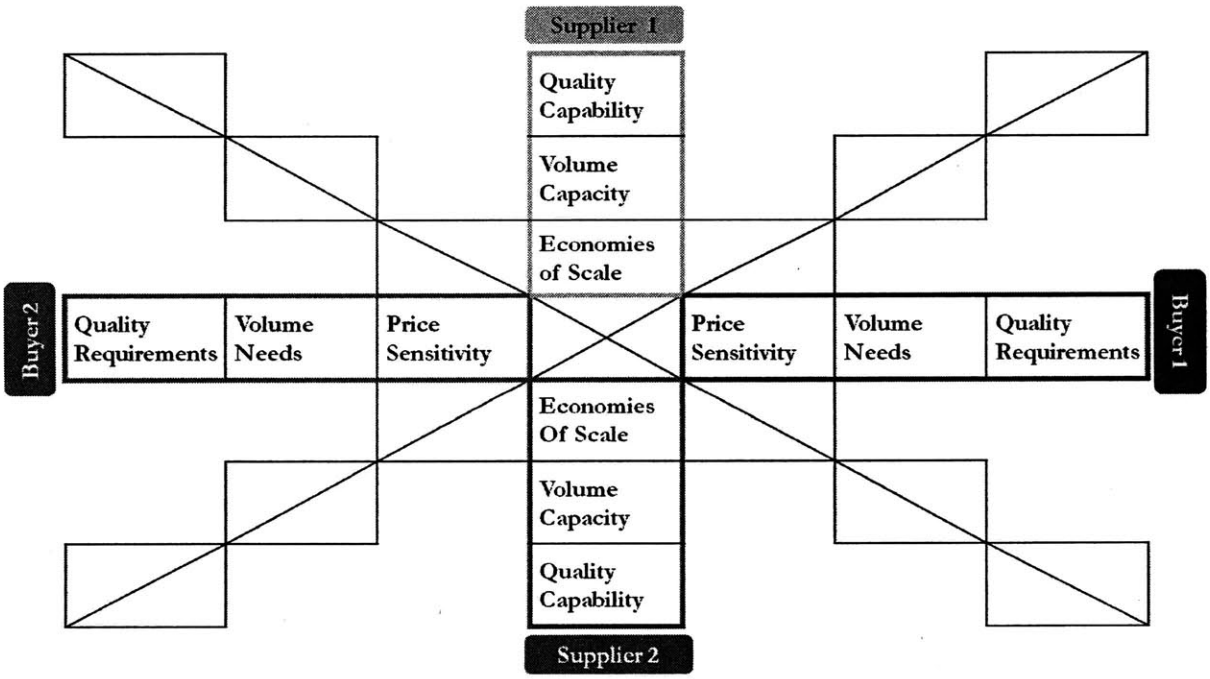
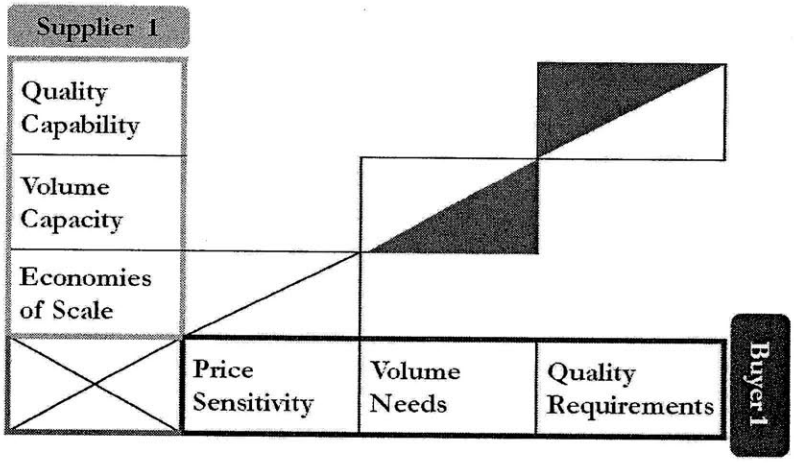


Figure 17. Attractiveness Chart for Four Groups

The followings describe how to fill out and read the attractiveness chart.

- Two buyers are on the x-axis: Buyer 1 on the positive side, and Buyer 2 on the negative side.
- On each side of the x-axis, three different factors, relevant needs or requirements of each buyer, are filled out: for example, buyer's quality requirements, volume needs, or price sensitivity.
- Similarly, two suppliers are on the y-axis: Supplier 1 in + side, and Supplier 2 in – side.
- On each side of the y-axis, similarly, three different factors, relevant capacities or capabilities of each buyer, are filled out: for example, supplier's quality capability, volume capacity, or economies of scale.
- Each quadrant shows the inter-attractiveness between one of two buyers and one of two suppliers in three different factors, such as price, volume, and quality. For example, the first quadrant of the chart shows the inter-attractiveness between Buyer 1 and Supplier 1.
- Each triangle shows the level of inter-attractiveness between two players in one of three factors, and the color of triangle displays the degree of attractiveness: blue for high attractiveness, yellow for middle, and red for low. For example, the blue triangle on the figure below shows the high attractiveness of Buyer 1's quality requirements to Supplier 1's quality capability, and the red triangle shows the low attractiveness of Supplier 1's volume capacity to Buyer 1's volume needs.



6.1 Dominant Supplier vs. Potential Suppliers in Glass Prefilled Syringe Market

First, the attractiveness chart is applied to glass prefilled syringe market. There are two buyers, big pharmaceutical companies and biotechnology companies, and two suppliers, the dominant supplier and other potential suppliers.

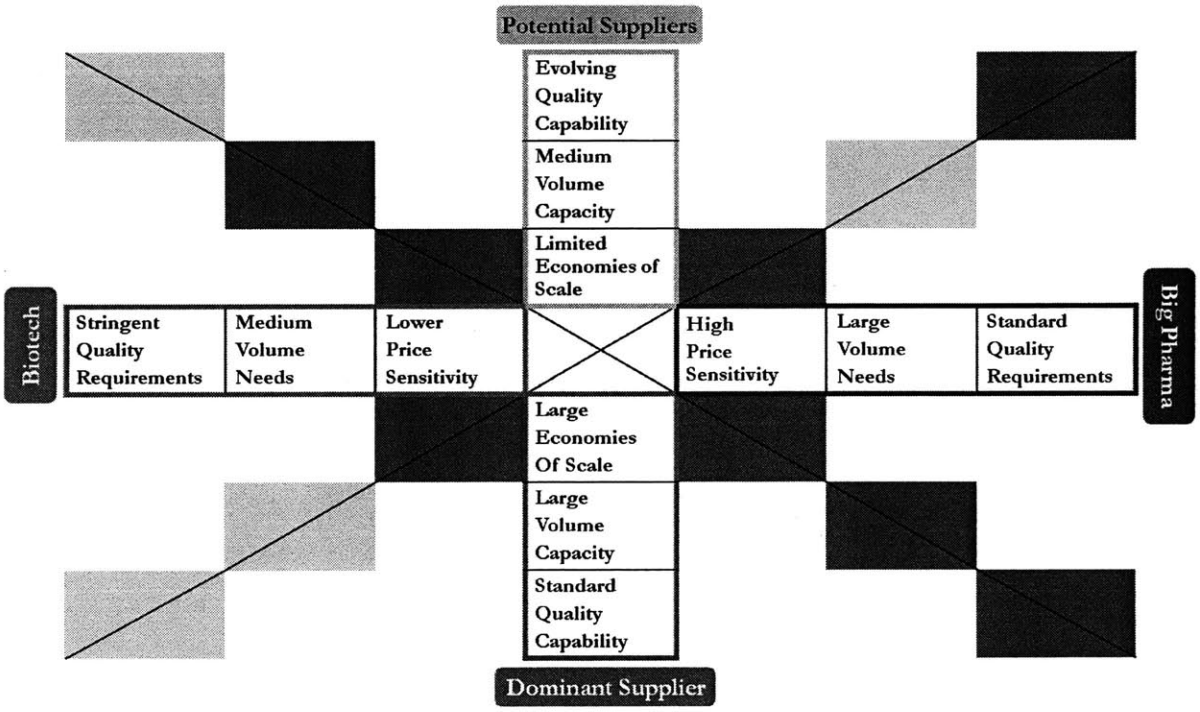


Figure 18. Attractiveness Chart in Glass Prefilled Syringe Market

As seen in Figure 21, price sensitivity, volume needs, and quality requirements are selected as buyers' three important factors while economies of scale, volume capacity, and quality capability are considered as suppliers' three important factors. For example, biotechnology companies have stringent quality requirements, medium volume needs, but lower price sensitivity whereas big pharmaceutical companies standard quality requirements, large volume needs, but high price sensitivity.

The attractiveness analysis shows that big pharmaceutical companies and the dominant supplier are perfect matches for each other. However, small potential suppliers are not good partners to big

pharmaceutical companies because suppliers' limited economies of scale cannot meet buyers' high price sensitivity. On the other hand, small potential suppliers should be more attracted to biotechnology companies than the dominant supplier is. This chart shows that biotechnology companies should make efforts on diversifying their supply base by working closely with small potential suppliers. As mentioned earlier, however, biotechnology companies should also maintain better relationships with the dominant supplier because it will take a time and efforts to elevate potential suppliers' quality capabilities high enough to get approval by regulatory agencies.

6.2 Glass Prefilled Syringe Suppliers vs. Plastic Prefilled Syringe Supplier

The attractiveness chart can be applied to analyze the attractiveness for this case.

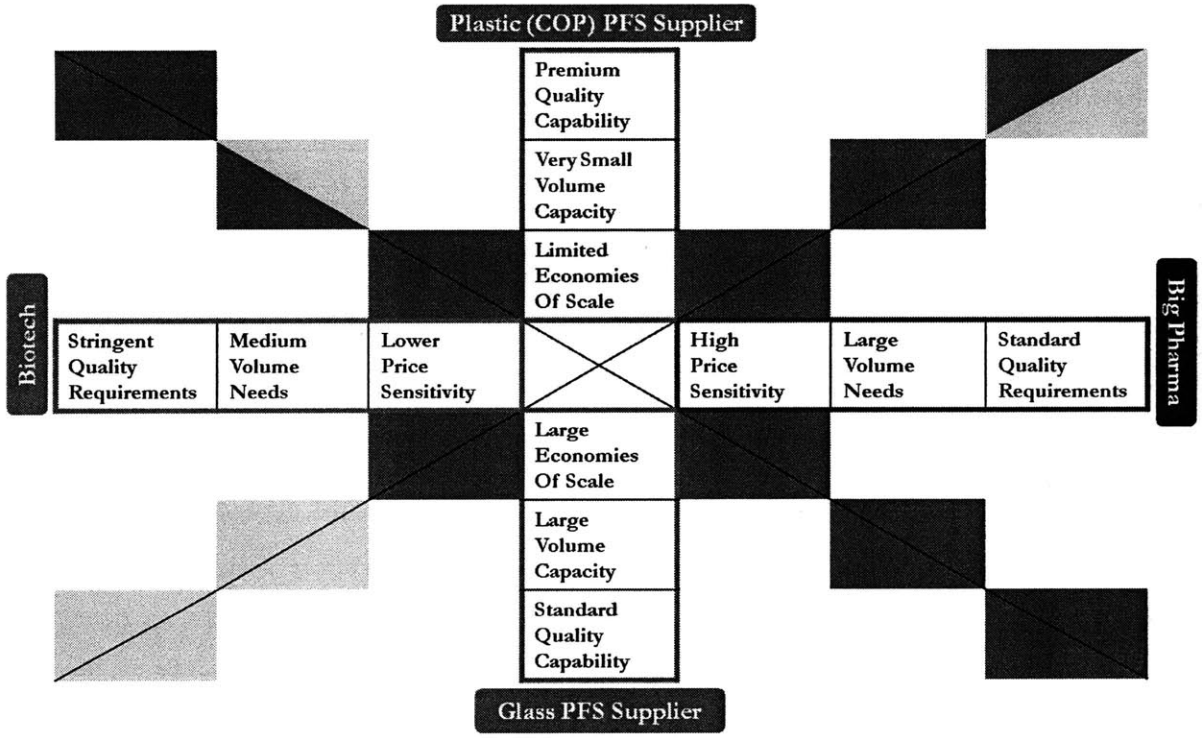


Figure 19. Attractiveness Chart for Glass vs. Plastic Prefilled Syringes

Unlike the previous chart, the plastic prefilled syringe supplier and glass prefilled syringe supplier are located on y-axis instead of the dominant glass prefilled syringe supplier and the small potential glass prefilled syringe suppliers. Compared with glass prefilled syringe suppliers, the plastic prefilled syringe supplier has premium quality capability, but very small volume capacity and limited economies of scale. However, the two weaknesses don't hamper biotechnology companies' interests in plastic prefilled syringes because biotechnology companies have relatively small volume needs and lower price sensitivity compared with big pharmaceutical companies. In addition, the volume capacity is expected to grow for the foreseeable future.

Hence, this chart suggests that the plastic prefilled syringe supplier is much better strategic match to biotechnology companies than glass prefilled syringe suppliers. More interestingly, we can find that the glass prefilled syringe market exists not for biotechnology companies but for big pharmaceutical companies.

COP-based plastic prefilled syringe, recently launched by Supplier Z, can provide biotechnology companies with potential opportunities to:

- Decrease quality related market complaints
- Reduce manufacturing related costs
- Lessen total cost of ownership,
- Minimize variations when used in devices
- Offer unique device opportunities

From experience in manufacturing, it will be challenging for any company to achieve zero "preventable" defects with glass prefilled syringes. From a quality perspective, as mentioned earlier, the plastic prefilled syringes can eliminate the need for silicone, tungsten, and adhesive, all of which are leachables which glass prefilled syringes typically have. In addition, the plastic prefilled syringes have high break resistance and low variability, both of which are critical advantages biotechnology companies can make use of when used for auto-injector system.

Compared with glass prefilled syringes, plastic prefilled syringes may have considerable advantages. Plastic prefilled syringes require identical and standard technology (injection molding). The biotechnology companies can leverage plastic technology for higher-volume prefilled syringes and other containers that may be needed for new device platforms.

Even though plastic prefilled syringes are expected to be more expensive than glass prefilled syringes due to current limited economies of scale, Amgen's total cost of ownership for drug products may be decreased due to the high quality of prefilled syringes. Hence, it can be hypothesized that the total cost of ownership will be decreased with switching to plastic syringes (see Figure 23).

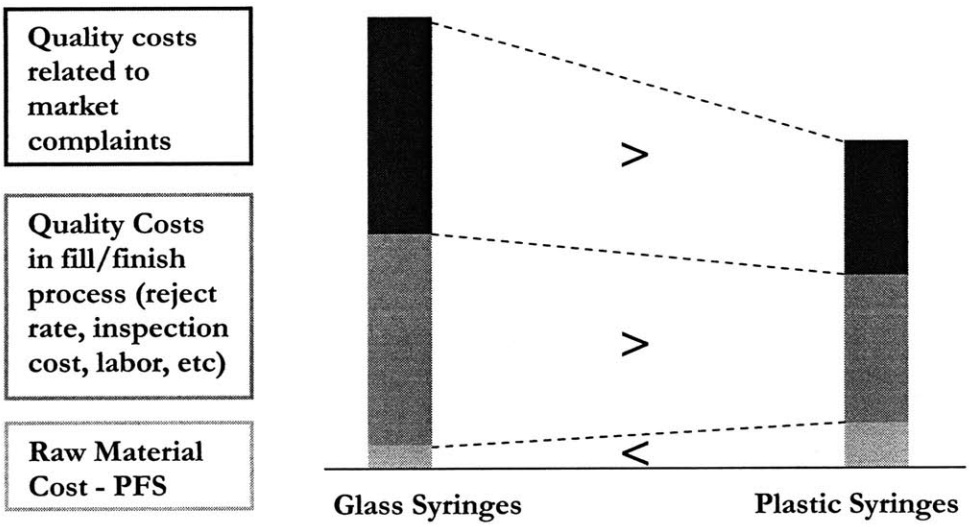


Figure 20. Schematic of Total Cost of Ownership

However, Amgen should also consider exploring the plastic prefilled syringe as a mid-to-long term strategy. Even though plastic prefilled syringes can offer many advantages over glass syringes, they are still a new technology in US. In general, new technologies have uncertainties, and a future market may be unpredictable.

Hence, Amgen should adopt the new plastic prefilled syringe technology by overlapping with glass prefilled syringes during the transition. Even though Amgen should start to make efforts on qualifying plastic prefilled syringe right now, it does neither guarantee that Amgen can take advantages of new technology right away nor that Amgen should put all of its effort into the plastic prefilled syringe market from the glass market.

7 Structuring Supplier Relationships

Now, the project turns to more complex questions of how the relationships with the suppliers in the network should be structured. As shown in Table 3, there is a wide spectrum of possible relationships from which Amgen might choose.

Table 3. Spectrum of Relationships with Suppliers or Customers[52]

Type of Relationship	Description
Arm's-length relationships	Traditional, cost-based, free-market, short-duration, purchase-order-driven relationships
Modified vendor relationships	Value-added services (e.g., supplier managed inventories)
Long-term contracts	Long-term supply contracts
Nonequity-based collaboration	R&D consortia Cross-marketing agreements Cross-production agreements Joint Purchasing activities
Minority equity investments	Invest in supplier
Licensing arrangements	Provide license to supplier in technology that host firm develops, but in which it wants to limit investments
Investment integration	Coordinate investment jointly
Joint ventures or strategic alliances	Allow firms to exchange certain goods, services, information, or expertise while maintaining a formal trade relationship on others
Asset ownership	Host firm retains ownership for critical assets in adjacent stages of the industry chain but contracts out all other aspects of ownership and control
Full ownership	Host firm fully owns activity

More toward vertical integration

[52] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 224

"On one end is an arm's length relationship, which is appropriate when a firm is procuring a commodity from an established market and has no need for close interaction on scheduling, quality, or other areas of performance. At the other end of the spectrum is full ownership, which is used when the activities or processes being performed are core, there is not an established outside market so the firm must complete the job internally, the economics of ownership are compelling, or there are product or technology reasons to integrate."[53]

7.1 Full or Partial Ownership of Prefilled Syringe Manufacturing Analysis

In order to solve the challenges with which Amgen has faced, Amgen may have to consider full or partial ownership of prefilled syringe manufacturing activities. Full ownership means Amgen owns the entire prefilled syringe manufacturing processes from glass-tube forming to washing, siliconizing, and sterilizing. Partial ownership means that Amgen performs only final syringe processing by buying bulk syringes from syringe manufacturers and executes washing, siliconizing, sterilizing bulk syringes. These two options may look attractive because they have potential to solve Amgen's challenges in the prefilled syringe market. For example, Amgen can ultimately control prefilled syringe quality itself and doesn't need to worry about the quality of supplier response due to its small prefilled syringe consumption. In addition, there are several bulk syringe suppliers in the market, and bulk syringes are considered a commodity.

However, both options have a number of risks as well:

- Due to Amgen's small volume needs, the internal process will not be able to achieve economies of scale
- Both options require high initial capital investments to build infrastructure
- Prefilled syringe manufacturing is not aligned with Amgen's core competencies. Amgen has had strong research and development to discover, develop, and deliver innovative human therapeutics[54] and strong drug manufacturing capabilities to produce vital therapeutics in

[53] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 224
[54] Amgen 2009 Fact Sheet

sufficient quantities as an important way to serve patients[55]

- Amgen has had no experiences in prefilled syringe manufacturing so that it may take a long time to become efficient

For example, initial capital investments for 1 single prefilled syringe wash/siliconization/sterilization process (air class 10,000) is estimated to be tens of millions USD or orders of magnitude more in existing filling/finish infrastructure or with new infrastructure respectively. Even if new infrastructure is built in an existing facility, there is a risk of regular facility audits conducted by regulatory agencies. On-going management costs for 1 single process will be approximately $1.5 million per year. In addition, 1 single process line can produce approximately hundreds of millions units of prefilled syringe per year – which is on the same order of magnitude of the entire biotech consumption annually. Amgen will be likely to suffer from high initial and on-going capital investments and low utilization rate.

[55] Amgen 2009 Manufacturing Fact Sheet

7.2 Structuring Supplier Relationship

Amgen can consider a different way to seek benefits of vertical integration without full or partial ownership of prefilled syringe manufacturing. Companies today have moved away from the ends of the spectrum as shown in Table 3, engaging with suppliers in a number of different ways. The type of relationship a firm chooses to engage in with any particular supplier depends on what role it wishes the supplier to play and how critical the sourced item is to the firm.

Table 4. Types of Suppliers by Criticality and Volume and Likely Types of Relationships[56]

	Item Purchased in Low Volume	Item Purchased in High Volume
Item Being Sourced is Critical to the Firm	**Bottleneck Suppliers** Nonequity-based collaboration Minority equity investments	**Critical Strategic Suppliers** Investment integration Joint ventures Strategic alliances Asset ownership
Item Being Sourced is Not Critical to the Firm	**Noncritical Suppliers** Arm's length Modified vendor contracts	**Leverage Suppliers** Modified vendor contracts Long-term contracts

In this framework, prefilled syringe suppliers are between bottleneck and critical strategic suppliers. For example, glass prefilled syringe suppliers can be bottleneck suppliers because Amgen purchases relatively low volume compared with other big pharmaceutical companies while prefilled syringe is still a critical item to Amgen. To non-dominant glass prefilled syringe suppliers, this option may look more attractive because they can be locked in a premium niche market with special needs.

Plastic prefilled syringe suppliers can be critical strategic suppliers because they can provide something for which it is difficult to find a substitute or alternative supplier. This is critical to creating premium quality level for Amgen's successful drug deliveries.

The option of investment integration is very likely to be attractive to the plastic prefilled syringe

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[56] Sara L. Beckman and Donald B. Rosenfield, "*Operations Strategy: Competing in the 21st Century,*" McGraw-Hill Higher Education, p. 226; Initially Reprinted from Handfield et al., "Avoid the Pitfalls in Supplier Development" *MIT Sloan Management Review*, 2000, p. 37~49

supplier for three reasons. First, the technology is targeting specifically biotechnology companies. Second, plastic prefilled syringes are still in the investment phase so they require investments and expertise. Finally, the supplier is likely to look for a committed large customer to share risk of evolving technology

8 Conclusions and Recommendations

8.1 Conclusions

This thesis thoroughly analyzed the prefilled syringe market including histories, growth drivers, demand and capacity forecasting, key players in supplier and buyer side, and complicated market dynamics. Next, it turned to discuss biotechnology companies' (including Amgen's) challenges along with current changes and issues in the market. Three facts stood out.

First, the prefilled syringe market has grown significantly with double-digit annual growth rates. It is also expected to grow further for the future with following growth drivers:

- Strong continuous growth of two markets, anti-coagulants and vaccines, which have consumed large portion of total prefilled syringe demands
- Continuing rise in number of biotech drugs which need to be delivered by injection route
- The trend towards home health care and self injection
- The strong advantages of prefilled syringes compared with other traditional drug containers such as vials and ampoules
- Increased pressure on the branded products differentiation and drug delivery system's increased role as a market differentiator

Hence, prefilled syringe has become the primary container of choice for most injectable drug delivery systems of pharmaceutical and biotech companies including Amgen.

Second, a big portion of the market consists of three large buyers and one dominant syringe supplier who will consume and supply a lot of existing syringe capacities. It should be noted that the biotech market has not been a large market segment for syringe suppliers. While the biotech market consumes a minor portion of total demand, it requires suppliers of the highest quality standards. This high quality standard is due to biopharmaceuticals' sensitive ingredients such as proteins and peptides. Both are unfavorable for biotech companies (like Amgen) to have bargaining power in the market. In addition, biotech companies' high dependence on quality level and the dominant supplier's relatively high quality capability made biotech companies solely rely on the dominant supplier,

exposed to risks of single sourcing. The dominant supplier's limited incentive to invest to meet biotech's high needs also added risks on biotech companies.

Third, in addition, there have been new changes in supply side of prefilled syringe market including:

- Increased competition between the dominant supplier and other supplier
- Introduction of COP-based plastic prefilled syringes which provide biotech companies with opportunities to resolve quality issues related to glass syringes
- The combined suppliers' capacity expansion plans which forecast market's supply will surpass demand for the future

These changes look favorable for Amgen to consider mitigating risks related to single sourcing by leveraging bargaining power, multi sourcing, or exploring new technology.

Hence, this thesis develops the theoretical or empirical analyses and discussions to answer three main questions:

- Should Amgen decide to single or multi source?
- Which supplier is a better strategic match to Amgen?
- How can Amgen structure beneficial relationships with those suppliers?

Finally, the answers to those questions develop a recommendation for short, mid, and long-term strategies which Amgen should consider in order to resolve its challenges and issues in the prefilled syringe market.

8.2 Recommendations

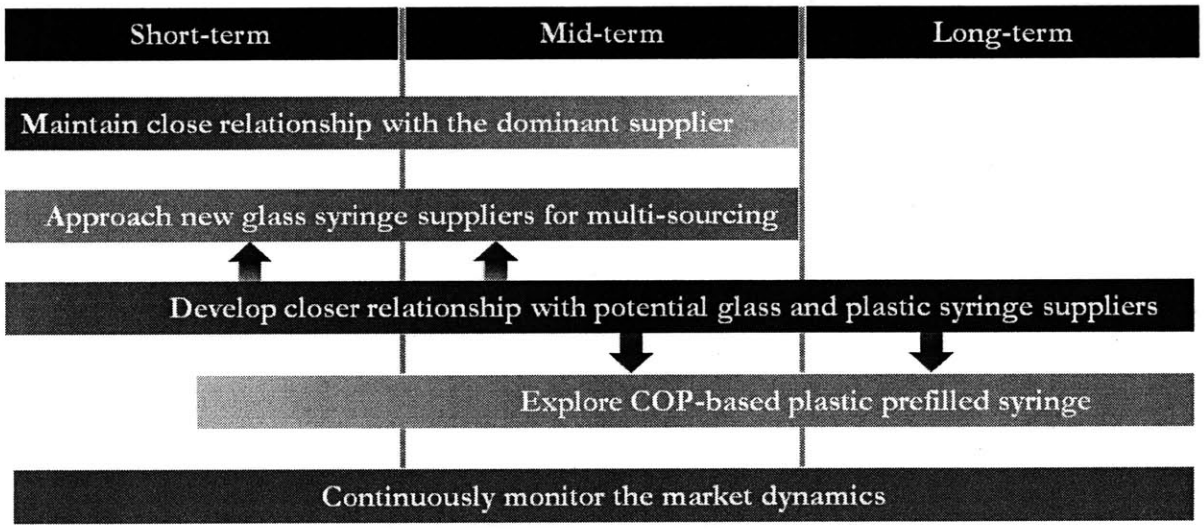

Figure 21. Recommendation for Amgen's Positioning Strategy in Prefilled Syringe Market

First of all, Amgen should work on multi-sourcing of prefilled syringes in the short-term in order to mitigate risks and to leverage over existing dominant supplier to drive service, quality, and price competition. Assuming multi-sourcing can be resource intensive and results may be unpredictable, Amgen should also maintain a strong relationship with the dominant supplier to prepare for uncertainties.

Secondly, Amgen should know that small potential suppliers may be more attracted to Amgen than the dominant supplier in glass prefilled syringe market and the plastic prefilled syringe supplier can be the best strategic match for Amgen. Given some uncertainties as plastic prefilled syringes have been recently developed and are new technology in US, Amgen should start a multi-sourcing approach to small potential glass prefilled syringe first and also keep working closely with plastic prefilled syringe supplier as a mid-term strategy.

Lastly, Amgen should develop closer partnerships such as investment integration or minority equity investments with two suppliers selected by attractiveness chart analysis as a supplier relationship management as well as vertical integration decision.

In addition, Amgen should monitor the market dynamics very carefully in order to response potential changes/issues quickly because the market is reshaping rapidly and has many uncertainties and risks both in supplier and buyer side. This can also be the reason why Amgen should have overlapping strategies covering transitions among short-, mid-, and long-term timeframe.

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