

**DEVELOPING A FRAMEWORK FOR GLOBAL DISTRIBUTION IN
THE BIOPHARMACEUTICAL INDUSTRY**

By

Swaminathan Sekar

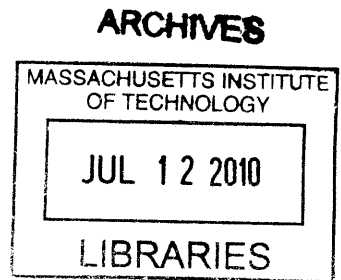
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Submitted to the MIT Sloan School of Management and the Department of Electrical Engineering
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ABSTRACT

This paper addresses two basic questions about the outbound distribution operations with a case study example of a large biopharmaceutical company. First, the research work focuses on developing an efficient, scalable truck distribution system to help reduce transportation cost, while maintaining the service level and capacity constraints. In doing so, the paper examines the Vehicle Routing Problem (VRP), a NP-hard combinatorial optimization in the context of biopharmaceutical customer demand fulfillment process. The thesis presents a model developed to perform distribution center decisions, with Amgen North America market as case study.

The second question addressed in this paper is a study on the number of distribution centers and possible locations. In a market with a certain geographic distribution of customers, and a desired number of distribution centers to operate, the analysis compares the different potential locations from standpoint of transportation cost, inventory level and site loading. The model is well suited for a company expanding into a new market to make decision on location of distribution centers to cater to a certain spread of customers in that region.

The paper presents analyses for a real case study to provide contextual example, as well as more broad recommendations in the field. Both models are scalable to markets outside North America for similar companies.

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1. INTRODUCTION

1.1. Project Drivers

The biopharmaceutical industry has grown significantly in the last few years, but the growth seen in its R&D and commercial aspect of business are more profound than that of its operations. In the case of market leaders, the scale and complexity concomitant with many products and SKUs for different markets makes it important to manage cost and efficiency of their operations (manufacturing and distribution).

The big drivers in biotechnology sector are cost, risk, availability and growth. In recent times, Amgen has been focusing on the risk profile at its different phases of operations. Firms usually hold enough safety stock to ensure no demand fluctuation or plant shutdown due to disaster would result in losing the opportunity to deliver the drug to a patient. Amgen's customers also place orders that vary in quantity and expected time to delivery. Amgen is committed to meeting customer turnaround time, and this leads to low utilization and high cost in their distribution process. With anticipated growth leading to more quantity and variety in products and packaging, there is a need to create a strategy to manage Amgen's global distribution and manage current processes in an optimal way to realize savings.

The scale and nature of businesses in US make logistics an important component of a successful operations strategy in almost all industries. The broad umbrella of logistics accounts for an estimated 9.9% of GDP in 2006 (\$635 billion annually on trucking costs)¹. Of this, the cost of distribution is estimated to take up about half². In biopharmaceutical industry, however, the entire cost of distribution may represent less than a fifth of the value added costs of goods. Yet, factors such as time-to-delivery, risk and inventory levels indirectly impact the top or bottom

¹ (Schulz, 2007)

² (De Backer, 1997)

line, making distribution a critical strategic component for this industry.

Based on the organization's need, Amgen defined the project scope that serves as the subject of this research. While the analysis on distribution center locations was a direct outcome of the original proposal, the VRP and Site 3 truck optimization work stream was developed as a consequence of initially mapping out the current distribution to identify potential opportunities in current operations. The thesis provides insight from literature and the methodology deployed to develop a distribution model for a specific context. It presents analysis pertaining to the Amgen case study, as well as more general recommendations in the field.

1.2. Problem Selection

Pharmaceutical and biotechnology companies are improving their supply chain for their current markets while creating robust processes and models to guide them in their expansion markets. With the threat of biosimilars and generics, there is an increasing need to reduce costs. Optimizing their supply chain creates opportunities to do so. The purpose of the business case is to examine the methodology of developing models to reassess and improve distribution process using Amgen, Inc as a model large biopharmaceutical company.

For the purpose of this thesis, the following names are used as a reference to Amgen sites of operation:

Site 1: Amgen primary location for packaging drug products

Site 2: Amgen primary distribution center in North America market

Site 3: Amgen secondary distribution center in North America market

Site 4: Logistic Service Provider (LSP) managed site in Canada for distribution in that market

Site 5: Amgen Europe distribution center for distribution to most non-North America markets

DC 1, DC 2, DC 3, ... : Locations of alternate distribution center being considered

Amgen's global distribution is a result of several regional strategies. Amgen will need to evaluate its current global distribution network to best manage costs, service levels, inventory levels, and risk. Options under evaluation include optimization, consolidation of logistics providers, and outsourcing of Amgen's warehousing/distribution operations.

The entire distribution operations can be segmented into three key phases – inbound material flow, material warehousing, and outbound material flow. This paper will focus on the outbound material flow for order fulfillment process, developing a custom vehicle routing system. The paper will study the rich literature in this field and use features of traditional VRP systems to develop a model to aid decision-making process at a distribution center.

Subsequently, the paper will also look at another aspect of the distribution operations, namely the footprint. In this segment, the paper will present a model based on the Great Circle Equation that will help determine transportation cost for any company operating from a few distribution centers (fulfillment centers) to deliver goods to a set of customers spread over the geography of a region.

The DC footprint analysis essentially analyzes at a region (market) and determines the transportation cost for fulfilling demand from the customers in that region for various combinations of numbers and locations of distribution centers. It is imperative to understand the transportation cost, the time-to-delivery (customer service), and volume of product flow through each distribution center (risk profile). These change based on the number of distribution centers, and their locations in that specific market. The model developed to analyze the DC footprint of the case study, Amgen North America, is applicable in ground transportation models anywhere in the world and not just for biopharmaceutical, but other industries too.

1.3. Problem Statement

The initial evaluation of current distribution operations in biopharmaceutical space led to two key areas of focus for this paper. The selection of these two topics as the scope of research is based on the following factors:

- The priority of the sponsor company (Amgen) for focusing on these issues
- The cost impact they deliver (see section 7 for the savings estimated through simulated pilot deployment)
- Low time to impact (identify improvement opportunities that need first attention and can be tackled during the time with sponsor company)

Operational

This paper will address the question of optimizing an existing distribution process. With the case example, the paper looks into whether Amgen can reduce its transportation costs through increased truck utilization without changes to customer service levels.

Strategic

This paper will address some general questions regarding determination of distribution footprint. It will answer these questions in the context of Amgen, the case study company.

Evaluate the distribution center (DC) footprint of a company based on its customer locations. Compare cost of similar DC network (e.g. potential 2-DC networks) to understand if the company incurs close to optimal transportation costs in current state.

Determine if the Periodic VRP (PVRP) structure of demand fulfillment (common in biopharmaceutical industry) is more cost effective with multi-DC network or direct shipments from packaging center.

Amgen currently runs its distribution operation out of Site 2 and Site 3. Products are packaged from Site 2 and transferred to Site 3. Hence, the paper seeks to address optimality of Site 2 – Site 3 DC network, cost analysis of other 2-DC networks against current state, and feasibility of direct distribution from Site 2. Based on initial analysis of current distribution network, the intern project scope was focused on North America distribution for model development and analysis.

1.4. Thesis Overview

This thesis is organized into five chapters as follows,

Chapter 1 outlines the motivation and problem addressed by the thesis and provides an overview of the thesis contents. Chapter 2 details the industry landscape, company background and the current distribution network at Amgen. A section of this chapter performs an organizational assessment of Amgen using the three lenses framework - the strategic, political and cultural lenses. Chapter 3 presents literature on the vehicle routing problem and associated concepts that are central to the outbound demand fulfillment model (truck routing model). The chapter also

presents some background on the great circle equation, used in computing physical distances between nodes in the model. Chapter 4 focuses on the thesis approach and states the major questions that need to be answered. In doing so, it explains the process of mapping current state, the key decision drivers, and the initial analysis outcome. These led to the hypothesis identified. Chapter 5 describes the formulations used to perform the analysis contained in this thesis. This chapter highlights process used to develop the model parameters (inputs, outputs) and illustrates the model applications through examples. Finally Chapter 6 discusses the recommendations for the two work streams and touches upon the challenges and next steps.

2. BACKGROUND

2.1. Biopharmaceutical Industry

The field of Biotechnology became a reality in 1982 with the introduction of the first drug, Humulin (Human Insulin), and has grown ever since. The biopharmaceutical industry is a segment of the pharmaceutical industry that focuses primarily on products consisting of ‘large molecules’ including living cells, proteins and DNA. This is in contrast with traditional pharmaceuticals that are typically produced through chemical synthesis. There were more than 450 biopharmaceuticals on the market in 2008, and countries such as China, India, Taiwan, South Korea and Singapore were fostering innovation with massive investments in new R&D centers of their own, primarily focused on stem cell technology.

Among the most well known products of the modern biotechnology industry are the mammalian polypeptides³, shown in table below -

Polypeptide	Market size
Erythropoietin (EPO)	\$ 7 billion
Human insulin	\$ 4 billion
Interferon-a (Intron A)	\$ 1.8 billion
Granulocyte-colony stimulating factor (G-CSF)	\$ 2.6 billion
human growth hormone (HGH)	\$ 1.7 billion

³ (Demain, 2004)

Interferon-β	\$2.1 billion
Recombinant hepatitis B vaccine	\$725 million
Somatotropin	\$ 700 million
Cerezyme (glucocerebrosidase)	\$700 million
Tissue plasminogen activator (tPA)	\$600 million

Table 1: List of commercially successful biotechnology drugs and their market size

Analysts predict that biotech products will drive growth in the pharmaceutical industry with a compound annual growth rate (CAGR) of approximately 11.6% through 2014. The global market size of publicly held biopharmaceutical firms was about \$89.7 billion, of which \$66.1 billion came from US. However, it continues to become more difficult and expensive to introduce a new drug in the U.S market. A majority of the growth in the future will come from other global markets – and in these markets, the firms will be selling more drugs to get a certain amount of revenue than in the United States.

This aspect has led the biopharmaceutical firms to focus on building robust global distribution strategies to manage the complexity in product SKUs and other requirements needed to cater to the markets. At the same time, potential competition from other players and bio-similar products have led these firms to focus heavily on reducing their costs to impact the bottom-line. The opportunities in supply chain and distribution in this industry provides avenues to achieve this goal.

2.2. Amgen, Inc.

Amgen, the world’s largest biopharmaceutical company, discovers, develops and delivers innovative human therapeutics to patients around the world. Headquartered in Thousand Oaks, CA, Amgen has approximately \$ 15 billion in product sales and 17,000 staff worldwide. Amgen has several manufacturing/distribution sites across continental US, Puerto Rico and Europe.⁴ As a leader in the biopharmaceutical industry, Amgen can offer valuable insight into the opportunities for innovation and efficiencies in the supply chain distribution process in this

⁴ *About Amgen – Fact Sheet, 2010*

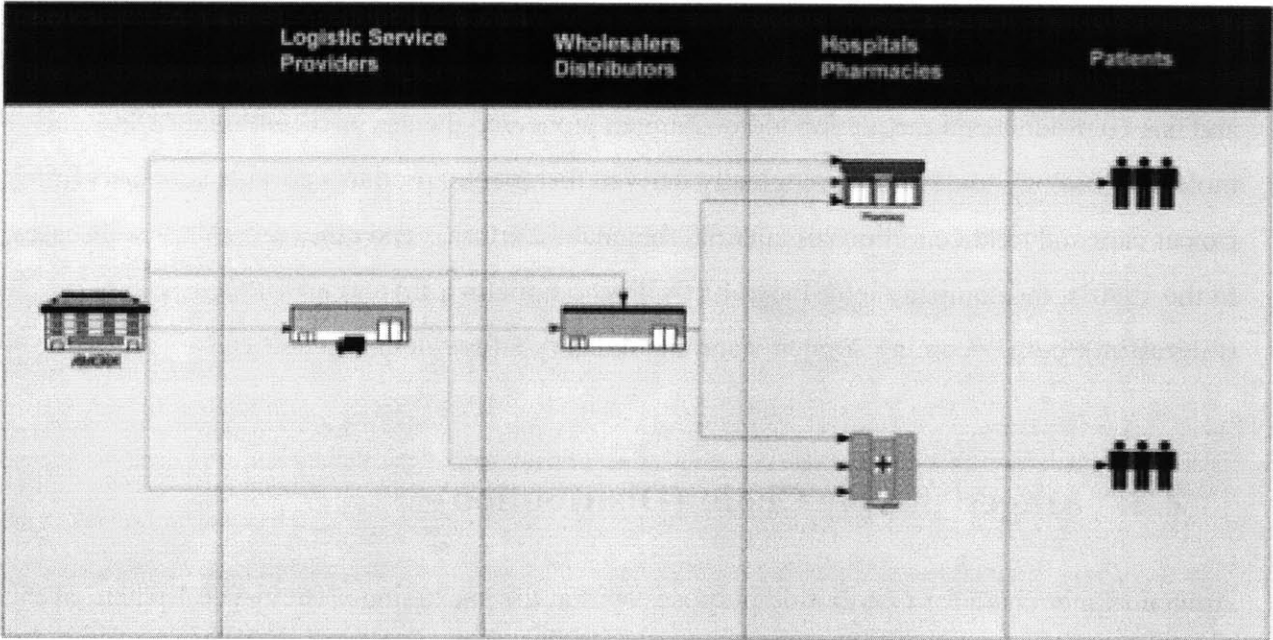
industry for relatively large-scale manufacturing.

Over the last 29 years, Amgen, Inc has applied a science-based approach to drug development, and has 10 products on the market today. Amgen pioneered the use of recombinant DNA and molecular biology to develop biologically derived therapeutic products provide supportive cancer care and treat conditions of anemia, rheumatoid arthritis and other autoimmune diseases.⁵ In the 1990's, the company introduced EPOGEN® (Epoetin alfa) and NEUPOGEN® (Filgrastim), both becoming Amgen's and the industry's first blockbusters.

2.3. Amgen Supply Chain (Distribution)

Amgen supply chain for distribution purposes start at the packaging plant in Site 1 where over 90% of Amgen's products are packaged. The products are then shipped via the US port of entry to Site 3 (Amgen primary distribution center, US) or to a depot (managed by logistic service provider) in Canada for the corresponding North America markets. Amgen Site 5 handles the distribution of products worldwide for most other markets. This includes the complex European distribution network requiring several SKUs, product packages, distribution requirements such as in-country presence, and engagement with several levels of supply chain before the product reaches the patient. Figure 1 describes the Amgen distribution structure discussed above.

⁵ *About Amgen – Fact Sheet 2010*



Blue line: Amgen controlled transport – direct (carriers contracted by Amgen)

Red line: Amgen controlled transport – indirect (sub-contracted to our LSPs)

Black line: transport not controlled by Amgen

* Source: Amgen Distribution Maps

Figure 1: Typical Distribution structure for Amgen

There are several types of companies involved in the distribution supply chain. They fall into 4 main categories that define their role in terms of activities, responsibilities, product ownership etc. The role of different participants in the distribution supply chain is elaborated table below:

Type of Operator	Role/tasks performed
Amgen Distribution Centers	Hold inventory and manage distribution to wholesalers, other distributors or hospitals/pharmacies.
Logistic Service Provider (LSP)	Performs logistics functions such as order processing, storage, and transportation. Does not take title of the products or assume risk of loss. Acts on behalf of manufacturer or distributor who hold title of products.
Distributors	Perform sales and promotion activities in the territory in accordance with agreed marketing plan and are responsible for distribution.

	<p>Responsible for applicable legal and regulatory compliance, e.g. control of advertising, recall.</p> <p>Assumes risk and takes title of the products and re-sells to its customers (wholesalers, hospitals, pharmacies).</p>
Wholesalers	<p>Do not perform sales & promotion activities</p> <p>Do not have primary obligations for regulatory or undertaking local registration. Like a distributor, assumes risk and takes title of the products</p> <p>Wholesaler can also operate as LSP, offering specific services for a fee (e.g., homecare delivery, nursing, marketing before the product ownership is transferred to wholesaler, which usually coincides with payment terms)</p> <p>Wholesaler distributes medicines to pharmacies or hospitals.</p>

Table 2: Description of distribution structure for Amgen

This thesis focuses on North America Distribution, primarily consisting of the Site 3 Amgen Distribution Center and its customers, predominantly wholesalers. The primary mode of transportation is using truck runs, and is responsible for delivery of over 90% of the commercial demand. The remaining (small volume) commercial demand and some samples are shipped as small parcel using logistic service providers.

In a pull-based supply chain, procurement, production and distribution are demand-driven so that they are coordinated with actual customer orders, rather than forecast demand. The supply chain is pull-based at this stage (from Site 3 onward) with customers (wholesalers) placing order request based on their inventory and demand levels. Typical to most supply chains in this industry, Amgen has a combination of push-based and pull-based with the push-pull boundary at the packaging and warehousing stage (Site 1 and Site 3).

The operations is marked by:

- Highly uncertain demand pattern
- Short time to demand fulfillment
- Need to meet demand without delay or shortage

Site 3 Distribution Center sends trucks on fixed days to each customer. Hence, the outgoing

truck capacity is subject to the demand level during that week. High order frequency and low order quantity result in low truck utilization.

2.4. Vehicle Routing Problem

The underlying principle of optimizing Amgen's distribution is the Vehicle Routing Problem (VRP). The method aims to minimize total transportation cost, subject to location of distribution centers and customers with a certain truck dispatch heuristic. It is one of the most discussed combinatorial optimization problems and is critical to the field of logistics, since Dantzig and Ramser introduced it in 1959.

Methods to reach a precise or approximate (heuristic) solution have been presented in literature for less complicated problems. Ever-changing constraints, input conditions, and decision drivers are factors that make finding such solution of global minimum cost in real-life complex scenarios computationally difficult.

2.5. Organizational Assessment

This project will impact the supply chain and distribution teams in different markets directly, but was being initiated and spearheaded by the Operations Strategic Planning team, the internal consulting team at Amgen. Successfully developing a distribution model would require a coordinated effort from different departments at Amgen such as Transportation & Logistics, Clinical Supply Chain, Commercial Supply Chain, Finance Operations, Global Strategic Sourcing and Planning, both in North America (US) and International Operations (Europe primarily). Some departments were primarily engaged to get access to data required for the project while others had a greater role because of the impact of the recommendations on their division.

The following is an assessment of the key organizations involved, highlighting some of the key challenges the project implementation could face. The implementation aspect of the recommendations is not examined in this section since it falls outside the scope of the project.

Three Lenses Analysis

A Three Lenses Analysis⁶ was performed in order to better understand how Amgen would respond internally to the proposed changes. The Three Lens Analysis, developed at the MIT Sloan School of Management, analyzes an organization from three perspectives. The Strategic Design Lens focuses on organizational structure and the grouping, linking and aligning of the organization. The Political Lens examines the contest for power within the organization among different stakeholders with different goals and underlying interests. The Cultural Lens looks at the history of the organization and the underlying assumptions with which it functions. The three lenses together can help provide a complete picture of an organization in transition and help uncover potential barriers to change.

In the following sections, the Strategic lens analyzes the company structure and current position with regards to industry, products and growth. The Political lens highlights the role and perspective of different groups. The Cultural lens looks at the behavior and communication habits the organization has with regards to current distribution and possible changes to it.

2.5.1. The Strategic Lens

Amgen at a high level has three main groups – Research & Development, Marketing (Commercial) and Operations. This project is being sponsored by the Executive Director of Supply Chain, and will be led by the Operations Strategic Planning (OSP) group. OSP is an internal consulting team that handled operations projects that are predominantly strategic in nature. The clients are the top management from Operations, and other departments relevant to the project. The focus on distribution and cost reductions aligns well with the strategic goals issued by the senior management for 2009. There are parallel initiatives aimed at fill-finish strategy and packaging strategy that were initialized. Together, the three projects will cover the strategic goals of operations department, and primarily assess cost, risk and inventory levels.

⁶ Carroll, J. S. (2006, June). *Introduction to Organizational Analysis: The Three Lenses*.

Though the OSP team manages the project, the impact of the recommendations is directly upon other groups that typically have team member representation in the project.

A team was put together involving people from Amgen US and International (Europe) locations, involving clinical and commercial supply chain, transportation, finance, global strategic sourcing and planning groups. The team reported to a governing board that consisted of senior management of these departments, including the project sponsor.

The US members represented North America or, in some cases, global distribution. The European members represented any supply chain activity in current and new markets outside of North America.

Amgen has had several initiatives on operations improvement including Lean, Inventory Management and such. The company however has several product SKUs and wants to ensure it designs a good supply chain network to manage the current and future demand by reducing cost and managing complexity.

In North America, which is the prime focus of this thesis, the illustrative sites (Site 2 and Site 3) are representative of the network responsible for both clinical and commercial distribution. The clinical trial products are split fairly evenly across the two sites, with each trial running out of only one site. Most of the commercial volume flows through Site 3.

2.5.2. Political Lens

It is critical to understand the right drivers that are critical to Amgen Distribution. In industries such as semiconductor where margins are small, this is the most critical driver for projects aimed at reevaluating distribution. There, the costs incurred by the company for operations (including distribution) are high. In the Biopharmaceutical industry, majority of the expenses go towards R&D activities and Commercial (Marketing, sales and such). The operations division represents a smaller percentage of firm's overall costs, but has to reduce cost. There is an inherent tension this causes among the different functional units.

On the other hand, the industry is very cautious about quality, safety, customer service (time to delivery) and stock availability. All these require significant increase in capital expenditure. In Amgen's case, the market expansion plans demand robust support in its distribution network.

These are critical factors alongside cost when evaluating the distribution network.

2.5.3. Cultural Lens

The company encourages employees to communicate across different groups, which helps develop relationships critical for managing a multi-functional team effectively. Amgen is very science-driven company and that resonates across different functional units of the company. Traditionally, the company had a motto of ‘Every patient, every time’ that led them to operate with high inventory and operating cost in ways that impacted the bottom-line. In recent times, the company has started to reassess its perspective towards delivering products to the market. This is primarily due to the need for reducing cost and managing their supply chain more efficiently.

Few of the hypotheses considered involved relocation or consolidation of facilities, and these could raise concern or false alarm. Hence, it is essential that the project findings be communicated in a well-planned manner. Confidentiality of data during the course of the project is necessary in order to prevent perceptions or conclusions getting formed in groups outside project members.

The main takeaways from the organizational analysis are that there is a strategic focus to reduce operations cost. There are significant opportunities to do so by optimizing their distribution spend, which makes this work very timely and relevant. This project involves several stakeholders from across the organization, and aligning incentives and getting consensus is a big challenge.

3. LITERATURE REVIEW

3.1. Fundamentals of Vehicle Routing Problem

The Vehicle Routing Problem (VRP) refers to a class of problems where optimal routes are determined to fulfill demand from a set of customer locations using certain truck capacity from an available set of warehouses. The objective of the VRP is to deliver a set of customers with

known demands on minimum-cost vehicle routes originating and terminating at a distribution center. The VRP arises naturally⁷ as a central problem in the fields of transportation, distribution and logistics. In some market sectors, transportation means a high percentage of the value added to goods. Therefore, the utilization of computerized methods for transportation often results in significant savings ranging from 5% to 20% in the total costs⁸.

The VRP falls under the category of nondeterministic polynomial time hard (NP Hard) problems⁹, with no exact known polynomial time exact solution algorithm¹⁰. The computational effort required for solving such problems increases exponentially with the problem complexity and sample size. The common approach is to use heuristic approaches to achieve sufficiently accurate (approximate) solutions in short time, based on an understanding of the specific problem characteristics.

The combinatorial Vehicle Routing Problem is a marriage of two well-studied NP Hard problems – the Traveling Salesman Problem (TSP) and the bin Packing Problem (BPP).

The TSP studies the shortest possible trip for a salesman, starting from his origin location, covering a set of customer locations, and ending back at his origin point. It assumes each location is touched once. The TSP aims to find the shortest length Hamiltonian cycle of a completely weighted graph $N = (L, R)$ where N represents the set of customer locations (nodes) and R represents the set of routes (edges) connecting the locations. Each route carries a weight (say cost c) that is a function of its length and corresponds to the distance between the two locations it connects.

The objective function:

⁷ (Dantzing & Ramser, 1959)

⁸ (Toth & Vigo, 2001)

⁹ (Lenstra and Rinnooy Kan, 1981)

¹⁰ (Garey and Johnson, 1979)

$$\min \sum_{i=1}^{n-1} \sum_{j=1}^{n-1} c_{ij} x_{ij}$$

where

$$x_{ij} = \begin{cases} 1 & \text{if the TSP routes include } (i,j) \\ 0 & \text{otherwise} \end{cases}$$

s.t

$$\sum_{i=1}^m x_{ij} = 1 \text{ for } j = 1, 2, \dots, m$$

$$\sum_{j=1}^m x_{ij} = 1 \text{ for } i = 1, 2, \dots, m$$

$$\sum_{i \in K} \sum_{j \in K} x_{ij} \leq |K| - 1 \text{ for all } K \subset \{1, 2, \dots, m\}$$

$$x_{ij} = 0 \text{ or } 1 \text{ for all } i, j$$

Problems in which no constraints are specified are known as "salesman" problems. The goal is to design a minimum tour for a single salesman (vehicle) using a single origin-destination with no capacity or tour-length constraints.¹¹

A version of this called m-tsp is the design of a pre-specified number, m, of distinct tours that collectively visit each of the demand points at least once while using a single common origin-destination. The objective is to minimize the total distance covered in the m tours. A vehicle routing problem is a case where there are constraints of the vehicle-capacity or maximum-distance types. The origins and destinations are usually referred to as depots. Here, the required number of vehicles and their routes are usually unknown. The solution aims to minimize an objective function that is representative of the cost of the system.¹²

The Bin Packing Problem (BPP) looks at arranging a set of products into bins with constraint on physical dimension (number, volume, weight etc.) of the products going into each bin. The BPP

¹¹Larson, R. C., & Odoni, A. R. (1981). *Urban Operations Research*. Prentice-Hall.

¹² Larson, R. C., & Odoni, A. R. (1981)

has known finite set of products with a certain volume or weight associated with each. A high cost is assigned to structure constraint on specific arrangement of products (e.g., high cost assigned when product i is placed after product j). A certain arrangement (ordered group) is defined as an ordered subset of products when total weight of the ordered group is within bin capacity, and cost between adjacent products in the group is infinite. The primary goal is to create a feasible solution with the minimum number of ordered groups.

In our context, we see the products as the locations that trucks have to stop at and arrange them in a certain sequence to reduce cost of transportation.

There are a few algorithms that have been developed to tackle this problem – The first-fit algorithm is a simple one that assigns products in the order they come, to the first bin they fit in. J. Ullman proved in 1973 that this algorithm could differ from optimal packing by as much as 70%. A different algorithm arranges the products from largest to smallest before assigning them sequentially to the first bin they fit in. In 1973, D. Johnson showed that this algorithm is never suboptimal by more than 22%. It was also shown that no efficient bin-packing algorithm could be guaranteed to do better than 22%. In some product arrangement scenarios, applying the packing algorithm after removing a product results in one more bin being required than the number obtained if the product is included¹³. The first such example was constructed by Sylvia Halasz and published by Graham¹⁴.

The BPP is conceptually equivalent to a VRP model in which all edge costs are taken to be zero (so that all feasible solutions have the same cost). VRP problem is solved in two stages, first relaxing the underlying packing (BPP) structure and then relaxing the underlying routing (TSP) structure. A feasible solution to the whole VRP problem is a TSP route that also satisfies the BPP constraints (the total demand along each of the n segments joining successive copies of the depot does not exceed capacity of vehicles). Since the TSP and BPP are inherently NP Hard problems, the merging of these two makes VRP significantly complex and difficult to solve in real-life scenarios.

¹³ (Hoffman, 1998)

¹⁴ (Graham, 1976)

3.2. Current forms of Vehicle Routing Problem

There are variants of VRP due to additional constraints that usually exist in real-life scenarios:

Abbreviation	Type of VRP	Description
CVRP	Capacitated VRP	Every vehicle has limited capacity
VRPTW	VRP with time window	Every customer order has to be delivered within a specific time window
MDVRP	Multi Depot VRP	Use many depots to fulfill demand
VRPPD	VRP with pick-up and delivering	Case where goods can be returned to warehouse by customer
SDVRP	Split Delivery VRP	Customers served by different vehicles
SVRP	Stochastic VRP	Variables like number of customers, their demands, serve time or travel time are random
PVRP	Periodic VRP	Delivery done on specific days
PVRPTW	Periodic VRP with time window	Deliver on specific times of the assigned days
DVRP	Dynamic VRP	Information such as demand level and customers for the period are dynamic inputs across time

Table 3: Types of Vehicle Routing Problem

Common real world scenarios are usually solved using heuristic approach rather than being solved exactly using algorithms. The most commonly available heuristic approach, such as the Savings Algorithm¹⁵ will be discussed in section 5.1.1. The Vehicle Flow Model¹⁶ showed typical VRP cases as being modeled as a mixed integer program (MIP). The variables associated with each route between nodes (locations) hold integer values.

¹⁵ Clarke and Wright, 1964)

¹⁶ (Bodin, 1983)

The pharmaceutical industry, including the Amgen case, will resemble a mix of Periodic VRP with Time Window and dynamic VRP due to specific customer service (order delivery) requirements and unknown demand pattern till close to order fulfillment.

The later sections in this paper describe the modified VRP structure used to develop the Truck Routing Model in the context of drivers that are critical for biopharmaceutical distribution process with Amgen as a case study.

Currently, there are a few commercially available vehicle routing software solutions. The prominent ones based on survey data¹⁷ from 1999 onward are listed below:

Product	Vendor	Year Introduced
JOpt.AAS	DNA Evolutions - Distributed	
Mobile Asset Route Optimization	Natural Algorithms GmbH	2009
QMms - Quant Methods for Management Science	FreshStart Logistics	2009
StreetSync Basic	QuantMethods	2009
Roadnet Anywhere	RouteSolutions	2008
JOpt.SDK	UPS Logistics Technologies	2006
StreetSync Desktop	DNA Evolutions - Distributed	
Route Planning Suite	Natural Algorithms GmbH	2005
DRTraCK	RouteSolutions	2005
Accellos One Optimize	Descartes Systems Group	2004
IBM ILOG Transportation Analyst	Appian Logistics Software, Inc.	2003
	Prophesy Transportation Solutions, an Accellos Company	1999
	IBM	

Table 4: Commercially available VRP software

3.3. The Great Circle Equation

In order to measure travel distances between two points on the surface of earth, the first step is to measure their orthodromic distance. The great circle distance or orthodromic distance is the shortest distance between any two points on the surface of a sphere measured along a path on the surface of the sphere (as opposed to measuring the straight line distance through the sphere's

¹⁷ Vehicle Routing Software Survey (2010):
http://www.lionhrtpub.com/orms/surveys/Vehicle_Routing/vrсс.html

interior).¹⁸

A great circle is a section of a sphere that contains a diameter of the sphere¹⁹. Sections of the sphere that do not contain a diameter are called small circles.

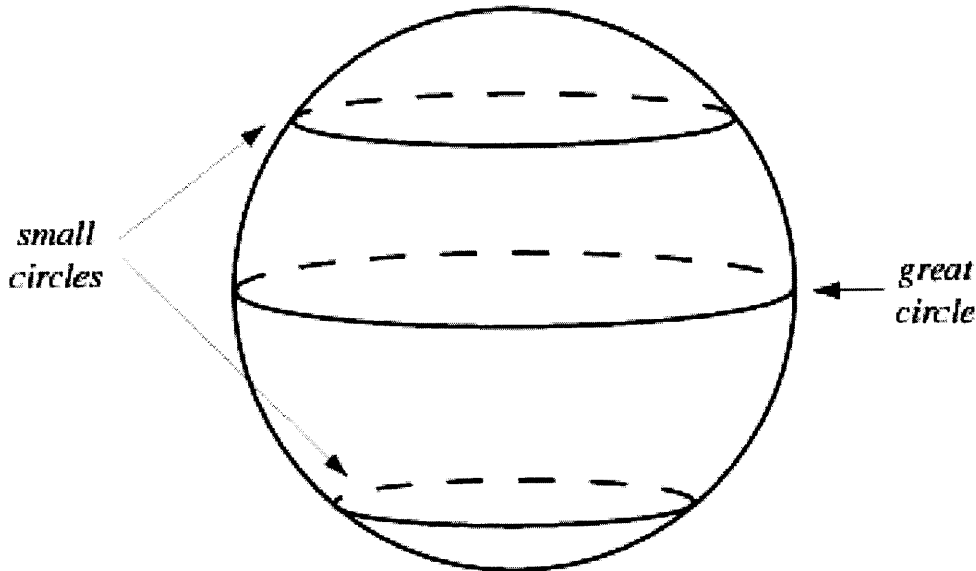


Figure 2: The great circle on the spherical earth surface

Unlike Euclidean space where distance between two points is measured using a straight line connecting them, the non-Euclidean geometry uses geodesics. On spherical surface, the geodesics are the great circles, circles that have centers coinciding with the center of the sphere. For any non-diametrically opposite points on a sphere, there is a unique great circle. Conversely, any two points on a sphere separate the great circle into two arcs. The length of the shorter arc is defined as the great-circle distance between those two points.

¹⁸ Weisstein, E. W. (n.d.). Retrieved from MathWorld--A Wolfram Web Resource: <http://mathworld.wolfram.com/GreatCircle.html>

¹⁹ Kern, W. a. (1948). *Solid mensuration with proofs* (2nd ed. ed.). Wiley, New York.

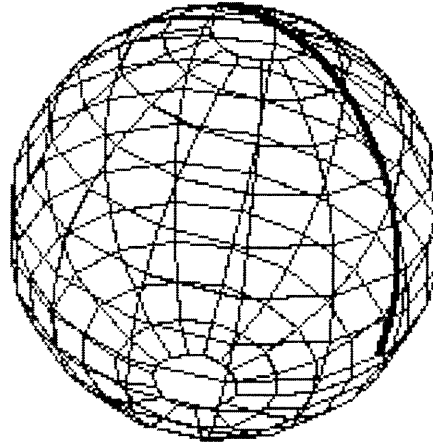
Φ_s, λ_s  Φ_f, λ_f

Figure 3: Latitude and Longitude of start and end points on earth surface

The great circle equation between two points is defined by (latitude, longitude) as (Φ_s, λ_s) and (Φ_f, λ_f) for start and finish points respectively, and $\Delta\Phi, \Delta\lambda$ which represent their differences.

Assume earth as a spherical surface,

$d = r \Delta\hat{\sigma}$. d is the arc length on a sphere of radius r and $\Delta\hat{\sigma}$ is the angular distance between the two points

The angular distance is computer using

$$\Delta\hat{\sigma} = 2 \arcsin \left(\sqrt{\sin^2 \left(\frac{\Delta\phi}{2} \right) + \cos \phi_s \cos \phi_f \sin^2 \left(\frac{\Delta\lambda}{2} \right)} \right).$$

Although this formula is accurate for most distances, it too suffers from rounding errors for the special case of antipodal points. A modified version for calculating the distance can be derived using the Vincenty's formulae. Vincenty's formulae are two related iterative methods used in geodesy to calculate the distance between two points on the surface of a spheroid, developed by Thaddeus Vincenty in 1975.²⁰ This is more accurate because it assumes the shape of earth to be an oblate spheroid.

²⁰ Vincenty, T. (1975, 04 01)

$$\Delta\sigma = \arctan \left(\frac{\sqrt{(\cos \phi_f \sin \Delta\lambda)^2 + (\cos \phi_s \sin \phi_f - \sin \phi_s \cos \phi_f \cos \Delta\lambda)^2}}{\sin \phi_s \sin \phi_f + \cos \phi_s \cos \phi_f \cos \Delta\lambda} \right).$$

The above formulae are used in this thesis work to measure the great circle distance between two locations that are either distribution centers or wholesaler sites. In order to translate the above distance to actual ground distances, the models developed in this paper uses $d = 1.25 * r * \Delta\sigma$. The circuitry factor of 1.25 is used to translate the great circle distance to road distance for trucking. In developing a model for Oak Ridge National Laboratories National Highway Network,²¹ Qureshi et .al. showed that using a circuitry factor of 1.22 gave a more accurate and consistent translation of great circle distance to road distance without statistical bias. A table of circuitry factors for different countries has been developed that showed the circuitry factor for United States based on 299 data points was 1.2 with a standard deviation of .17.²² However, note that the presence of physical bodies such as lakes, rivers and mountains significantly alter the circuitry factor approximation between some nodes. Typical example in the United States involves cities located across the Lake of Michigan.

3.4. Distribution center footprint

The number of distribution centers to be built, and their respective locations are two of the most important decision issues for logistics managers. The typical factors of consideration include inventory levels and cost, warehousing and operating costs and transportation costs (both inbound and outbound). The locations also need to take into account customer service requirements, availability of transportation infrastructure and 3rd party logistics service providers. There are many branch and bound algorithms for locating warehouse (or DC) footprint have been developed. Efrogmson presents an integer program based approach to solving the special class of discrete programming problems such as plant (DC) location. Branch and bound has been used here to successfully solve location problems with 50 or higher plants (DCs).²³ Elson shows

²¹ (Qureshi A M, 2002)

²² (Ballou, H R, 2001)

²³ (M. A. Efrogmson, T. L. Ray, 1966)

how mixed-integer programming can be successfully applied in specific cases of warehouse location problem. The paper discusses the flexibility of mixed-integer models in developing decision-making tools to determine warehouse locations (footprint).²⁴

Work by Nozick and Turnquist (1998) has shown how incorporating inventory costs in a location model can affect optimal decisions on the number and locations of DCs. A subsequent work built an iterative procedure that can alternate between solving a location problem (given an inventory policy), and solving an inventory optimization (given the number and locations of DCs) to integrate the inventory and location decisions.²⁵ The work by Nozick and Turnquist look at distribution centers primarily from the perspective of inventory setup, while the work on this paper looks at the transportation costs incurred in making DC location decisions.

Chen proposed a new multiple criteria decision-making method to solve the distribution center location selection problem under fuzzy environment. In the proposed method, triangular fuzzy numbers are used to represent the weight of each criteria and preference of each alternative, and the same is format is used to represent the relative output value (evaluated score) of each DC pair. A stepwise ranking process is proposed to rank all the DC location options considered.²⁶

The general formulation of the fixed-charge facility location model is as follows²⁷

$$\begin{aligned}
 & \min \sum_k f_k X_k + \phi \sum_i \sum_k G_i d_{ik} Y_{ik} \\
 & \text{s.t. } \sum_k Y_{ik} = 1 \quad \forall i \\
 & \quad Y_{ik} \leq X_k \quad \forall i, k \\
 & \quad X_k \in \{0, 1\} \quad \forall k \\
 & \quad Y_{ik} \geq 0 \quad \forall i, k.
 \end{aligned}$$

where f_k is the fixed cost of locating a facility at site k

G_i is the demand at wholesaler i

d_{ik} is the distance from site k to wholesaler i

²⁴ (Elson, 1972)

²⁵ (Nozick, Turnquist, 1998)

²⁶ (Chen-Tung Chen, 2001)

²⁷ (Daskin, 1995)

ϕ is the cost per unit distance per unit demand

$X_j = 1$ if a facility is to be located at candidate site k

$= 0$ otherwise,

and Y_{ik} is the fraction of demand at location i which is served by a facility at k

Nozick and Turnquist developed a fixed-charge location model that considers trade off the costs of opening new warehouses against the transportation costs of serving demand from them.

Transportation costs can be reduced by opening more DCs as that will reduce the distance of commute, but each new facility has associated setup, fixed and variable operating costs that increases the overall cost of operating multiple DCs.²⁸

In the later sections, we use the concepts of mixed integer models to develop a DC footprint model to analyze the DC footprint of our case study from the perspective of transportation costs.

4. IDENTIFYING OPPORTUNITIES

The process applied to tackling the question of evaluating Amgen's distribution was to first map the current distribution to best understand cost and volume across different markets. Other factors like regulatory requirements vendor capability need to be considered too. The data is analyzed to extract key findings through understanding current map and identifying opportunities. Key hypotheses are generated based on the analysis and opportunities. This process leads to the model development phase described in Chapter 5.

4.1. Map Current Global Distribution

All interviews, data collection, and analyses were performed at Amgen, Inc. Data was obtained from sites in US and Europe (Sites 1-5). Interviews of over 30 subject matter experts across departments at Amgen and external vendors went into developing the work for this thesis. Inputs from groups in Commercial Supply Chain, Clinical Supply Chain, Transportation, Finance, Planning, Commercial Operations, Regulatory and Manufacturing were integral to the business case.

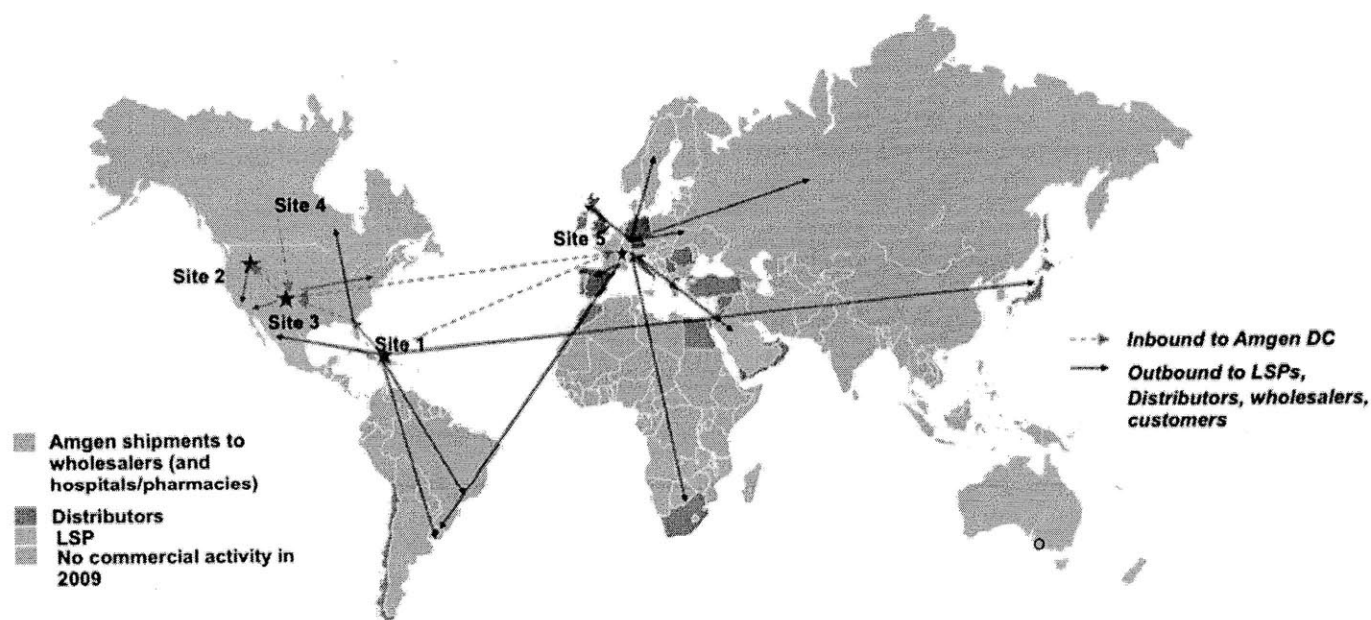
²⁸ (Nozick, Turnquist, 2001)

An overview of the different Amgen markets across these factors is listed in Table below

Region	Cost & Volume	Customer Service	Risk & Regulatory	Suppliers
NACO	Lower cost/unit, over 60% volume	Fixed day delivery to wholesalers	Limited implications to Supply Chain	Pan-American suppliers
ICO	Higher cost/unit, ~30% volume	LSP, Distributor, Wholesaler, home care	Local stock required	No Pan-European logistic provider
Intl Expansion	Mexico, L.A. Small volumes		Cross-border shipping difficult	Limited capability and footprint

Table 5: Overview of distribution across different markets

Amgen’s commercial distribution process begins at Site 1. The figure below shows the overall product flow.



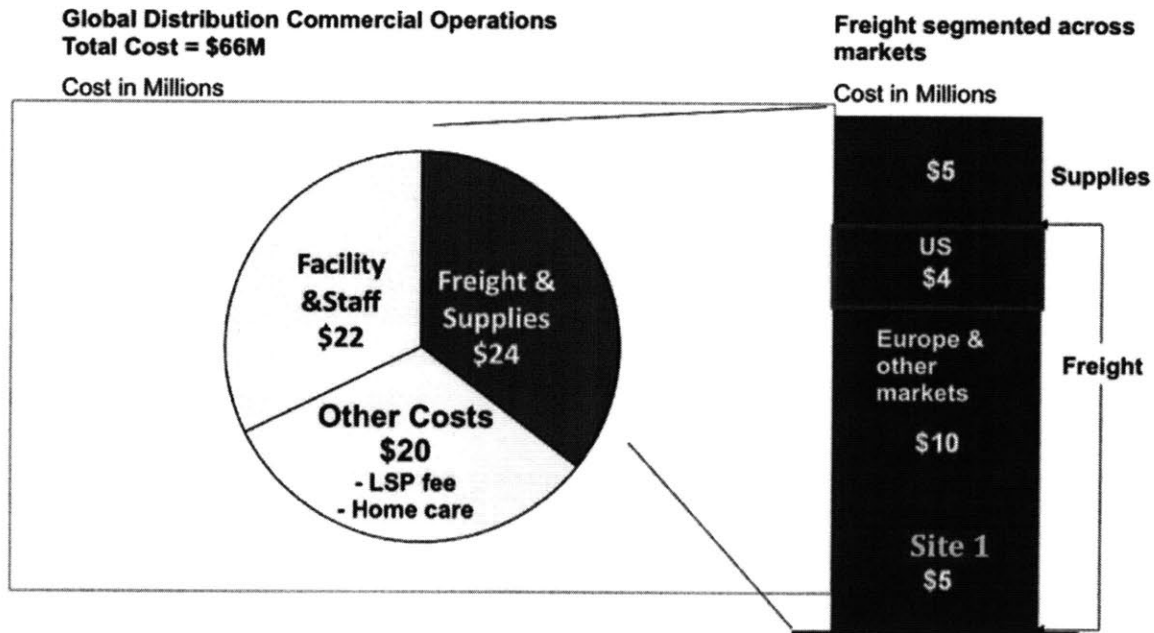
For illustrative purpose only

Figure 4: Global distribution map with product flow starting from Site 1 packaging stage

In the market of focus, North American Commercial Operations (NACO), the products reach US port of entry by ship and from there to Site 3 by trucks. The Primary Distribution Center is Site 3, and the first economic customers in North America are predominantly wholesalers. Amgen does about 90% of its commercial order fulfillment via trucks.

4.2. Develop Decision Drivers

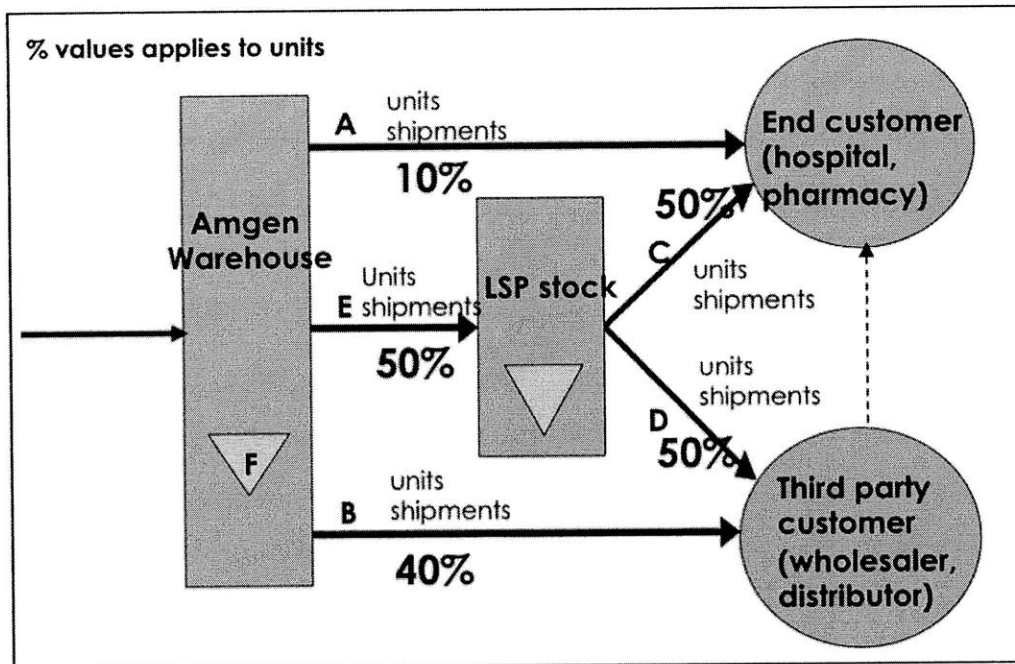
Mapping the current distribution will help understand the total cost of distribution in dollars and as percentage share of overall operations cost.



For illustrative purpose only, numbers are not representative of actual spend

Figure 5: Total operations costs, segmented to reflect distribution spend

Subsequently, transactional data is used to map annual volume of product flow across different segments of the supply chain (and across different channel modes). Figure 6 below shows the various channel partners engaged in moving a product from Amgen packaging site to a patient.



For illustrative purpose only

Figure 6: Product flow across different supply chain channels in ICO market

Mapping order pattern of wholesalers, by week and by product helps determine potential multi-city routes that can cater to all customer orders while subject to capacity constraint of trucks. Demand forecast for current and expansion markets are gathered to understand the future trend in volume and revenue growth across different markets. This analysis showed that larger volume of products would be sold in non-US markets to achieve a certain revenue figure compared to US.

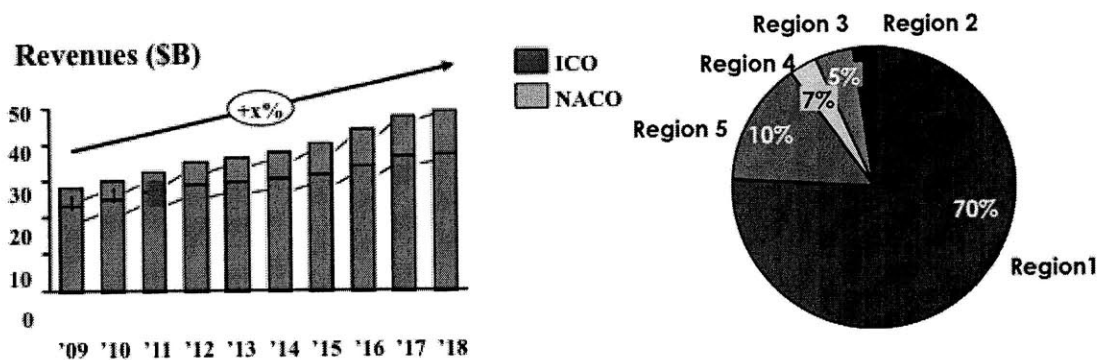


Figure 7: Forecast model used to understand future distribution need

Data was gathered from SAP to understand customer service and order fulfillment pattern and determine how the Periodic VRP (PVRP) can be adapted to Amgen case study.

Finally, specific biopharmaceutical constraints such as temperature and other transportation conditions are identified. Three temperature modes, Room Temperature, 2-8C and Frozen, are needed to transport the various drug products and raw materials during different stages of production, warehousing and delivery.

Based on these, a set of key decision drivers is identified (see Table 6: Decision drivers of distribution network development process). The decision drivers help guide the model development by defining the variables to be included.

<i>Phase of Project</i>	<i>Decision Drivers</i>
<i>Identify future distribution network (regional nodes and channels)</i>	Current/future demand forecasts Customer service level expectations Regulatory considerations Other (counterfeiting risk, parallel trade)
<i>Determine who manages distribution node/channel (Amgen, LSP or Distributor)</i>	Supplier capabilities; Global/regional footprint Amgen footprint Financial impact Risk Mitigation
<i>Optimize current distribution</i>	Customer ordering and fulfillment pattern Truck insurance limit Transit (driving) time Shipping condition

Table 6: Decision drivers of distribution network development process

4.3. Analyze Data and Initial Findings

The transactional data obtained from SAP and the budgeting data from Finance will be used to reconcile the annual expense incurred for distribution. There are many components to this expense such as transportation expenses, packaging expenses, LSP fees (fee paid to a logistic service provider for his warehousing, transportation and customer support, and accounting services. Here, the costs that can be impacted by the optimization to distribution network can be

identified. A template structure was developed to capture the financial data from different sources, ranging from supply chain teams to finance operations teams.

Estimated annual costs	Site 1	Site 2, 3	Site 5	Total
<i>Freight & Supplies (millions)</i>				
Commercial Freight				
LSP freight				
packaging supplies				
Total				
<i>Other Distribution costs (millions)</i>				
LSP services				
LSP services (Canada & AU)				
home care				
Total				
<i>Facility & Staff</i>				
Labor & Occupancy costs				
<i>Annual Global Commercial Distribution Costs</i>				
<i>Annual Clinical Distribution Costs</i>				
shipments to depots				

Table 7: Cost-to-serve detailing distribution cost components across all markets

A cost-to-serve model was built and transactional data from SAP and Operations Finance group were used to analyze the current distribution process. This model would relate the pallet demand from each wholesaler to the truck schedule to determine truck loading. A pallet is a large container used to transport products from a distribution center to customer on trucks. Pallets are

of the same size and a truck holds 22 pallets at full capacity. In some cases, the product costs are high and hence the insurance limit (on cost of goods carried on each truck) is reached before the pallet limit.

Description of North America Distribution

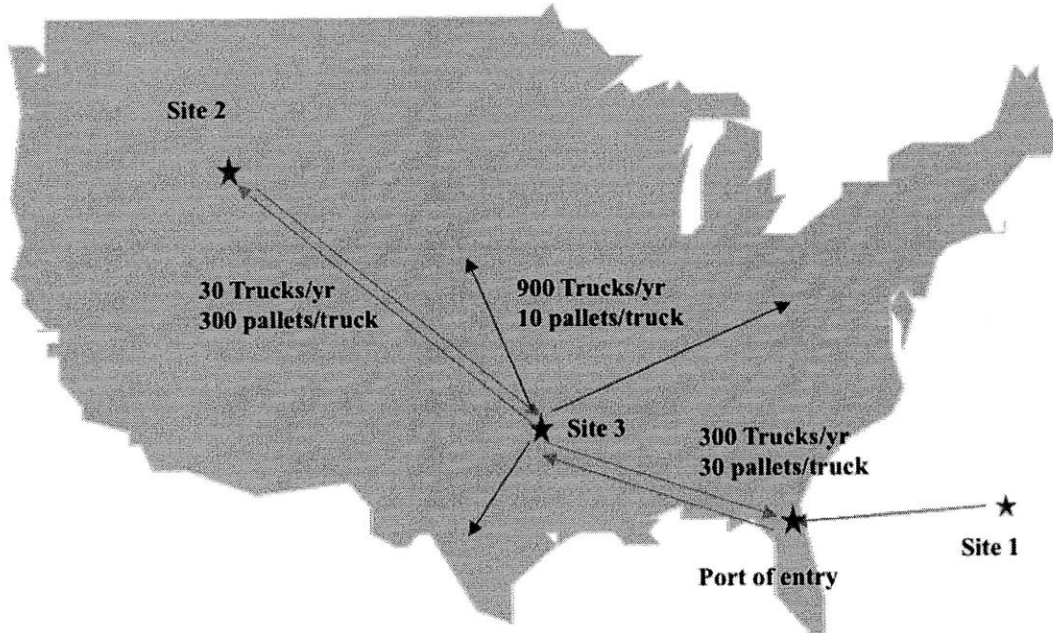
Packaged goods from Site 1 are shipped via ocean containers to Florida and from there via trucks to Site 3 (prime distribution center) twice every week. The trucks that carry products between port of entry and Site 3 have a larger configuration and 20% higher pallet space compared to trucks used for demand fulfillment at Site 3. Site 3 holds inventory of about 4-5 months to cover for the demand fluctuations (operational inventory) and meet demand during site recovery if a event (such as natural disasters) results in temporary closure of Site 1 or other earlier stages of supply chain (strategic inventory). Inventory is moved between Site 2 and Site 3, to meet demand variations and allow release of products with earlier expiry date (FIFO) first. Site 2 handles a small volume of commercial order fulfillment (~15%), predominantly to the customers in west coast region of US.

Based on initial data analysis, following key observations were noted –

- Most of the truck delivery today happens in a direct routing mode, where a truck leaves from the Amgen distribution center at Site 3 to a wholesaler location and returns to Amgen.
- Multi-city routes are used for less than 10% of products sent on outbound trucks. These are done for 5 wholesalers in northeast and central US regions on a fixed route basis. In Figure 11, the historic multicity route involved customer 1, 2 and 3. The model presented later in this paper will consider other customers in that region to create dynamic multicity routes based on weekly demand. The senior manager for distribution at Site 3 assigns trucks to wholesaler routes in an adhoc (manual) manner. Automating this can aid the decision making process.
- Outbound trucks carry over 90% commercial products at very low truck utilization
- Order pattern was erratic; customers were allowed to place an order anytime during the course of the week in order to get their shipment for that week. This made scheduling and capacity planning difficult. For instance, the top wholesaler customer had a 3x variation in

demand within each month of 2008. Hence, in a given week, the customer could need either a full truck or a $1/3^{\text{rd}}$ of truck space to meet their order quantity. Here, the opportunity to consolidate truck space using dynamic multi-city routes becomes evident.

- Trucks were dispatched to wholesaler sites on a pre-determined fixed schedule. Hence, in weeks with low demand, the truck capacity was significantly underutilized.



For illustrative purpose only

Figure 8: Map of US distribution flow

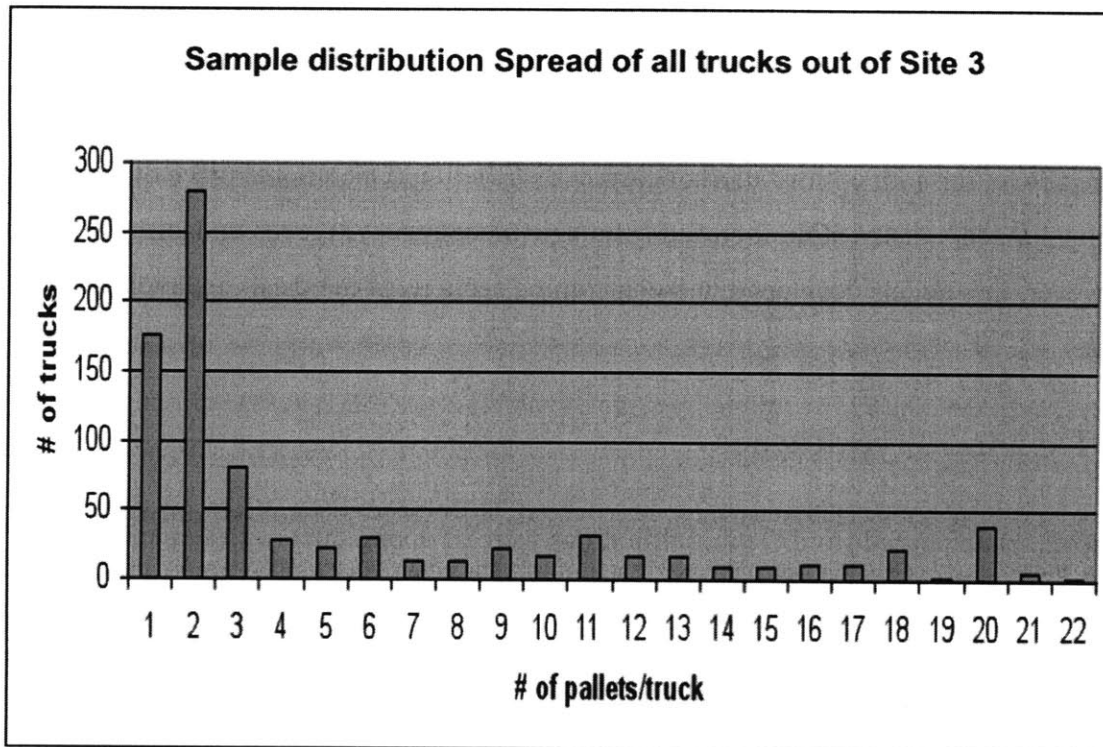


Figure 9: Sample representation of distribution spread of all outgoing trucks to wholesalers

Apart from these internal observations, several interviews were conducted with vendors who provide logistic services, warehousing and transportation, to understand their capabilities in the different markets. The key findings were –

- The North America region had few dominant players (like UPS, DHL) with capabilities to handle transportation, warehousing and customer service across the region. They also handle cold-chain (frozen temperature) and room temperature conditions for the drug products.
- Europe has several regional players having varying levels of capability. No pan-European player has emerged yet to enable consolidation of vendors in that market.
- Other expansion markets, such as Latin America, have several challenges ranging from availability of LSP companies, high cross-border taxation, and security-safety issues. It is easier to ship products from Miami (US) or Panama (tax-free zone) to countries in Latin America than to ship across those countries.
- Clinical distribution requirements and processes are vastly different from that of commercial distribution. Hence, consolidation of logistic providers across them is very

difficult. Most players have stronger niche in either commercial or clinical distribution capabilities. No player was dominant in both spaces.

Based on the above, for both optimization of current distribution (Operational piece of the thesis) and analyzing Amgen's distribution footprint (Strategic piece), we will focus on North American region. However, the models developed in the upcoming sections of the thesis are applicable to other markets.

4.4. Develop Hypotheses

The hypotheses that emerged from the initial findings were of operational or strategic nature. Thus, two work streams were developed as detailed here.

4.4.1. Operational

- There is significant cost saving opportunity in rationalizing the truck dispatch heuristics.
- Creating multi-city routes will reduce some legs of transportation and improve truck capacity utilization, potentially saving \$400K annually.
- Current customer service model (fixed day delivery to a wholesaler) can be met while running a dynamic multi-city route.

In order to realize these changes, there should be a process-driven approach to decision-making and execution at the distribution center. The first goal then is to develop a model that handles the various constraints and variables to deliver recommendations that enable decision-making and demand fulfillment. Chapter 5 will describe the model in greater detail.

4.4.2. Strategic

The aim of the 'DC Footprint Model' is to

- Develop business scenarios and evaluated multi-DC options in North America
- Validate current network based on Site 2 – Site 3 Distribution Center locations
- Make it robust and scalable to other regions for distribution analysis

The intention here is to develop distribution footprint for Amgen in a given market. The analysis

will be based on capital and operating expenditure of running a distribution center (warehousing, transportation). Developing a model that will help understand Amgen's transportation cost, site loading and inventory profile while varying the number of distribution centers and their locations across US. The hypotheses we explore here include confirming that current location for Amgen's distribution centers in Site 2 and Site 3 are a good choice given the customer footprint.

5. METHODOLOGY AND TOOLS –MODEL DEVELOPMENT

This chapter will explore the methodology used to validate the hypotheses developed and realize the cost savings identified. Both 'Truck Routing Model' developed for operational hypotheses and the 'DC Footprint Model' developed for strategic hypotheses rely on the Great Circle Equation as underlying engine for their main calculations.

Typically, the physical zip codes of customer (wholesaler) sites and current/potential distribution centers are available. These can be converted using a master database of all zip codes mapped to corresponding latitudes and longitudes. The Great Circle Equation then helps dynamically determine the approximate distance between these two points in physical travel distance terms.

5.1. 'Truck Routing Model' – Operational

The truck routing model was developed to realize the saving opportunities identified in the analysis of current distribution process. The model would enable multi city routing, higher truckload utilization and more defined, automated process to aid weekly operations decisions.

5.1.1. Model fundamentals

The most common algorithm for designing the heuristics of a single-depot VRP problem is the Savings Algorithm of Clarke and Wright. Consider a depot (D) and n customer sites. With n vehicles, we can dispatch one vehicle to each demand site. The total length of this $2 \cdot d(D, i)$ where d represents distance between depot and customer site.²⁹

²⁹ (Clarke and Wright, 1964)

Using a single vehicle to serve two points, say i and j , on a single trip, the total distance traveled is reduced by the amount

$$S(i,j) = 2*d(D, i) + 2*d(D, j) - [d(D,i) + d(I,j) + d(j,D)] = d[D,i] + d(D,j) - d(i,j)$$

The saving $s(i, j)$ realized by creating a 2-site route is typically between 5-20% and can be as high as 50%. While it is more desirable to create these routes as $s(i,j)$ gets larger, i and j cannot be combined if doing violates one or more of the constraints of the VRP. In the Amgen case, we cannot combine some customer sites due to the Periodic VRP nature of our case where fixed day deliveries are done to wholesaler sites.

In the case of multiple depots (or multiple origins in unconstrained, traveling-salesman-type problems), the algorithm also needs to assign demand points to specific depots. This new "degree of freedom" further increases the computational complexity of the problem. Multi-depot VRP problems are solved entirely on heuristic algorithms. The most common one are "cluster first, route second" variety, where demand points are assigned to depots first, following which it is solved as a single depot VRP problem for each depot.³⁰

An extension of the Clarke and Wright's savings algorithm to multi-depot VRP's has been developed that avoids the early partitioning of demand points to depots.³¹ This work was then combined with the cluster formation approached detailed above to form an efficient algorithm capable of handling large-scale deployments with several nodes.³²

Several versions of VRP have been formulated as mathematical programming problems by various investigators. Literature shows the largest vehicle routing problems of any complexity to have been solved exactly reportedly involved less than 30 delivery points.³³ However, the heuristic approaches that have discussed can be used even with thousands of delivery points.

³⁰ Larson, R. C., & Odoni, A. R. (1981)

³¹ (Pullman, 1972)

³² (Golden, 1976)

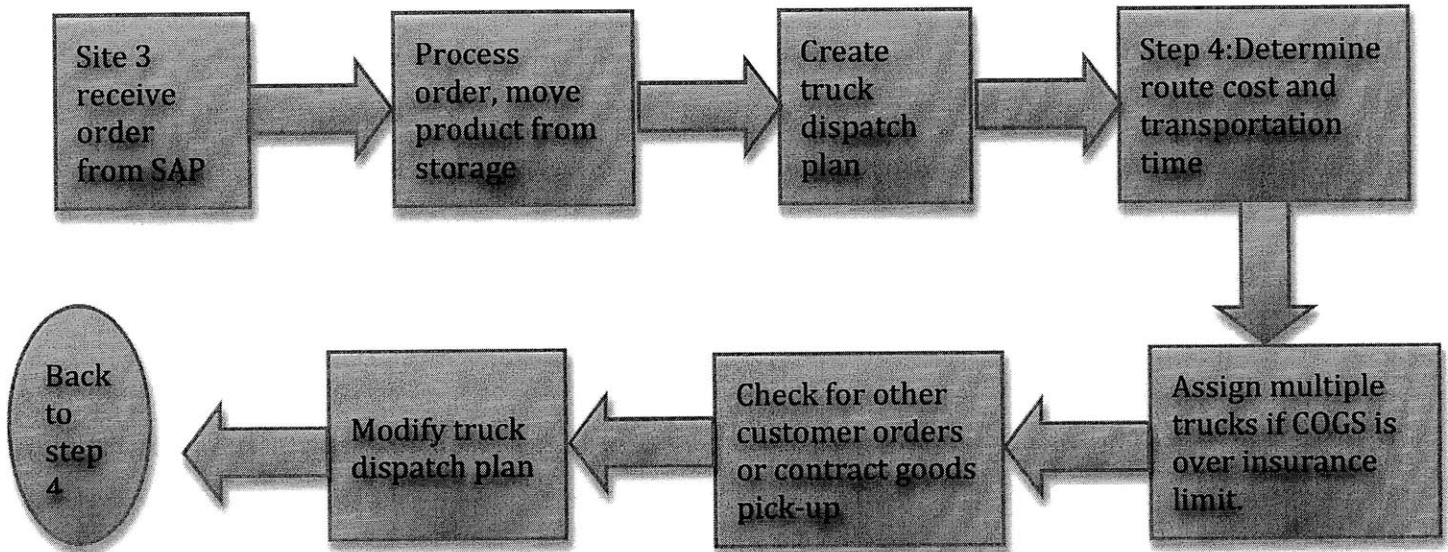
³³ (Christofides, 1974)

The case study for this paper, Amgen, had site 2 and site 3 as depots for the North America market. The above method has been adopted for modeling the Amgen ‘truck routing model’. First, the customer sites were assigned to the two depots. Then, in looking at the second step (single depot VRP structure), the model adopts periodic VRP with time window and dynamic inputs (combination of PVRPTW and DVRP). The main different in the ‘truck routing model’ is in the way we treat the multi-city nodes. More than 2 customer sites were considered as part of the multi-city route. The factors that determined whether a site was part of a multi-city route included distance, expected customer service terms, day of delivery and typical order size. As a first step to the heuristic approach, several multi-city routes were created, starting from Site 2 and Site 3, and touching a specific group of customers. The model, however, would determine if a specific customer site would be active as part of the multi-city route in a given week, based on several constraints such as existence of demand from that customer, urgent delivery request, truck capacity, and comparative cost of direct truck delivery to customer.

Cost was a big driver in deciding to build an in-house model. The project team had the necessary resources for building a model and understood the needs of Amgen’s distribution process. The model required to manage Amgen’s distribution was more basic (hence easier to build) compared to the typical scenarios where these commercial software solutions were used. Hence, it was decided that the model to optimize the vehicle routing process would be built in-house.

5.1.2. Model Description

The current distribution happens primarily out of Site 3. The delivery day for each wholesaler is preset, and demand orders are received through up until 1-2 days before the truck dispatch day. The first phase of model development was a series of interviews with transportation and distribution teams from senior management to the ground staff handling daily operations at Site 3. The pain points and needs from their perspective that would be necessary to realize the savings were understood. The current distribution process is mapped below



Currently, the order processing is done manually. Below is a list of processes that are managed manually, that have been identified as necessary elements to include in the model.

Variable	Description
Customer Demand	Demand from wholesalers are received by Distribution team through SAP
Insurance limit	The high value of biopharmaceutical drug products puts a limit on the COGS that can be carried in each truck. Hence, sometimes orders need to be split across multiple trucks occasionally.
Delivery time, wait time and wholesaler open hours	Wholesalers have different receiving hours. The travel time and rates differ. Trucks cannot be kept on wait roadside due to high value of goods. These create conflicting constraints that are managed manually on case-by-case basis.

Multi-city routing	There are only few predetermined multi-city routes, in cases where wholesalers are within reasonable proximity or order pattern is fairly known. There is no mechanism to create multi-city routes on a regular basis based on demand.
Cost of Transportation	There is no mechanism to compare weekly cost of running a direct shipment to that of possible multi-city route based on that week's demand

Table 8: Description of variables critical to model development based on interviews

The model presented in this section has elements of typical logistic and planning models. However, the model incorporates specific factors based on the needs expressed during the interviews. Hence, it has a broader set of output variables and control variables, some of which are specific to Amgen's case.

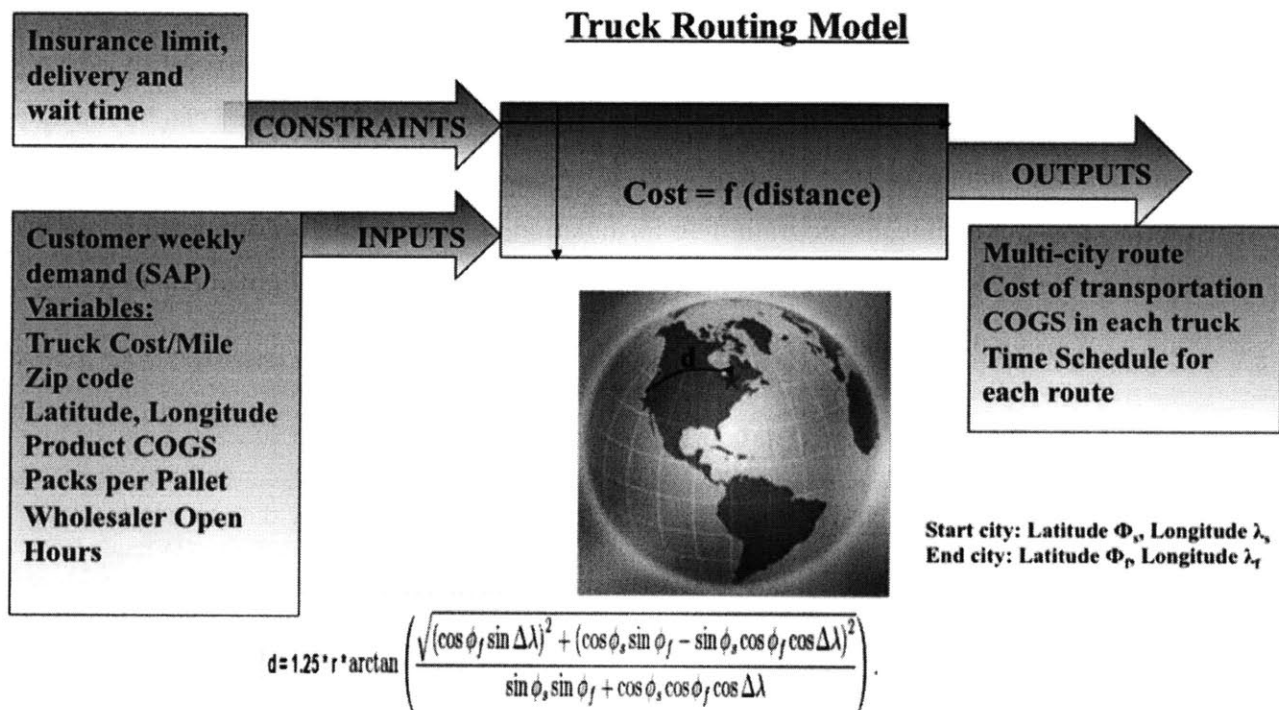


Figure 10: Truck routing model

The input to the model is the demand data in packs, by customer name, for the planning period. The first step the model does is to segregate the SAP demand data by product, and convert the packs to pallets. The model also extracts other wholesaler details like distance and receiving open hours from an editable master customer list. The model has predetermined groups of wholesaler sites, with locations in a specific region grouped together. For our case of Amgen in North America, we have 4 zones: North, Northeast, Southeast and Thousand Oaks (West). There are two main factors that were considered in creating the zones –

1. The wholesaler locations are fixed and known, hence the distances and their footprint relative to Amgen DC is already available and that make it easy to rule out some site clustering options.
2. There are constraints on the delivery date and time-to-delivery for most wholesalers, e.g. trade operations contracts with specific customers on predetermined delivery day. This makes it impractical to group some customers together.

With this model, managers can input the demand data and determine the multi-city routes for that week. The model provides practical application in the decision making process for managers by giving outputs that are currently done in a manually, such as determining insurance value of products on a truck, schedule of departure and arrival of truck and transportation cost. It is easy to reconfigure, flexible to considering various scenarios of truck deployment and can be run as frequently, and for data over any period of time.

The model has a mixed integer programming formulation with binary on/off options for considering a site as part of multi-city route. This will be explained in the Implementation section below where the output of model is described.

5.1.3. Model Assumptions

Assumes fixed speed of transit from one location to another, fixed delivery date to wholesalers and small parcel (vendor managed) urgent order fulfillment.

The model has assumed one-hour unloading time at each wholesaler site and a uniform cost/mile of \$1.85 based on gas prices. These assumptions can be changed to reflect varying unloading time at wholesaler locations, or varying prices for different routes.

5.2. 'DC Footprint Model' – Strategic

5.2.1. Model Description

The 'DC Footprint Model' calculates the distances using the modified form of great circle equation to determine distances between potential Distribution Centers. The model assigns wholesalers to active distribution centers (DCs) based on closest proximity. The model allows turning on/off any of the DCs and hence considers various combinations. Each scenario output shows transportation cost, operating cost, site loading (volume of products flowing through each DC) and risk profile based on inventory levels. The next section (Implementation) will explain the output of this model and present scenarios of business cases developed with Amgen as case example.

5.2.2. Model Assumptions

The 'DC Footprint Model' assumes variable operating cost of new DCs based on existing location costs. It considers variable cost as a function of the volume of products, and hence increases linearly with volume instead of step increases.

The set-up cost was taken as zero because the chosen locations had an existing Amgen or UPS site. However, set-up cost can be added when the model is scaled to other global markets.

5.3. Implementation

5.3.1. 'Truck Routing Model' – Operational

The model output will create dynamic multi-city routes for all wholesalers based on location and order demand. This increases truckload utilization to 40-60% of full truck capacity, a 400% increase compared to current operations. The transportation cost reduces because of less frequent return trips to Site 3. Additionally, the model has some future saving opportunities. The model also simulates changes to delivery patterns (day, frequency) to show reduction in transportation cost by ~25%. This can be used to initiate discussions with the commercial group (trade

operations) to trigger negotiation with wholesalers for revising the customer service terms.

5.3.1.1. Model output – Amgen Business Case

As an illustration, the ‘Truck Routing Model’ is run for the Amgen weekly demand data. To do that, the data from SAP is copied into the ‘SAP Demand’ tab of the excel model. The model reads the headings of each column to extract customer name, product name and order quantity (packs). These fields are read by another section of the model that consolidates all orders by customer and converts it to pallets.

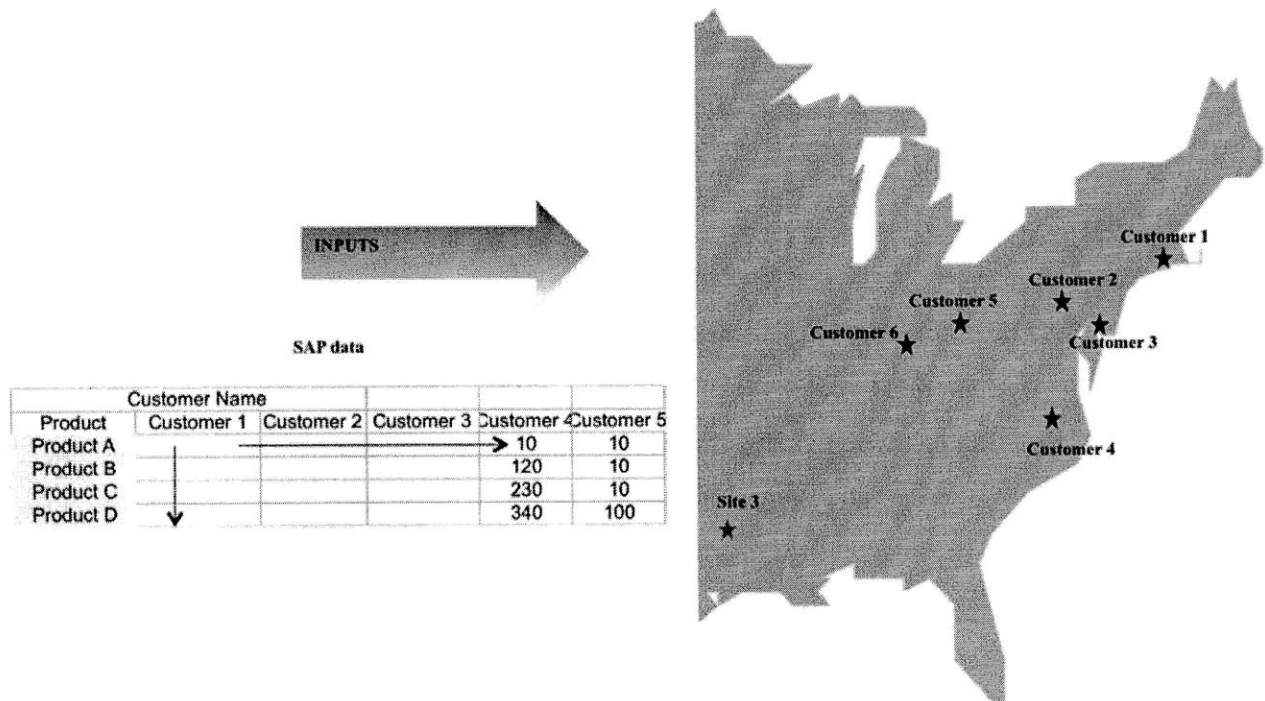


Figure 11: SAP input to Truck routing model in Amgen case example

The model will then identify the active wholesaler zip codes (with orders for that week), and map the latitude and longitude of those sites. In this case, it will pick customer # 4, 5 and 6 and make customer # 1, 2 and 3 inactive. The figure below lists some of the numerical calculations done by the model that will then feed into the output sheet.

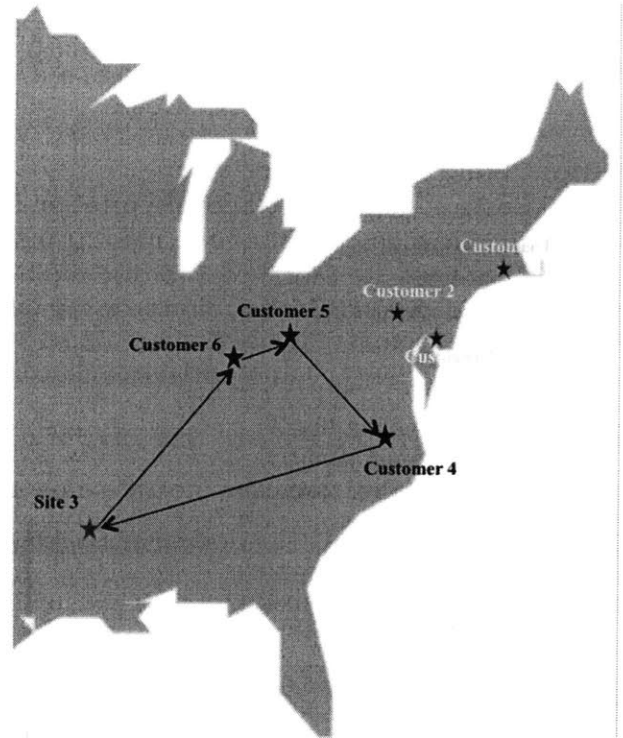
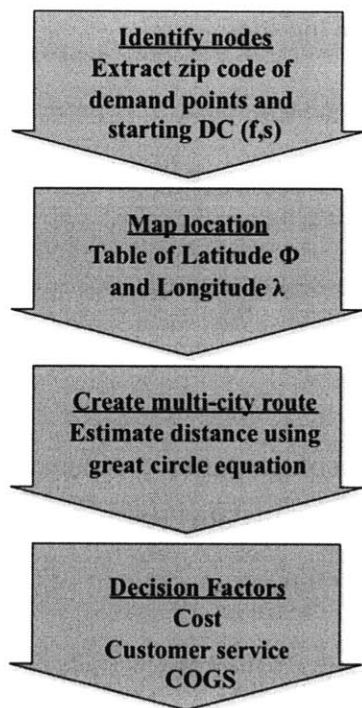


Figure 12: Flowchart of model execution and map of multi-city route based on given weekly demand

The output sheet does a series of basic calculations to create a decision framework that will guide the manager on planning the scheduling process.

Output Field	Description
Multicity Pallets Demand	Demand in pallets if Multicity option is 'on', 0 if option is 'off'
Total Pallets multicity	Gives total pallet count to ensure it is within truck capacity (~22 pallets)
COGS Value	COGS of product carried for each customer
Total Route COGS	There is a limit on total COGS of products on a truck, this tab helps confirm compliance to it

Table 9: Output variables related to truck loading

Output Field	Description
Distance between legs	Miles from one point to next in the multi-city route
Travel time	Travel time to reach a site
Reach Date & Time	Date and time of arrival at wholesaler site
Unloading/hold time	Hold time if truck reaches before opening hours of wholesaler
Start Date & Time	Date and time of departure from wholesaler site
1-way Distance	Distance of direct truck shipment from SITE 3 to

from DC

Wholesaler

Table 10: Output variables related to transportation logistics

Output Field	Description
Travel Cost	Cost of transportation for that leg
Overnight Charges	Cost of overnight transport when applicable
Total Route Cost	Total cost for the multi-city route
Direct Truck Cost	Cost of direct 1-stop deployment (Site 3-Wholesaler-Site 3)

Table 11: Output variables related to Transportation cost

Hence, for the Amgen case example, the below table is a portion of the output the manager will get. This will help the manager to understand the customer service and delivery schedule for each option and make decision on direct vs multi-city routing option.

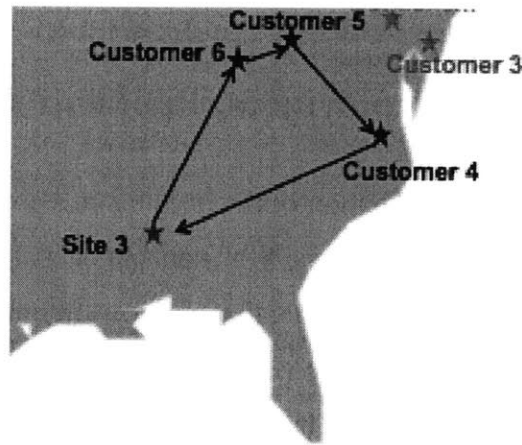
The table below has the portion of output that is data based on wholesaler or SAP data already present. Based on data, the customer 1, 2 and 3 do not have any demand for the considered week. Customers 4, 5 and 6 have a pending order that reflects in the ‘Actual Pallet Demand’ tab. The Manager has chosen to keep ‘on/off Multicity’ option as 1, which allows all wholesaler sites to be considered while making the multi-city route. The last two columns give the COGS of products to be carried by truck that week.

Zone	Customer ID	Customer City	Zip Code	Receiving Opening hour	Receiving Closing Hour	On/Off Multicity	Actual Pallet Demand	Multicity Pallets Demand	Total Pallets multicity	COGS Value	Total Route COGS
northeast	Amgen	Site 3	40200			1					
		Customer									
northeast	10055093	1	43100	7	19	1	0	0		\$-	
		Customer									
northeast	10024423	2	43111	7	19	1	0	0		\$-	
		Customer									
northeast	10019569	3	18000	7	19	1	0	0		\$-	
		Customer									
northeast	10012208	4	02100	7	19	1	1	1		\$118,295	
		Customer									
northeast	10059442	5	08988	7	19	1	1	1		\$101,988	

		Customer							
northeast	11111111	6	08988	7	19	1	1	1	\$140,885
northeast	Amgen	Site 3	40200			1		3	\$361,168

Table 12: Model output with input, demand data and COGS by customer and zone

Based on this, below is the map that shows the Manager a graphic representation of the multi-city routing for the considered week.



Site location for illustrative purpose only

Figure 13: Multi-city route recommended for the given week based on demand data

The Manager then will consult the second portion of output that will guide him on his decision-making process. It shows precisely how far the different sites are, what the relevant multicity route stops are (in this case, Site 3, Wholesalers 4, 5 and 6 and back to Site 3), and what the time of delivery at each site is. This is the ‘scheduling’ portion of the output. The last few columns compare multi-city route cost (listing all its components – ‘travel cost’, ‘overnight charges’ and total) to the option of direct shipment from DC to the three wholesalers separately.

Multicity Stops	Miles between legs	Travel time (Hrs)	Reach Date&Time	hours on stop at site	Unload /hold time	Start Date & Time	Travel Cost	Over night Charges	Total Route Cost	1-way Distance from DC	Direct Truck Cost
40200				0	0:00	11/10/09 9:00 AM					
40200	0	0	not a stop	0	0:00	11/10/09 9:00 AM	\$-			0	\$-
40200	0	0	not a stop	0	0:00	11/10/09	\$-			0	\$-

						9:00 AM				
40200	0	0	not a stop	0	0:00	11/10/09			0	\$-
			11/11/09			9:00 AM	\$-			
02100	1000	20	5:00 AM	3	3:00	11/11/09	\$1,849	\$1,000	1000	\$3,698
			11/11/09			11/11/09				
08988	319	7	3:00 PM	1	1:00	11/11/09	\$590		708	\$2,617
						11/11/09				
08988	0	0	not a stop	0	0:00	11/11/09	\$-		708	\$2,617
			11/12/09			11/12/09				
40200	708	15	7:00 AM	0	0:00	11/12/09	\$1,308	\$4,749		

Table 13: 'Truck routing model' output comparing multi-city and direct delivery

Customer locations are for illustrative purpose only

5.3.1.2. Model deployment, Pilot and Training

The model was deployed at the distribution center in Site 3 in a controlled environment setup. It was piloted over a two-week period with real SAP demand data at Site 3 and the model costs were compared to actual incurred costs during that period. After making final edits to the model, the training phase began. The Site 3 Senior Manager handling distribution and the IT specialist were trained on all aspects of the model. The training included understanding the equations and model set-up, learning how to edit the model, and an instruction sheet that detailed all the steps involved in using or changing the model. The model ownership was then transferred to the Site 3 team.

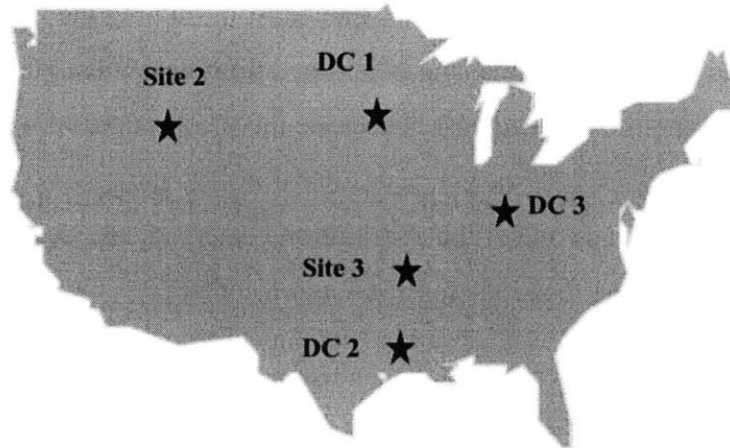
5.3.2. 'DC Footprint Model' – Strategic

The 'DC Footprint Model' output considers 6 DC locations – current locations in Site 2 and Site 3, distribution from packaging Site 1, and 3 UPS hubs. The model evaluates transportation costs varying locations and number of Distribution Centers. It is a cost-to-serve model with cost, quantity and customer service consideration.

Input: customer, demand and DC options

Output: transportation cost, variable operation cost

Model allows turning DCs on/off, permits all network combination of DCs, and dynamically assigns customers to DCs for fulfillment based on closest proximity.



For illustrative purpose only

Figure 14: US Map with potential DC locations

5.3.2.1. Model output

The ‘DC Footprint Model’ was able to

- Develop business scenarios and evaluated multi-DC options in North America
- Validate current network based on Site 2 – Site 3 locations
- Scale to other regions for distribution analysis

5.3.2.2. Analysis and Discussion

The business scenarios analyzed for the Amgen case study using this model is detailed below. All analyses take transportation cost (and in some cases, variable operating cost) into consideration.

Analysis 1: Study of two-DC networks for Amgen North America

The cost of running all combinations of 2-DC scenarios were studied from perspective of transportation cost to fulfill customer demand from each network.

The cost of running a DC 1 –Site 3 network had lowest transportation cost, \$130K lower than the current Site 2 – Site 3 combination. However, this is based purely on transportation cost of

operation, and does not include the synergies gained from running the DC from Site 2 where Amgen already has physical presence and other operations activities. The DC 1 site will require additional CAPEX, and the reduced cost is because the wholesalers on west coast are located in that region.

With Thousand Oaks fixed as one of the distribution centers, the model showed the SITE 3-SITE 2 combination to be the best locations for distribution centers.

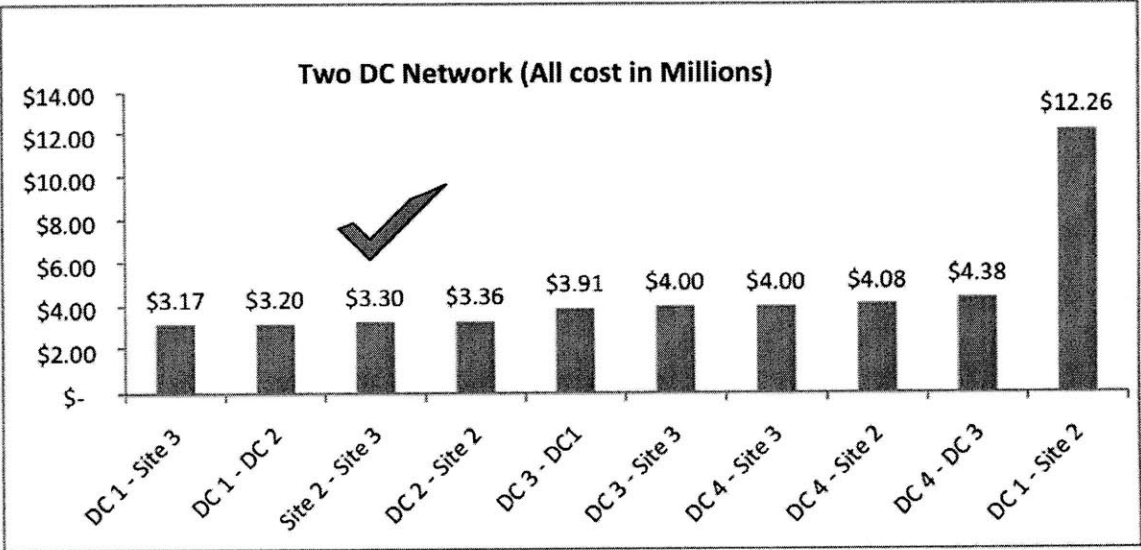


Figure 15: Model output two-DC network transportation cost

Analysis 2: Study of one-DC networks for Amgen North America

In business case analysis answers the following questions:

- 1 What is the best DC location to have a single distribution center in North America?
- 2 Can Amgen ship directly from packaging center at Site 1 to wholesaler locations?
- 3 How does cost of running two-DC network compare to that of single-DC

The model output is shown in figure below. Site 3 is the best location for a single DC network, and is better than the option of shipping directly to wholesalers from Site 1 through DC 3 at port of entry.

This is due to the nature of customer demand fulfillment that Amgen has committed to – Amgen distribution policy involves sending a truck to a wholesaler site on fixed days of a week

regardless of the order size. Hence, there are many trips to wholesalers with smaller order quantity. Transportation cost is a result of preset fixed delivery schedule to customer site. Higher cost of direct from Site 1 (through DC 3) is due to longer distance truck runs from DC 3 (port of entry) to most of the wholesaler locations. Site 3 is better positioned here to function in a ‘hub and spoke’ model. The products are transferred from Site 1 to Site 3 using fewer truck runs (full truck loading) and this functions as a hub. From Site 3, wholesaler order fulfillment is done using smaller truckloads, but very frequent and shorter distance trips (spokes).

Lastly, the transportation cost of running current 2-DC network is cheaper by at least \$1 Million/yr compared to single DC network (Site 3) making the current set-up a suitable one to continue operating as.

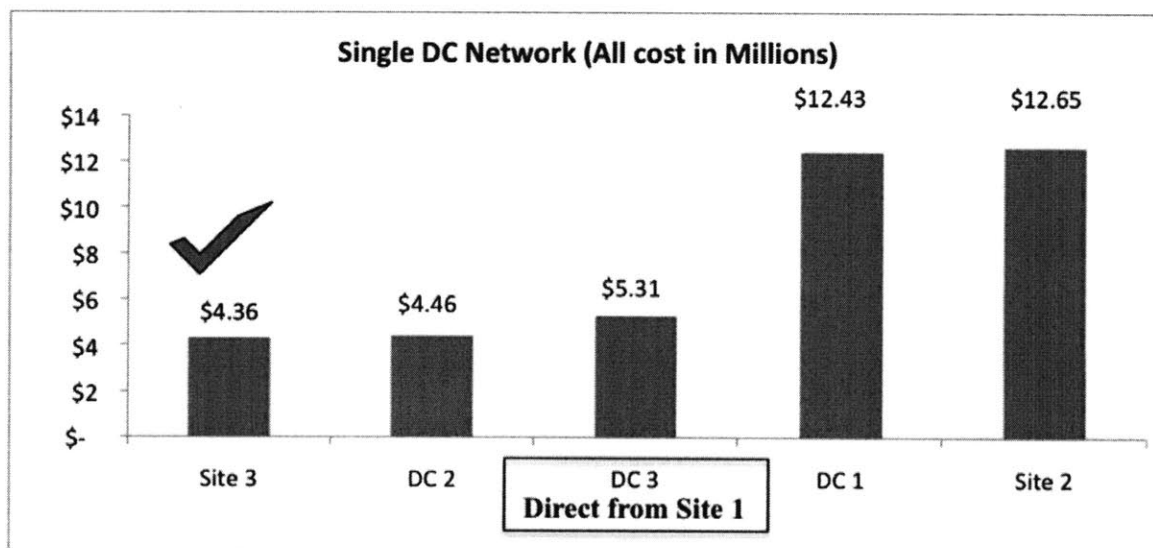


Figure 16: Model output one-DC network transportation cost

Analysis 3: Study risk profile and inventory levels across the various 2-DC networks

Based on proximity of the DCs to wholesaler locations, the model assigns wholesaler demand fulfillment to closest DC in the network. This analysis considered the demand data for a one-year period (2008-09) and looked at how the demand will be fulfilled in each 2-DC network combination. The model output shows a more even distribution of inventory and risk profile in the Site 3 - DC 3 network scenario. In this case, a 64%-36% split of inventory allows for

moderate site loading and lessens risk from Site 3 shutdown.

In all other 2-DC networks, the Site 3 distribution center handles over 90% of the commercial demand and will result in a high level of inventory flow through one site.

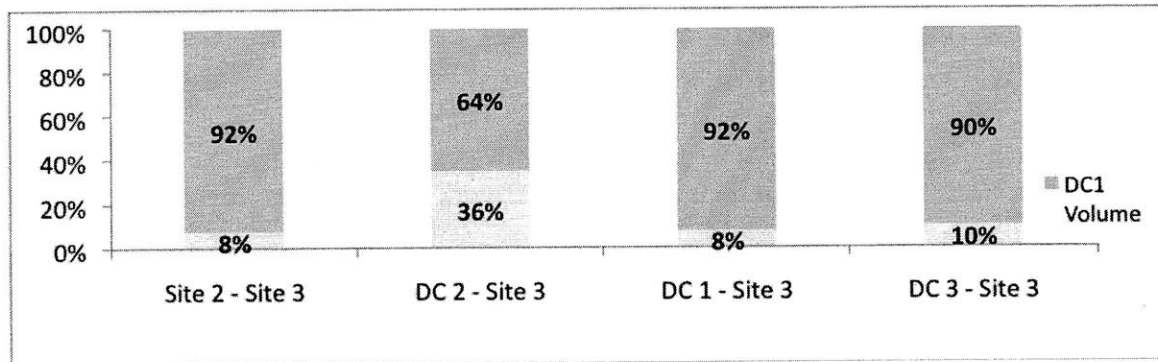


Figure 17: Site loading and inventory profile for 2-DC combinations involving SITE 3

This last analysis on site loading has limited implications for the current North America market, but the largest impact of this type of analysis for Amgen will be when making DC location decision in Europe and Expansion markets. In determining the location of Distribution Centers in the new markets, this model can help understand transportation cost, volume of product flow through each DC and the inventory and risk profile.

Analysis 4: Cost Saving Opportunities with minor changes in current DC network

This business scenario assumes the existing operations – Site 1 as a packaging location, and Site 2 – Site 3 as distribution centers. An earlier analysis had shown that there is not much value in shifting all distribution activity from Site 3 to Site 1. Here, assuming this current footprint, model identifies cost saving opportunity through fulfilling order demand of two wholesalers directly from Site 1.


The change is possible due to the following factors –

- 1 The wholesalers referred as #1 and #2 in table below approximately 2-3 pallets/week and take order delivery once a week
- 2 Both wholesalers take order delivery once a week

- 3 The wholesalers delivery can be accommodated by truck scheduled for transfer of products from port of entry point to Site 3

It is easy to fill this order size from Site 1 and ship direct to wholesaler, and will reduce transportation cost by \$340,000 annually. The table below shows the cost incurred in the two routes of delivery.

Wholesaler Name	Current Mode Cost		Cost Direct from Site 1
	Site 1 to Site 3	Site 3 to Wholesaler	
Wholesaler 1	\$ 70K	\$ 248K	\$ 121K
Wholesaler 2		\$178K	\$ 33K
Total Cost	\$ 496K		\$ 154K



Potential Savings \$340K

Table 14: Saving opportunity in direct from SITE 1 distribution for select wholesalers

The next step involves understanding if Site 1 has the capability to handle direct distribution, and if the cost of changes in packaging and distribution at Site 1 is less than \$340K saving identified.

6. SUMMARY

6.1. Operational – ‘Truck routing model’

The thesis addressed the question of whether opportunities to optimize current distribution channels existed. There are opportunities to improve the distribution model, automate decision-making steps, and create a structure to aid fulfillment processes. Developing the ‘Truck Routing model’ did this. As a case study, the model helped create multi-city routes to improve truck utilization to 60% and reduce transportation cost by ~ \$400,000 annually.

In answering the questions developed as part of the problem statement, the thesis detailed our the process used to identify opportunities, methodology & tools used to develop a model, and the implementation and training to realize the savings identified.

6.2. Strategic – ‘DC footprint model’

In this section, the thesis evaluated Amgen’s Distribution Center footprint. There were some key questions that were addressed in the process –

Is there an opportunity for direct distribution from packaging center Site 1?

Can we establish additional or alternate distribution centers?

Is the current location of DCs optimal based on our customer footprint?

The ‘DC footprint model’ analyzed Amgen’s distribution footprint from the standpoint of transportation costs. Business scenarios were developed to evaluate single- and multi-DC options in North America. The model validated current network based on Site 2 – Site 3 locations as a good option. With the current fulfillment strategy pursued by Amgen, the option of distributing from Site 3 was more economical than direct distribution from Site 1. The model helped analyze the inventory and risk profile, and identify cost savings through small changes to current distribution. The model can be scaled to other regions for distribution analysis.

6.3. Challenges and Next Steps

‘Truck Routing Model’

Operations Impact

The team will perform further pilot tests and validate the model at Site 3 Distribution Center, get management approval for use, and deploy for North America Distribution Operations.

Model ownership has been transferred to Distribution team and implementation is in progress.

Need to create an ownership team that will be responsible for owning various components of the model.

Commercial Impact

Use model to monetize cost savings through changes in customer fulfillment pattern.

Provide feedback to trade operations to evaluate feasibility of changing wholesaler contracts in order to reflect the desired changes in demand fulfillment.

Other Markets

Use model for optimizing truck distribution in other markets

'DC footprint Model'

Model can be used to analyze the European distribution network (truck channel)

Extend model for Middle East and Latin America in determining Distribution Center footprint, resulting transportation costs, and DC site loading (volume of product flow through each DC of the network).

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