UNDERSTANDING SOCIAL AMPLIFICATION OF RISK: POSSIBLE IMPACT OF AN AVIAN FLU PANDEMIC

by

Aamir Sundrani

B.S. Chemical Engineering, The University of Texas at Austin, 1999

Submitted to the Sloan School of Management and the Engineering Systems Division in partial fulfillment of the requirements for the degrees of

Master of Business Administration
and
Master of Science in Engineering Systems

In conjunction with the Leaders for Manufacturing Program at the
Massachusetts Institute of Technology
June 2007

Signature of Author _____
Sloan School of Management
Engineering Systems Division
May 11, 2007

Certified by _____
Charles L. Cooney, Thesis Advisor
Professor, Department of Chemical Engineering

Certified by _____
Kimberly M. Thompson, Thesis Advisor
Visiting Associate Professor, Sloan School of Management
Associate Professor, Harvard School of Public Health

Certified by _____
Daniel E. Whitney, Thesis Reader
Senior Lecturer, Engineering Systems Division

Accepted by _____
Richard de Neufville, Professor of Engineering Systems
Chair, Engineering Systems Division Education Committee

Accepted by _____
Debbie Berechman, Executive Director of Masters Program
Sloan School of Management

UNDERSTANDING SOCIAL AMPLIFICATION OF RISK: POSSIBLE IMPACT OF AN AVIAN FLU PANDEMIC

By

Aamir Sundrani

Submitted to the Sloan School of Management and Engineering Systems Division
on May 11, 2007 in partial fulfillment of the Requirements for the
Degrees of Master of Business Administration and
Master of Science in Engineering Systems

Abstract

Today, stakeholders expect organizations to be able to endure external shocks. Hence, the real potential of an avian flu pandemic has many corporations developing business continuity plans for the disruptions that a pandemic may cause. For the pharmaceutical/biotechnology industry, the major concerns of a pandemic include high employee absentee rates, lack of accessibility to the medical facilities, and disruption to the product supply chain.

This work introduces social amplification of risk theory to evaluate the potential impact of a pandemic to a business due to heightened fear. It uses a case study of Genzyme Corporation and evaluates pandemic related risks to two of its major products. By applying a system dynamics framework to evaluate the mechanisms for the amplification of risks, a solution is proposed. The lessons introduced in this work can help organizations evaluate the true risks of catastrophic events.

Thesis Supervisor:	Charles L. Cooney
Title:	Professor, Department of Chemical Engineering
Thesis Supervisor:	Kimberly M. Thompson
Title:	Visiting Associate Professor, Sloan School of Management Associate Professor, Harvard School of Public Health

This page is intentionally left blank.

Acknowledgments

I wish to extend my appreciation to the Leaders for Manufacturing Program and Genzyme Corporation for their financial support and opportunity to work on this project. I want to especially thank my supervisor John McFadden and sponsor Mark Bamforth for sharing their time and knowledge with me. Their support throughout the internship has been instrumental to its success. Special thanks to Jeff Goldberg and other Genzyme employees who have provided feedback and supported the project.

I would like to recognize my thesis advisors, Charlie Cooney and Kimberly Thompson for their patience, support and guidance. Their recommendations have strengthened the project.

Lastly, I want to convey my deepest gratitude to my family for their sacrifice and support throughout the last two years. I couldn't have made this journey without them.

This page is intentionally left blank.

Table of Contents

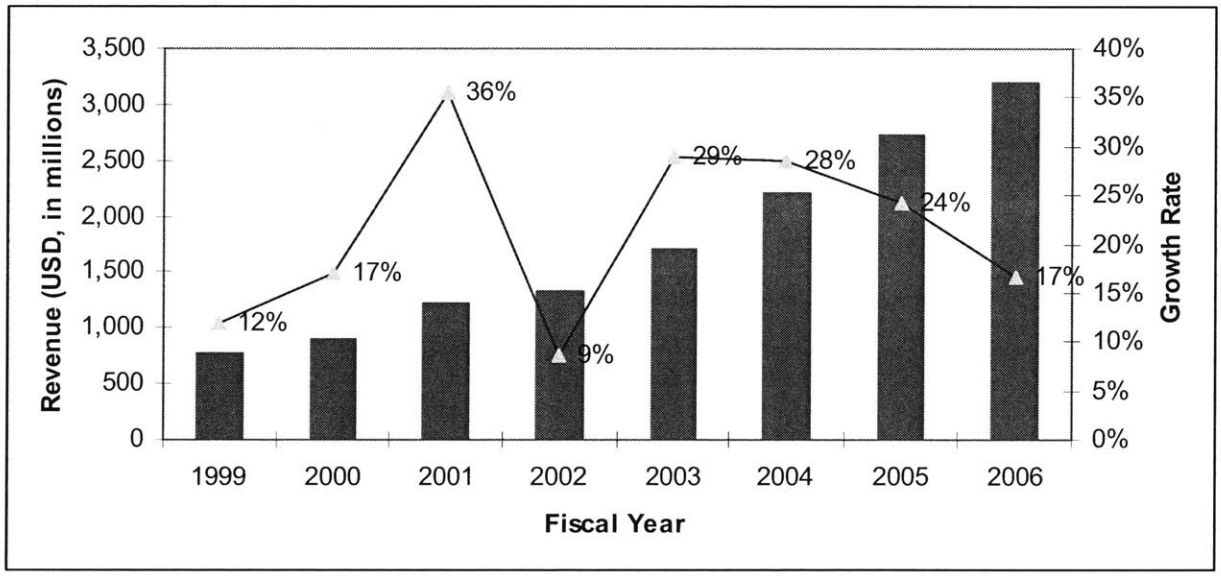
This page is intentionally left blank.

Chapter 1: Introduction

1.1 Company Overview

With annual revenues exceeding $3 billion, Genzyme Corporation is a leading biotechnology firm dedicated to addressing serious unmet medical needs. Founded in 1981, Genzyme targets therapies and services for rare inherited disorders (also known as orphan diseases), kidney diseases, orthopedic surgical needs, organ transplant and immune diseases, cancer and diagnostic testing. Most of the drugs supplied by Genzyme have few if any substitutes and they are either life critical or drastically improve the quality of a patient's life. Today, the firm employs over 9,000 employees and helps patients in nearly 90 countries (*1*). For the last six years (except in 2002), it experienced double digit growth rates in revenues (see Figure 1-1) (*2-9*).

Figure 1-1: Genzyme's Revenue from 1999-2006 (*2-9*)



As Genzyme grows and expands into new product and geographical markets, its manufacturing blueprint becomes more complex. Table 1-1 shows the breakdown of product families by Genzyme's major manufacturing sites (*9*):

Table 1-1: Manufacturing/Servicing sites of Various Product Families (*9*)

	Renal	Therapeutics	Transplant	Biosurgery	Genetics
Belgium (Geel)		x (2009)			
England (Haverhill)	x				
Ireland (Waterford)	x	x	x		
United States (MA – Allston and Framingham, NJ, NM, CA)		x		x	x
France (Lyon)			x		

1.2 Project Motivation and Setting

Genzyme continues to grow and increase the number of people globally who rely on its products. In the age of terrorist attacks, natural disasters, and flu pandemics, supply chain management represents a primary concern, and it is imperative that Genzyme prepare for external shocks and work toward minimizing impacts on the company's business operations.

Potential Impacts from External Shocks

The need to prepare for disruptions is not an academic exercise. Disruptions have negatively impacted many corporations, especially those that are ill prepared to handle them. Yossi Sheffi, in his book The Resilient Enterprise (*10*), opens with the powerful example in which a fire at a Philips semiconductor fabrication plant in Albuquerque resulted in supply shortage of cell phone chips for the company's two largest customers, Nokia and Ericsson. While Nokia was able to manage the shortage by immediate action and diverting some of its orders to other suppliers, Ericsson did not have contingency plans in place and suffered a $2.34 billion loss. Eventually, Ericsson exited from the phone handset production market.

The recent devastation of Hurricane Katrina in 2005 severely impacted the New Orleans Blood Center's ability to operate (*11*). The Blood Center, a non-profit service organization, is the primary provider of blood and blood components to over forty hospitals in Southern Louisiana and Mississippi (*11*). The floods from Hurricane Katrina destroyed $2m worth of equipment

(*12*) and drove staff members to evacuate the area (*11*). It took the center over twelve months to obtain adequate funding from the Federal Emergency Management Agency to support construction of a new facility and purchase of new operating equipment (*13*). During this time, according to The Blood Center Community Development Manager, Suzy Potter, many of the hospitals relied on other blood centers, outside of New Orleans, to meet their blood requirements (*14*).

These examples highlight the importance of learning from the experiences of others in identifying operational/supply chain weaknesses and of using scenario planning of possible future events to create a robust enterprise. One potential event of great interest right now is an avian flu pandemic.

Avian Flu Pandemic

News headlines on spread of avian influenza and its potential toll on human lives have alarmed governments and corporations around the globe. By the end of 2006, transmission of influenza from birds to humans infected 263 individuals in 12 countries resulting in 158 deaths (*15*). If the new flu strain is able to mutate, due to antigenic shift, to a form in which humans can transmit the disease efficiently to other humans, a pandemic is likely to occur (*16*). Once a fully transmissible human influenza outbreak occurs, it is possible for the virus to circle the globe within three months (*17*). A pandemic usually occurs in two or three waves (*17*), each lasting six to eight weeks (*18*) and hence, could last for a total of one to three years (*19*). Also, each wave may affect different regions of the world. Therefore, unlike a discrete disruptive event like the September 11, 2001 terrorism attack or the 2004 tsunami in Southeast Asia, a major pandemic is likely to impact most organizations in some fashion. The World Health Organization (WHO) has designed a six-phase pandemic alert system (see Fig. 1-2) to communicate to the world the current status of the threat (*20*).

Figure 1-2: World Health Organization Pandemic Alert System* (*20*)

Stages of Pandemic Influenza		
Inter-pandemic phase New virus in animals, no human cases	Low risk of human cases	1
	Higher risk of human cases	2
Pandemic alert New virus causes human cases	No or very limited human-to-human transmission	3*
	Evidence of increased human-to-human transmission	4
	Evidence of sustained human-to-human transmission	5
Pandemic	Efficient and sustained human-to-human transmission	6

*As of March 2007, the world is at WHO pandemic Stage 3.

Possibility:

Three major pandemics occurred each century for the last four centuries. The last major pandemic occurred in 1968. Characteristics of the three latest large pandemics include (*21*):

1) 1918 Spanish flu (H1N1 virus subtype) – caused >50m deaths worldwide (about 2% of population at the time); mortality rates were high among infants, elderly, and healthy individuals
2) 1957 Asian flu (H2N2 virus subtype) – caused 1m deaths worldwide; mortality rates were high among infants and elderly
3) 1968 Hong Kong flu (H3N2 virus subtype) – caused 700,000 deaths worldwide; mortality rates were high among infants and elderly

The current strain of influenza virus, H5N1, is similar to that of Spanish flu (*22*). The risk of pandemic increases as each additional human case gives the virus an opportunity to improve its transmissibility in humans (*23*).

Potential impact:

The potential impacts of the avian flu pandemic are highlighted by health agencies around the world, including the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC). According to WHO, the next pandemic will spread much more rapidly and infect more people than in the past because of the greater global population, greater world-wide travel and higher density urban settings (*17*). Furthermore, the flu is expected to cause more serious illness and greater number of deaths, since more people today live with chronic medical conditions and immune suppressing diseases (*24*). WHO estimates that the world will face up to 233 million outpatient visits, 5.2 million hospital admissions (*25*) and 2 million to greater than 7.4 million deaths during the next pandemic (*17*). These estimates are based on 1957 pandemic. According to Shigeru Omi, director of WHO's Western Pacific Region Office, in the worst case scenario, the death toll could reach 100 million (*26*).

To protect its citizens, most countries plan to close ports and airports, suspend schools in affected areas and quarantine affected areas (*27*). The following are also expected at the time of a pandemic:

Strain on the medical system (*28*)

As a pandemic expands across many geographical areas simultaneously, hospitals and other medical care facilities are expected to be overwhelmed by patients who become ill (and by the worried well) (*29*) and short-staffed as doctors, nurses, and other health care workers may themselves become ill or be afraid to come to work (*25*). One of the likely results of the medical system running at or beyond full capacity (*30*) is that most of the elective and non-life saving procedures will assume lower priority (*18*).

Run on consumer products/drugs

At the onset of a pandemic, when human-to-human bird flu transmission is confirmed, the WHO will raise the pandemic alert system to Stage 4. At Stage 4 or earlier, most governments will urge citizens to maintain a stock of non-perishable items (*31*). People will be encouraged to also plan for cold and flu-like symptoms and to replenish their medicine cabinets (*31*). With such warnings, people will most likely immediately rush to the markets to stock-up on consumer goods and drugs, which could create a temporary shortage of numerous products (*29*). This type of behavior is often observed following warnings of a potential catastrophe, such as a strong hurricane (*32*).

Business disruption

The avian flu pandemic is expected to cause major disruptions to most businesses especially in today's "closely interrelated and interdependent systems of trade and commerce" (*17*). WHO estimates worldwide economic damages could exceed $800 billion (*33*). In general, corporations can expect the following:

- High employee absentee rate: the Department of Homeland Security predicts a 20-40% absentee rate at the height of a pandemic (*29*), based on the following factors:
  - Personal illness
  - Taking care of sick family members
  - Taking care of children whose schools have been temporarily suspended
  - Fear of contagion

- Supply disruptions throughout the chain, including (*30*):
  - Suppliers unable to meet demand
  - Production disruptions
  - Transportation disruptions

- Travel disruptions (*30*)

1.3 Thesis Structure

With the reasonably high probability of a near-term pandemic and a general sense that responsible businesses must be prepared, this thesis explores key areas that Genzyme should highlight during business continuity planning in order to minimize the impact of potential disruptions.

Chapter 2 introduces the concept of social amplification of risk theory using a system dynamics framework. It provides two real world examples to illustrate the use of the theory: (1) the Three Mile Island nuclear meltdown in 1979 and (2) a Genzyme incident involving Renagel 800mg tablet withdrawal in 2001.

Chapter 3 describes Genzyme's efforts to prepare for an avian flu pandemic. It also outlines potential mechanisms for risk amplification/attenuation during a pandemic. The chapter then analyzes the potential impacts of a pandemic on Genzyme's ability to deliver Cerezyme and Myozyme to patients and after scenario analyses it offers recommendations to minimize possible negative impacts.

Chapter 4 provides a conclusion and recommendation for a future project that Genzyme could undertake to create a more robust enterprise.

This page is intentionally left blank.

Chapter 2: Social Amplification of Risks (*34*)

The reaction to a disruption is typically based on how the risks associated with the disruption are perceived, which may or may not correspond to the actual risks. Psychological, social, institutional, and cultural processes that shape perceptions may heighten or attenuate the response to the risk event (*34*). In this chapter, a system dynamics model is used to illustrate the applicability of the social amplification of risk theory to a couple of real world examples. Before evaluating the impact of social amplification of risks, Section 2.1 illustrates and introduces system dynamics modeling techniques and Section 2.2 introduces the social amplification of risk framework.

2.1 System Dynamics Modeling

System dynamics is an approach for analyzing and solving complex problems with a focus on policy analysis and design. The approach uses a perspective based on information feedback and delays to understand the dynamics of complex physical, biological, and social systems. System dynamics provides a means to evaluate dynamic complexity, understand the sources of policy resistance, and design more effective policies (*35*).

To demonstrate how a system dynamics model could be applied to a business setting, Figure 2-1 shows a simple causal loop model of a common decision most pharmaceutical companies make – how much to spend in research and development. Most companies allocate a percentage of their sales to R&D spending. As shown by the "Innovation" positive feedback loop, the innovations or new products that stem from R&D results in higher revenues, which in turn increases R&D spending. Positive feedback loops are self-reinforcing and therefore, an "R" is placed inside the loop. The arrows indicate the causal relationship, while the positive sign at the arrowheads indicate the effect is positively related to the cause. If the "Innovation" loop were operating on its own with this simple structure, both the sales and R&D spending would increase or decrease exponentially.

However, the positive feedback loop is not isolated and in the simple example shown here it is paired with a negative feedback loop "Costs." As the company's R&D spending increases, so do the operating costs. However, as costs increase, R&D spending decreases to ensure acceptable profitability. A negative sign at the arrowhead indicates the effect is negatively related to the cause. Negative feedback loops are balancing (or self-correcting) and denoted by "B" inside the loop.

As the reinforcing and balancing loops operate simultaneously, the strength of each loop dictates the results from the interactions. In this simple example, a corporation will continue to increase its R&D spending as long as the return from the R&D investment (i.e. in the form of innovation or revenues) is greater than proportional costs. Note, in reality, time delays, which are not represented in this simple example, exist between the R&D spending and the investment return.

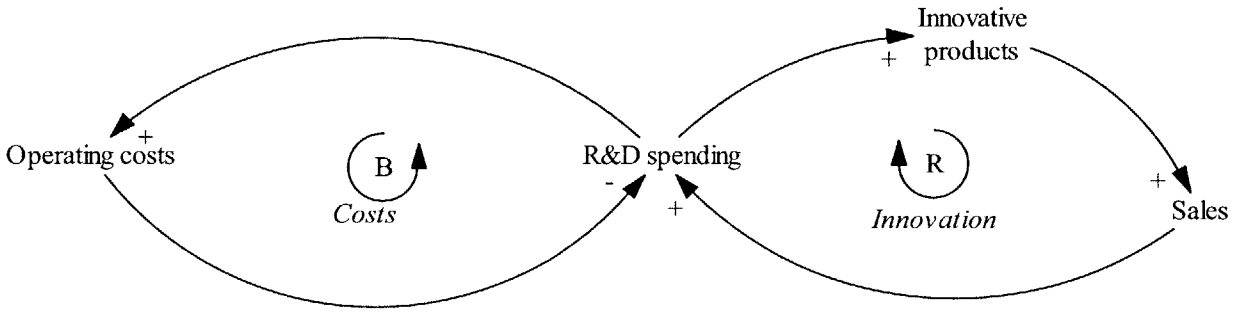


Figure 2-1: R&D Spending Causal Loop

The system dynamics framework is also used to explain the oscillation or the "Bullwhip Effect" experienced by many supply chains. Variability in demand orders amplify as one moves upstream in the supply chain (i.e., further from the customer) (*36*) as a consequence of lack of coordination among the various parts of the supply chain. As customer demand changes, the suppliers, manufacturers, and distributors respond according to their, often incomplete, understanding of the real demand, and they adjust the rate at which resources are ordered and used (*37*). Further, decision makers fail to account for the time delays in the negative feedbacks that regulate the state of the system, ignoring the supply line of corrective actions that have been initiated but have not yet had their effect (*38*). The result is oscillation or a "Bullwhip Effect" in

the supply chain, characterized by production and inventories that repeatedly overshoot and then undershoot the appropriate levels (*39*).

2.2 Social Amplification of Risk Framework

Kasperson et al. described the concept of social amplification of risk based on their observations of responses to a large range of technical risks. Technically, risk is defined as a product of the probability of events and the magnitude of specific consequences. However, social amplification of these risks drives the public responses and results in higher-order impacts. Social amplification of risk involves two stages: transfer of information about the risk and the interpretation and response to the information (*34*).

The first stage of amplification occurs with transfer of information about the risk. Information about the risks is extrapolated from prior direct experience or communicated by other persons or the media. Usually, direct experience with risk events instills fear about other risk events and hence, heightens the perception of risk. When risks are communicated through other channels, such as news media or friends and family, the volume of information, the extent of dramatization, and the symbolic connotations of information contribute to the degree of amplification of risk (*34*). Today, the Internet provides an easy medium to communicate real-time information to millions of people around the world, which may exacerbate amplification of risk (*40*). Moreover, the type of information channel, whether it is news media or a personal network, is an important factor in amplification of risk. Since the media cover mostly dramatic or risk events, high amounts of media coverage of an event amplify the public perception of the risk (*34*).

Interpretation and response to the information about a risk event is the second stage of amplification of risk. As complex risks are simplified for evaluation and communication purposes, individual or group biases are introduced. Lastly, the unfamiliarity of a risk event triggers the "signal value" or signals the seriousness of the event. In general, people feel more at risk when there is uncertainty about a hazard and when they feel that they have no control (*34*).

For this reason, people may worry less about the risk of smoking and a high fat diet than about the unproven or remote risks of electromagnetic fields or collision with an asteroid.

Often social amplification of risks results in behavioral responses that elicit second- and third-order impacts, which many times cause undue harm to individuals, corporations, or other parts of society. To highlight a real world example of social amplification of risk, consider the pandemonium created by the Three Mile Island (TMI) accident. On March 28, 1979, as a result of equipment malfunction and operator error, a partial nuclear core meltdown of the TMI's Unit 2 reactor frightened the residents across Pennsylvania (*41*). That evening Walter Cronkite of CBS reported "we are faced with the remote but very real possibility of a nuclear meltdown at the Three Mile Island atomic power plant" (*42*). While the Nuclear Regulatory Commission (NRC) later concluded the situation posed little danger (*42*), the uncertainty caused by conflicting reports of utilities and regulators (*41*), combined with media coverage, heightened the fear. Approximately 140,000 residents voluntarily evacuated the region (*42*). The event resulted in greater public opposition to nuclear power, stricter regulations, and reduced operation worldwide, impeding one of the major potential energy sources (*34*).

Figure 2-2 provides a system dynamics model outlining the principles of social amplification of risk using the TMI example. The "Media impact" reinforcing loop shows the direct correlation between the media coverage and the increase in perceived risks. Complementary to the "Media impact" loop is the "Too much info" loop, which shows that volume of information on the TMI event, whether it came from the media or personal network, also raised perceived risks. The TMI event instilled fear in the general population about nuclear technology and resulted in opposition to nuclear power and other higher-order impacts, such as stricter regulations. This demonstrates the overall risk of nuclear plant near-miss events may significantly exceed the risk estimates produced by a traditional risk analysis that does not typically include amplification.

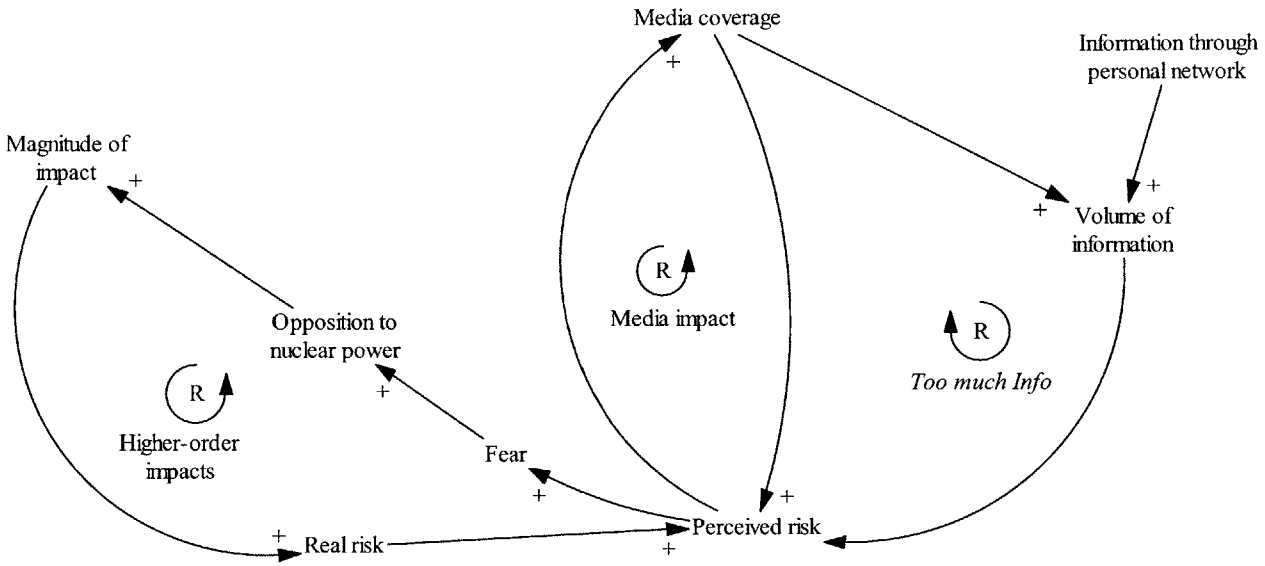


Figure 2-2: TMI Risk Amplification

2.3 Framework in Practice

To demonstrate the impact of social amplification of risk to Genzyme, this section considers the Renagel® 800mg withdrawal incident in 2001, which resulted in several unforeseen consequences for the company.

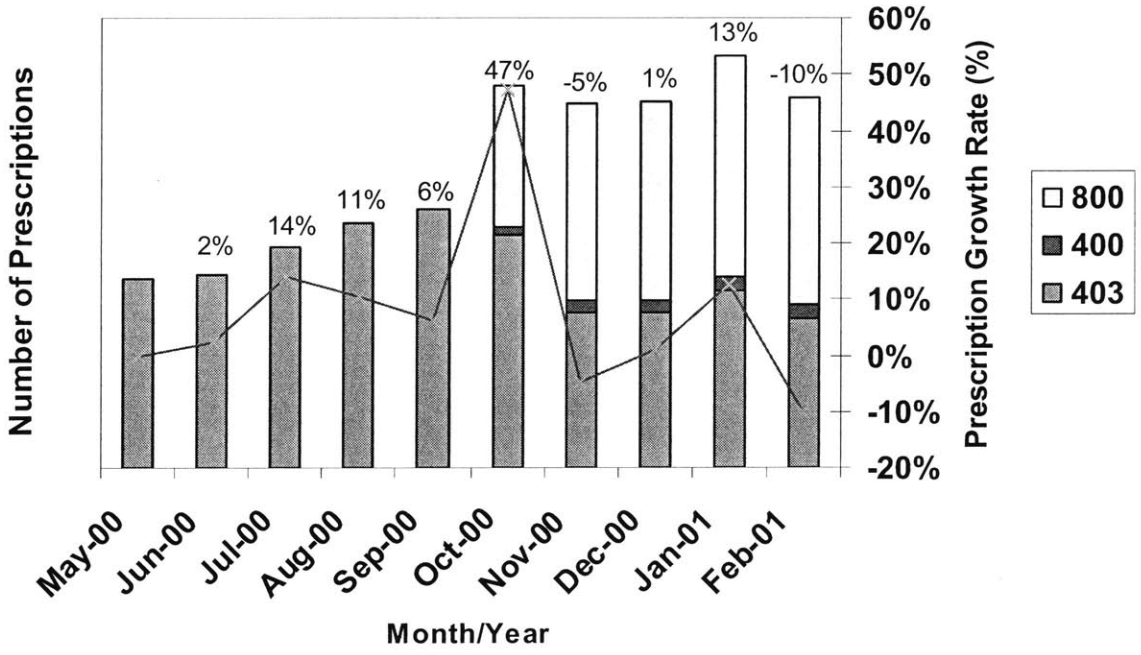
Product description

In 2006, the Renal business accounted for 21% of Genzyme's total revenue or $608m, and Renagel currently accounts for 85% of the revenues of Genzyme's Renal business (*9*). Launched in November 1998, Renagel is indicated for the control of serum phosphorus in patients with Chronic Kidney Disease on hemodialysis (*9*). It is unique in that it controls phosphorus without the accumulation of calcium or metals that can lead to hardening of tissues (*43*).

Introduction of 400mg and 800mg tablets

Renagel therapy began with 403mg capsules. However, in September 2000, Genzyme introduced 400 and 800mg tablets in response to many patients' preference for taking a tablet form (*3*). Furthermore, the 800mg tablets allow patients to take fewer pills, which many patients value because they take several supplementary pills for their disease. Following the launch of the tablet form, the demand for 800mg pills increased faster than expected due to several factors, which include the benefits of Renagel's superior non-absorbed polymer technology and the larger 800mg dose. Figure 2-3 shows a spike (47% increase) in number of new Renagel prescriptions following the introduction of 800mg dosage form (*44*).

Figure 2-3: Renagel New Prescription Data for May 2000 – Feb 2001 (800mg, 400mg, 403mg) (*44*)



Value chain

Figure 2-4 provides a simple description of the value chain for Renagel in 2001 that helps show the roles of the various players on risk amplification at the time of Renagel 800mg withdrawal.

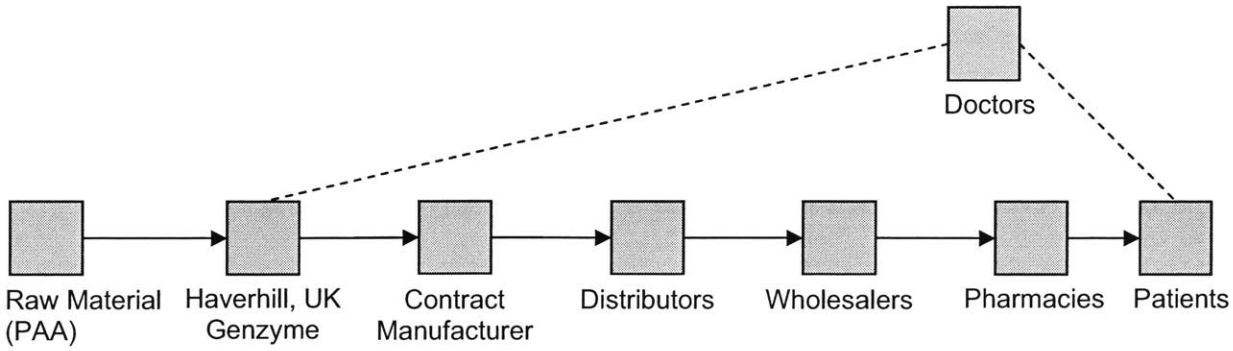


Figure 2-4: Renagel Value Chain

The primary raw material, polyallalymine hydrochloride (PAA), is received by Genzyme's Haverhill, UK production site and converted to the active pharmaceutical ingredient (API), Sevelamer hydrochloride. The API is then shipped to a contract manufacturer to convert the powder into tablets. The final product is distributed by the wholesalers to the individual pharmacies, from which patients buy their prescribed Renagel. One of the significant players in the value chain is the doctor (nephrologist). The patients rely on their doctor to prescribe the appropriate treatment based on his/her knowledge of safety and efficacy of the product. Hence, Genzyme's sales force ensures that doctors are well-informed about the risks and benefits of using Renagel.

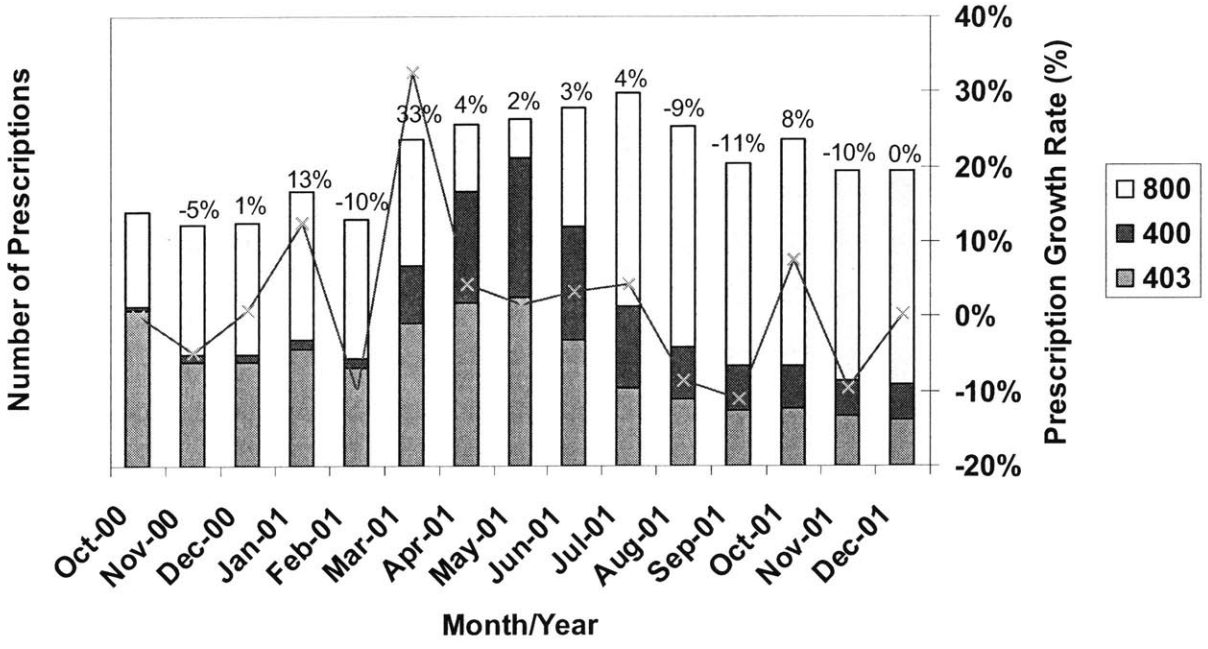
Problem

At the end of 2000, Genzyme's contract manufacturer for Renagel encountered a manufacturing quality problem with the 800mg tablets. After unsuccessful attempts by the contract manufacturer to fix the problem, Genzyme decided to stop production of the 800mg tablet from March to May 2001 and help its contract manufacturer retool (*45*).

First-order impact of the withdrawal:

When Genzyme announced its plan to withdraw the 800mg tablet from the market in March 2001, the company aided the nephrologists to temporarily switch patients from the 800mg tablet to an equivalent dose of 400mg tablets or 403mg capsules. As shown in Figure 2-5, the new prescription rates soared approximately 33% during March to account for the switchover from 800mg to other dosage forms (along with the growth rate), and they continued through April and May (*44*). During the same time period, Renagel revenues continued to grow due to the strong demand. The revenue increased from $28.6m in 2001 Q1 to $40.4m in 2001 Q2 (*46, 45*).

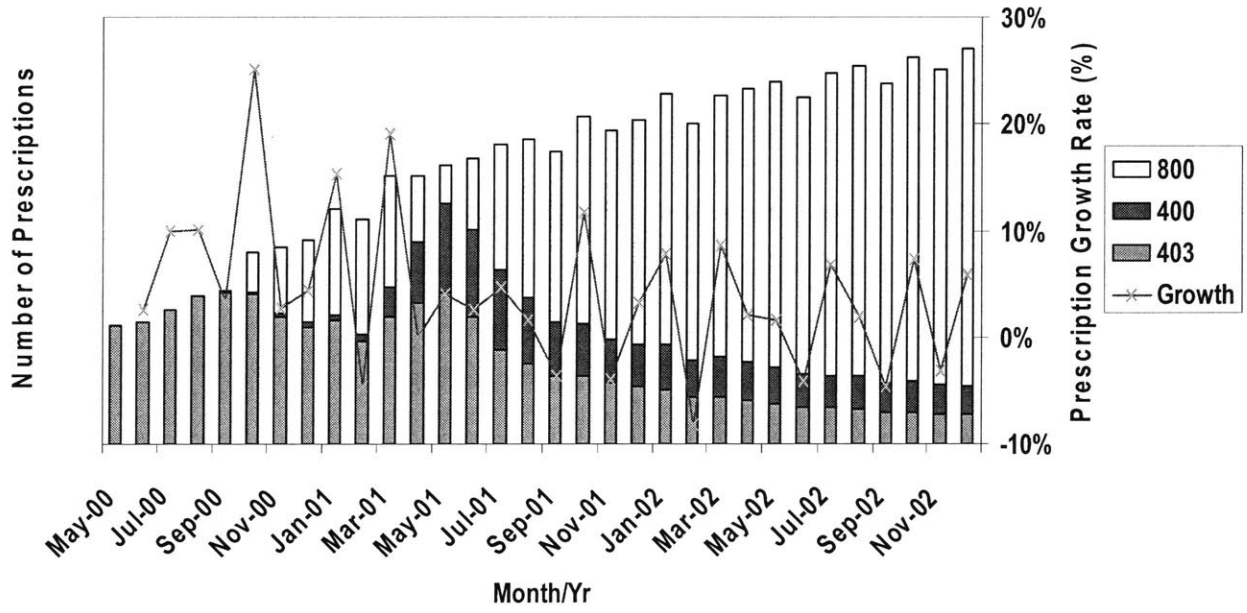
Figure 2-5: Renagel New Prescription Data for (800mg, 400mg, 403mg) (*44*)



Reintroduction of Renagel 800mg tablet:

After resolving the production issues, Genzyme reintroduced the Renagel 800mg tablets to the market in June 2001 (*45*). As expected, the overall demand growth rate continued on its trajectory as indicated by the 16% increase in total number of prescriptions from June to December 2001 (total number of prescriptions increased 18% from January to May 2001) (see Figure 2-6) (*44*). However, the new prescription rates for Renagel during the months of June and July 2001 (see Figure 2-5) continued to hover at high levels, similar to those at March and April (30+% greater than February 2001). The conflicting data between the total prescription and new prescription rates were not apparent and hence, Genzyme read the persistent higher number of new prescriptions as an increase in true demand instead of as a consequence of patients switching back from 400mg/403mg dosage form to 800mg tablets.

Figure 2-6: Total Number of Renagel Prescriptions (800mg, 400mg, 403mg) (*44*)



Response by wholesalers

Once Genzyme reintroduced the 800mg tablet, the wholesalers increased their 800mg tablet order rate to replenish their safety stocks, which the wholesalers used during the withdrawal period, and to build inventory levels of 12-18 weeks of demand. The move to increase inventory levels occurred in response to higher demand expectations and very likely, to protect the wholesalers from future product shortages, especially given higher anticipated demand.

The surge in wholesaler order rates resulted in approximately 30% increase in Renagel revenues in the third and fourth quarters of 2001 (see Table 2) (*47, 4*). Genzyme did not realize the wholesalers were building Renagel inventory and believed the increase in sales was due to growth in actual demand. As a result, the company provided optimistic future sales forecasts for 2002 (*48, 49*). In the beginning of 2002, the company came to realize the wholesalers' inventory position. To prevent wholesalers from further building-up inventory (and avoid similar future events), the company decided to establish formal inventory management agreements (IMA) with them. In addition, for the next few quarters, Genzyme reduced its shipments of Renagel to the wholesalers in order to drive down wholesalers' Renagel inventory levels to six weeks (*45-47*).

Table 2-1: Renagel Revenues (from 2001 Q2 to 2002 Q2) (4, 45-47, 50, 51)

Year/Quarter	Revenue (in USD thousands)	Increase in Revenues (in USD thousands)
2001 Q1	$28,595	
2001 Q2 (withdrawal period)	$40,408	+$11,813
2001 Q3	$52,356	+$11,948
2001 Q4	$55,641	+$3,285
2002 Q1	$29,532	-$26,109
2002 Q2	$39,543	+$10,011

Modeling the response

Figure 2-7 uses a system dynamics model to demonstrate how amplification of risk in this case may have driven wholesalers to respond to the reintroduction of Renagel 800mg tablets.

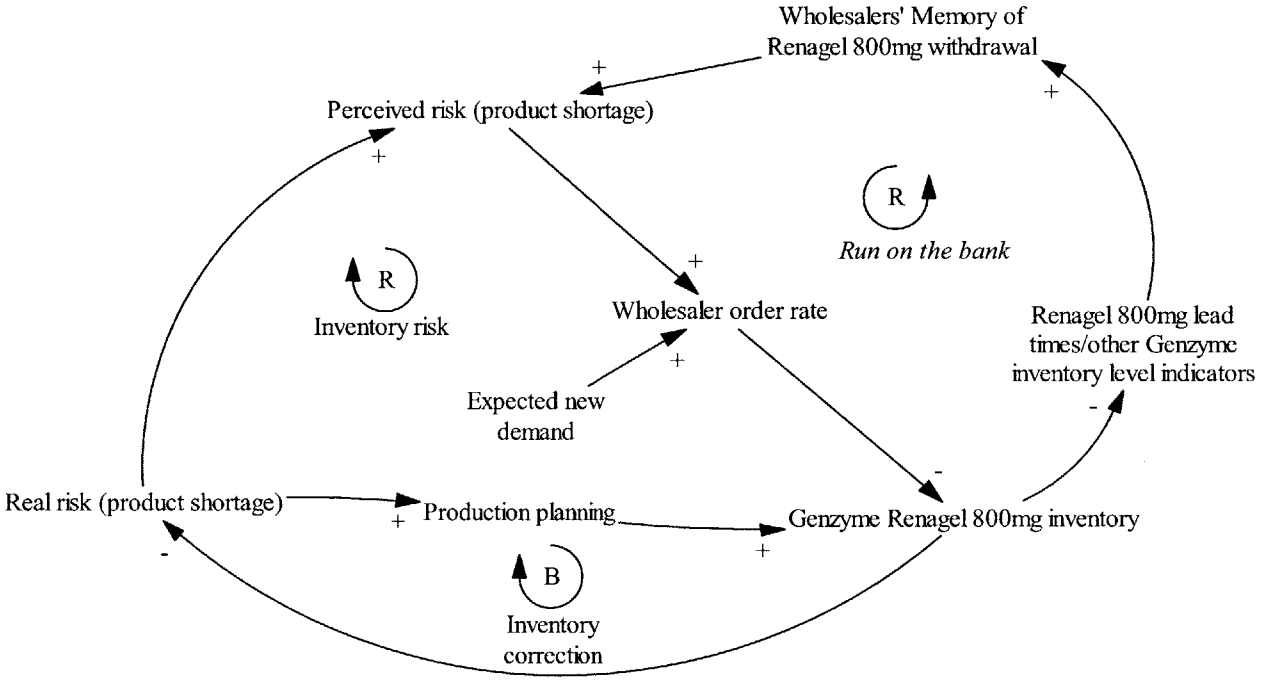


Figure 2-7: Response to Renagel 800mg Tablet Withdrawal

The "Run on the bank" loop (shown alone in Figure 2-8) shows that the withdrawal of Renagel 800mg tablets in 2001 may have heightened the wholesalers' perception of risk (of future Renagel 800mg tablet shortage). This arises from a direct causal connection between the "Wholesalers' Memory of Renagel 800mg withdrawal" and "Perceived risk" as wholesalers' memory of the Renagel incident incites concern of a reoccurrence (of product shortage). Wholesalers react to the higher perceived risks and higher than expected demand rates by increasing their order rates in order to allow them to build higher than normal inventory levels and hedge against future incidents. As the increase in order rates depletes Genzyme's inventory levels, it leads to longer product lead times, which further invoke wholesalers' memory of the Renagel incident. This strengthens the "Run on the bank" reinforcing loop. While in this

example the wholesalers cause the "Run on the bank," in different situations other members of the supply chain, such as patients or the pharmacies, can similarly do so.

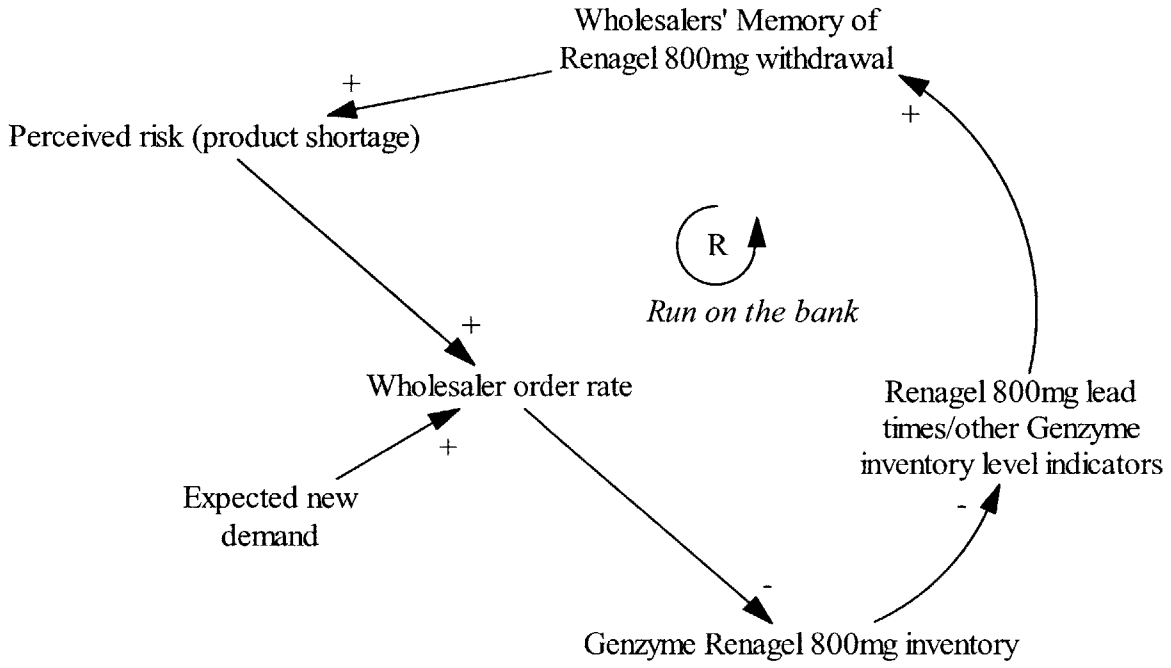


Figure 2-8: "Run on the bank" Reinforcing Loop

Likewise, the "Inventory risk" reinforcing loop (see Figure 2-9) demonstrates how the increase in "Perceived risk," which drives down Genzyme's Renagel 800mg inventory, increases the "Real risk" of product shortage. As "Real risk" increases, by definition, so does the perceived risk.

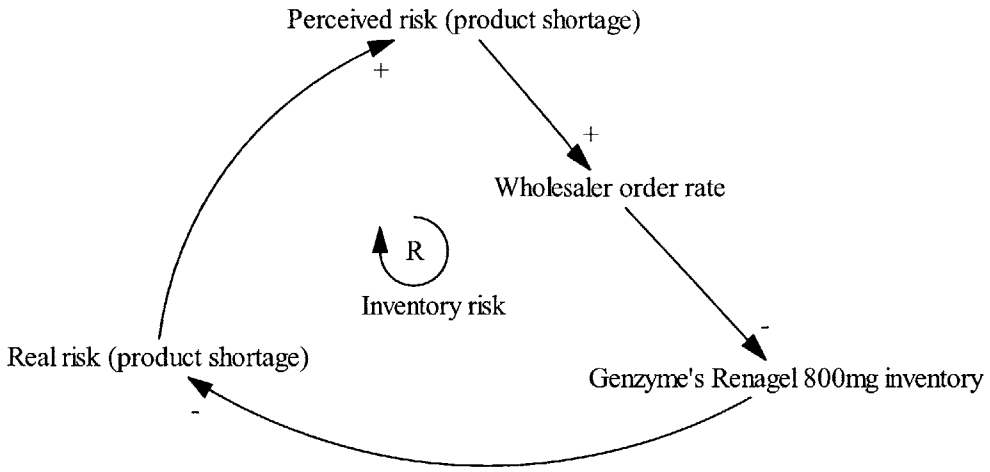


Figure 2-9: "Inventory risk" Reinforcing loop

The "Inventory correction" loop (see Figure 2-10) shows that the higher wholesaler order rates that cause depletion of Genzyme's inventory result in an increase of "Real risk" of product shortage. The shortage will prompt Genzyme to increase its Renagel production rates to maintain target inventory level. The "Inventory correction" loop is a balancing loop designed to prevent further strengthening of the "Run on the bank" and "Inventory risk" loops by calming wholesalers' fears of Genzyme running out of product.

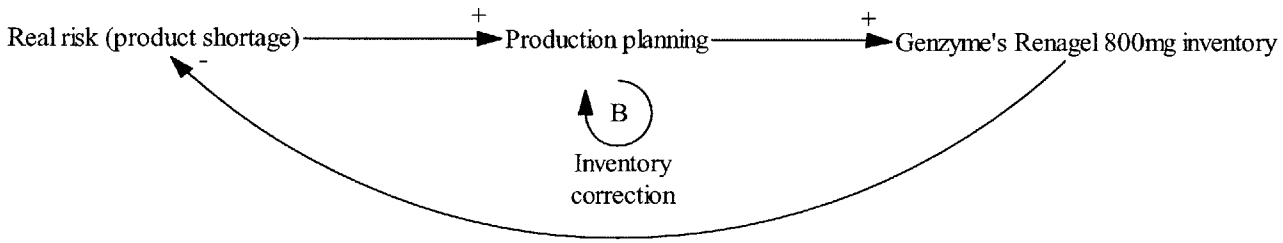


Figure 2-10: "Inventory correction" Balancing Loop

In response to the Renagel incident, Genzyme made couple of key long-term strategic decisions to avoid similar future incidents.

1) Increase inventory levels

While Genzyme's wholesalers appear to have reacted to the 2001 Renagel 800mg withdrawal and the increased demand expectations by increasing their inventory levels of Renagel, so too did Genzyme. After experiencing product shortage first-hand with Renagel 800mg tablets, Genzyme decided to raise its inventory levels (*5*). The "Inventory build-up" balancing loop in Figure 2-11 illustrates that Genzyme's increase in inventory levels should decrease perceived risk of product shortage.

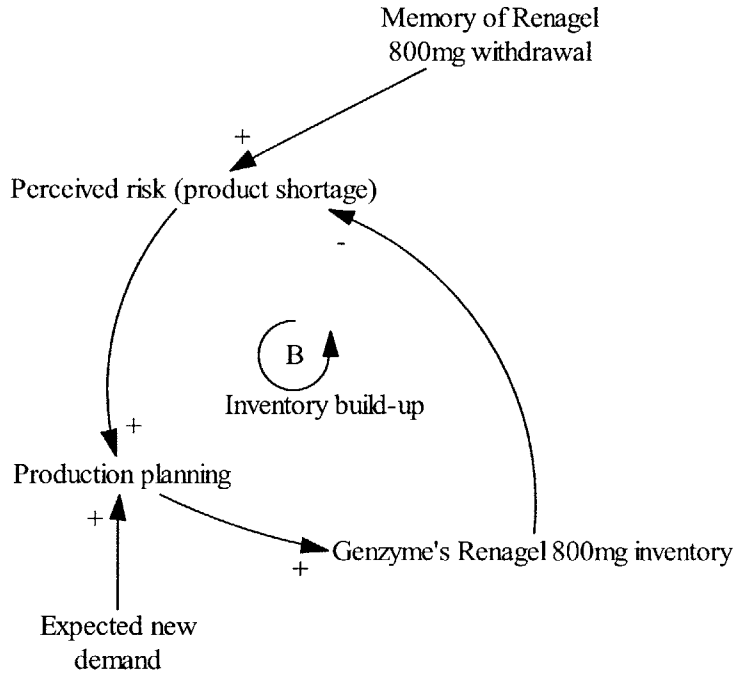


Figure 2-11: "Inventory build-up" Balancing Loop

2) Move tablet production to Genzyme

The Renagel incident substantiated Genzyme's earlier decision (and pressured the company) to move the entire manufacturing process in-house. The company felt that it could not rely on a contract manufacturer to continue to invest in adequate process equipment required for Renagel's high growth rates. Hence, Genzyme expanded its UK facility and built tablet manufacturing

capabilities in Ireland (*6*). By end of 2003, the company had successfully transferred most of the operations in house.

Higher-order impact of withdrawal:

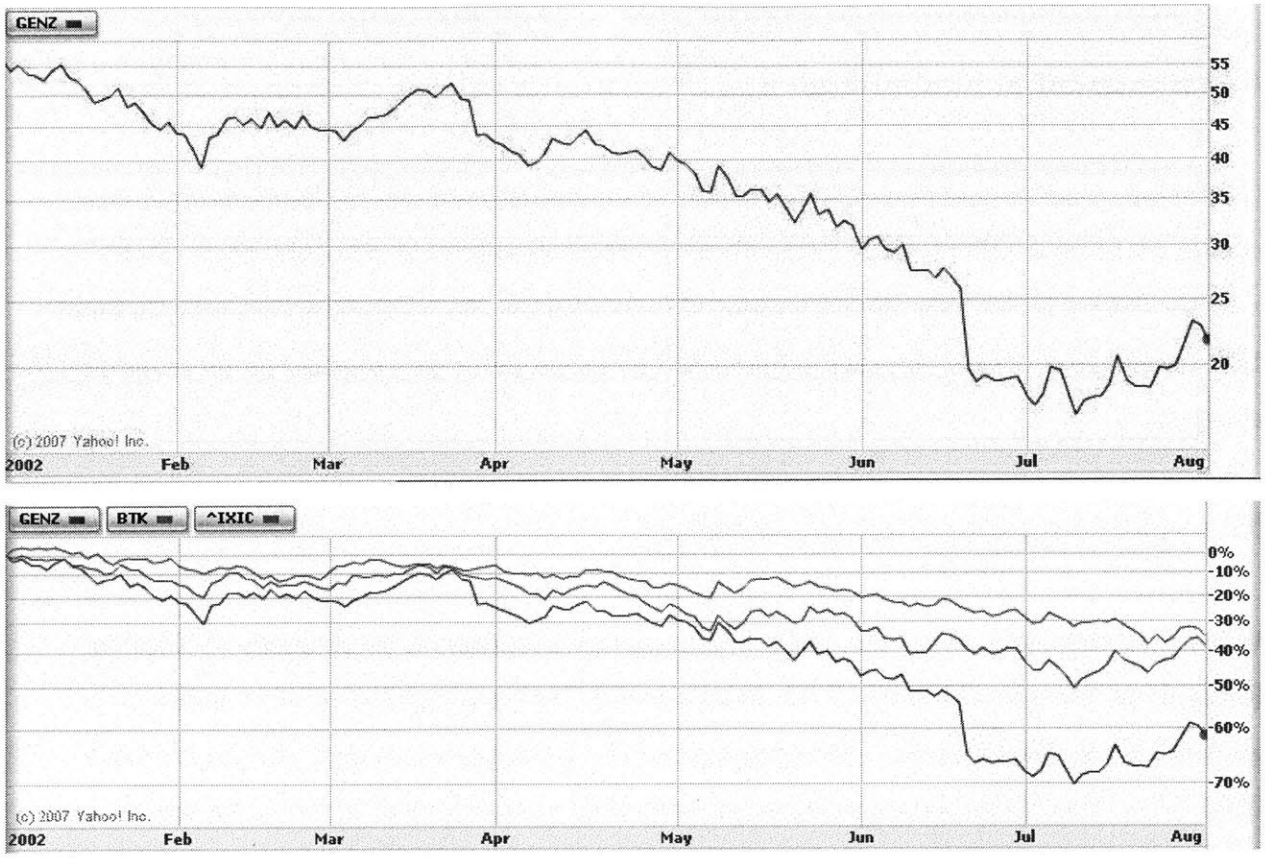
During the withdrawal period of Renagel 800mg tablets, it is not evident that Genzyme faced significant adverse effects, since Renagel sales continued to grow at a healthy pace. However, once the 800mg tablet form was reintroduced to the market, the wholesalers' reaction to build 12-18 weeks of inventory appears to have resulted in a higher-order impact not anticipated by the company.

Excess inventory leading to a stock price decline

When Genzyme reduced the shipment of Renagel to wholesalers to work down wholesalers' Renagel inventory level in early 2002, this impacted Genzyme's ability to meet earnings guidance for the first quarter. The company issued a warning on earnings forecast in March 2002 (*52*). The official earnings release in April 2002 confirmed that first quarter earnings per share (EPS) were $0.12 below the forecast, EPS of $0.21 versus EPS expectation of $0.33 ($0.33 was pre-March estimates, since the company lowered the guidance from $0.33 to $0.21-$0.23 in March) (*53*). The shortage in earnings was directly attributed to Renagel sales, since the first quarter sales of Renagel were approximately $30m instead of the forecasted $60m (*52*). Similar to the first quarter of 2002, Genzyme missed earnings in the second quarter (*54*) due to its continued efforts to reduce wholesalers' Renagel inventory levels to six weeks.

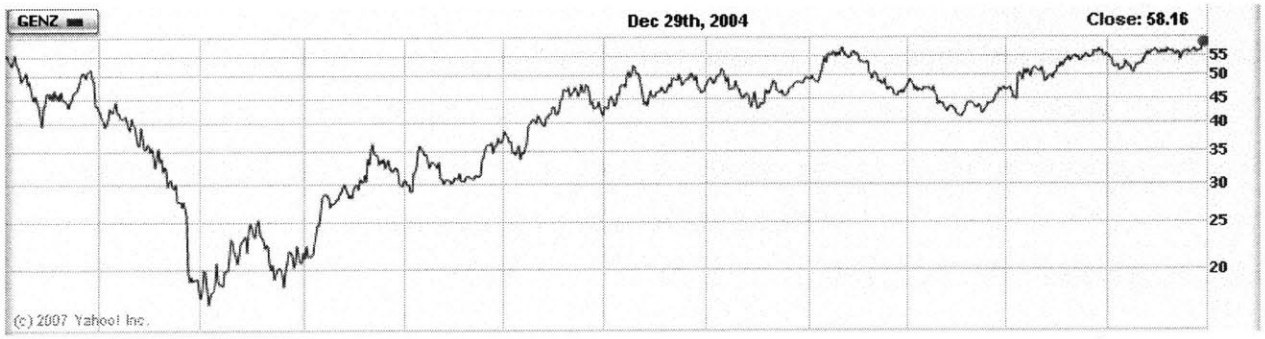
Largely due to missed earnings and a loss of credibility that ensued, most analysts downgraded Genzyme's stock (*53*). As a result, Genzyme's stock (ticker symbol: GENZ) price declined from $58.50 on January 2, 2002 to $16.88 on July 10, 2002, a 71% drop in value. During the same time period, NASDAQ (^IXIC) and the AMEX biotech (^BTK) indices decreased 32% and 50% respectively (see Figure 2-12) (*55*).

Figure 2-12: Genzyme Stock Performance Jan 2002 to Aug 2002 (*55*)



It took Genzyme approximately 2 ½ years (December 29, 2004, share price $58.16) to achieve share price valuations similar to that in January 2002 (See Figure 2-13) (*55*).

Figure 2-13: Genzyme Stock Performance Jan 2002 to Jan 2004 (*55*)



2.4 Conclusion

The Renagel incident in 2001 clearly demonstrates how response to a disruption based on perception of risk could magnify the impact of a disruption. The temporary withdrawal of Renagel 800mg from the market (i.e., a short disruption) did not directly cause a decline of the stock price. However, the wholesalers' decision to increase inventory levels due to fear about experiencing another withdrawal in the midst of high demand and Genzyme's response may have ultimately caused this higher-order impact. Hence, the risk of product shortage should include not only the immediate impacts, but also the possible higher-order and longer-term impacts.

The Renagel example also illustrates the possible time delay between the disruption and the impact from the disruption. In general, the impact of a certain event (or decision) does not necessarily surface at the time of the event. It can be delayed in part due to poor information, lack of alternatives, or speed of the response (see "Bullwhip Effect" in Section 2.1). In the case of withdrawal of Renagel 800mg tablets, Genzyme failed to correlate the disruption event from March to June 2001 with the wholesalers' decision to build inventory after the reintroduction of the Renagel 800mg tablets. When the company realized its wholesalers had increased their inventory levels of Renagel, the company was convinced that the wholesalers' response was due to misread of demand.

This page is intentionally left blank.

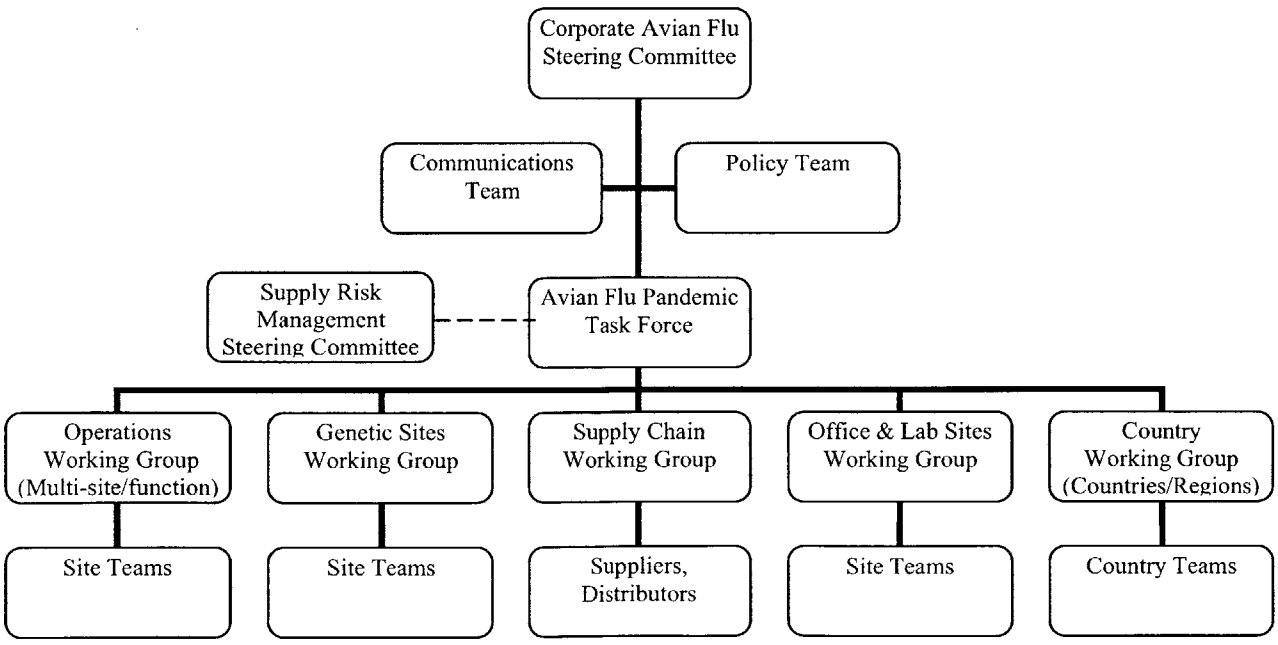
Chapter 3: Preparing for an Avian Flu Pandemic

This chapter describes the major elements of Genzyme's business continuity plan for a possible avian flu pandemic. It then takes the predicted consequences of a pandemic discussed in Chapter 1 and uses social amplification of risk theory to derive additional risks Genzyme should consider in preparation for a possible pandemic. Section 3.4 shows sensitivity analyses on absentee rate and probability of site quarantine to determine required safety stock level and number of safety stock locations. The chapter ends with recommendations about how to mitigate these potential risks.

3.1 Genzyme's Preparations for Pandemic

Like many other corporations, Genzyme realizes the importance of preparing for disruptions that could adversely impact its business. In its effort to prepare the company for a possible pandemic, Genzyme established several teams to develop, implement, and oversee business continuity strategy for an avian flu pandemic. Figure 3-1 shows the overall team structure.

Figure 3-1: Genzyme's Avian Flu Pandemic Planning Teams



The goal of the business continuity strategy is to help protect the health of the employees and to minimize the impact of a pandemic on the business. Appendix I provides the actions required by Genzyme at each WHO pandemic phase. Genzyme has identified four primary areas of preparation.

1) Disease prevention

Genzyme is committed to the health and safety of its employees. Hence, the goal of the disease prevention focus area is to provide employees a safe workplace and access to necessary resources to combat/prevent the influenza. Genzyme plans to accomplish the goal by:

a) Using precautionary measures
    a. Educating employees on elements of "cough/sneeze hygiene" etiquette
    b. Providing employees funding and/or access to annual influenza immunizations
    c. Restricting workplace entry only to people free of influenza symptoms (during WHO Stages 4, 5, and 6)
    d. Utilizing infection control measures such as distributing alcohol-containing hand gels to employees ("dispenser on every desk"), installing hand gel dispensers in common areas and increasing frequency of cleaning (during WHO Stages 4, 5, and 6)
b) Encouraging social distancing (e.g. enable working from home, more use of teleconference meetings, avoid face-to-face contact)
c) Purchasing/stockpiling and providing employees access to anti-viral drug (once infected by avian influenza)

2) Human resource policies

Genzyme expects to face many human resource issues during a pandemic, since many employees will be absent from work for various reasons including personal illnesses, family member illnesses and/or needs for care, and fears of getting infected. The goal of human resource policies pertaining to a pandemic is to help Genzyme maintain a healthy work environment while

limiting the negative impacts on business.

The HR policies expand existing policies governing employee absences for personal or family illnesses. Employee absentee policies will address the amount of time employees must remain absent from work following the onset of, or exposure to, flu symptoms and address financial concerns during this time.

3) Travel policies

While many countries may close their borders during a pandemic, Genzyme has created policies to ensure employees do not put themselves in danger by traveling to regions afflicted by the avian influenza. The policies are based upon the World Health Organization's Six Stage Pandemic matrix outlined in Chapter 1. Table 3-1 summarizes Genzyme's travel policies.

Table 3-1: Genzyme's Travel Policies (*56*)

Action	WHO Phase			
	3	4	5	6
Monitor events/travel	✓	✓	✓	✓
Flu info & supplies	✓	✓	✓	✓
Prior approval		✓	✓	✓
Quarantine*		✓	✓	✓
Travel prohibited				✓

*A person who has returned from a pandemic-afflicted region must wait 10 days before returning back to work

4) Communication

Adequate communication will be the key in preparing Genzyme for a pandemic. Hence, the company has developed a detailed communications plan specific to a pandemic. The plan serves two major goals:

1) Raise awareness about the potential pandemic and educate about responsible actions

2) Provide guidelines for external communications required during this time period, including communications with patients, customers, and investors

The company also has invested in an internal website dedicated to a pandemic and maintains FAQs (frequently asked questions) for employees.

5) Operations

Creating a robust operations strategy will be critical for Genzyme to deliver products and services to patients during a pandemic. The operations strategy outlines the following components:

1) Risk assessment materials and scenario planning guide (see Appendix II for a sample scenario exercise)
2) Supply and distribution:
    - Ensure suppliers are prepared for a pandemic
    - Ensure contingency plans are in place for supply shortage - multiple suppliers or inventory
    - Ensure transportation companies and distribution channels are prepared for a pandemic
    - Ensure medical facilities, including infusion and dialysis centers, are prepared for a pandemic
3) Manufacturing:
    - Plan for high absentee rate
        - Prioritize resources at each site and across sites by identifying "essential" functions, core skills, and core people; cross-train staff in different functions and create back-ups for core people and skills
        - Prioritize products
    - Set appropriate inventory set point of finished goods based on appropriate risks
    - Evaluate outsourcing options
4) Regulatory priorities and initiatives
5) IT infrastructure requirements (for employees working from home)

3.2 Risk Amplification during a Pandemic

A pandemic, similar to other risk events, may instigate responses that may result in amplification or attenuation of risk. The following outlines some of the mechanisms that affect perceived risk. Depending on timing, country, employer, and other circumstances, there may be different or additional sets of mechanisms.

Mechanisms:

Media

The media play an important role in keeping the public informed about risk events. Hence, during WHO's Stage 4 of a pandemic, widespread news media coverage of the event should be expected. The death toll may be communicated on a regular basis by this group as well as information on how to protect oneself. On one hand, since media coverage is identified with risk events and it frequently dramatizes disruptions, it will most likely increase people's perception of risk associated with a pandemic. On the other hand, the information provided by the media can help calm people's fear and decrease the perception of risk.

Personal network

Besides receiving information about risk events through the media, people frequently engage in discussions about the risk events at work, home, or social gatherings. At the time of a pandemic, the topic will be on the minds of most people and will be brought up frequently during conversations. Personal networks will add to the volume of information about a pandemic and may cause greater sense of panic. However, personal networks can also be a great source of information for people on the topic of avian influenza. For example, an individual's physician could help to educate the patient on the influenza and provide tips on minimizing risks of getting infected. Therefore, the personal network can either amplify or attenuate perception of risks.

Employers

While information provided through the media and personal network could increase or decrease the perception of risks during a pandemic, information provided by employers is intended to prevent risks from escalating. Most corporations, such as Genzyme, are preparing their respective companies to continue operations during a pandemic. As part of these preparations, companies are educating their employees about a possible pandemic, providing easier access to annual flu vaccinations, and stocking-up on influenza protection supplies (see Chapter 3-1). The preparations give employees a sense of control, which may help to reduce fear of a pandemic.

System Dynamics model of mechanisms:

Figure 3-2 provides a system dynamics framework of a scenario using the three mechanisms discussed above. While the media and personal networks can cause either an increase or decrease of perceived risks, this scenario assumes the media coverage and personal networks increase perceived risk. The higher the perceived risks the greater the media coverage and information flow through the personal networks. The result is a combination of three reinforcing loops, "Too much info," "Media impact," and "Personal ntwk impact." On the other hand, the "Employer impact" is a balancing loop that mitigates the impact of the reinforcing loops by seeking to reduce fear. If some employers are not active in educating and protecting their employees, then the media and personal networks may have a far greater influence on perception of risks than employers and this may cause net amplification of risks.

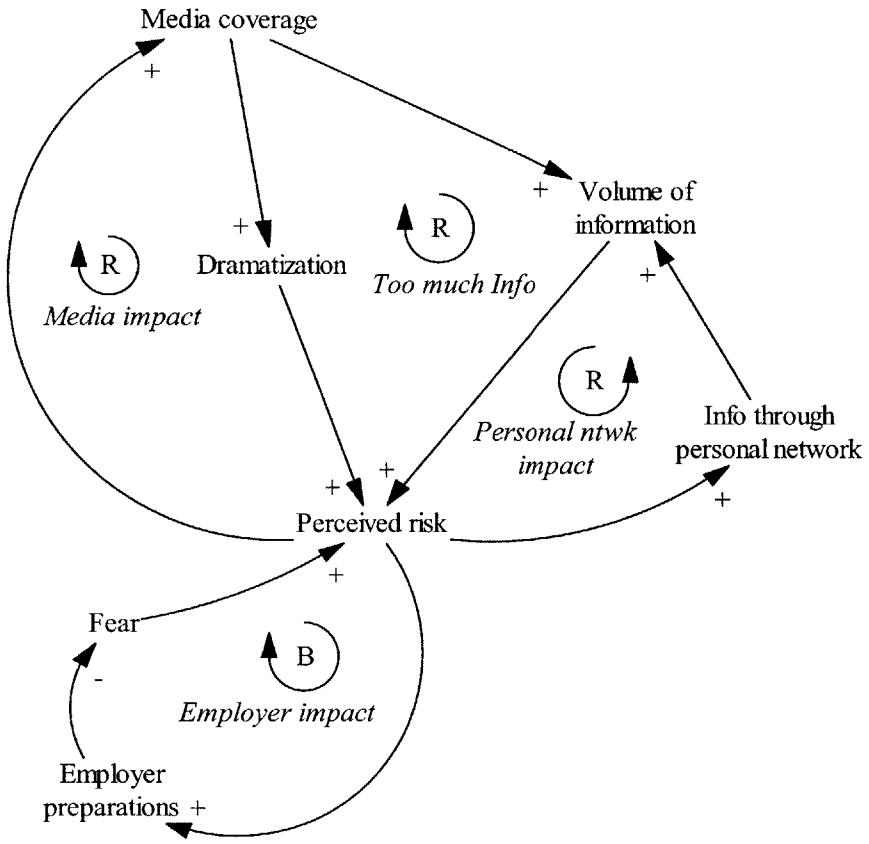


Figure 3-2: Mechanisms for Increasing Perceived Risks

Implication of higher perceived risks:

If fear or the overall perception of risk increases due to the mechanisms outlined above, it may result in greater impact including greater employee absentee rate and greater strain on the medical system. For example, as more people fear getting infected (or as the general level of fear rises) the number of people staying home to avoid public places will increase. Moreover, with heightened anxiety, people who experience even minor flu symptoms may panic and visit a doctor or hospital, which could further overwhelm the medical system.

3.3 Major Concerns for Genzyme

The Three Mile Island incident and the Renagel withdrawal example demonstrate that people may react out of fear instead of considered rational judgment when they face disruptions that amplify real risks. Similarly, as noted in Section 3.2, the perceived risk may exceed the real risk in the event of an avian flu pandemic. This section examines the impact of a pandemic and the implication of the higher perceived risks as it relates to two of Genzyme's lysosomal storage disorder products, Cerezyme® and Myozyme®, because:

1) Both products treat life-threatening diseases and have no equivalent alternatives
2) Both products are administered by intravenous infusion and require medical intervention
3) Both products have finite shelf-life due to their biological nature
4) The products are at different stages of the product lifecycle, which makes comparison to them more useful

Cerezyme and Myozyme product and distribution information:

Cerezyme product info

Cerezyme, Genzyme's highest revenue product, is the only safe and effective enzyme replacement therapy for Gaucher Type 1 disease (also approved for Type 3 Gaucher disease in European Union) (*9*). Gaucher disease is an inherited genetic condition that causes fatty deposits to build up in certain organs and bones due to lack of glucocerebrosidase enzyme, which helps the body to break down a certain type of fat molecule (glucocerebroside) (*57*). Symptoms of Gaucher disease include anemia, spleen, and liver enlargement and bone deterioration (*57*). Children and adolescents with Gaucher disease may experience a delay in growth and development (*58*). With the introduction of Cerezyme (imiglucerase for injection) in 1994 and with its predecessor (Ceredase – 1991), clinicians have been able to address the disease process itself, and therefore, alleviate and even reverse many effects of Type 1 Gaucher disease (*59*).

Growth of Cerezyme

There are fewer than 10,000 people worldwide affected by Gaucher disease (*57*) and Genzyme serves approximately 5,000 patients. While the market is relatively mature, Genzyme continues to add 5-7% new patients every year. The greatest obstacle to growth is identification of new Gaucher patients. Since the disease is rare, many doctors are not able to diagnose the problem (*60*). However, Genzyme has been successful in educating hematologists, oncologists, geneticists, metabolic specialists, and Ministries of Health about the disease resulting in better rate of detection.

Myozyme product info

Myozyme is the first and only approved treatment for Pompe disease (*9*), an inherited rare neuromuscular genetic disorder that occurs as a result of a defect in a gene that is responsible for making an enzyme called acid alpha-glucosidase (abbreviated as GAA), which breaks down glycogen (*61*). Absence of this enzyme leads to a build-up of glycogen in the lysosomes of cells (*61*). Pompe disease manifests with a broad spectrum of clinical symptoms, with variable rates of progression ranging from rapidly progressive and often fatal within the first year of life, to severe cardiac and skeletal muscle involvement, to relentlessly progressive disease resulting in significant morbidity and premature mortality from skeletal and respiratory muscle involvement (*9*).

Growth of Myozyme

Pompe disease affects 5,000 to 10,000 patients around the world (62). In 2006, Myozyme was granted marketing approval in United States, Canada, and Europe. Sales in 2006 were $59.2 million (*9*). With treatment costs exceeding $200,000/year per patient (*63*), this implies that Genzyme currently provides Myozyme to approximately 300 patients. As with that of Cerezyme, the growth rate of Myozyme depends on identification of new patients with the disease. Additionally, since the product is still fairly new, the growth also depends on getting

approval for the treatment in additional countries and for different patient population (such as late-onset Pompe disease patients).

Diagnosing Pompe disease can be challenging because many of the symptoms are similar to those of other diseases. In addition, symptoms often develop slowly and may not show up at the same time. Therefore, a conclusive diagnosis of Pompe disease generally requires an enzyme assay test that demonstrates that the patient has deficient enzyme activity. This is determined by performing tests on a tissue (muscle, skin) or blood sample to verify that the patient's GAA enzyme activity is low or absent. Due to the necessary testing equipment, the assay tests are typically conducted at a medical facility (*64*).

Distribution of Cerezyme and Myozyme

The distribution model for Cerezyme and Myozyme is different than that of Renagel. Genzyme has tens of thousands of Renagel patients and hence, depends on pharmacies across the world to fill Renagel prescriptions. Since the company does not have strong distribution capabilities and relationships with pharmacies, the company must partner with wholesalers to distribute Renagel. On the other hand, Cerezyme and Myozyme have small patient populations that allow Genzyme to develop personal relationships with most of the patients. With intimate knowledge of the patients, the company is able to deploy a more direct distribution model.

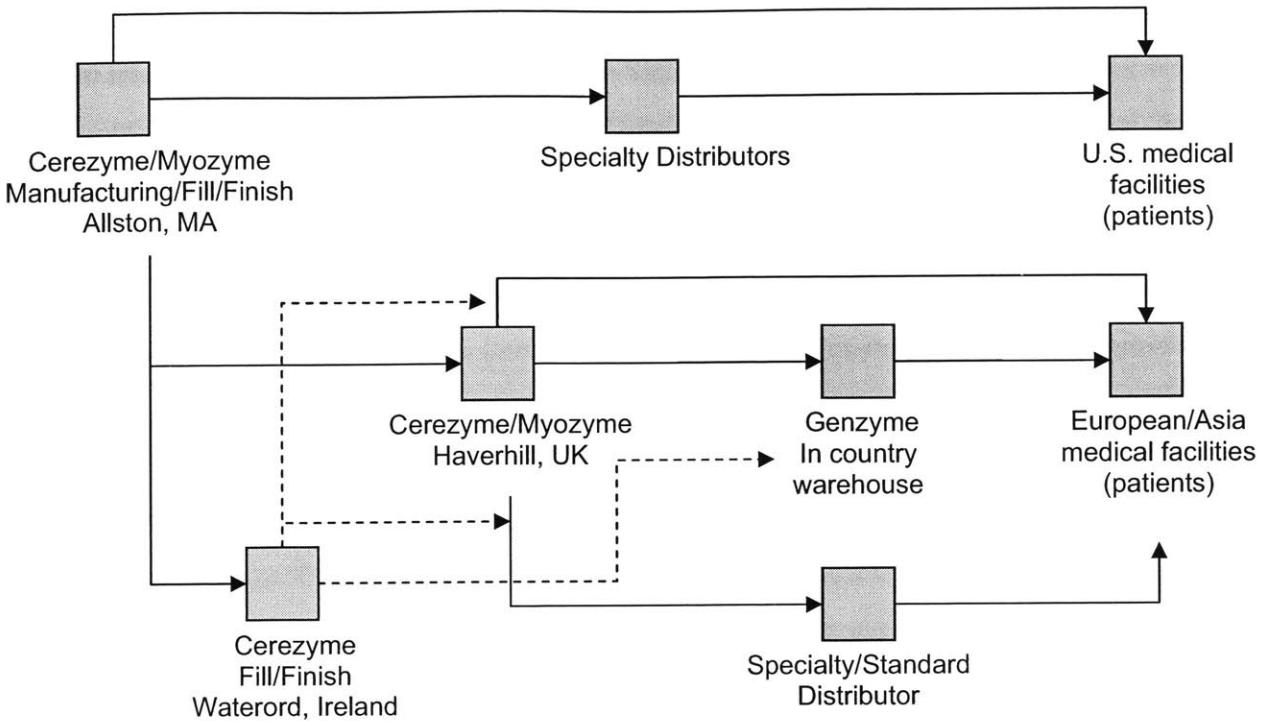
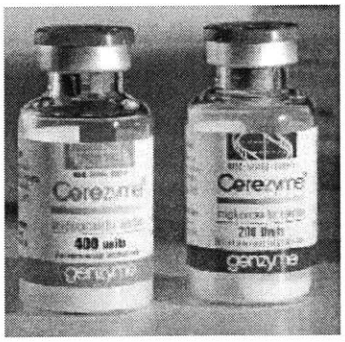


Figure 3-3: Cerezyme and Myozyme Distribution Chain

Figure 3-3 shows the distribution chain of Cerezyme and Myozyme for US and Europe/Asia markets. Both Cerezyme and Myozyme are produced, finished, and filled at the Allston facility (*9*). The company also fills and finishes Cerezyme for several non-US markets at its Waterford facility (*65*). The products are white to off-white powder and packaged in small glass vials as shown in Figure 3-4.

Figure 3-4: 200 and 400 Unit Cerezyme Vials



Cerezyme and Myozyme are intravenously infused and thus, the products are shipped to the patient's physician location, hospital or another medical facility (*66*) where the infusion into the patient takes place (marking the end of the distribution chain). The distribution method employed by the company depends highly on the geographic market it serves. For example, in the United States, Genzyme either sends the products directly to the medical facilities or partners with specialty distributors to serve many of the Cerezyme and Myozyme patients. Along with delivering the therapy to patients, the specialty distributors also provide patient support services, such as assistance in filing reimbursement claims.

The distribution chain for the European or Asian markets is more complex. First, the products are shipped to Genzyme's Haverhill site for labeling of vials (according to specific country requirements). Once the vials are labeled, Genzyme supplies the product to the appropriate medical facilities using three methods:

1) By shipping the vials directly to the medical facilities
2) By partnering with distributors to distribute the vials to various medical facilities
3) By shipping the vials to a Genzyme operated "in-country/regional warehouse" from which it is shipped to the medical facilities

The method utilized depends on country requirements and/or patient needs. For example, the third option is chosen many times to satisfy country import laws. Moreover, transportation between sites and/or medical facility locations is handled by integrated carriers, such as UPS. While regional shipments typically use ground transportation, shipment of product from the Allston facility to Europe is air freighted via commercial aircrafts.

Inventory location

Once Cerezyme and Myozyme are manufactured at the Allston facility, the product vials (or bulk) are stored at cold temperatures (2 - 8°C) at the Framingham site until it receives purchase orders. The average shelf life of Cerezyme is two years (unopened vials) (*67*), while that of Myozyme is 18 months (*68*). Genzyme does not keep inventory at any other site.

Expected impact of a pandemic on distribution of Cerezyme and Myozyme:

Due to the magnitude of impact expected during a pandemic, Genzyme should address several business continuity-related concerns specific to Cerezyme and Myozyme.

1) Slow down in production rates

Currently, Myozyme and Cerezyme (and other lysosomal storage disorder products) are all produced at the Allston facility and share production capacity and other resources. Hence, a high absentee rate in that facility would likely slow down production rates since the critical operation functions, such as maintenance and quality control, rely heavily on employee resources. Similarly, there is a high probability that Genzyme's suppliers will face production slow down that may cause raw material shortages and further contribute to slow down of Cerezyme and Myozyme production rates. With inadequate production rates, Genzyme increases the risks of not meeting patient therapy requirements.

The company might be hard pressed to move employees from other non-critical product manufacturing facilities to Allston. However, the likelihood of those employees willfully transferring to Massachusetts during a time when families are coping with the impact of a pandemic is very small (and it may not be possible if travel is truly restricted).

2) Disruption in distribution

As noted above, finished goods of Cerezyme and Myozyme are stored at the Framingham facility. Once a purchase order is placed, Genzyme uses commercial airlines and integrated carriers to transport and deliver Myozyme and Cerezyme to medical facilities around the world. During a pandemic it is possible that with high absentee rates the transportation companies will be operating at lower service levels. This problem along with the closure of country ports (as mentioned in Chapter 1), will likely impact the speed of distribution of products and services to the patients. Furthermore, by continuing to

maintain inventory at one location, the company risks the possibility of a government quarantine of the site, which could prevent Genzyme from shipping the product altogether. Thus, patients may be forced to skip treatment(s).

3) Limited access to medical facilities

With the medical facilities overwhelmed with influenza related illnesses and priorities given to immediate life-threatening illnesses, Myozyme and Cerezyme patients will likely endure longer waiting periods for infusions. This can result in lower compliance rates.

The clinical trials and identification of new Pompe patients will also be impacted by the medical facilities'/doctors' shift in priorities to flu related illnesses. Depending on timing of a pandemic, this will result in delay of Myozyme approval in other countries and impact its growth.

4) Run on the products

As people rush to stock-up on consumer goods and drugs at the onset of a pandemic, Genzyme will face increased demands from its patients (and/or wholesalers) for most of its products ahead of the immediate need resulting in "Run on the bank" (as shown in Figure 2-8).

In the case of Renagel, this will be possible if patients convince their doctors to write the prescriptions and they are able to fill the prescriptions from the pharmacies. The sudden increase in order rates will draw down inventory levels and may cause a temporary product shortage.

However, since Genzyme knows most Cerezyme and Myozyme patients personally and maintains complete control of the distribution channels, the company can avoid "Run on the bank" problem for these products.

Consequence of higher perceived risks on distribution of Cerezyme and Myozyme:

The fear induced during a pandemic may result in greater perceived risks and magnification of the above impacts. The employee absentee rates may be worse than predicted and further slow down Genzyme's production rates. For similar reasons, Genzyme may experience greater difficulty in distributing its products across the globe due to lower operating rates of commercial airlines and transportation companies. Also, with higher perception of risks, the countries may further tighten up their borders and restrict movement of goods into their respective regions, delaying the delivery of the treatments. Lastly, the greater fear may contribute to more healthy people using and hence, further overwhelming the medical system and thereby, making the medical facilities less accessible to Cerezyme and Myozyme patients. Without taking appropriate measures to mitigate impacts of a pandemic, Genzyme risks not only losing sales and hampering growth, but also of not being able to adequately provide its patients the therapies they depend on.

3.4 Scenario Analysis

As described in Section 3.3, Genzyme could potentially face many disruptions due to a pandemic. This section will present sensitivity analyses on two of the major concerns, absentee rate and probability of quarantine of the Framingham inventory facility. Since a pandemic is expected to arrive in waves and each wave affects different regions of the world, it is possible to develop several scenarios of the impact of a pandemic to derive costs and benefits of keeping safety stock at multiple locations. The analyses will help Genzyme determine the appropriate amount of safety stock it should maintain for a pandemic and number of safety stock locations.

Assumptions for scenario analysis:

1) 5,000 Cerezyme patients - while Genzyme continues to find more patients for its Cerezyme therapy, the product is highly mature and therefore, demand is relatively steady and predictable
2) 100% production capacity utilization

3) One-to-one linear relationship between number of employees and production quantity
4) Probability of site quarantine ranges from 1-10%
5) 100% probability of 20-50% employee absentee rate
6) Average annual therapy cost to patient for Cerezyme = $100,703 K (2006 total Cerezyme revenue) / 5,000 patients = $201,407/patient/yr
7) Pandemic wave lasts 8 weeks
8) 5% physical holding cost – this is assuming Genzyme uses existing facilities and all locations have the same holding cost
9) r (cost of capital) = 15.23% (*69*)
10) C = 19% of sales – based on %COGS for all of Genzyme products (*9*)
11) The various inventory locations are in different countries or parts of the world

Safety Stock:

According to inventory theory, the purpose of safety stock is to protect the company from demand surges or unexpected supply disruptions (*70*). Since demand for Cerezyme is assumed to be constant, safety stock is intended to protect the company from the impact of a pandemic.

Safety stock sensitivity analysis

There are many estimates for employee absentee rate during a pandemic. The safety stock calculations will evaluate sensitivity analysis on the range of 20-40% absentee rate cited in Chapter 1. The analysis also accounts for possible absenteeism associated with social amplification of risk by adding 10% to the range resulting in an absentee range of 20-50% (see Table 3-2).

Safety stock required (in terms of revenue) = number of patients x average annual price of drug per patient x absentee rate x number of weeks of disruption

The safety stock is based on revenue loss due to lack of availability of therapy during a pandemic wave that lasts for eight weeks. For example, if Genzyme decides to plan for 40% absentee rate,

then it should carry safety stock of Cerezyme that correlates to approximately $61.5m of revenue.

Table 3-2: Required Safety Stock (based on production loss from employee absenteeism - in terms of revenue)

Absentee Rate at Allston Facility					
20%	**25%**	**30%**	**35%**	**40%**	**50%**
$30,769,231	$38,461,538	$46,153,846	$53,846,154	$61,538,462	$76,923,077

Number of safety stock locations:

In addition, the company needs to decide the number of different locations to hold safety stock at. Currently, Genzyme is holding inventory at its Framingham site. While the probability of site quarantine by a government agency is small, Table 3-3 shows sensitivity analysis of expected revenue loss (or opportunity cost) based on different probabilities and safety stocks calculated in Table 3-2. For example, if Genzyme were to carry safety stock worth $61.5m of revenue (correlating to 40% absentee rate) at the Framingham site, the expected revenue loss at 5% probability of site quarantine is approximately $3.1m.

Expected revenue loss (from quarantine) = Probability of quarantine x Safety stock required

Table 3-3: Expected Revenue Loss of Holding Safety Stock at *One* Location

	Absentee Rate at Allston Facility						
Probability of quarantine	**20%**	**25%**	**30%**	**35%**	**40%**	**45%**	**50%**
1%	$309,857	$387,321	$464,785	$542,250	$619,714	$697,178	$774,642
2%	$619,714	$774,642	$929,571	$1,084,499	$1,239,428	$1,394,356	$1,549,285
3%	$929,571	$1,161,963	$1,394,356	$1,626,749	$1,859,142	$2,091,534	$2,323,927
4%	$1,239,428	$1,549,285	$1,859,142	$2,168,998	$2,478,855	$2,788,712	$3,098,569
5%	$1,549,285	$1,936,606	$2,323,927	$2,711,248	$3,098,569	$3,485,890	$3,873,212
6%	$1,859,142	$2,323,927	$2,788,712	$3,253,498	$3,718,283	$4,183,068	$4,647,854
7%	$2,168,998	$2,711,248	$3,253,498	$3,795,747	$4,337,997	$4,880,247	$5,422,496
8%	$2,478,855	$3,098,569	$3,718,283	$4,337,997	$4,957,711	$5,577,425	$6,197,138
9%	$2,788,712	$3,485,890	$4,183,068	$4,880,247	$5,577,425	$6,274,603	$6,971,781
10%	$3,098,569	$3,873,212	$4,647,854	$5,422,496	$6,197,138	$6,971,781	$7,746,423

In order to gain insight on whether Genzyme should hold safety stock at more than one location, Table 3-3 provides a sensitivity analysis of expected opportunity costs for a scenario with two inventory locations.

The "Third Law of Probability" (given below) is used to calculate the probability of quarantine of both safety stock locations simultaneously.

$P(A_1 \text{ and } A_2) = P(A_1) \times P(A_2)$ or $P(A_1 + A_2 + A_n) = \pi P(A_i)$

$P(A_1)$ – probability of event A_1 occurring

$P(A_2)$ – probability of event A_2 occurring

$P(A_n)$ – probability of event A_n occurring

π – multiplication

Table 3-4: Expected Revenue Loss of Holding Safety Stock at *Two* Different Locations

		Absentee Rate at Allston Facility						
Prob. of quarantine (of each location)	**Prob. of quarantine of both locations simult.**	**20%**	**25%**	**30%**	**35%**	**40%**	**45%**	**50%**
1%	0.01%	$3,099	$3,873	$4,648	$5,422	$6,197	$6,972	$7,746
2%	0.04%	$12,394	$15,493	$18,591	$21,690	$24,789	$27,887	$30,986
3%	0.09%	$27,887	$34,859	$41,831	$48,802	$55,774	$62,746	$69,718
4%	0.16%	$49,577	$61,971	$74,366	$86,760	$99,154	$111,548	$123,943
5%	0.25%	$77,464	$96,830	$116,196	$135,562	$154,928	$174,295	$193,661
6%	0.36%	$111,548	$139,436	$167,323	$195,210	$223,097	$250,984	$278,871
7%	0.49%	$151,830	$189,787	$227,745	$265,702	$303,660	$341,617	$379,575
8%	0.64%	$198,308	$247,886	$297,463	$347,040	$396,617	$446,194	$495,771
9%	0.81%	$250,984	$313,730	$376,476	$439,222	$501,968	$564,714	$627,460
10%	1.00%	$309,857	$387,321	$464,785	$542,250	$619,714	$697,178	$774,642

Cost/benefit analysis will help Genzyme determine whether it makes economical sense to carry twice the safety stock (at different locations).

Benefits

The sensitivity analyses above show that expected loss of revenues decreases drastically as the number of safety stock locations increases from one to two. For example, if Genzyme were to carry safety stock worth $61.5m of revenue at both the Framingham and Waterford sites, the expected revenue loss at 5% probability of quarantine (of both sites simultaneously) is approximately $156K.

Costs

Table 3.5 provides holding costs of safety stock (per location) at different employee absentee rates.

Total safety stock holding cost (H) = Physical holding cost (h x C) + Opportunity cost of capital (r x C)

$$H = (h \times C) + (r \times C) = (h + r) \times C$$

$H = (h + r) \times C$

$H = (0.05 + 0.1523) \times (0.19 \times \text{Revenue})$

Table 3-5: Safety Stock Holding Costs per Location

Absentee Rate at Allston Facility						
20%	25%	30%	35%	40%	45%	50%
$1,190,997	$1,488,746	$1,786,496	$2,084,245	$2,381,994	$2,679,743	$2,977,493

Interpretation:

From evaluating Table 3-5 and Table 3-2, it is evident that the safety stock holding costs are dramatically lower than the opportunity costs for the various absentee rates. For example, at 40% absentee rate, the safety stock holding costs for inventory worth $65.1m of Cerezyme revenue is $2.4m. Hence, in this case, Genzyme could hedge its risks against the financial impact of a pandemic by spending less than 4% of possible revenue loss on safety stock. Also, the sensitivity analyses show that the difference in expected revenue loss between carrying safety stock at one and two locations is greater than safety stock holding costs (for quarantine probabilities of greater than 3%). For example, at 40% absentee rate and 5% probability of quarantine of a safety stock location, Genzyme decreases its expected revenue loss by $2.9m if it were to carry the required safety stock at two locations and incur an additional $2.4m of safety stock holding costs. Therefore, from an economical point of view, it is advantages for Genzyme to carry safety stock at an additional location if the probability of quarantine (or other disruptions preventing the distribution of product) of the Framingham facility is believed to be greater than three percent.

Decisions for contingency planning:

Genzyme will need to make several decisions as it develops business continuity plans for a pandemic. The decision tree below illustrates the basic decisions Genzyme needs to evaluate:

- For what percent of absentee rate does the company build safety stock – determines level of safety stock
  - ✓ i.e., for 20% or for 50% or for something in between
- For what probability of quarantine to plan – determines number of safety stock locations
  - ✓ i.e., for < 3% or for > 3%

The sensitivity calculations above do not incorporate non-economical benefits of holding safety stock at multiple location(s). Accounting for non-economical benefits, such as patients' health, could have significant bearing on the decisions.

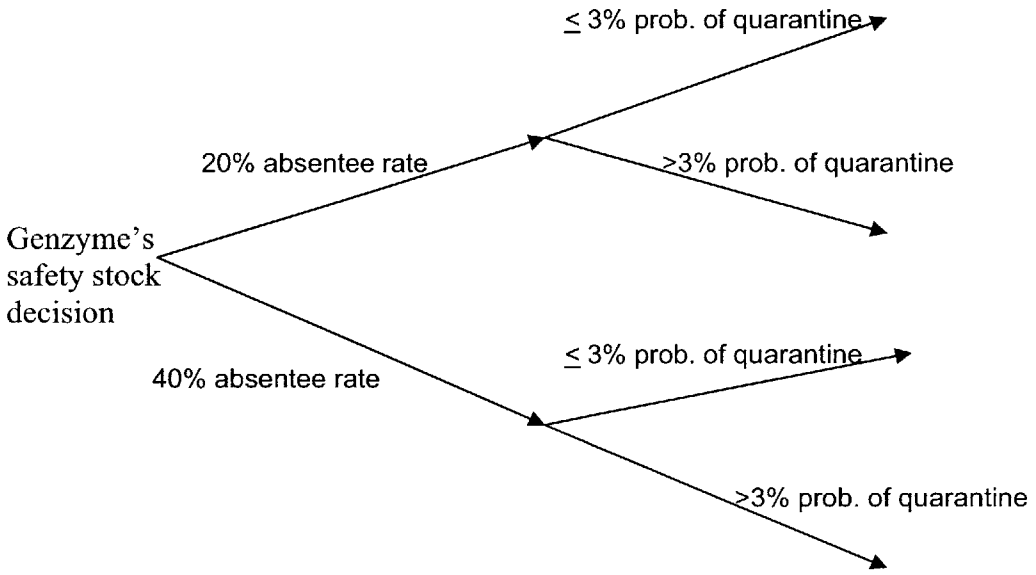


Figure 3-5: Decision Tree for Genzyme's Safety Stock

Sensitivity analysis for Myozyme:

Sensitivity analyses for Myozyme are similar to those for Cerezyme, since the price of the therapy and the cost structure (assumption based on shared resources) are similar to Cerezyme. The primary difference between the two is the number of patients that take the therapy. There is roughly sixteen times the number of Cerezyme patients than Myozyme patients. As a result, Genzyme will need to carry dramatically lower safety stock of Myozyme.

3.5 Recommendations

The following recommendations address the impact of a pandemic on the distribution of Cerezyme and Myozyme:

1) Increase redundancy
2) Maintain inventories at other locations
3) Build capabilities to provide infusions at patients' homes
4) Continue with development of communication plan

Increase redundancy:

Since the lysosomal storage disorder drugs, including Cerezyme and Myozyme, are produced at the same facility, the company will need to build redundancy into its processes in order to address lower production rates. The redundancy can be accomplished by building:

1) Greater safety stock of raw material and finished goods

While holding greater inventory of raw material and finished product is expensive, it can be used to protect the company against supply and production disruptions. Hence, the company should revisit calculations for safety stock levels and account for the 6- or 8-week production disruption associated with a pandemic wave (see Section 3-4). Note that the shelf lives of Cerezyme and Myozyme are greater than the predicted duration of a pandemic.

2) Additional capacity

Genzyme can build extra capacity that will allow the company to increase production rates and increase inventory ahead of a pandemic. As an alternative to building its own capacity, Genzyme could partner with a contract manufacturer to obtain access to capacity during a pandemic, although this would require licensing of the facility and associated expenses. The additional capacity could be used in addition to or in lieu of building greater safety stock. However, the company will need to compare the cost of carrying extra capacity (or the option with a contract manufacturer) with the costs associated with carrying high levels of inventory.

The concern with building extra capacity is complying with Food and Drug Administration (FDA) regulations. Due to the complex nature of biologics, FDA has imposed stricter regulations on biological manufacturing processes. In contrast to chemically-synthesized small molecular weight drugs, which have a well-defined structure and can be thoroughly characterized, biological products are generally derived from living material -- human, animal, or microorganism -- and hence, are complex in structure and usually defined by their manufacturing processes. Therefore, changes in the manufacturing process, equipment, or facilities prompt FDA to require additional clinical studies to demonstrate the product's safety, identity, purity, and potency (*71*). This is also the case with holding idle capacity for long durations of time or using contract manufacturing sporadically. The FDA wants to ensure the manufacturing process has not changed once approved. Running additional clinical studies may be cost prohibitive for Genzyme.

Maintain inventories at other locations:

While the major carriers and airlines are developing their own business continuity plans for a pandemic, Genzyme should hedge risks of disruption to delivery of its products by maintaining safety stock of Cerezyme and Myozyme at additional locations. Moreover, Genzyme can further lower its risks by locating safety stock closer to its patients. Maintaining inventories at additional locations and closer to the patient will also allow Genzyme to mitigate impact from

possible country port closures and quarantine of the Framingham site at the time of a pandemic (see Section 3-4).

Some of the plausible locations for holding safety stock are Haverhill and Waterford sites and Genzyme's country/regional warehouses. Genzyme can also work with its distribution partners in many of the countries to maintain a certain level of safety stock.

Build capabilities to provide infusions at patients' homes:

The limited access to medical facilities during a pandemic is a concern to Cerezyme and Myozyme patients (and to Genzyme) since they depend of the medical facilities to provide infusions. Genzyme can ease this concern by developing home (or portable) intravenous therapy capabilities or partnering with companies that provide this service.

Use communication to address fear:

As noted in Section 3.3, the employer plays a big role in influencing perceived risks. One of the significant methods of reducing people's level of fear is by communicating effectively with them. Hence, it will be important for Genzyme to share many of the communication pieces with others in the distribution chain. For example, tips on protecting against avian influenza should be communicated to not only Genzyme employees, but also its suppliers, patients and others in the distribution chain.

Genzyme is developing a specific communications strategy to manage media, investors, and government officials during the time of a pandemic. Thus, this recommendation requests the company to consider how it may also help members of its distribution chain reduce fear within their respective organizations and thus, decrease absentee rates.

Chapter 4: Conclusion

4.1 Summary

If history is any indication of the future, Genzyme should expect a major pandemic in the near future. A pandemic's impact will be felt in every country and organization, and hence, it will be important for Genzyme to prepare the company for a pandemic on a global basis. As Genzyme develops business continuity strategy for a pandemic, it should consider the following:

- Understand and account for higher perception of risks

Most people react to perception of risks rather than to real risks. During a pandemic, the images of dead bodies, people wearing face masks, and volume of information on the proliferation of a life-threatening virus may incite fear among the masses and may drive behavior that increases the impact of a pandemic. In the case of Cerezyme and Myozyme, the worse case scenario include border closures, government quarantine of Genzyme's Framingham facility, high employee absentee rates, and overcapacity of the medical system. To hedge against risks of supply disruption, Genzyme should maintain 6-8 weeks of safety stock of Cerezyme and Myozyme (and raw materials) at more than one location, preferably close to the patients. Moreover, to ensure Cerezyme and Myozyme patients receive timely infusions during a pandemic, Genzyme should help provide its patients an alternative to receiving intravenous infusions at medical facilities. Appropriately managing risks will enable Genzyme to continue to conduct business in the midst of a pandemic and minimize impact to its sales and/or growth rate.

- Minimize social amplification of risks

Genzyme like other companies can play an important role in mitigating the social amplification of risks. By providing access to information and disease prevention tools to its employees, the company protects the health of employees as well as drives the perception of

risks closer to real risks, which minimizes the higher-order impacts. For similar reasons, the company may benefit by sharing disease related knowledge and tools with partner companies in the distribution chain.

In conclusion, understanding and managing behavior that stems from fear will be critical for Genzyme to successfully operate through the next pandemic.

4.2 Future Work

While it is important for Genzyme to consider increasing its safety stock of raw materials and finished products to account for a potential pandemic (or other similar disruptions), the underlying question for the company is how much inventory to build of what products at which locations. The company needs to address this question as part of developing contingency plans for a pandemic.

Scope of project:

Currently, each business in the company builds safety stock based on its own criteria. A future project team should evaluate and develop a coherent inventory model that addresses various external disruptions including a pandemic. The model should incorporate two aspects:

1) Overall quantity of raw materials and finished products to stock
2) Optimal number of inventory locations to address disruptions

The goal of the project is for businesses to assimilate this model with their current inventory model in order to more accurately account for disruptions.

APPENDIX

I. Genzyme's Pandemic Implementation Plan

Purpose of Implementation Plan: To assist the Task Force and/or Crisis Management team in understanding the actions required at each pandemic phase in order to protect the employees and mitigate business impact during a flu pandemic.

According to the World Health Organization, we are currently in Phase 3.

INTERPANDEMIC PERIOD

Phase	Action	STRATEGY: PLANNING
Phase 1, 2 (After Phase 6, the WHO Phase reverts back to Phase 1 and 2)	▪ Revise pandemic plans on annual basis ▪ Develop leadership plan for each site, for all levels of Mngmt ▪ Monitor situation globally Post Pandemic Actions (Actions after Phase 6 Pandemic): ▪ Arrange for counseling of those that were affected by Pandemic ▪ Identify key learnings and document	

PANDEMIC ALERT PERIOD

Phase	Action
Phase 3	▪ Convene the Task Force Team/Steering Team and set up regular review times ▪ Ensure product prioritization reflects current suite of products ▪ Work with vaccination manufacturers to ensure access to avian flu vaccine as it is developed after understanding the virus strain ▪ Identification of critical roles; skills required for critical roles, and employees with the skill set required ▪ Cross-train personnel to ensure critical functions can be performed in the midst of absenteeism ▪ Review and complete applicable items on pandemic/business continuity checklist (see "Influenza Pandemic Business Continuity Planning Guide" for checklist) ▪ Decide on whether to make antiviral drugs available to employees ▪ Manage availability of hand sanitizers/tissues/etc. to employees ▪ Anticipate and prepare for increased demand for annual flu vaccine ▪ Ensure IT infrastructure can handle work force working offsite ▪ Review/ensure arrangements and training for working remotely (for critical and non-critical tasks that can be done remotely) ▪ Contact distributors/suppliers and be aware of their policies and procedures ▪ Develop inventory levels for all Phases ▪ Contact local authorities and health providers and get up to date news, advice and local/county wide pandemic plans ▪ Track travel to/from affected regions ▪ Communications Plan for Phase 3 includes the following: - Pandemic portal site serving as the central resource of information for employees, providing information on corporate plans and current updates - Memo from Henri announcing initiative - Updated slide deck available on portal site ▪ Conduct simulations ▪ Ensure any relating policies (or recommendations) are developed or updated:

	- Travel - Sick leave compensation - Work arrangements - Social distancing - Reporting ▪ Execute actions per Travel Policy for Phase 3
Phase 4	▪ Actions under Phase 3 will continue where appropriate. ▪ Initiate appropriate actions per Corp Communications Plan for Phase 4 ▪ Trigger Phase 4 work arrangements ▪ Begin process of distributing daily email messages (or by other methods) to members of mngmt, reporting current status of influenza outbreaks and/or other reporting needs ▪ Increase any specialized and comprehensive cleansing services ▪ Ensure inventory levels for Phase 4 ▪ Execute the following to prevent the spread of flu virus: - Place signage, information, posters and leaflets in appropriate places throughout the sites - Strongly recommend annual flu vaccination to all employees ▪ Review leadership plan and advise all managers to review critical work in progress with his or her designated successor ▪ Activate crisis command center ▪ Communicate policies/recommendations for Phase 4 through Pandemic Portal
Phase 5	▪ Actions under Phase 4 will continue where appropriate. ▪ Ensure inventory levels for Phase 5 ▪ Increase cleaning frequency ▪ Trigger Phase 5 work arrangements ▪ Limit access points (establish check point) ▪ Track senior executives ▪ Once pandemic strain flu vaccine is available, inoculate critical personnel before the rest of the employees ▪ Communicate policies/recommendations for Phase 5 through Pandemic Portal

PANDEMIC PERIOD

STRATEGY:

Phase	Action
Phase 6	▪ Actions under Phases 4 and 5 will continue where appropriate. ▪ Ensure inventory levels for Phase 6 ▪ Trigger Phase 6 work arrangements ▪ Communicate policies/recommendations for Phase 6

II. Sample Scenario Exercise

Genzyme: Avian Flu Pandemic Simulation

Global News:

In late September of 2006, an outbreak of unusually severe respiratory illness is identified in a small village in southern China. At least 25 cases have occurred, affecting all age groups; 20 patients required hospitalization, 5 of whom have died to date. Surveillance in surrounding areas is increased, and new cases begin to be identified throughout the province. Viral cultures collected from several of the initial patients are positive for type A influenza virus. The isolates are sent to the World Health Organization (WHO) Collaborating Center for Surveillance Epidemiology and Control of Influenza at the Centers for Disease Control and Prevention (CDC) in Atlanta, for further characterization. CDC determines that the isolates are type A H7N3, a subtype never before isolated from humans.

This information is immediately transmitted back to the Ministry of Health in China and throughout the WHO network. CDC, in collaboration with WHO, dispatches a team of epidemiologists and laboratory personnel to further evaluate the outbreak and disseminates a Health Alert Network (HAN) advisory notifying clinicians and U.S. state health departments to be on the alert for patients with severe respiratory illness and a history of travel to the region of Asia where the human cases occurred. Isolates of the H7N3 virus are sent to the WHO Collaborating Centers and to the U.S. Food and Drug Administration (FDA), so that work can begin to produce a reference strain for vaccine production. Influenza vaccine manufacturers are placed on alert. The outbreak caused by the novel influenza virus begins to make headlines in every major newspaper and becomes the lead story on major news networks. Key U.S. government officials are briefed on a daily basis as surveillance is intensified throughout Southeast Asia and the Pacific Rim.

At Genzyme:

Jim Zyme, manufacturing director at the Haverhill site, recently returned from his visit to southern China. He had been searching for a contract manufacturer for the xxx product.

Three days after his return from China, Jim experiences high fever and vomiting that sends him to the local hospital in Haverhill. After thorough examination, the doctors conclude that Jim has been infected with the H7N3 virus. Per requirement, the hospital reports the case to the Haverhill health authorities.

Haverhill health department determined that Jim had come into contact with 15% of the operations personnel and engineers as well as many people in the community. Haverhill health authority issued quarantine on all potential candidates of the influenza for the incubation period of 10 days.

At the same time, a public relations nightmare blossoms as the UK media grabs hold of the story and Genzyme becomes the public face of a potential pandemic. CNN repeatedly has asked Genzyme CEO, Henri Termeer, to make a statement. (play statement made by Henri).

By mid-November, human cases of H7N3 have been reported in Ireland, UK, Hong Kong, Singapore, South Korea, and Japan. Although cases are reported in all age groups, young adults appear to be the most severely affected, and case-fatality rates approach 5%. Public unease grows because vaccine is not yet available and supplies of antiviral drugs are severely limited.

Most governments have set-up a protocol to screen all passengers flying from the affected regions. The governments are also restricting all travel to the affected regions.

Due to public fear of the spread of the H7N3 influenza, the residents demand that Ireland shut its borders.

In early December, human cases are identified in the United States. CDC reports that the H7N3 virus is isolated from ill airline passengers arriving from Hong Kong and Tokyo in Los Angeles, Honolulu, Chicago, New York, and greater Washington DC area, including Baltimore. State and local agencies are asked to intensify influenza surveillance. Vaccine manufacturers are asking when the vaccine seed viruses will be available.

Points to consider:

1) What are the key communication pieces that will be needed to address the above issues? What are the key messages? Within the company who should deliver the various communication pieces?

2) What is the potential impact of the quarantine? How do you address the shortage of employees? How do you protect other employees?

3) As borders close down in various parts of the world, what are supply chain contingency plans?

4) What are the issues around employee health and how should it be addressed (ex. surveillance, communication, reporting)?

5) What other key issues Genzyme needs to address at this point?

6) What specific assistance will be needed from external agencies/organizations?

7) What steps are should be taken to prepare the company for the events of the next 2-3 months?

8) On what medical care-related areas do safety and health teams need to collaborate with the hospitals, emergency rooms and outpatient providers?

Part B

Global News:

It is now late December. Local outbreaks have been reported in major cities throughout the United States, including_NY, Cambridge, Framingham, Allston, Westborough, the impact has begun to be felt in earnest as evidenced by a noticeable increase in the number of persons presenting to emergency rooms with symptoms consistent with influenza. Phones at physician offices and the health department begin to ring constantly. More people are seeking medical care than actually need it, due to fear about the new strain of virus.

Rates of absenteeism in schools and businesses begin to rise. Similarly, personnel in key positions (health care, law enforcement, and other emergency personnel) are absent due to illness or caring for ill family members.

At Genzyme: Approximately, 20% of key personnel in Framingham, Cambridge, Westborough are absent. Most sites have triggered "Product prioritization plan (PPP)"

Nationwide, accounts of illness are reported by the media. Citizens begin to clamor for the vaccine, but it will still be another month or two at the earliest until the first vaccine is available. After it starts to become available, the vaccine will need to be given to certain high priority groups because there won't be enough at once for the entire population. Angry phone calls to elected officials reflect frustration and lack of understanding about why the limited vaccine is being targeted only for certain personnel and will not be distributed to the general public.

Some local pharmacies have run out of antiviral medications and other related supplies (including hand sanitizers, masks) and are unsure whether they can expect to receive more. Although the health department has issued guidelines to physicians on antiviral medication use and has emphasized the importance of prioritizing persons with underlying illnesses who have recent onset of influenza symptoms, anecdotal information suggests that physicians have been prescribing antiviral medications more broadly.

Maryland is experiencing higher than average incidence rate and is considering declaring state of emergency.

Points to consider:

1) What are the issues that Part B presents and how Genzyme could mitigate the impact of these issues?

2) How do you plan to ensure that the critical products continue to be manufactured? What will be required of the various departments to trigger the "Product prioritization plan" in the face of employee shortage?

3) How do you minimize impact of reduction of staff?

4) What are the implications of border closure, travel restrictions and inadequate transportation means on the supply chain of the products? (ex. alternative distribution pts and methods)

5) What temporary concessions/policies will be required of the regulatory agencies during this time?

6) Do you have infrastructure in place for employees to work from home? What alternative communication methods could be appropriate under different circumstances? (Insert the scenario of internet crashing)

Part C

Global News:

It is now mid February. The eastern part of US is overwhelmed by the number of influenza cases. Rough surveillance estimates indicate that 40% of the population is ill with H7N3 influenza.

Local hospitals and outpatient clinics are extremely short-staffed; an estimated 30% to 40% of physicians, nurses and other health-care workers are absent due to illness, caring for family members, or simply because of fear for their safety. Intensive care units are overwhelmed, and soon there is a shortage of mechanical ventilators for treatment of patients with severe respiratory syndromes or postoperative needs. Family members are distraught and outraged when loved ones die within a matter of days. Funeral homes are overwhelmed by the numbers of dead (approximately 325 in the past 3 weeks) and are unable to keep up with the need for services.

Hospitals and other health facilities around the world have postponed all non-essential procedures until further notice. Since many of Genzyme's products require infusion, this policy has a huge bearing on Genzyme's patients.

The first supplies of vaccine will arrive next week and are targeted to health-care workers and first responders.

Law enforcement, emergency medical personnel, health care, and local utility companies (power and water) also have personnel shortages, resulting in some cutbacks in routine services. Reports of internet disruptions are increasing. Grocery stores are suffering shortages of food supplies due to the nationwide impact resulting from ill truckers who usually deliver those supplies. FEDEX and UPS have announced they would not be able to honor on-time delivery guarantees since they are short staffed.

For Genzyme: Transportation companies in the Baltimore area are experiencing significant business disruptions.

Many area residents (particularly those with chronic, unstable medical conditions) are afraid to venture out for fear of becoming seriously ill with influenza. Hundreds are staying home, and their essential supplies—such as food—are becoming depleted.

Points to Consider:

1) How does Genzyme address patients access to Genzyme products?

2) How will Genzyme assist families of employees and communities it operates in?

3) How does Genzyme continue operations? (ex. lock-in critical employees)

4) What other issues Genzyme is likely to face?

Part D

It is now late March, and the number of ill persons has been on the decline for 3 weeks. Hospital staff is exhausted. All those available to assist in providing health care have been pulled in.

Vaccine is finally becoming available on a larger scale.

Points to consider:

1) What are some of the business resumption issues to consider?
2) Assuming potential deaths of employees or their loved ones, what do you need to consider?
3) How do you ensure returning employees are healthy?
4) What are some short term and long term issues to consider coming out of a pandemic?
5) What are key data we can collect during and after a pandemic?

This page is intentionally left blank.

Bibliography and Notes

1) Genzyme Corporation. "Who We Are." Accessed on April 2, 2007. <http://www.genzyme.com/corp/structure/corp_home.asp>

2) Securities Exchange Commission. Genzyme 10-K Report 1999.

3) Securities Exchange Commission. Genzyme 10-K Report 2000.

4) Securities Exchange Commission. Genzyme 10-K Report 2001.

5) Securities Exchange Commission. Genzyme 10-K Report 2002.

6) Securities Exchange Commission. Genzyme 10-K Report 2003.

7) Securities Exchange Commission. Genzyme 10-K Report 2004.

8) Securities Exchange Commission. Genzyme 10-K Report 2005.

9) Securities Exchange Commission. Genzyme 10-K Report 2006.

10) Sheffi, Yossi. The Resilient Enterprise. Cambridge, MA: MIT Press, 2005. 3-10.

11) Schwander, Tina. "Blood Center of New Orleans – New Orleans, Louisiana." Accessed on April 2, 2007. <http://www.miblood.org/news_events/press_090605.html>

12) Muckraked. "Gulf-Area Charities Still Need Your Help." June 4, 2006. Accessed on May 8, 2007. <http://www.muckraked.com/wordpress/2006/06/04/gulf-area-charities-still-need-your-help/>

13) U.S. Department of Homeland Security. "FEMA Obligates Over $2 Million For Blood Center In New Orleans." Accessed on May 8, 2007. <http://www.fema.gov/news/newsrelease.fema?id=31220>

14) Potter, Suzy: The Blood Center Community Development Manger. Acquired information by speaking with Suzy Potter. January 2006.

15) World Health Organization. Accessed on May 8, 2007. <http://www.who.int/csr/disease/avian_influenza/country/cases_table_2007_04_11/en/index.html>

16) Pandemicflu.gov. Accessed on May 8, 2007. <http://www.pandemicflu.gov/faq/pandemicinfluenza/1070.html>

17) World Health Organization. Accessed on May 8, 2007. <http://www.who.int/csr/disease/influenza/pandemic10things/en/>

18) U.S. Department of Health and Human Services (HHS). November 2005. Accessed on May 8, 2007. <http://www.hhs.gov/pandemicflu/plan/pdf/HHSPandemicInfluenzaPlan.pdf>

19) GlobalSecurity. Accessed on May 8, 2007. <http://globalsecurity.org>

20) World Health Organization. Accessed on May 8, 2007. <http://www.who.int/csr/disease/avian_influenza/phase/en/index.html>

21) Pandemicflu.gov. Accessed on May 8, 2007. <http://www.pandemicflu.gov/general/historicaloverview.html>

22) World Health Organization. Accessed on May 8, 2007. <http://www.who.int/csr/disease/influenza/H5N1-9reduit.pdf>

23) World Health Organization. Accessed on May 8, 2007. <http://www.who.int/csr/disease/avian_influenza/avian_faqs/en/index.html#areall>

24) Centers for Disease Control and Prevention. CDC Influenza Pandemic Operation Plan. December 20, 2006. <http://www.cdc.gov/flu/pandemic/pdf/cdc_oplan_122006.pdf>

25) World Health Organization. "WHO checklist for influenza pandemic preparedness planning." Department of Communicable Disease Surveillance and Response Global Influenza Programme. 2005. Accessed on May 8, 2007. <http://www.who.int/csr/resources/publications/influenza/FluCheck6web.pdf>

26) Enserink, Martin. "Who Adds More "1918" to Pandemic Predictions." Science. December 17, 2004. Accessed on May 8, 2007. <http://www.sciencemag.org/cgi/content/full/306/5704/2025b>

27) Pandemicflu.gov. Accessed on May 8, 2007. <http://www.pandemicflu.gov/faq/planningresponse/1083.html>

28) U.S. Department of State. Bureau of International Information Programs. "Health Services Could Be Overwhelmed in a Pandemic, Experts Say." Washington, D.C. March 9, 2006. Accessed on May 8, 2007. <http://usinfo.state.gov/gi/Archive/2006/Mar/11-871715.html>

29) Homeland Security. Pandemic Influenza: Preparedness, Response, and Recovery. Guide for Critical Infrastructure and Key Resources. September 19, 2006. <http://www.pandemicflu.gov/plan/pdf/cikrpandemicinfluenzaguide.pdf>

30) Pandemicflu.gov. Accessed on May 8, 2007. <http://www.pandemicflu.gov/general/index.html#impact>

31) Zwillich, Todd. Flu Pandemic Guide: Stock Up on Basics. WebMD. January 6, 2006. <http://www.foxnews.com/story/0,2933,180914,00.html>

32) Government of Jamaica. "Prepare for Disaster: Recover Faster." Accessed on May 8, 2007. <http://www.jis.gov.jm/special_sections/labourDay2005/preparingForAHurricane.html>

33) Brahmbhatt, Milan. "Avian and Human Pandemic Influenza – Economic and Social Impacts." World Bank. Geneva, November 7-9, 2005. Accessed on May 8, 2007. <http://www.who.int/mediacentre/events/2005/World_Bank_Milan_Brahmbhattv2.pdf>

34) Kasperson, Roger E., Ortwin Renn, Paul Slovic, Halina S. Brown, Jacque Emel, Robert Goble, Jeanne X. Kasperson, and Samuel Ratick. "The Social Amplification of Risk: A Conceptual Framework." Risk Analysis, Vol. 8, No. 2, 1988.

35) Sterman, John D. Business Dynamics: Systems Thinking and Modeling for a Complex World. Boston: Irwin McGraw-Hill, 2000. 4-5.

36) Lee, Hau, V. Padmanabhan, Seungjin Whang. "The Bullwhip Effect in Supply Chains." Sloan Management Review (pg 93-102). Spring 1997.

37) Bean, Michael. "Bullwhips and Beer: Why Supply Chain Management is so Difficult." Forio Business Solutions. Accessed on May 8, 2007. <http://forio.com/resources/bullwhips-and-beer/>

38) Sterman, John D. Business Dynamics: Systems Thinking and Modeling for a Complex World. Boston: Irwin McGraw-Hill, 2000. 695-698.

39) Sterman, John D. Business Dynamics: Systems Thinking and Modeling for a Complex World. Boston: Irwin McGraw-Hill, 2000. 665.

40) Beal, Vangie. "Internet-based Communications." August 5, 2005. Accessed on May 8, 2007. <http://www.webopedia.com/DidYouKnow/Internet/2005/internet_communications.asp>

41) Three Mile Island 1979 Emergency website. Accessed on May 8, 2007. <http://www.threemileisland.org/virtual_museum/march28_1979.html>

42) Three Mile Island 1979 Emergency website. Accessed on May 8, 2007. <http://www.threemileisland.org/virtual_museum/march30_1979.html>

43) Genzyme.com. Accessed on May 8, 2007. <http://genzyme.com/business/biz_home.asp>

44) IMS Health Incorporated. Script data provided to Genzyme Corporation.

45) Securities Exchange Commission. Genzyme 2001 Quarter 2 10-Q Reports.

46) Securities Exchange Commission. Genzyme 2001 Quarter 1 10-Q Reports.

47) Securities Exchange Commission. Genzyme 2001 Quarter 3 10-Q Reports.

48) Wang, Elise. Genz: Solid 2002 Financial Outlook. Salomon Smith Barney. Jan 24, 2002.

49) Augustine, Mark. GENZ Posts Q3:01 EPS of $0.30 On Renagel Sales of $52.4M; Raising Estimates. USbancorp Piper Jaffray. October 18, 2001.

50) Securities Exchange Commission. Genzyme 2002 Quarter 1 10-Q Reports.

51) Securities Exchange Commission. Genzyme 2002 Quarter 2 10-Q Reports.

52) Augustine, Mark. Renagel Fizzles; Investment Community Sizzles. USbancorp Piper Jaffray. March 27, 2001.

53) Renaud, Ronald, Hayley Xuereb, Alexandra Lee. 1Q02 Earnings: Another Disappointment – Downgrading to Neutral. Bear, Stearns & Co. Inc. April 18, 2002.

54) Chovav, Meirav, Katherine Kim, Hoki Luk. Reported in-line 2Q02 EPS of $0.25; Maintaining EPS ests. UBS Warburg. July 12, 2002.

55) Yahoo Finance Charts. Accessed on May 8, 2007. <http://finance.yahoo.com/charts#chart1:symbol=genz;range=2y;indicator=volume;charttype=line;crosshair=on;logscale=on;source=undefined>

56) Genzyme Corporation. "Genzyme: Pandemic Planning Guide." November 2006.

57) Cerezyme.com. Accessed on May 8, 2007. <http://www.cerezyme.com/patient/about/cz_pt_about-gaucher.asp>

58) Cerezyme.com. Accessed on May 8, 2007. <http://www.cerezyme.com/patient/about/cz_pt_about-symptoms.asp>

59) Cerezyme.com. Accessed on May 8, 2007. <http://www.cerezyme.com/patient/treatment/cz_pt_treatment.asp>

60) Cerezyme.com. Accessed on May 8, 2007. <http://www.cerezyme.com/patient/about/cz_pt_about-diagnosis.asp>

61) Pompe.com. Accessed on May 8, 2007.
<http://www.pompe.com/patient/learning/pc_eng_pt_learning.asp>

62) Kugler, Mary. "Pompe Disease." About: Rare Diseases. July 19, 2003. Accessed on May 8, 2007.
<http://rarediseases.about.com/cs/pompedisease/a/071903.htm>

63) Heuser, Stephen. "High-priced Genzyme drug is OK'd." The Boston Globe. April 29, 2006.

64) Pompe.com. Accessed on May 8, 2007.
<http://www.pompe.com/patient/diagnosing/pc_eng_pt_diagnosing.asp>

65) For the sake of simplicity, this section does not refer again to the fill/finish capabilities at the Waterford site.

66) Throughout the rest of the paper, the end recipient of Cerezyme and Myozyme will be referred to as "medical facility".

67) LSDregistry.net. Revision: August 28, 2003. Accessed on May 8, 2007.
<www.lsdregistry.net/gaucherregistry/hcp/safety/greg_SmPC.pdf>

68) EMEA.EU.int. March 29, 2006. Accessed on May 8, 2007.
<http://www.emea.eu.int/humandocs/PDFs/EPAR/myozyme/H-636-PI-en.pdf>

69) NYU Stern paper. "Estimation Inputs for Valuation: Estimation of Discount Rates." Accessed on May 11, 2007.
<http://pages.stern.nyu.edu/~adamodar/New_Home_Page/lectures/dcfinput.html>

70) Anupindi, Ravi, Sunil Chopra, Sudhakar D. Deshmukh, Jan A. Van Mieghem, Eitan Zemel. Managing Business Process Flows. New Jersey: Pearson Education, Inc., 2000. 138. 140, 188-189.

71) U.S. Food and Drug Administration. Frequently Asked Questions. July 26, 2006.
<http://www.fda.gov/cder/biologics/qa.htm>