5-4-2010

Problems Facing the Pharmaceutical Industry and Approaches to Ensure Long Term Viability

Donald A. Baines
University of Pennsylvania, djtz00@gmail.com

Submitted to the Program of Organizational Dynamics in the Graduate division of the School of Arts and Sciences in Partial Fulfillment of the Requirements for the Degree of Master of Science in the Organizational Dynamics at the University of Pennsylvania Advisor: Richard Bayney

Problems Facing the Pharmaceutical Industry and Approaches to Ensure Long Term Viability

Abstract
This paper examines the Pharmaceutical (Pharma) industry and the changes that have occurred particularly over the last 10 years as a result of the overall economic downturn, the rising cost of healthcare and the costs associated with the development and sales of pharmaceuticals. One response of big Pharma to this has been the recent spate of partnerships, mergers and acquisitions, consolidation, diversification, licensing agreements and downsizing in both human and capital resources. Four major challenges facing the complex Pharma industry are highlighted and discussed. These include the decline in the discovery, approval and marketing of new chemical entities (NCE) with fewer and fewer blockbuster drugs making it to the market, competition from generics drugs, regulatory pressures and the weak growth in the US market (the largest market) and therefore the need to explore other markets to name a few. In addition to the research driven aspect of the paper, a summary of the interviews conducted with executives and other industry practitioners (to get their personal views) is presented. Finally referencing some of the strategies adapted by some companies, this thesis identifies Organizational Dynamics areas of concentration and the role they can play within companies in their plans to ensure long term viability. The analysis focuses on the commercial aspects of the industry and offers some steps that will be useful in changing the current business model and setting the stage for future success.

Disciplines
Organizational Behavior and Theory

Comments
Submitted to the Program of Organizational Dynamics in the Graduate division of the School of Arts and Sciences in Partial Fulfillment of the Requirements for the Degree of Master of Science in the Organizational Dynamics at the University of Pennsylvania Advisor: Richard Bayney

PROBLEMS FACING THE PHARMACEUTICAL INDUSTRY AND APPROACHES TO ENSURE LONG TERM VIABILITY

By

Donald A. Baines

Submitted to the Program of Organizational Dynamics
in the Graduate division of the School of Arts and Sciences
in Partial Fulfillment of the Requirements for the Degree of
Master of Science in the Organizational Dynamics at the
University of Pennsylvania

Philadelphia, Pennsylvania

2010

PROBLEMS FACING THE PHARMACEUTICAL INDUSTRY AND APPROACHES TO ENSURE LONG TERM VIABILITY

Approved by:

Richard Bayney, Ph.D., Advisor

Keith Hornbacher, MBA, Reader

Martin, Stankard, Ph.D., Reader

ABSTRACT

This paper examines the Pharmaceutical (Pharma) industry and the changes that have occurred particularly over the last 10 years as a result of the overall economic downturn, the rising cost of healthcare and the costs associated with the development and sales of pharmaceuticals. One response of big Pharma to this has been the recent spate of partnerships, mergers and acquisitions, consolidation, diversification, licensing agreements and downsizing in both human and capital resources.

Four major challenges facing the complex Pharma industry are highlighted and discussed. These include the decline in the discovery, approval and marketing of new chemical entities (NCE) with fewer and fewer blockbuster drugs making it to the market, competition from generics drugs, regulatory pressures and the weak growth in the US market (the largest market) and therefore the need to explore other markets to name a few. In addition to the research driven aspect of the paper, a summary of the interviews conducted with executives and other industry practitioners (to get their personal views) is presented.

Finally referencing some of the strategies adapted by some companies, this thesis identifies Organizational Dynamics areas of concentration and the role they can play within companies in their plans to ensure long term viability. The analysis focuses on the commercial aspects of the industry and offers some steps that will be useful in changing the current business model and setting the stage for future success.

ACKNOWLEDGEMENTS

My appreciation is extended to Dr. Richard Bayney my capstone advisor as well as my two capstone readers, Keith Hornbacher MBA and Dr. Martin Stankard for their advice and input during the writing of this paper. I would also like to thank my fellow classmate Tara Lukievics who partnered with me in the interview section for the capstone as well as my cohorts who shared this learning experience with me. A special thanks to my family, Junette, Tariq and Zoei for their patience and encouragement as I spent long hours away at class or at home working on class assignments and projects.

LIST OF TABLES

LIST OF FIGURES

TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

Background

The Pharmaceutical industry and big Pharma (< $3 billion annual sales) in particular are now experiencing the same phenomenon that many other industries have faced in the past where many companies have been forced to try and reinvent themselves in the face of challenges in their business environment. It happened with the computer industry for example International Business Machine Corporation (IBM) moving to a service model, the steel industry (outsourcing and diversification) and more recently, the technology sector with the bursting of the dotcom bubble. One thing has become clear. Only the companies that are willing to change or modify their strategies and follow that with excellent execution of these strategies will have long term success.

The issues involved are very complex and cover a wide variety of areas including research and development, commercial, political and geographical to name a few. This paper explores the commercial or business issues and their impact on the current Pharma business model. It will also look at strategies being devised to address the lack of innovative new products being developed and approved and the negative impact they have on revenue growth. It will also provide some steps and suggestions that will be helpful in addressing the issue based on changing the changing environment. It will examine the strategies that can be used in focusing research and development as well as changing business models that can be used to mitigate the loss in revenue caused by the patent expiration and a lack of blockbuster medicines to replace them, both in the developed and Emerging Markets.

The performance of companies that attempt to change their business models via a variety of approaches, primarily mergers and acquisitions (M&A) will also be examined. While it is difficult to predict or project how companies will fare after a significant change it its operating model or structure,, the early results are very important because investors and analysts are very often quick to reward or punish companies based on their ability to deliver on their pre-merger or pre reorganization promises.

A perfect example of this was the difference in early evaluation between the Pfizer and Wyeth vs. the Merck and Schering Plough mergers. In the February 17th 2010 issue of FiercePharma Tracy Stanton wrote:

> Not only have analysts predicted solid growth for the new Merck, but have been praising management for its discipline and commitment. While as you know, Pfizer execs got an earful of criticism—and a stock price hit—when its forecast post merger sales substantially lower that it had predicted earlier.

A few weeks later on March 2nd, 2010 the same reporter wrote

> Suddenly, Pfizer is the belle of the hedge-fund ball. Reuters reports that "some of the savviest" of hedge funds are eyeing the company, now that it has on hand the new drugs and vaccines it bought along with Wyeth. Apparently, these professional investors believe the rationale around that $68 billion deal: That Wyeth's products will make up for Lipitor's fall off the patent cliff.

Many big Pharma companies have responded to the current business climate by engaging in a variety of strategies aimed at paving the way for future success. Examples of this are, Merck's recent merger with Schering Plough, a move aimed at consolidation based on perceived pipeline synergies, the Pfizer buyout of Wyeth and Roche's acquisition of Genentech. Others have pursued the path of diversification as is the case with Johnson and Johnson, Novartis or Abbot that have significant business activities outside of the traditional pharmaceutical arena engaging in areas such as consumer

products, healthcare services, medical devices and medical diagnostics. Yet other companies have taken the path of focusing on the 'Emerging Markets' that are in some ways considered largely untapped potential like AstraZeneca and GlaxoSmithKline's focus on China and India respectively.

These are examples of changes that point to the fact that many Pharma companies do not see the current situation as a temporary setback. Many are making the decision to work with former competitors (Eli Lilly, Merck and Pfizer working on Oncology in Asia,) or revamp their research capabilities as seen with Eli Lilly and Covance recently signing a 3 year biotechnology services agreement where Lilly will test bioproducts at Covance's new biotech facility (Lilly February 26, 2010 press release). Companies are also trying to improve their manufacturing capacity and efficiency (many with a variety of Six Sigma process improvements) and commercial models (Merck embarking on a new way of engaging with their customers) in order to be successful in the future.

There is no doubt that the Pharma industry is facing challenging times, and only the companies that are able to (1) execute on the strategy they develop as well as (2) carefully assess and manage the risks, (3) make the right portfolio and business decisions and (4) improve their processes will be able to have long term success.

Chapter 1 outlines some of the issues being faced by the industry as well as some projections on where the solutions may be found. Chapter 2 takes a look a ways in which some companies have already responded by trying to find ways to modify the way they do business, including looking for ways to buy or partner to get assets they currently do not have in their portfolio.Chapter 3 recaps the views expressed by subject matter experts

on the industry. These interviewees were selected based on their extensive experience in the Pharma industry including research and development, global marketing, mergers and acquisitions, portfolio management, consulting, sales and marketing experience.

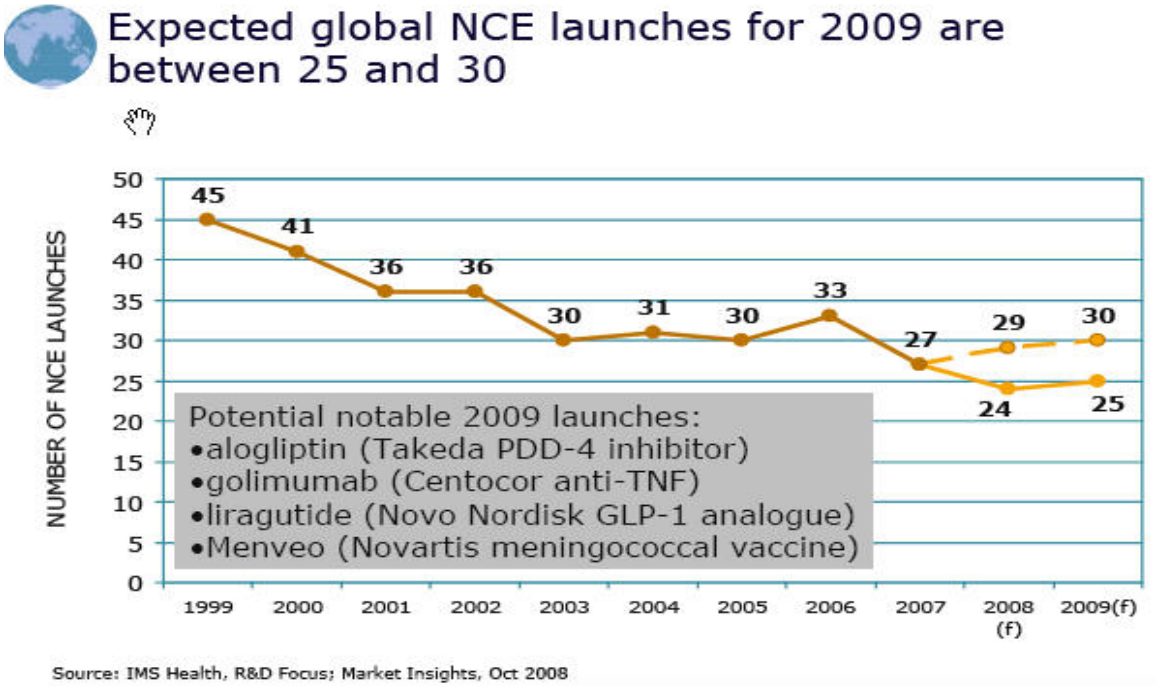
Chapter 4 examines past mergers in more detail, looking at examples where companies made the decision to merge assets and the resulting performance of the combined entity. This is very important because in the future more and more companies may chose to go this path and it will be very important to understand how close they came to achieving their targeted objectives, both in the short and long term. In chapters 5, 6 7, 8 and 9 potential approaches and solutions to address the main issues will be proposed, incorporating some of the disciplines, processes and tools from the Organizational Dynamics program at the University of Pennsylvania while chapter 10 brings it all together in a summary that reiterates the sense of urgency and steps needed to address the issues impacting this very complex and now fast paced industry.

PHARMACEUTICAL INDUSTRY ISSUES

Limited Approval of New Chemical Entities)

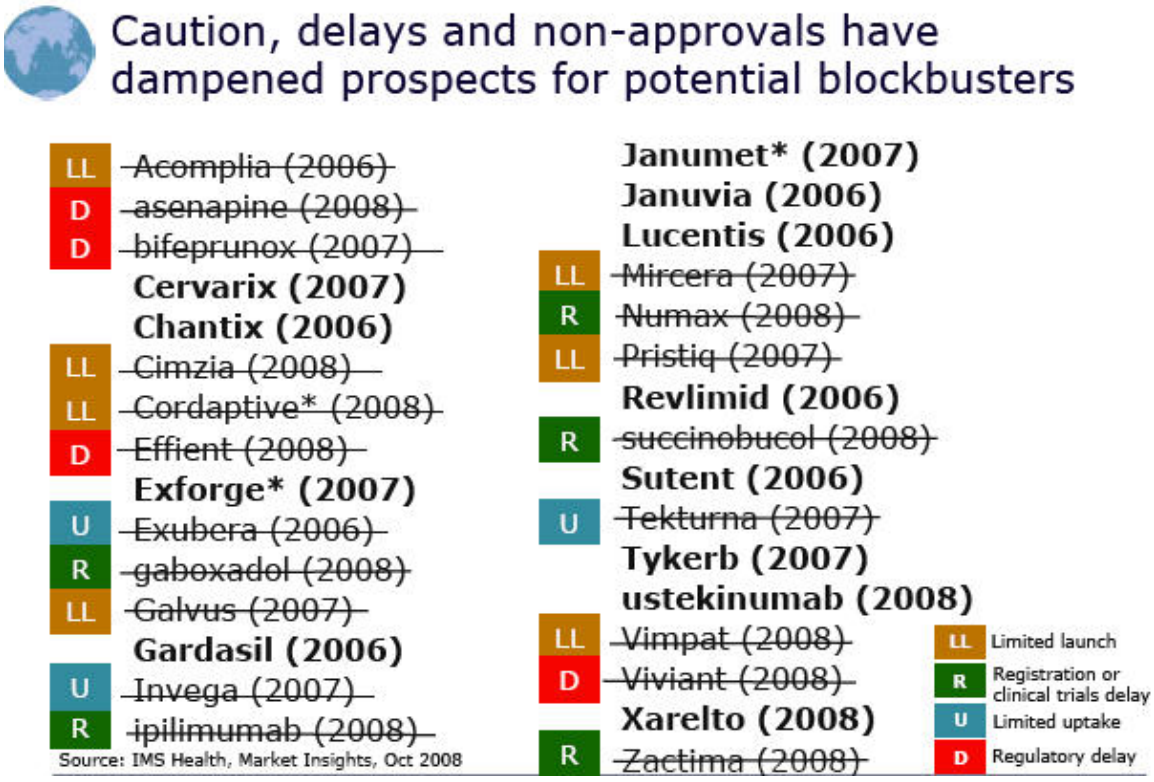
New Chemical Entities (NCEs) are the compounds that emerge from the process of drug discovery. Research done by IMS research shows that there has been a significant decline in the number of NCEs launched over the last ten years. A plot of the IMS data (Figure 1) shows a decline in the NCE launches from 45 in 1999 down to approximately 27 by the end of 2009. This phenomenon has not been restricted to just a few therapeutic areas or companies and is compounded by the fact that the value of the launches that have occurred are significantly less than in the years when blockbusters drugs provided significant increase in revenue

Figure 1 - Expected NCE Launches for 1999-2009



The reason for this decline has been attributed to many factors including increased scrutiny and higher safety standards dictated by the Food and Drug Administration (FDA) authorities, broad portfolio of early stage therapeutic products being looked at but with not much success in creating novel medicines in the vast majority of the areas, despite advances in technology and processes. Regardless of the reasons, the companies have to deal with the reality that there are less new products being approved and therefore they are failing to achieve their potential to provide treatment for patients and commercial benefits to their companies. Figure 2 shows the fate of some promising drugs over the last few years.

Figure 2 - Product Delays and Non-Approvals



While the solution to this problem starts in the area of research and development (R&D), the business aspects is of critical importance. It takes about 10–12 years to bring a medicine to market from discovery through launch. While it may be possible to

decrease this time using better processes and technology, fixing the business model where each company invests in R& D from discovery through product launch (lifecycle management) is just as critical. Additionally, companies need to make better portfolio decisions that enables them to sharpen the focus of their investments and where possible look for opportunities to work with other entities to share the cost of R&D as well as the business risks.

Increased Generic Competition

Generic drugs have always been a big challenge for the established big Pharma companies. Big Pharma companies spend many years and millions of dollars (approximately $802 million estimated by the Congressional Budget Office, CBO) from discovery to product launch. In 1976 the estimate was $137 million dollars and by 1990 it had increased to $445 million dollars. These companies are able to take advantage of their hard work and investments while their patents are in effect, but as soon as these patents expire, the generic drug makers are able to undercut the big Pharma profit margin within 6 months by producing lower cost, and in most cases very effective alternatives (See Figures 3 and 4).

Figure 3 – High Level Breakdown of R&D Cost

DiMasi and Others' Estimate of Average Research Costs and Times for Successfully Developed New Molecular Entities

	Average Length of Research Phase		
	Preclinical Phase (4.3 years)[a]	Clinical Trials and FDA Approval (7.5 years)	Total (11.8 years)
Research and Development Costs (Millions of 2000 dollars)			
Direct costs	121	282	403
Opportunity costs[b]	214	185	399
Total Costs	**335**	**467**	**802**

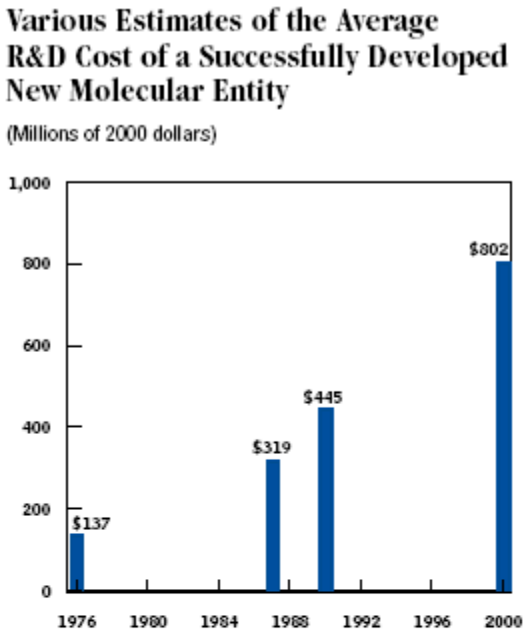
Source: Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics*, vol. 22, no. 2 (March 2003), pp. 151-185.

Note: FDA = Food and Drug Administration.

a. The estimate for the duration of the preclinical phase is based on the comprehensive drug database maintained by the Tufts University Center for the Study of Drug Development.

b. Opportunity costs are the costs associated with keeping capital tied up in a specific drug-development project for a given period (that is, the forgone interest or earnings that a company might have gained from investing its capital in other ways). DiMasi and others assumed the forgone rate of return to be 11 percent per year.

Figure 4 - Estimates of R&D Costs



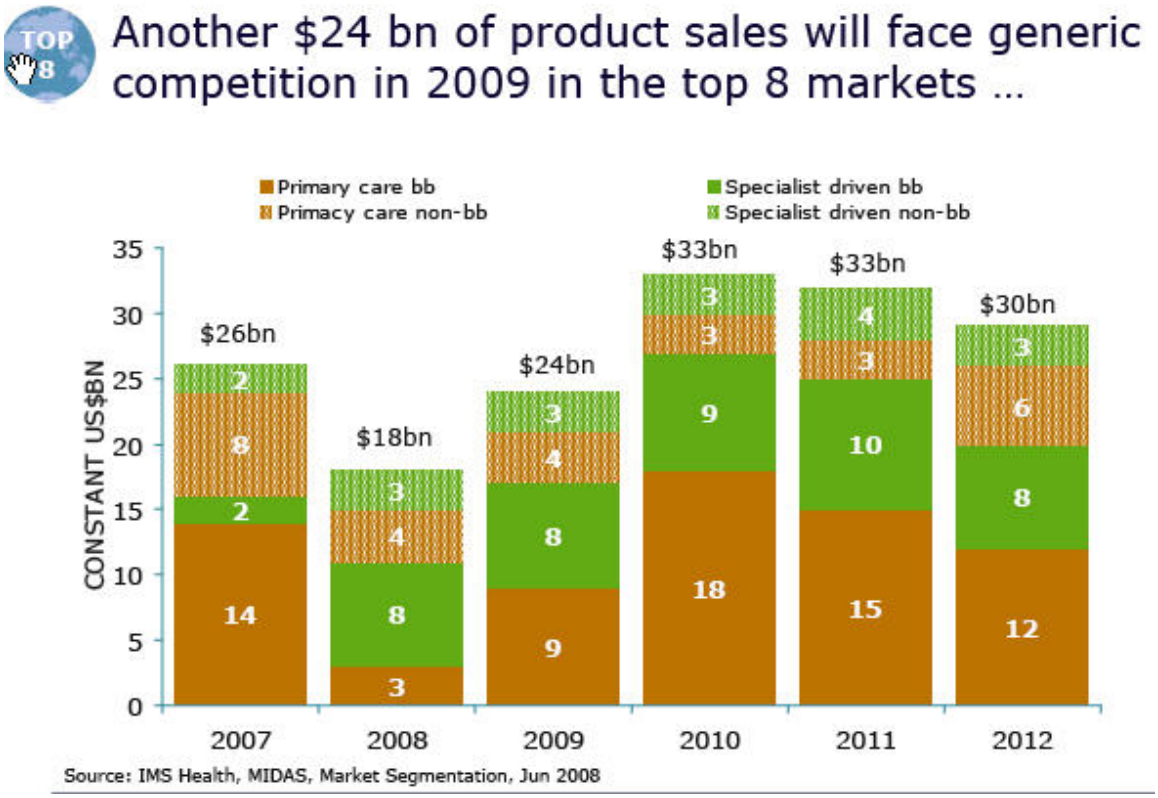
Source: Congressional Budget Office based on R.W. Hansen, "The Pharmaceutical Development Process: Estimates of Current Development Costs and Times and the Effects of Regulatory Changes," in R.I. Chien, ed., *Issues in Pharmaceutical Economics* (Lexington, Mass.: Lexington Books, 1979), pp. 151-187; Joseph A. DiMasi and others, "Cost of Innovation in the Pharmaceutical Industry," *Journal of Health Economics*, vol. 10, no. 2 (July 1991), pp. 107-142; U.S. Congress, Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks, and Rewards*, OTA-H-522 (February 1993); and Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics*, vol. 22, no. 2 (March 2003), pp. 151-185.

Notes: R&D = research and development.

The year shown for each estimate is the year in which the cost survey was performed, not the year in which the results were published.

The recent economic downturn, healthcare reform in many countries and less disposable income for customers have made the generic option more attractive to payors, insurance companies and consumers concerned with managing their costs. As a result the generic drug makers have been making inroads in the product sales of the branded products and this along with patent expiration has led to projections of an increase in generic sales of $12 billion dollars from $18 billion in 2008 to $30 billion in 2012 (see Figure 5).

Figure 5 - Generic Sales Projections Through 2012



Generic drugs are here to stay, and many will argue that they play a very important part in dampening the rising cost of healthcare for consumers, especially with the ever increasing medical and insurance costs. In this environment big Pharma companies need to get creative and change or modify their business model to be successful. Options available to them could include, improving their product lifecycle process to provide additional value to patients on compounds that currently exist, partnering with biotech and generic companies to discover additional indications and uses for their products. Another approach that could be considered is to develop their own generic drug infrastructure and competence so they can tap into certain markets where the cost of brand drugs may be prohibitive, but the generic versions could help them to gain

access to the market or region once the patent life has expired. This would help them to develop brand recognition.

Regulatory Changes and Political Impact

The recent (2006–2010) economic downturn has in many situations intensified and refocused people's attention on regulation in the Pharma industry. Some of the arguments in the fall of 2009 healthcare debate in the United States are a prime example. The debate has been driven both by the need for the improvement in the regulatory process to meet the current needs of all the stakeholders as well as the stated and in some cases implied need to ensure that the expected benefits are aligned with the cost for the insurance, products and services.

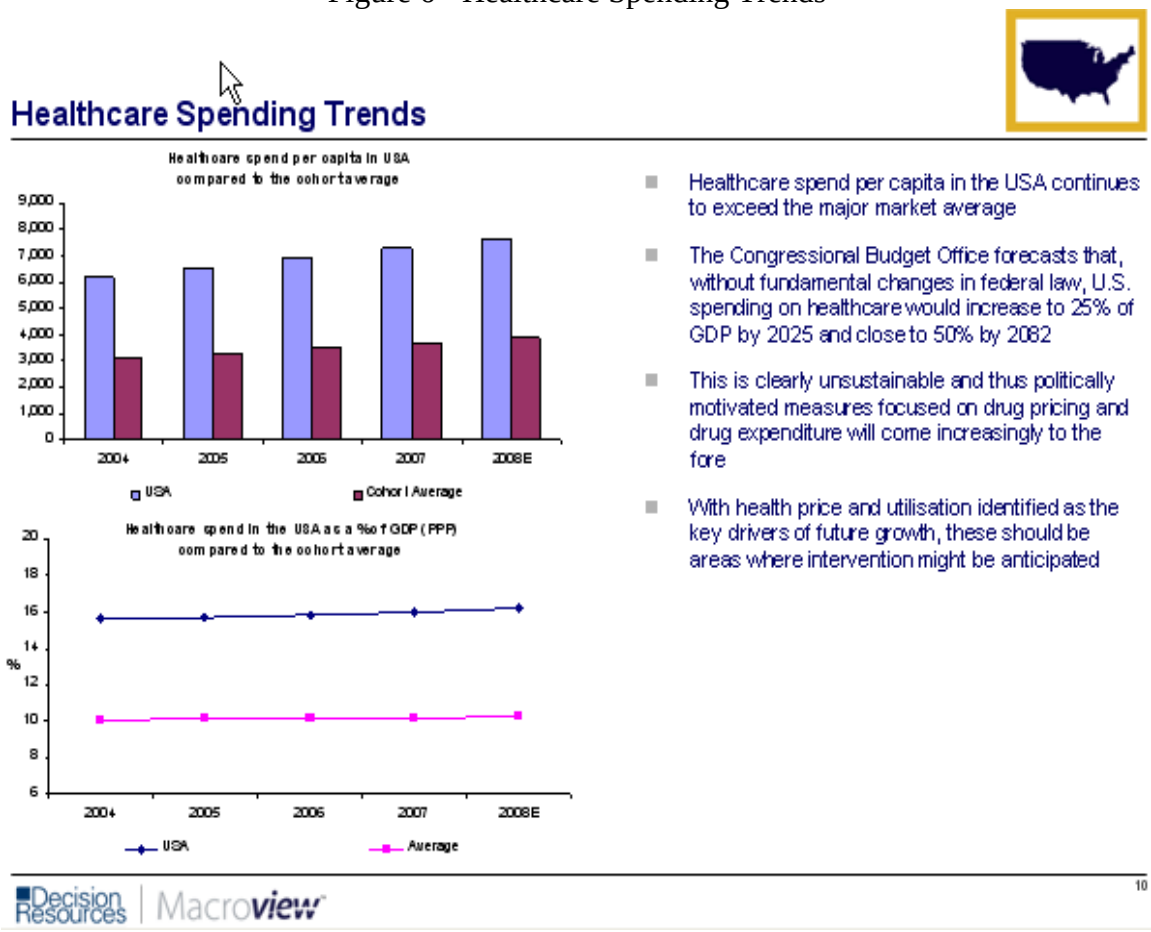
This reality will prompt and in many cases force big Pharma companies to revamp their cost structures as governments, insurance companies, payors and patients focus on reducing the spending on healthcare. Figure 6 shows the cost forecast by the Congressional Budget Office which will rise to 25% of the US GDP by 2025 if the current trend continues.

These cost and other related issues could be seen more as the symptom of the underlying problem. The real issue is that there is a need for Pharma companies to be able to demonstrate the value they bring to their patients and other stakeholders. In other words, show the value that can be provided to the patient by the products they submit for approval, especially where they are in therapeutic areas that are already being addressed while the needs of many others are not met or are underserved.

The Food and Drug Administration (FDA) in the Unites States and other like organizations in other countries have as one of their main mandates, the health and safety

of the society. Big Pharma could partner with these agencies by leveraging some of the cutting edge technology they (big Pharma) have to speed up their processes, a win-win proposition (see Figure 6). This would also require a higher level of communication and openness than currently exists so the needs and safety of patients are put first in all interactions.

Figure 6 - Healthcare Spending Trends



Regulation also impacts many other issues and stakeholders concerned about issues like Global Warming (the effects of manufacturing plants on the environment) Animal Rights groups (resistance to testing in animals) and many other groups. These groups often have not only the monetary resources but also the political connections that

can make it very difficult for Pharma companies to operate to their full potential in many countries and markets. Pharma companies would be well served to understand the concerns and improve these relationships and not get into a situation where they have trouble marketing and selling their products after clearing the high hurdle of research and development and passing product efficacy and safety clinical trials.

The Emerging Markets (Changing Disease Patterns, Patient Demographics)

The United States is by far the biggest market for Pharmaceuticals. Many companies recognize the need to start putting more resources and infrastructure in other regions and countries that have the potential to become significant sources of growth in the very near future. China and India are the countries that readily come to mind, but countries like Brazil, Russia and even Poland are being looked at as markets that still have significant areas where the needs of patients with certain diseases are not being met.

In Figures 7 and 8 the IMS research identifies the following countries as the E7, China, India, Brazil, Russia, Turkey, Poland, South Korea while others include Mexico or Indonesia in the place of Poland or S. Korea. Regardless of what countries are identified as the E7, these are meant to define the non-industrialized countries with significant economic, political, developmental and other growth potential that need to be included in their business planning to achieve success on a global scale.

Many regions have diseases which are not fully understood and may have different medical needs because differences in genetics, diet, climate or other factors which are unique to their environment. It is important that companies recognize that they need to invest in clinical trial and other investigative work before they attempt to introduce their portfolio of current products to the region. This like the other problems

listed requires rigorous assessment and understanding of the ways of doing business, culture and a host of other physiological and social factors, especially in places where people have practiced one form of medicine for years. In these cases the solution may be a combination of current and new approaches and therapies and not simply going in with the goal of replacing treatments that have been used for generations.

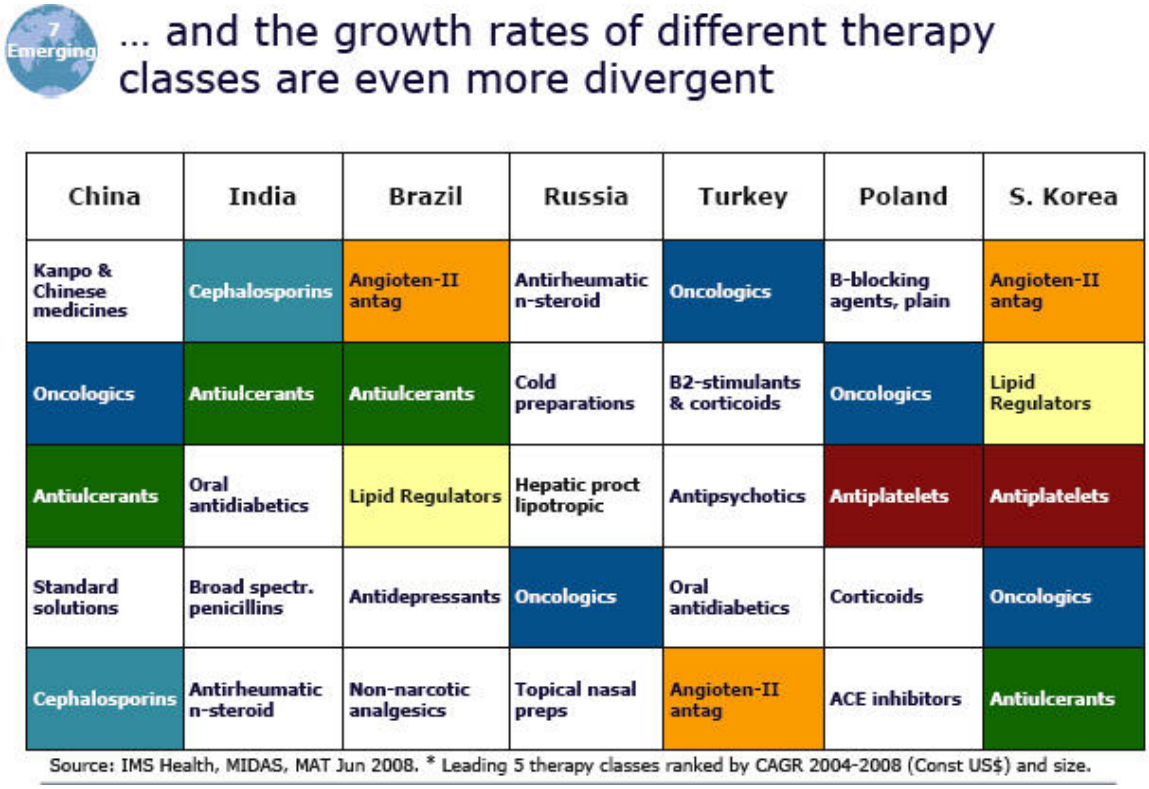
Figure 7 - E7 Health Demographics

Demographics differ substantially across the E7

	Country	Life expectancy M / F	Urban population	Causes of death	GDP per capita (US$, PPP)
>1 Billion	**China**	70 / 74	44%	Cancer, CV (urban) Respiratory, CV (rural)	6,164
	India	66 / 71	28%	Heart/CV, respiratory, perinatal, diarrhea	3,044
>100 Million	**Brazil**	69 / 76	84%	Heart/CV, perinatal, injury, diabetes	10,402
	Russia	59 / 72	73%	Heart/CV, poisoning/ injury, cancer,	16,280
<100 Million	**Poland**	71 / 80	62%	Heart/CV, respiratory, cancer	17,727
	Korea	74 / 81	81%	Heart/CV, cancer, diabetes	26,380
	Turkey	70 / 75	65%	Heart/CV, perinatal, COPD	12,439

Source: WHO World Health Statistics; Economist Intelligence Unit, 2008.

Figure 8 - E7 Therapy Classes



Big Pharma companies have a responsibility to their shareholders, investors, employees and patients to operate in a way that will ensure their viability for the long term. That is the only way that they will be able to continue to provide and improve the medicines that societies depend on them to produce. The data above illustrates the huge opportunity that the Pharma industry has for meeting the need of patients in therapeutic areas, as well as and by inference the financial gains they can have in geographies that have been a focus of their business plans but have huge and diverse unmet needs.

Companies should plan to diversify their business models to invest in regions where there are opportunities to meet the needs of the people as well as broaden their operations. This does not simply mean moving operations to countries where relatively lower labor cost may make it possible for them to lower their operating costs and take

advantage of manufacturing and supply chain logistics. It also requires them to take a real look at disease patterns and needs and not merely take their current portfolio of products and try to force fit them into these new regions. To put it directly, Emerging Market strategy should include the required level of concern for patient needs as well as the necessary business benefits to be effective and increase the potential for long term success.

CHAPTER 2

PHARMACEUTICAL INDUSTRY RESPONSE

The issues outlined in chapter 1 are not an exhaustive list of the things big Pharma has to rectify, but they represent significant areas which need to be addressed. Many organizations have been rethinking their business and operational models based on their individual situation. Table 1 provides a snapshot of some of the actions taken by some of the Pharmaceutical companies in recent years, and from a commercial standpoint shows the willingness of Pharma companies to change their way of doing business.

Table 1 – Actions Taken by Pharmaceutical Companies (2006 – 2009)

Company	**Action**	**Reason for Action**
Merck & Co	Acquisition of Schering Plough in a reverse merger (11/2009)	Leverage synergies, particularly with the product pipeline.
Pfizer	Buyout of Wyeth (10/2009)	Solidify #1 ranking and increase revenue
Roche and Genentech 'Partnership'	Roche acquired Genentech in a 'friendly' agreement (3/2009)	Increase focus on innovation; Pharma-biotechnology innovation
AstraZeneca	Major investments in China (on going)	Invest in infrastructure to meet the needs of the local customers and patients
GlaxoSmithKline	Major investments in India (on going)	Increase presence in the region targeting regional unmet medical needs
Johnson & Johnson	Purchased Pfizer's Consumer Healthcare department (2006)	Continued focus on diversification
Norvadis	Agreement to acquire an 85% stake in the Chinese vaccines company (11/2009)	Strategic initiative to build a vaccines industry leader in this country and expand the Group's limited presence in this fast-growing market segment.
Bayer	Acquired the portfolio and OTC division of privately owned Sagmel Inc (2008)	Increase HealthCare sales and market share in the Commonwealth of Independent States

While there have been mergers in the past, the pace and frequency of these activities have increased over the past few years (see Chapter 5) as companies identify and try to create synergies for their R&D capabilities, improve their pipeline, and manufacturing efficiency and improve their marketing and sales processes. In some ways the actions listed above indicate a break from the past where partnerships, mergers and other forms of sharing rarely occurred and many tried to grow mostly from within.

The reality of the need for innovative products, services and new therapies are influencing and dictating the need for these changes. Companies are realizing that if they keep doing things the way they have always done them, they most likely will continue to get the same results, which have been on a downwards spiral of late, relative to the 1980s and 1990s.

The April 16, 2008 edition of **Piribo**, the online destination for business intelligence for the biotech and Pharmaceutical industry made the following points:

- The Pharmaceutical markets in India, China and Turkey are expected to grow the fastest among all the E7 nations.
- The E7 nations are expected to account for nearly half of the 6.99 Billion global populations in 2012.
- Cardiovascular, cancer and other chronic diseases have taken over communicable diseases as the biggest killers in these nations.
- The Pharmaceutical market in most of these regions is still dominated by acute therapies, but with the growth rate of chronic therapies far exceeding that of acute therapies, the therapy mix of the market will be much different in the next five years from what it is today.

Many companies have made the first step of recognizing that there is a need to change. The problem however comes with ensuring that the proper due diligence is done and the right decisions are made based on their specific situation. Changing bad practices and adapting the behaviors necessary for success is also a very big challenge. The

industry is very complex and as can be seen in Table 1. Many companies are starting to make changes that they think will work better to prepare them for the future. The headlines referenced below shows that a healthy debate is on going regarding what is the best approach for the long term viability of the industry.

Andrew Jack, a multiple award winning journalist has been writing for the Financial Times since 1990, specializing in health and pharmaceuticals since 2004. In the March 12, 2009 edition of the Financial Times article titled, "Pharmas try different routes to survive' Andrew Jack wrote, "Rarely in the field of pharmaceuticals have so many companies adopted such varied strategies in order to survive the intensifying structural pressures in their industry"

He then goes on to describe what he sees as the as the three main approaches namely;

1: Acquisitions like the Pfizer and Merck examples above

2: Specialization by companies like Shire and AstraZeneca that previously concentrated on 'small molecules' with limited benefits and

3: Geographical Diversification as mentioned above by GlaxoSmithKline and AstraZeneca.

In the January 31, 2010 edition Jack wrote. "Large pharmaceutical groups should abandon their own early stage drug development and switch to less costly licensing from biotech companies, according to a new analysis".

The views expressed below in the June 2, 2009 edition of Jack's article in the Financial Times is another good example of the disparate views and opinions on how the issues can be resolved:

> I have not seen value creation through pharmaceutical mergers in the past 10 years," says **Steve Arlington**, head of the pharma R&D practice at PwC, the professional services firm. "The industry has suffered from disruption through mergers, post-merger activity. Can big pharma become too big? You see a loss of leadership. The internal machine becomes very complex, and compliance overtakes leadership." But **Daniel Vasella**, chairman and chief executive of Novartis, who had an active role in the Swiss company's creation through the merger of Ciba-Geigy and Sandoz in 1996, as well as several big takeovers since, is more positive. He argues that some companies might have been in a far worse shape if they had not combined. "An industry which has mounting pressure has a tendency to consolidate," he says. "It's a normal process. We have not yet reached the point of lethal size which is destructive.

In the February 12, 2010 article of Business Week, Fred Hassan, the former CEO of Schering Plough before the merger with Merck is quoted as saying:

> "Large drugmakers will need to merge in order to fund expensive, complex areas of research, such as Alzheimer's disease, Hassan said today in an interview on Bloomberg TV. Smaller companies also will be forced to sell themselves as they run out of cash in the tight credit markets, he said. "One reason deals are necessary is because the innovation investments are becoming larger and larger and it makes it easier when people can combine their resources to make the big, deep bets that you need to make for difficult diseases," Hassan said. "That is why you are going to see more of these deals."

These are just a small sample of the views, opinions and recommendations that can be found daily in online, television shows Pharma industry trade magazines, books and articles submitted by well known and knowledgeable 'experts'. From the research two things are very clear, one, the issues are very real and companies need to act and two, there is not one magic solution that is guaranteed to work.

The January 11, 2010 edition of the Fierce Pharma newsletter carried the following statement:

> "Think the Pharma mega merger is done ... over ... finito? Think again. Some analysts and money men are saying that the drug industry is still ripe for consolidation. After all, no one company has more than 8 percent of the global

> market for prescription drugs. And given that market shares are in the single digits, says noted venture capitalist G. Steven Burrill of Burrill & Co., "That would generally indicate that we have a ways to go on consolidation." Yep, says Simon King, a senior analyst at Datamonitor. He told Chemical & Engineering News, "There's definitely a couple of large M&A events left in Big Pharma."

These and other such views and opinions make it apparent that regardless of what has happened in the past or is currently happening with mergers, diversification and other changes, the need to be able to strategize and execute on these plans is paramount for long term success.

The question then becomes, 'what can the industry do to attain a high degree of success in implementing the various commercial strategies being attempted'? The potential answers are many, broad in scope and range from the philosophical to the very scientific and technical approaches. It involves moving cautiously and deliberately and at the same time making decisions quickly to capitalize on opportunities when they present themselves.

At the organizational level, companies also need to revisit the way they interact with government agencies, insurance companies, physicians and patients who as their main stakeholders collectively dictate their long term profitability, viability and existence.

CHAPTER 3

INTERVIEW SUMMARY

While it was important to do extensive industry research to better understand the challenges being faced as well as the response by both individual companies and the industry, additional work was done to gather information by interviewing professionals with extensive Pharma industry experience as well as marketing and academic expertise. The sample size was limited, 6 interviewees (see appendix A), representing over 140 years of collective experience with knowledge and expertise in Marketing, Sales, Research and Development, Consulting, Academia and Business Development at executive level.

The responses to the questions (Appendix B) showed that there was agreement with the view that the current business model was not working. While there was acknowledgement that it all starts with the pipeline, the collective responses indicated that there were many other factors that contributed to the problems being faced by big Pharma. These factors include, ineffective product lifecycle management, ineffective selling models resulting in limited access and usage, ineffective articulation of the Pharma value proposition and lack of creativity and innovation in providing the medicines and services to meet the growing and diverse unmet medical needs of society.

The table below summarizes the responses with the number of similar answers indicated in the parentheses. The responses are not verbatim but represent the main points expressed using the 'affinity diagram' process approach.

Table 2 – Results of Interview on the Pharma Industry

Changes in Pharma over the last 5-10 years	**Commercial Issues/Experience**	**Companies Need to Address Commercially**	**Commercial Imperatives**
Less blockbuster drugs being approved (6)	Limited access to doctors via sales reps (4)	Lack of diversity in the pipeline/ therapeutic areas targeted (5)	Develop global strategies specific to targeted regions e.g. Emerging Markets (4)
Healthcare reimbursement and issues have become more visible (4)	**More regulatory focus driven, much driven by politics and safety concerns (4)**	Perception that they are not focused on the patients (2)	**Assess and address unmet needs (4)**
More market share being captured by generic drugs (3)	Shrinking pipeline resulting in reduced number of products to market (3)	Ineffective, inflexible selling model (3)	Develop new/better go to market models (3)
More consolidation; e.g. (Mergers and Acquisitions) M&A (5)	Increased 'consumerism' - more demands - price pressure (3)	Lack of creativity and innovation (3)	***Effectively implement business and culture changes after M & A (4)***
Flat to declining sales (2)	Commercial model is 'dead' - ineffective - value not articulated (2)	Perception of arrogance by many stakeholders - doctors, patients, policy makers (3)	Communicate more clearly and openly with customers (2)
Higher presence of biotech companies (2)	Too much focus on blockbuster drugs for commercial success (3)	Effectively communicate value proposition (3)	***Make M&A and partnerships strategic and focused (5)***

Note***:*** Conducted to gain additional Pharma industry perspectives. Sample size= 6 interviews; parenthetic numbers indicate frequency of mentions

While it would not be prudent to draw any absolute conclusions from such a limited group of participants, it is clear from the interview participants agree with most of the literature in the various books, newspapers, magazines and online publications referenced. It would be very hard to find an informed Pharma professionals or industry

analysts who would disagree with the findings above based on all that is has happened over the past few years.. The news, articles and even Wall Street discuss these happenings almost daily and of course, there is no shortage of proposed solutions on ways to fix the issues.

What may be more difficult is to find people who will agree on any single approach to rectify the problem. It was interesting to note that most of the respondents saw the competition from generic drug companies as a drain on the big Pharma revenue base, but no one suggested focusing the efforts at taking back market share from the generic companies once the patents have expired as a strategy. Instead, the views expressed suggested that big Pharma is in control of its destiny, and the focus should be on things like, creating innovative medicines, diversifying the product and service portfolio and fixing the ineffective business and selling models.

With the Pharma industry being very complex, from the research and development of a molecule to the administering of the prescribed drug, there was no consensus on the best way to fix the commercial issues listed in the research or the interviews. Each organization will need to assess its situation based on all the factors such as history, culture, areas of competence, business models etc, which are too many to be covered in this capstone thesis.

The approach proposed in the next few chapters should provide some valuable insights into how organizations can take the initial steps to incorporate some valuable tools and processes to address the very daunting task facing each and every organization in the industry. Chapter 4 will provide some details on how mergers and acquisitions have been approached and performed in recent years.

CHAPTER 4

OVERVIEW – PAST MERGERS AND ACQUISITIONS

Most organizations look to mergers and acquisitions (M&A) and other such partnerships as the one of their first option to addressing the problems they face. The big Pharma companies look to the smaller companies and biotech to provide competences or additional resources to help spur R&D as well as Marketing and Sales (M&S) growth, and the smaller companies in turn get much needed funding to continue their work, either as partners or as a part of the larger company.

In a study, *Big Pharma Mega Mergers 1995 – 2014* published in December 2009, Datamonitor classified four M&A growth strategies (see Table 3).

Table 3 - Grouping of Big Pharma Companies by M&A Growth Strategy (adapted from Datamoniter)

Four Classes of M& A Strategy			
Buy Growth Companies	Buy Scale Companies	Multi M&A Companies	Organic Companies
Roche-Genentech Johnson & Johnson Abbott-Solvay	Merck-Schering-Plough GlaxoSmithKline Sanofi Aventis AstraZeneca Bayer AG	Pfizer-Wyeth Novartis	Eli Lilly Bristol-Myers Squibb

1. Buy Growth Companies– activity primarily aimed at increasing the growth of prescription sales
2. Buy Scale Companies – activity to increase product pipeline, R&D, M&S etc.
3. Multi M&A Companies – employ two or more of the strategies
4. Organic Growth Companies – avoid M&A as a core strategy

The goal is to take a look at examples of M&As that have occurred and to provide some

perspectives on how each combined company performed. It is not meant to be an in-depth study of the various kinds of M&As (see Table 4, *(adapted from Big Pharma Mega Mergers 1995–2014, Page 13)*

Table 4 – M&A Overview 1995-2014

Year	**Acquirer**	**Target**	**Value($bn)**	**Combined Rx Sales ($bn)**
1996	Ciba-Geigy	Sandoz	36.0bn	14.4bn
1997	Roche	Boehringer Mannheim	11.0bn	11.9bn
1999	Astra	Zeneca	37.7bn	14.8bn
	Sanofi	Synthelabo	n/a	7.9bn
	Johnson & Johnson	Centocor	4.9bn	12.0bn
2000	Pfizer	Warner-Lambert	90.0bn	22.6bn
	Glaxo Wellcome	SmithKline Beecham	85.3bn	28.6bn
	Abbott	Knoll	6.9bn	6.5bn
2001	Johnson & Johnson	Alza	12.3bn	14.9bn
	Bristol-Myers Squibb	Dupont	7.8bn	12.9bn
2003	Pfizer	Pharmacia	60.0bn	46.1bn
2004	Sanofi	Aventis	82.0bn	38.2bn
2005	Novartis	Hexal	8.3bn	25.0bn
2006	Novartis	Chiron	5.1bn	29.5bn
	Bayer	Schering	24.9bn	
2007	AstraZeneca	MedIumme	15.6bn	30.7bn
2008	Eli Lilly	ImClone	6.5bn	18.8bn
2009	Roche	Genentech	46.9bn	36.1bn
	Pfizer	Wyeth	68bn	60.0bn
	Merck & Co.	Schering-Plough	41.1bn	41.9bn
	Abbott	Solvay	6.6bn	19.8bn
2010	Novartis	Alcon	TBC	43.0bn

Snapshot of M&A Results

The performance of the combined companies was assessed using a variety of financial measures such as:

- Profit margin (Earnings Before Interest and Taxes/total revenues)
- Capital turnover (total revenues/capital employed)
- Return on capital employed (EBIT/capital employed)
- Market capitalization

Of the 22 transactions large scale (large scale = valued above $5 billion) M&A activity studied Datamonitor found that only 3 delivered fast growth performance over the next 5 year period. The study results had the following observations, "Only three M&A events have delivered fast growth performance over subsequent five year period"

- Only the small-sized acquisitions have delivered a subsequent fast sales growth performance over the next five years (Centocor, Knoll and Genentech)
- No big or medium sized acquisitions have contributed to fast sales growth performance in the next five-year period.
- Nearly all big and medium sized acquisitions have delivered a flat sales growth performance in the five year period after the merger
- Only 2 large scale acquisitions have provided medium sales growth performance in the 5 years after the merger (Warner-Lambert, acquired by Pfizer and Zeneca, acquired by Astra).

While only 3 of the large M&A organizations gained the targeted fast growth performance pace in the first 5 years, it is important to note that the small or flat growth in many ways stabilized their balance sheet in an environment where many of them are

facing patent expiry over the next few years as the so called 'patent cliff' looms. This is seen as relative success to many because without this small growth many companies would have had a steep decline in growth as their branded products lost patent protection.

> Generally speaking, however, big Pharma companies seem to be playing "follow the leader" too much, says Wharton management professor Saikat Chaudhuri whose work focuses on mergers and acquisitions. "They don't do a good job of portfolio management. They tend to all go after the same things. They tend to be conservative and place their [M&A] bets on [a narrow range] of drugs." Knowledge@ Wharton February 3, 2010).

The current (spring 2010) healthcare situations will continue to impact the companies as the after effects of the recent recession continue to reverberate around the world. This is truly a global economy and the business environment continues to evolve even as companies continue to implement new approaches to improve their product pipeline and look for new patients and markets to serve. While doing this they need to do rigorous business assessments to ensure that their strategies are financially sound, informed by strong portfolio management to target areas where they can provide novel medicines in therapeutic areas not addressed, establish rigorous process improvement to ensure that they maintain and improve their operations to gain efficiency and minimize safety issues and institute comprehensive risk management in almost everything they do.

Additionally, the one area that should not be underestimated is the effort it will require to integrate companies after a merger. They will also need to setup organizations to make the partnerships successful and do the due diligence to ensure that they are able to operate and conduct business in countries where business and cultural norms are far different their current experiences.

CHAPTER 5

LIMITED APPROVAL OF NEW PRODUCTS (NCE)

To address the limited approval of new products companies need to continue to look for ways to discover and develop new medicines in different therapeutic classes while effectively managing and optimizing the product life cycle for current products. This requires investments not just in R&D but also in market research and other areas to ensure that the molecules entering the pipeline are included in their strategic plans. It also means the decisions need to be made to take advantage of the value of molecules in the pipeline that do not align with the strategy, but may be of value to other organizations. This may involve exploring different kind engagement with smaller Pharma companies, generic drug makers, biotech companies as well as competitors who may be better able to take advantage of the value already created in the early stage R&D and integrate them in their pipeline based on their strategies.

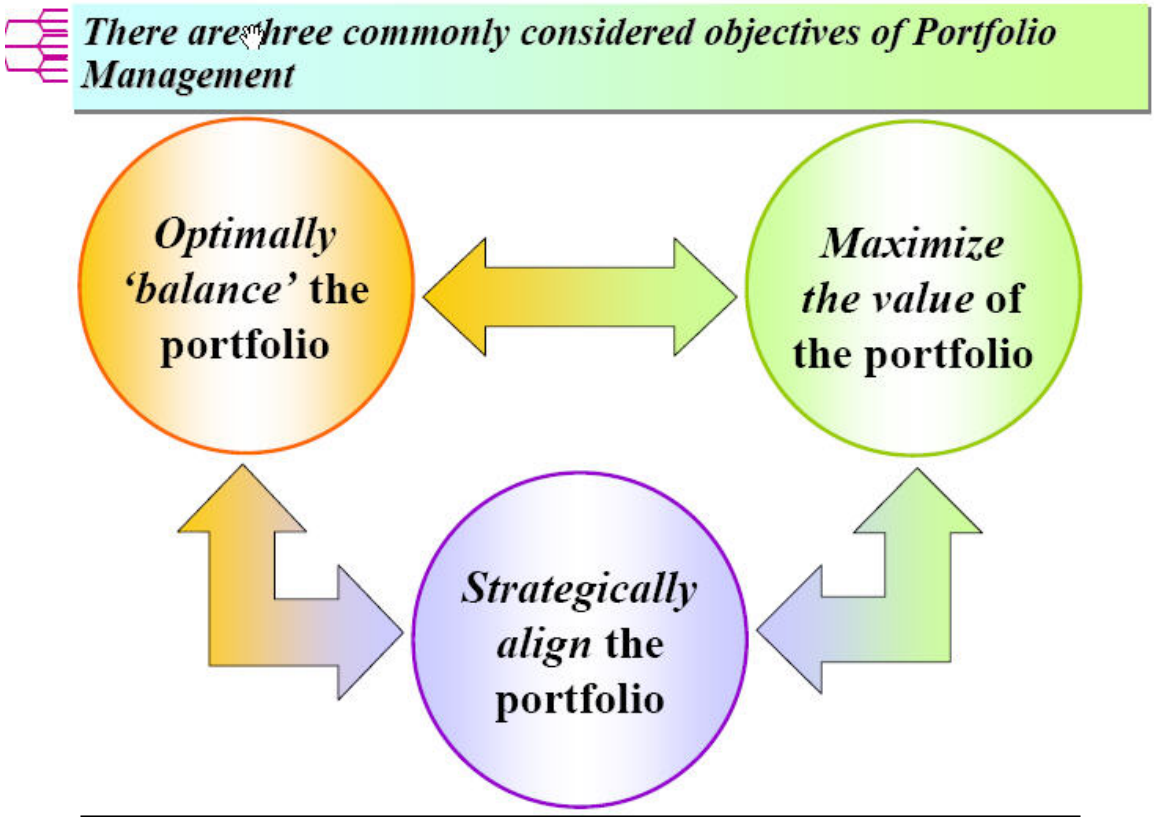
Portfolio Management

One discipline taught in Organizational Dynamics that would be useful in helping companies do a proper assessment of their business model is Portfolio Management. For the purposes of this paper portfolio management will be defined as "the active management of a collection of assets whose consolidated purpose is to aid in the attainment of one or more organizational/enterprise goals under constrained resource conditions" (Bayney 2007).

With limited resources being available to them, companies need to prioritize their portfolio of products and where they have areas that align with their strategy, optimize

the molecules in the pipeline and maximize the overall value contained in the portfolio (see Figure 9).

Figure 9 – Portfolio Management Objectives (adapted from Bayney 2007)



For Pharma companies a big part of this process will include looking at areas where there are opportunities to address un-met needs. An example of the kind of change needed in the industry going forward was the announcement on February 23, 2010 of the formation of the Asian Cancer Research Group Inc., (ACRG) by three major Pharma companies, Eli Lilly, Merck & Co. and Pfizer. The objective of this independent not-for-profit entity is to speed up the early stage R&D and therefore the treatment for patients affected with the most commonly diagnosed cancers in Asia.

If the ACRG lives up to it potential, (and that will be very challenging by virtue of having to overcome all the issues of change management, culture and integration just

to name a few things) there is a possibility that it can have a positive impact on all the issues listed in chapter 1. This represents work in just one disease area (oncology), but has the potential to significantly decrease the amount of spending if each company did it alone ($335 million in the pre-clinical phase) as well as increase the potential for early successes because of the collaboration and sharing of expertise and experience. It can also help with the Emerging Market Strategy because the types of cancers found in Asia may be different than those currently being addressed in the US and Europe because of demographic, hereditary, genetic, environmental and other factors. Finally it could serve as a useful model for future collaborations across the industry if it is successful along with some of the steps outlined in Table 5.

Table 5 - Key Steps to Address Limited Approval of New

Action	**Intent**
1. Develop strategy and determine therapeutic areas of focus	Sharpen focus and make strategic and communicate long term business goals
2. Assess current pipeline or molecules and medicines and determine where they align with the strategy	Make informed portfolio decision based on strategy, resources available and sound business cases
3. Establish a process to augment portfolio elements that align with the strategic therapeutic areas by forming partnerships or establishing business relationships with entities conducting preclinical studies	Minimize upfront costs and mitigate R&D risks by investing in late stage development from other organizations.
4. Divest valuable pipeline elements that do not align with the strategic therapeutic areas of focus	Maximize benefits from R&D efforts already expended.
5. Update and improve where possible all processes in the product life cycle from basic R&D through product approval	Look for opportunities to optimize the portfolio by increasing the speed of R&D, improve safety and reduce operational costs
6. Invest time and effort to understand and plan for the organizational and cultural dynamics that can lead to failure even if the science and technology works as planned	Avoid the mistake many companies have made in not understanding and addressing these critical areas

CHAPTER 6

INCREASED GENERIC COMPETITION

The February 25, 2010 report by Bloomberg has an article in which Eli Lilly's CEO John Lechleiter is quoted as saying "increasing the efficiency and speed of developing innovative products is the company's key to offset an anticipated $10-billion loss in annual sales due to generic competition by the end of 2016". The executive remarked that his and the company's response "has to be, 'Where do we find and how do we bring forth new innovation as quickly and cost-effectively as possible?' That's what we're working on." Many companies in the industry are modifying their strategies in response to the challenges they face and as is the case with most things, planning and executing these strategies effectively will be critical.

Generic drugs are here to stay, and many people believe that they play a critical role in making patient care more affordable and are just as effective. From a commercial standpoint there may be many ways that big Pharma companies can benefit from establishing different levels of partnerships with generic companies or even establishing their own generic drug businesses, especially in countries where their branded products may not have a presence. This is not to suggest going away from the model of trying to develop blockbuster drugs, especially in areas where there are untreated diseases. It is suggesting that diversifying their business models in a way that addresses therapeutic areas that have not been addressed with the added benefit of spreading their business opportunities and risks.

To do this will require developing a different mindset with regards to how they operate with the current and future environment. This may include embracing the role that generic drugs can plan in the Pharma ecosystem and taking advantage of the opportunities this presents as seen below in Table 6.

Table 6 - Key Steps to Address Increased Generic Competition

Action	Intent
1. Assess the current product portfolio and determine how to maximize the value by looking at new markets, seeking additional indications that can benefit patients and the company's bottom line	Focus on lifecycle management and develop standard processes and tools to make this a part of the organization functions under normal operating conditions.
2. Revisit the business model and look for opportunities to partner with existing generic drug makers to ensure that patient safety is impacted because of differences between the brand and generic drug	Maintain patient safety and develop and maintain brand loyalty
3. Assess business model and look for areas where establishing a generic business through M&A or organic growth maybe beneficial. This could be especially important in developing countries where there is currently little or no availability and accessibility of cutting edge medicines	Address un-met medical needs, enlarge the global business footprint and diversify sources of revenue
4. Invest more in biologic therapies	Broaden potential sources of treatments for patient care

CHAPTER 7

REGULATORY CHANGES AND THE ASSOCIATED POLITICAL IMPACT

All the factors outlined in chapter 1 are very important, but the issue of regulatory changes and the associated political fallout has one of the biggest impacts on big Pharma companies because this is the final hurdle companies have to overcome to get their medicines to patients after investing hundreds of millions of dollars.

In the recent years many companies have embarked on a process to implement what has been called 'New Commercial Models', which is basically changing the way they interact with all their stakeholders and customers including governments and regulatory agencies, doctors, patients and other caregivers. While a big aspect of this is focused on the marketing and sales of products, there is also a component that tries to show improved openness and sharing with agencies, especially in the areas of transparency on product efficacy and safety. This is not only practical, but it also has a political aspect in trying to show good faith and a sense of partnership with the agencies.

There is also more emphasis on stemming the flow of 'me too' products being approved to encourage or even force Pharma companies to be more innovative and invest in therapeutic and disease areas where medicines and healthcare solutions are lacking. This is an area where companies could really begin to add value to agencies like the FDA by provide technological help in looking for ways to assess safety and efficacy concerns in addition to being more open and therefore develop a more trusting working relationship.

Big Pharma companies have for a long time been characterized as big spending, greedy and solely motivated by profit, especially when there are discussions about the

price of prescription medicines. This has led to some restrictions being put on many marketing and sales activities, especially where it pertains to sales representatives giving gifts and other valuables to physicians and other prescribe the medicines. Some companies have even made the extra step of disclosing the amount of money given to subject matter experts and other people they engage to promote, sponsor or discuss their products.

In the current and most likely future environment, these companies will have to improve and help shape the way they are perceived, and bring to the front the good work they are doing not just in producing pharmaceuticals, but also in other areas that benefit society and the environment.

Big Pharma companies have for years been involved in philanthropic and other human causes that benefit the wider society. Examples of this include Merck's efforts to help cure River Blindness in some parts of Africa, Latin America and the Middle East, and GlaxoSmithKline's efforts to eliminate Lymphatic Filariasis in tropical countries. These and other like contributions should not directly influence regulation, but in a world where perception is reality, the political benefit and goodwill from society can be immeasurable. Table 7 describes some of the key steps that need to be taken to start to reverse the negative perceptions.

Table 7 –Key Steps to Address Regulatory Changes and the Associated Political Impact

Action	Intent
1. Streamline portfolio and focus efforts on new and novel medicines that will meet the needs not currently being addressed by existing treatments, e.g. Alzheimer's disease	Make targeted investments in areas that helps advance the treatment of diseases not currently being addressed. This also demonstrates the behaviors that regulatory agencies, healthcare providers and patients want to see
2. Develop a process or standard to clearly and transparently communicate product safety risks and efficacy to regulatory agencies	Re-establish a working relationship with these stakeholders built on trust and openness
3. Continue to seek ways to demonstrate the value of the medicines to healthcare professionals, other caregivers and patients	Re-establish the value add and trust with these stakeholders who have significant political and advocacy standing
4: Partner with the FDA and regulatory agencies to use technology to make the approval process more efficient leading to quicker approval as well as earlier discovery of risk and safety issues	Make the process better by identifying pass or fail indications so the 'wait' period for valuable resources can be decreased

CHAPTER 8

THE EMERGING MARKETS (CHANGING DISEASE PATTERNS, PATIENTS DEMOGRAPHICS)

Of the four issues focused on in this paper, taking on the opportunities and threats associated with doing business in the Emerging Markets and addressing issues such as changing disease patterns and patient demographics may be the issue with the most uncertainties and intricacies, even when considering the odds of a molecule becoming a successful medicine. While the Emerging Markets present vast and untapped areas for Pharmaceutical companies to explore, there is also the uncertainty and potential risk that need to be considered when contemplating the level of investment that would be required to develop and establish a long term and sustainable business.

With the slow growth in revenue in the US compounded by the recent global economic downturn, Pharma companies have been making attempts to establish a presence in the so called Emerging Markets (E7 in Chapter 1). They are making this decision because they currently do most of their business in the US and other developed countries, primarily in Europe. In many ways this represents the new frontier for these companies. This needs to be approached in the same way that a company would approach any new venture, with caution and the right amount of due diligence to maximize the potential opportunities and minimize the threats. One strategy would be to use the approach of a SWOT analysis. A few examples of the opportunities presented are:

1. Rapidly growing economies and populations
2. Opportunities to learn more about Eastern Medicines and to see where they can inform or augment Western Medicine to meet patient need

3. Expansion of healthcare infrastructure, systems and to deliver access to drugs.
4. More people with disposable income to spend on medicine.
5. Changing medicinal preferences from low cost generic to branded medicine when economies of scale can be realized (new concept)

The threats associated with including the Emerging Markets as a strategy for revenue growth include:

1. Limited knowledge of the markets and culture. This could lead to companies creating serious cultural and business transgressions leading to unfavorable perceptions of their brands.
2. Political instability in some regions that could put huge investments in jeopardy when there is a change in regime.
3. Difference in laws and the ways they are interpreted and implemented.
4. Too much dependence on the countries in the Emerging Markets leading to a lack of focus on the developed markets which still provide the majority of the revenue and stability.
5. Lack of acceptance of the medicines by a broad section of the targeted populations resulting in unrealized growth.

This is not just about the research and development. It is also about understanding the medicinal needs of the people, the culture, way of doing business and developing a partnership with these region and seeing and treating them as equals, and not just as revenue potential.

If this is done right, Big Pharma companies will benefit greatly not just in terms of financial profits, but just as important they could potential reshape some of the

negative perceptions by addressing the medicinal needs in areas where the current treatment is not enough. Table 8 details some key steps to follow to embark on the journey of winning in the Emerging Markets.

Table 8 - Opportunities in the Emerging Markets (Changing Disease Patterns, Patients Demographics)

Action	Intent
1. Take the time to assess the medicinal needs of the people in the regions and countries they want to do business in. Do not just try to introduce products to other people just to find a source of additional income	Develop the business based on the needs of the people in the Emerging market as well as the business need of the Pharma company
2. Make strategic choices in regions, countries to invest in based on thorough research and analysis of the opportunities and threats.	Doing the due diligence to ensure that there is a fit for the individual companies
3. Partner with regulatory authorities in the targeted countries in the Emerging Markets (China, India, Brazil etc) to establish guidelines for safety and efficacy targets.	Engage with this key stakeholder in the regions to create world class standards that will create a solid base for future work built on the best technology and knowledge developed over decades.
4. Invest in existing companies (small Pharma, generics biotech) to learn about the business environment, build R&D, manufacturing, supply chain, marketing and sales infrastructure	Demonstrate long term commitment, establish relationships and build trust
5. Develop an organization staffed and trained to support the execution of the strategy. In addition to scientific and business areas this would include investing or acquiring competence in areas like Change Management, Integration Management and other necessary skill-sets necessary to deal with the dynamics of a growing and changing organization	Ensure in addition to the normal functional areas, the need for the 'softer skills' are understood and acquired or developed

CHAPTER 9

LONG TERM AND SHORT TERM RECOMMENDATIONS

In the 1980s and 1990s, Pharma companies enjoyed very profitable years because of the many breakthroughs in medicines, high product margins and for many years, a favorable and growing global economy. That is no longer the case, and to succeed now and in the future they have to look for new ways and areas of growth as well as look at their operating costs and make efforts to bring them in line with their new reality. The quick and obvious choice that many companies make is to do things like reducing R&D, sales headcount, marketing and promotional spending, consolidate manufacturing infrastructure and look for M&A opportunities as discussed in previous chapters.

The reduction in headcount can bring limited savings but that is not by itself a long term solution that supports a growth strategy. Many of the suggestions made in the previous chapters can be successful, but they will take time because the Pharm industry is a very complex one. Reprioritizing the pipeline and determining the portfolio of therapeutic areas on which focus on will take time. Setting up different business models to capitalize on the benefits of generic partnership and getting into that business will take time. Changing the perception and realizing the benefits of working more in partnership with regulatory agencies and other stakeholders will take time, and getting to understand and engage in business in the Emerging Markets is also long term proposition.

Looking at the current operations and finding ways to be more efficient, eliminate redundancies, limit health and safety risks in all areas from R&D through sales and marketing has the potential to save companies millions of dollars. The rest of this chapter will take a look at ways in which process improvement, tied to business outcomes, can

help to put companies in a better footing for their business. This is not just doing random acts or process improvement or coming up with process improvements that do not translate to the bottom line. It is taking a look at all aspects of the operations and seeing where improvements can be made in addition to planning to address the problems identified.

Short Term Fixes based on Quality/Quality Improvement

> Genzyme shares fell 22 percent in the last 12 months as the company struggled with drug shortages stemming from a virus contamination at its main manufacturing plant in Boston (Bloomberg February 22, 2010).
>
> Eli Lilly has received an FDA warning letter for quality issues in the manufacturing of Humalog at its Carolina, Puerto Rico facility. Based upon inspections last year, FDA cited the facility for faulty API test methods (PharmaManufacturing.com February 25, 2010)

The headlines above are just a few areas where Pharma companies are hemorrhaging significant amount of money and development potential. The loss is not just in terms of the actual dollars lost or the resources tied up, but it also includes the opportunity cost for the areas where these could have been invested. Process improvement is a tool, and like any tool its effectiveness and potential is best realized if it is applied correctly, and aimed at helping the organization's operations and ultimately the bottom line.

The Pharma industry could also learn from other industries. The history of the consumer electronics industry is well known, with the rise and subsequent decline of companies like RCA and others that initially had leading research and development

capabilities but at some point lost out to competition because of their inability to respond to the changing market environment.

There are many reasons that could be cited for the shift in leadership in the consumer electronics and computer hardware development from US companies to companies in Asia, particularly Japan, and at the top of the list would be the quality improvement or process improvement movement in addition to the lower cost of labor. Process and quality improvement had many leaders like Dr. W. Homer Sarasohn and Dr. W. Edwards Demming who were some of the main contributors to teaching the Japanese executives and workers quality management.

The turnaround attributed to post war Japan is well documented, but for the purposes of the issues being faced by the Pharma industry today what is important to note is that by changing out dated and inefficient ways of doing business, the Japanese electronic industry went from being insignificant to the United States industry post World War II to being world leaders by the 1990s.

The same parallel is true for the Japanese automobile industry where quality was their biggest selling point until the recent (2009 & 2010) escalation of the issues with Toyota cars. Not surprisingly, part of the explanation given for the recent issues was the extensive focus on revenue growth at the expense of quality. Only time will tell what the long term impact will be on Toyota, but it is safe to assume that this will cause them losses in the hundreds of millions if not billions of dollars in addition to placing the onus on them to rebuild their reputation for safe and reliable cars, which they had developed over a period of decades. The Pharma industry will hopefully learn from the mistakes made by Toyota as the try to reinvent themselves and their way of doing business.

Long Term Approach Based on an Understanding of the Issues Identified

It is very important that the current quality issues be addressed to help with reducing operational cost for the short and near term. Just as important is the need for Pharma companies to look ahead and to not make the mistake of focusing on revenue growth and expansion at the expense of quality. To do so would be short sighted and have the potential damaging their brand for a very long time. Below are some steps that can be taken to create a balance between the need to address the issues identified and maintaining and improving quality (see Table 9).

Table 9 - Process Steps to Address the Issues Faced by the Pharma Industry

Process Steps
1: Develop an understanding of the organization's high level strategy and therapeutic areas of focus
2: Develop a map of the Pharma industry value stream across the product life cycle (R&D through to Sales)
3: Develop a preliminary business case for decisions that have to be made regarding M&A and other partnerships and assess the cost of integration
4: Create a SIPOC for each area (e.g. R&D, Marketing etc) to see where there may be gaps or lack of alignment based on the organization's competence or capabilities
5: Make buy, build, acquire or partner decisions based on the need identified above as well as the organization's strategy and integration capabilities
6: Update the business case and financials and create an implementation and integration office to execute the strategy.

Each step is explained in the section that follows.

1: Develop an understanding of the organization's high level strategy and therapeutic areas of focus

This could help with addressing the objectives listed in the Commercial Imperatives column in the interview summary (Table 2), particularly where there is a need to decide on and focus on the long term strategy. This has to be done at the highest

levels of the organization and clearly cascaded and communicated throughout the organization. Tools that could be used to address this included Brain Storming, Affinity Diagram and Stakeholder Mapping. It could also be used to help with setting the direction based on the business and healthcare environment as well as the organization's current business, strengths and competencies.

2: Develop a map of the Pharma industry value stream across the product life cycle

The value stream map is a good tool for helping to understand all the components in a business, process, system or any entity that have some form of life cycle. In this case, a value stream map can be developed based on the 4 problem areas identified directly by the research and restated by the interview participants. The lifecycle below (Table 10) goes from the identification of a therapeutic area to focus on to the delivery of the product and services required to meet the patient need.

Table 10 - Example of One Representation of the Pharmaceutical Value Stream

Area of Focus	**Components Associated with this Proposed Product Lifecycle Value Stream**						
	Identify Therapeutic Opportunity	R&D	FDA & Compliance	Manufacturing & Production	Marketing	Sales	Services
Lack of NCE Approvals	High	High	Medium	Medium	Medium	Medium	Medium
Generic Competition	Medium	Low	Low	High	High	Medium	Medium
Regulatory Changes & Political Impact	Medium	Low	High	Low	Medium	Medium	Low
Emerging Markets	High	Medium	Low	High	Low	High	Medium

High = High correlation between the area of focus and the value stream components
Medium = medium co-relation area of focus and the value stream components
Low = Low co-relation between the area of focus and the value stream components

Note: The co-relations above are relative because it is recognized that as an industry all the factors are related in one or many different ways.

The value stream map above would be a good tool for helping the organization to decide on where to focus their resources and energies, based on their strategies and competencies. For example, if the Emerging Markets is the area in which a company was placing its strategic bet, the table above suggests that Identifying Therapeutic Opportunity, Manufacturing and Production and Sales should be the highest priority followed by R&D and Marketing. This value stream in this case would help to decide on relative importance of each component to achieving their objective.

3: Develop a preliminary business case for the decision that needs to be made regarding M&A and other partnerships and assess the cost of integration**.**

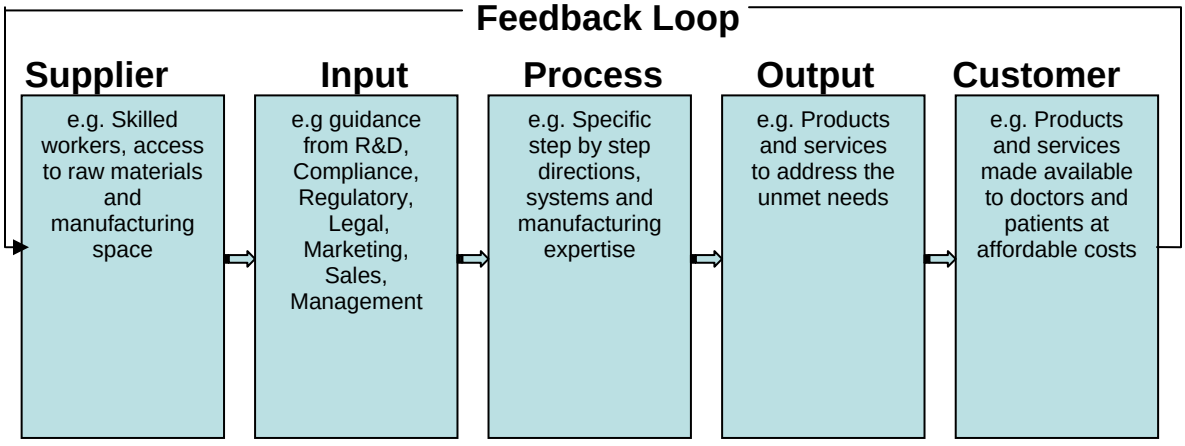
After making the strategic decision to focus on a particular therapeutic area, it is very important that the company creates a business case using the best information available, taking into consideration all the costs and expenses that will be associated implementing the strategy. In these situations GAAP (General Accepted Accounting Principles) are a good baseline for companies to use. It is also important to have a good understanding of the financial stability or not of companies that will be engaged in the proposed M&A or partnership. This is especially important when the business agreement is being done with entities or organizations that may be in countries that have different accounting, financial, quality, safety, legal and contracting rules and standards.

4: Create a SIPOC for each area (e.g. R&D, Marketing etc) to see where there may be gaps or lack of alignment based on the organization's competence or capabilities:

A SIPOC (Supplier Input Process Output Customer) diagram which is tool usually used as part of a Six Sigma process can be very useful in helping an organization dig deeper to better understand the details involved in a particular process or operation. As an example, this process could be used to address the R&D component that is a high priority in the area of Emerging Markets. This is a very good tool for getting to understand potential issues and hidden costs.

If a company is looking to invest in R&D in the Emerging Market, it is very important that they develop an understanding of where and how the resources, (human, capital and natural) will be acquired and deployed. Knowledge of local transportation access, laws, customs and politics is also very important to attain to be able to properly assess the feasibility of setting up operations in the targeted country and is critical for understanding supply chain considerations (see Figure 10).

Figure 10 - Example of a SIPOC (that could be created for the Manufacturing and Production Component to address Emerging Market Concerns)



The same process could be used in every component associated with the value stream map of the life cycle because taking a 'system approach' to assessing the suppliers, inputs, processes, outputs and customers can help to eliminate unwanted surprises and hidden costs or problems.

5: Make buy, build, acquire or partner decisions based on the need identified above as well as the organization's strategy and integration capabilities.

Once the proper assessment has been done using the value stream map to understand the key areas and priorities, the business case to determine the feasibility of the endeavor and the SIPOC to understand what is required in more details, the organization needs to decide on the best way to more forward.

Some of the decisions that have to be made in the Manufacturing and Production component to the value stream map to address the Emerging Market opportunities include;

1. Should manufacturing space be rented or purchased?
2. Should workers be recruited and trained locally or should they be brought in from other regions or countries?
3. Should all the production be done in-house or should certain aspects be subcontracted to local companies?
4. How will safety and compliance issues be addressed and should what impact will that have on downstream marketing and sales?

These are just a representational set of questions that will need to be addressed.

On one hand there has to be focus on creating the most efficient manufacturing and production process, but just as important is the need to recognize that from a political

and business standpoint, there may be a need to use local workers, contractors and respect customs that may not be the most efficient in order to be gain local acceptance and conduct business. The answers to these questions have to be answered and reflected in the business case and other assessments to ensure that these realities are reflected in the decisions being made.

6: Update the business case and financials and create an implementation and integration office to execute the strategy

With any business activity, doing the assessment and making the decision to implement the strategy are just the first steps. Strategies and solutions need to be well thought out and not done in isolation which could lead to implementing tactics which do not support or compliment each other or align with the strategy. In order to realize the targeted objectives, it will be necessary to setup the necessary organizational structures, programs and projects needed to meet the objectives. A system of checks and balances to monitor and control the process is also critical. Throughout the implementation process it will be necessary to maintain the financial rigor and due diligence needed to ensure that the decisions and investments made continue to make good business sense.

CHAPTER 10

CONCLUDING THOUGHTS

Observations

The issues outlined in the Pharma industry and the potential long term impacts are very real. It is a combination of the economic issues being faced globally as well as the industries inability to produce new products and services that meet the evolving needs of patients, current and future. If there is any doubt that companies are aware of the problems and are trying to make strategic and tactical moves to change, one only has to take a sampling of the headlines in Pharma magazine publications to get some perspectives. Below are the headlines captured from FiercePharma.com in just one week, that highlights some of the issues companies are facing as well as the actions they are taking to position themselves for future growth:

Astellas launches $3.5B bid for OSI (March 1, 2010)

California county sues GSK over Avandia (March 1, 2010)

AZ pitches social-media rules to FDA (March 2, 2010)

UK calls summit over medicine shortages (March 2, 2010)

Pfizer rejoins Patiopharm race with $4B bid (March 3, 2010)

Teva regains exclusivity on Merck meds (March 3, 2010)

FDA aims to step up criminal prosecutions (March 4, 2010)

How will new BMS chief replace $11B? (March 4, 2010)

Few pharmas to profit off CV growth (March 5, 2010)

GSK faces up to $6B Avandia liability (March 5, 2010)

The headlines clearly show that companies are not sitting back and waiting for things to change. Most are actively looking for ways to gain valuable assets as well as look for ways to engage with the FDA and deal with competition from generic drug makers. Companies also have to deal with the legal actions that often follow any reports or accusation of product risk or safety issues, again a big drain on their resources as well as revenue.

Research Summary

There is no magic solution that can address all the issues outlined in this thesis. The Pharma industry and individual companies will have to look deeply within themselves and make a conscious decision to change. Every industry has certain characteristics which tend to be more or less representational of the companies in the industry. In general big Pharma companies have grown up over the years from the mid 1970s to the early 2000s with the understanding that if they pour money into R&D and start with a large number of candidate molecules, at some point it will pay off with one or two major drugs from the batch.

The current realities no longer support that philosophy. The lack of approval of new and innovative products with very high patient value makes it hard for companies to realize the growth they had in earlier years. The proliferation of generic drug makers along with a slew of patents expiring means that the revenue stream for branded products can go from hundreds of millions of dollars to tens of millions of dollars or less in a matter of 6 months. The scrutiny and pressure from regulatory agencies to abide by higher safety standards minimize risks and prove greater efficacy means that more time, effort and money have to be invested in upgrading processes and infrastructure. Added to

that is the every present legal and political risks that have to be managed and mitigated whenever there are accusations or reports of product issues. Slower growth in the developed countries necessities looking at the opportunity to develop business and operations in the Emerging Markets, but along with these opportunities there are also significant threats and this is still an area in which most big Pharma companies have limited expertise.

Interview Recap

One common view expressed in the interviews conducted with the Pharma professionals was that the current Pharma model from research and development through marketing and sales is broken. This was very much in line with the results of the research. The interviewees were encouraged that there was evidence that some companies were changing and trying to add more value and me effective in some areas, but in general they felt that there was no organized or concerted effort being made to bring about the major changes that will be needed to turn the industry around. They felt that there is room for collaboration that can reduce operating cost and other industry costs and still have a place for healthy competition based on introducing innovative medicines to help with patient care meet the needs of stakeholders and shareholders at the same time. The Partnership between Eli Lilly, Merck and Pfizer will hopefully be a model for how this will be able to work.

Considerations

Chapters 5 through 9 outline some key steps that that companies can make in both the short and long term to make the changes necessary to be proactive and in some cases respond to the issues being faced in the industry. Not only is it important to identify the

right steps to do, it is also important to do these steps in the right way. In other words, in order to be successful, the first steps may be getting the required funding, skilled employees, processes, infrastructure and strategy from well meaning executives and senior managers. However, it is also very important to realize that making all these things work well together in order to achieve the desired results is not automatic.

The dynamics involved in getting an organization to functions at its best to achieve the targeted objectives is very complex, and has to be understood and planned for at every level. This will require global and regional understanding of history, cultures, beliefs, values and societal norms. At the country level it will require knowledge of the culture, politics, business and constitutional law, infrastructure, supply chain and the people. At the organizational level a lot of work has to be done to assess and understand not only what motivates and inspires creativity and productivity of the current employees, but also any employees that may become a part of the organization as a result of a M&A or other forms of partnerships. It would take significant effort in the areas of Change Management, Integration Management, Process Management, Portfolio Management, Program Management and Project Management to be able to plan and execute any strategy that is developed.

It would be possible to write a complete thesis on any one of the organizational topics listed above, referencing concepts like the theory of needs (Maslow), looking at what motivates individuals or how people behave as individuals versus in a group, organizational or country setting. It could also consider how people respond to threats and rewards, real or perceived. These thoughts are central to any work that would be needed to implement the changes needed for companies to make the shift from 'business

as usual' to a new way of thinking and functioning. The steps listed above assumes that the leaders of the companies not only have the skills, knowledge, experience, will and intelligence quotient (IQ) needed to make these changes, it also assumes that these leaders have the emotional intelligence quotient (EQ) needed to understand the psychological and sociological factors at play.

Conclusion

When looking at the industry from a global standpoint it is clear that there are opportunities to address un-met medical need in many therapeutic areas and regions of the world. It is also clear that with this very complex industry, making the changes necessary will not be easy, and it will not happen overnight. To be successful in the future Pharma companies will have to find ways to deliver the medicines and solutions needed to meet the diseases of today and the future. Companies need to find a way to make science and technology work with business needs in an efficient way to benefit all stakeholders. As companies embark on this journey, they need to devote as much time and effort to clearly communicate their strategies to employees, customers and other stakeholders, planning for change and structuring their organizations for success.

Many companies are well on the way to changing their organizational strategies as well as their operations to meet the challenges they face. Mergers and acquisitions and other forms of partnerships have been a big part of these changes, and their long term strategic impact and performance is still being played out so it is too early to draw conclusions. It is important for individual companies and the Pharma industry to listen to their stakeholders and spend time assessing their options, strategies and most importantly, understanding the long term needs of patients before they invest heavily in any particular

area. This will go a long way towards demonstrating that they are serious about meeting patient needs, and the stakeholders at every level will benefit as a result of these actions.

REFERENCES

Bayney, Richard (September 2007) ***Managing Project Portfolio***. DYNM 621

Bloomberg, Arlene Weintraub and Meg Tirrell (February 25, 2010). ***Lilly Chief Tests Drug Search to Offset Sales Loss***

Bloomberg, Lopatto, Elizabeth (February 22, 2010) ***Icahn Wants to Join Genzyme's Board, Bring Others***

Bloomberg, Pettypiece, Shannon (February 12, 2010). ***Former Schering CEO Hassan Sees More Deals Among Drugmakers***,

Congressional Budget Office (October 2006). ***Research and Development in the Pharmaceutical Industry***

DATAMONITOR (December 2009). ***2009 Pharmaceutical M&A Overview***

DATAMONITOR (December 2009). ***Big Pharma Mega Mergers 1995 - 2014***

IMS (October 24, 2008). IMS ***Pharmaceutical Market Forecast: New Reality for 2009***

Jack, Andrew (March 12, 2009). ***Pharma Split on Nature of Mergers as Kill or Cure***, Financial Times

Jack, Andrew (January 31, 2010). ***Big drug groups urged to buy in test products***, Financial Times

Knowledge@Wharton (February 3, 2010) ***Pharma is at pain to replace Blockbusters: Has it Found The Cure?***

PharmaManufacturing.com **(February 25, 2010)** ***Lilly Cited for Quality Issues in P.R. Humalog Facility***

Stanton, Tracy **(March 2, 2010)** ***Hedge Funds puts bucks behind Pfixer, FiercePharma***

Stanton, Tracy (February 17, 2010) ***Analysts cheer results from post-merger Merck,*** FiercePharma

Stankard, Martin F (2008). ***The Art and Science of Process Improvement***, *Context, Strategies and Tools*, Pages (10 – 35)

GLOSSARY

Affinity Diagram *– Tool that gathers large amounts of language date (opinions, ideas, issues) and place them into groupings or categories based on their natural relationships*

Big Pharma *– Top 10 global Pharmaceutical companies based on 2008 sales. Big Pharma is also used to describe companies with revenues in excess of $3 billion per year*

Blockbuster Drug *– a drug that achieves annual revenues of over US 1 billion dollars at a global level (Ref - Pharmaceutical Sector Inquiry, Preliminary Report (DG Competition Staff Working Paper),* 28 November 2008, page 17 (pdf, 1.95 MB

Commonwealth of Independent States *– A regional organization whose participating countries are former Soviet Republics formed during the breakup of the Soviet Union.*

EBIT (Earnings Before Interest Tax) *– Financial measure of a company's earning power from ongoing operations before interest payments and income taxes are deducted. It normally does not include income and expenses from unusual, non-recurring or discontinued activities.*

Emotional Intelligence Quotient (EQ) *– The ability, capacity, skill to perceive, assess and manage the emotions of one's self, others and groups*

Generally Accepted Accounting Principles (GAAP) *– The Americanized term used to refer to the standard framework of guidelines for financial accounting used in any given jurisdiction which are generally known as accounting standards*

IMS Health – *Company that provides pharmaceutical intelligence, information and consulting services to the healthcare market*

Lymphatic Filariasis *- a disfiguring disease prevalent in tropical and sub-tropical countries. Transmitted by mosquitoes, it can lead to severe swelling of the arms, legs, breasts and genitals and thickening of the skin.*

Patent Cliff *– Term to describe the loss of revenue of $140 billion in annual sales by 2016 as key product patents expire and the generic version enter the market. This is expected to get to its peak in 2011/2012 when name brand drugs like Pfizer's* ***Lipito****r, GlaxoSmithKline's* ***Advair,*** *Sanofi-Aventis and Bristol-Myer's* ***Plavix*** *and AstraZeneca's* ***Seroquel***

Mid sized pharma – *Pharmaceutical companies positioned 11 – 50 based on 2008 sales*

River Blindness *- River blindness is a debilitating disease that threatens the health and livelihood of more than 100 million people in parts of Africa, Latin America and the Middle East. Transmitted through the bite of black flies, river blindness causes intense itching and painful skin lesions, and it can eventually lead to the permanent loss of sight*

Small pharma *– Pharmaceutical companies positioned 51 – 150 based on 2008 sales*

SIPOC diagram - a tool used by a team to identify all relevant elements of a process improvement project before work begins. It helps define a complex project that may not be well scoped

APPENDIX A

CAPSTONE INTERVIEWEES

Name	**Title**	**Brief Summary of Experience**
Mr. Blair Gibson	Executive Director of Portfolio Strategy & Planning (Merck & Co.)	23 years in the Pharma industry with global experience in Portfolio Strategy and Planning, Product Launches and New Products Management
Dr. David Reibstein	Author, Consultant & Professor of Marketing (The Wharton School, University of Pennsylvania)	30 years experience as a professor of Marketing with major awards and publications. Extensive Global Consulting with major corporations
Garry Neil M.D.	Corporate VP, Corporate Office of Science and Technology (J&J Services Inc)	Broad experience in science, medicine and pharmaceutical development (18 years Pharma). Senior positions within J&J, most recently Group President, Johnson and Johnson Pharmaceutical Research and Development
Ms. Janet Keyser	Executive Director, Development Integration (Merck & Co.)	Responsible for integration of Transformational Change in Research Laboratories Division of Merck & Co., Various leadership positions in Clinical Quality Assuarance and Global Process Development (29 years experience)
Mr. Marvin Johnson	National Sales Director, Neuropsychiatry (Merck & Co.)	25 years experience in the Pharma industry in Marketing and Sales including Global Franchise Brand Leadership.
Mr. Michael Lombardo	Executive Director, Marketing Process Management (Merck & Co.)	19 years experience in the Pharma industry in Marketing and Sales including Global Franchise Brand Leadership and Process Management

APPENDIX B

CAPSTONE QUESTIONAIRE

1: In your opinion, how has 'Big Pharma' changed over the past 10 years?
2: What are the 5 top critical factors that have led to these changes and how would you rank them in terms of the impact they have caused? Rank each on a scale of 1 – 5 (with 1 being the highest impact and 5 being the lowest impact)
3: What are the top 3 to 5 commercial issues that companies need to resolve to ensure future success, and why? Please be specific and categorize the issues as short-term (1 to 3 years) or long-term (3 to 5 years).
4: What are the top 3 to 5 scientific (research and development driven) issues that companies need to resolve to ensure future success, and why? Please be specific and categorize the issues as short-term (1 to 3 years) or long-term (3 to 5 years).
5: How would you describe the 'Big Pharma's' strategic plan to increase innovation and productivity?
6: Why have most previous mega mergers failed to deliver long term benefits to buyers and shareholders and how do you think companies such as Pfizer and Merck will avoid repeating industry's past mistakes
7: Many companies are making strategic decisions to change their business models (R&D and commercial) by taking a variety of approaches for example, diversification, partnerships, mergers and acquisitions to name a few. What are the top 3 to 5 things that companies need to do now to ensure that the successful implementation of these strategies?
8: What approaches are 'Big Pharma' companies taking to manage merged/acquired portfolio of assets?
9: In once sentence, please explain the importance of the following for ensuring top line growth for 'Big Pharma?' ▪ R&D ▪ Marketing and Sales ▪ The Emerging Market/Globalization ▪ Demographics