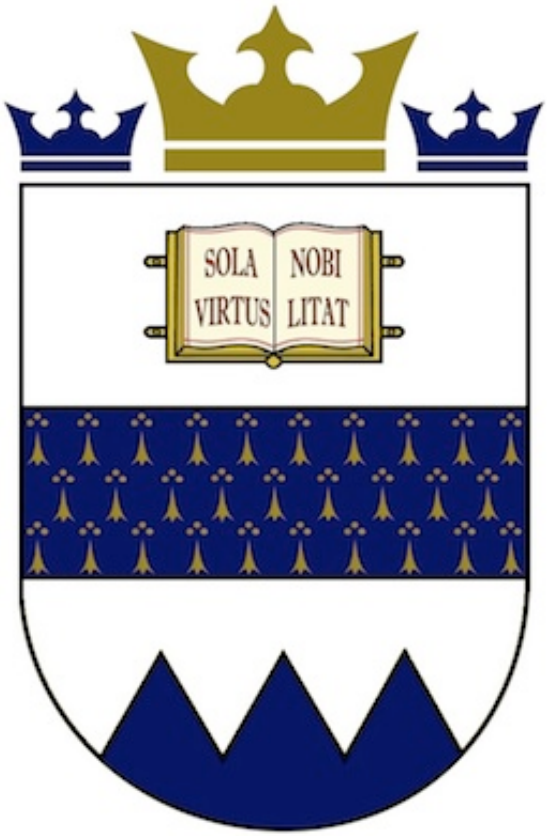


UGSM-Monarch Business School
Doctoral Research Plan

The Impact of Leading Regulatory Strategies on the First Cycle Approval of a New Drug Application in the USA

PROGRAM:	D.Phil. Business Research
SUBMISSION DATE:	08-July-2013
CANDIDATE:	Mr. Samrat Sisodia, MS, MBA.
PROPOSAL SUPERVISOR:	Dr. Ronald Movrich, Ph.D., J.D.
DISSERTATION SUPERVISOR:	Dr. Ronald Movrich, Ph.D., J.D

Final Draft For Approval Purposes

RESEARCH DOMAIN OVERVIEW

Approximately 100 million people die every year in the world. Of these an estimated 65 million people die due to various disease of which 25 million of those die due to incurable disease (WHO, 2013). Needless to say, the speedy approval and availability of potent new drugs to fight those diseases presents exciting possibilities worldwide for healthcare systems, doctors, and patients. New drug development has saved millions of lives globally and improved the quality of life for countless patients over the years (Papanicolaou, Skyes, & Mossialos, 2004). The focus of today's drug development is remarkably varied and has progressed significantly in comparison to a decade ago (Tonkens, 2005). Current government regulations and market expectations are vastly different; drug development today is more focused towards statistically proving the safety, efficacy, and quality (SEQ) of a drug rather than simply depending on its clinical effects (Wechsler, 2004). Over the years, the Food and Drug Administration (FDA) of the USA has revised regulations to establish conclusive evidence of SEQ before granting permission to commercialize a drug for human use (D.Pilling, 1999).

Drug discovery, research and development (R&D) is an extraordinarily complex and lengthy process which requires many interdisciplinary tasks and a large industrial base (Maglennon, 2012). A typical drug development program consists of four elimination phases: 1. drug candidate selection, 2. preclinical, 3. clinical, and 4. submission, review and approval (SRA) (Adams & Branter, 2006). These phases are commonly known as the "interphase drug development" and represent continuous evolution of drug candidates from bench chemistry to animal and human

trials. Upon completion of the first three elimination phases, drug companies prepare for the SRA phase by submitting a formal application to the FDA known as the New Drug Application (NDA) (Shane, 1992).

The success of the NDA is measured by the time required to obtain approval. The NDA approval times are usually categorized as: first, second and third cycle approval. These cycles represent the number of FDA review deficiencies and industry response cycles. All pharmaceutical companies thrive to secure the “first cycle approval” on an NDA in order to launch the product after the shortest possible FDA review time (Rockoff, 2013). Moreover, the first cycle approval of an NDA establishes confidence in investors and lends much needed credibility to the drug prescribers (Hoag, 2006).

Traditionally, the regulatory affairs (RA) department of drug companies lead the SRA phase but over time the RA departments have assumed the lead role in interphase drug development strategies (Gopinath, Bhadauria, Gunjan, & Insha, 2012). The change in the role of the RA departments was largely due to several FDA regulations which were issued within the past decade (GPO, 2012). These regulations required regulatory and scientific interpretation which led to the additional RA department responsibility for interpreting the regulations and defining the regulatory and scientific strategies for a drug development program (Getz & de Bruin, 2000). Surprisingly, even after having such a profound role in the success of a drug the impact of regulatory strategies on the drug approval process is not well researched nor thoroughly understood (D.Pilling, 1999).

Existing understanding of the impact of regulatory strategies on a successful drug development program is usually drawn from the summary basis of approval (SBA) published by the FDA or various pharmaceutical literature whose conclusions are largely anecdotal (Maglennon, 2012). Rockoff (2013) shows that leading regulatory strategies are not formally categorized and there is an apparent lack of clarity on the mechanism and degree of influence these leading regulatory strategies have on a successful drug development program. Therefore, understanding the various regulatory strategies and their effect on drug development programs would advance the domain knowledge both academically and professionally. Thus, the goal of the contemplated research is to meet the following four objectives:

1. To examine the role of the RA department on a successful drug development program;
2. To categorize the leading regulatory strategies applied during the drug development programs;
3. To understand the factors influencing the nature of regulatory strategies applied during the drug development program;
4. To generate a conceptual model or framework that assists in understanding the relationship between the types of regulatory strategies and the first cycle approval of an NDA in the USA.

Because this research does not appear to have been completed elsewhere the contemplated research will contribute original knowledge towards defining the types of leading regulatory strategies and understanding the impact of various leading strategies over the first cycle approval on an NDA. This will be acomplished through a triangualtion of data from the drug industry, leading academics and government regulatory agencies.

PROVISIONAL RESEARCH QUESTION

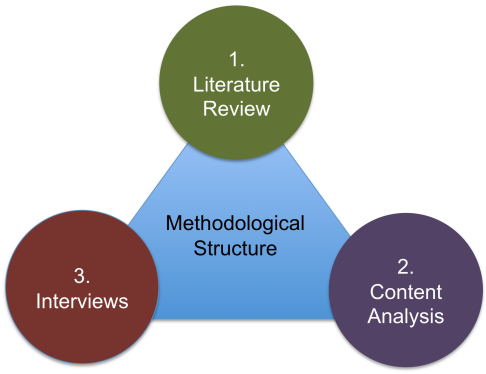
Given the above discourse, a provisional research question has been developed as follows:

> "What are the charactersitic of a new conceptual model or framework that maximizes the ability of pharamceutical companies to obtain first cycle approval on New Drug Applications within the USA?"

RESEARCH METHODOLOGY

Figure 1 shows that the aim of the contemplated research is to respond to the provisional research question by way of a triangulation of research data, being: 1. literature review of existing seminal academic authors (desk research); 2. content analysis of existing corporate data (desk research), and; 3. interviews with primary stake holders in industry (field research).

FIGURE 1
Methodological Structure
Triangulation of Data

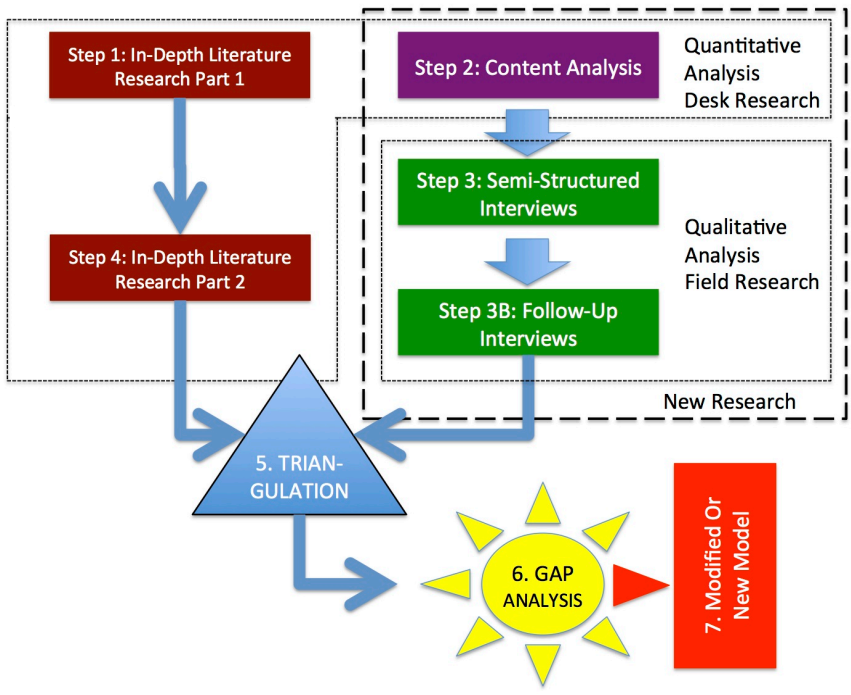


Source: UGSM-Monarch Business School Switzerland

Figure 2 illustrates the steps within the Monarch Standardized Research Process Flow that will be followed within the contemplated research, as:

1. **In-Depth Literature Review-Part 1:** In-depth review of the seminal authors within the study domain will be the first step completed in order to provide a solid academic foundation to the research.
2. **Content Analysis:** An analysis based on data obtained from annual reports, white papers, supporting commercial documents and other commercial data sources will be examined.

FIGURE 2
Monarch Standardized Research Process Flow



Source: UGSM-Monarch Business School Switzerland

3. **Two-Step Semi-Structured Interview Process:**

   Step 1. **Preliminary Interviews:** The development of preliminary interview questions will be informed by and synthesized from the

review of the literature and content analysis. Stakeholders to be interviewed will be industry participants considered knowledgeable with respect to the research at hand. A minimum sample of thirty (30) unique participants will be interviewed. Interviews will be held in person at a location amenable to the subjects and are expected to be approximately thirty (30) minutes in length. Telephone interviews will be used in the case that physical interviewing is impossible due to resource or time constraints. Interviews will be tape recorded unless objected to by the participant in which case manual notes will be taken.

Step 2. **Follow-Up Interviews:** of a more specific and narrow view informed by the first round of interviews, content analysis and literature review will be concluded with a smaller sub-set of 15 respondents obtained from the first round sample. These interviews will seek to uncover deeply held personal beliefs and understandings on the research subject that will further uncover important aspects in responding to the provisional research question.

4. **Step 4-In-Depth Literature Review-Part 2:** A second more in-depth literature research review will be completed to further refine the scope and consideration of the existing knowledge within the academic field to add more expertise and specificity to the research analysis.
5. **Step 5 & 6-Triangulation of the Data & Gap Analysis:** A triangulation of the data will be considered and analyzed in order to determine whether or not the

existing academic knowledge is congruent with the practical application of the field on a commercial basis. The result of this analysis should dictate whether or not a “Knowledge Gap” exists between the academic (theoretical) and the practical (applied) domains.

6. **Step 7-Development of New Model:** Building on the Gap Analysis a thorough analysis of the existing frameworks within the academic domain will be made. This analysis will inform whether or not the existing frameworks sufficiently address the requirement for practical application within the industry and whether or not they may be further improved or modified.

RESEARCH TIMELINE & BUDGET

TABLE 3
Provisional Research Timeline

		Year 1				Year 2				Year 3			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
PART A	Pre-Literature Review	■	■										
	Literature Review Part 1			■	■	■	■						
	Research Plan		■										
	Chapter 1			■									
	Chapter 2 & 3				■	■	■						
	Content Analysis				■								
		Official Submission of Chapters 1, 2, 3 and Slide Presentation To Obtain Authorization To Continue On To Field Research											
PART B	Interviews Part 1							■					
	Literature Review Part 2							■	■	■	■		
	Interviews Part 2										■		
	Data Analysis									■	■		
	Chapter 4, 5, 6									■	■		
	Manuscript Perfecting									■	■	■	
	Submission												■

Source: UGSM-Monarch Business School Switzerland

The contemplated research is expected to conclude over a 36 month period. A breakdown of the time allocation by the different phases of the research is outlined in Table 3 above.

TABLE 4
Provisional Research Budget

	In US Dollars
Conferences and Memberships	2,000
Hotel Accommodations	1,500
Travel	4,000
Books & Articles	1,500
Laptop & Statistical Software	1,000
Miscellaneous Expenses	1,500
TOTAL	11,500

The research will be privately funded. No requests for supplementary grants, assistantships or scholarships will be made. The total budget of the project is approximately $11,500. No additional resources or funding will be requested of UGSM-Monarch Business School Switzerland. The budget is presently funded and research may begin immediately upon approval.

BIBLIOGRAPHY

1. Adams, C. P., & Branter, V. V. (2006). Estimating the cost of new drug development: Is it really $802 million? *Health Affairs*, 25(2), 420-8.
2. D.Pilling. (1999). Trials and tribulations: Getting a new drug to market can take years. david pilling examines the range and the efficacy of the regulatory hurdles that companies must clear. *Financial Times*.
3. Getz, K., & de Bruin, A. (2000). Speed demons of drug development. *Pharmaceutical Executive*.
4. Gopinath, E., Bhadauria, R., Gunjan, J., & Insha, Z. (2012). Pharmaceutical Regulatory Affairs Review. *International Journal of Advanced Research in Pharamceuticals & Bio Sciences*, 292-301.
5. GPO. (2012). *www.gpo.gov.* Retrieved from http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf
6. Hoag, H. (2006). *Rules rule.* Nature.
7. Maglennon, S. (2012). Remodelling pharmaceutical R&D and the role of regulatory affairs. *Regulatory Rapporteur*.
8. Papanicolaou, S., Skyes, D., & Mossialos, E. (2004). EMEA and the evaluation of health-related quality of life data in the drug regulatory process. *International Journal of Technology Assessment in Health Care,*, 20(3), 311-24.
9. Rockoff, J. D. (2013). Drug discovery gets an upgrade; pharmaceutical companies are using powerful computers to increase their chance of success. *Wall Street Journal (Online)*.
10. Shane, A. (1992). New Drug Development a Long , Arduous Process. *Drug Topics*.
11. Tonkens, R. (2005). An Overview of the Drug Development Process. *Physician Executive*.
12. Wechsler, J. (2004). FDA eyes manufacturing innovation: To boost drug development. . *harmaceutical Technology*.
13. WHO. (2013). *Death Distribution Across the World*. Retrieved July 06, 2013, from WHO Media Center Fact Sheet: http://www.who.int/mediacentre/factsheets/fs310/en/index.html