The Impact of International Trade Agreements on Health: Patent System Harmonization and Medicines in Mexico

by

Benjamin C. Warren
B.Comm (International Business), University of Alberta, 1997
J.D., University of British Columbia, 2001
LL.M. (International Health Law), University of British Columbia, 2003

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in

THE FACULTY OF GRADUATE STUDIES
(Population and Public Health)

The University of British Columbia
(Vancouver)
April 2012
© Benjamin C. Warren, 2012
Abstract

Patent system harmonization obligations found within international trade agreements have been subject to intense scrutiny over the past two decades due to the potential negative implications for public health in developing countries. In 1994, NAFTA became the first trade agreement to include patent system harmonization obligations. Mexico as a signatory to NAFTA was the first developing country to adopt the patent system of developed countries via patent system harmonization. This makes Mexico a particularly relevant case study on the subject. The central research question addressed in this dissertation is: Does NAFTA patent system harmonization promote access to medicines in Mexico, while incentivizing pharmaceutical R&D? This dissertation undertakes a comparative legal analysis, a scoping study, and qualitative stakeholder analysis to address the central research question. Evidence is provided that compulsory licensing as a safeguard is inadequate as a downstream measure in the promotion of access. A key finding is that international trade agreements should be drafted with optimal pharmaceutical patent protection standards in mind. Further, patent system harmonization results in a net health benefit that can be maximized through the provision of feedback evidence to decision-makers in order to develop responsive laws and policy. This dissertation proposes that: if we reform the granting of patent terms from a fixed twenty year life period to a flexible and adjustable term determined through an assessment of health and economic conditions that exist during any given time period, we will improve both global equity in access to medicines and reduce economic inefficiencies in our current model for pharmaceutical R&D, while maintaining adequate incentives to conduct pharmaceutical R&D. The proposed reform is akin to the use of interest rates as an economic growth and stabilization tool in monetary policy. It would require government patent offices to analyze global conditions in pharmaceutical access and R&D, and accordingly adjust the number of years of patent protection awarded. This novel contribution to the academic literature informs Canadian, Mexican, and developing country decision makers on how to design appropriate policy for the benefit of public health.
Preface

This multi-method interdisciplinary research dissertation was wholly completed by the Ph.D. Candidate in the School of Population and Public Health, Faculty of Medicine, in advancement of his academic career in Global Health and his professional career as a practicing lawyer in the areas of Health, IP, and International Law.

Identification and design of the research project was done in cooperation with the supervising committee. Data collection was conducted entirely by the Candidate in a series of visits to Mexico City in 2008–2009. Data analysis was conducted entirely by the Candidate with the concomitant support of a secondary raw data analyst.

A selected list of scholarly publications that the Candidate has co-authored over his tenure as a doctoral student that in part arose from the work conducted in the dissertation is included here.


Preparation of four additional manuscripts for publication directly resulting from the body of this research work is currently underway. Ethics approval for the qualitative study was received from the University of British Columbia Research Ethics Board on September 08, 2008 (File No. H07-01972 - LATA Study).
# Table of Contents

Abstract .............................................................................................................. ii  
Preface ............................................................................................................... iii  
Table of Contents .......................................................................................... iv  
List of Tables .................................................................................................. vi  
List of Figures .................................................................................................. vii  
List of Abbreviations ..................................................................................... viii  
Acknowledgements ........................................................................................ x  
Dedication ......................................................................................................... xi  
Chapter 1: Introduction ................................................................................... 1  
  1.1 Introduction .............................................................................................. 1  
  1.2 The Global Debate .................................................................................... 7  
  1.3 Rationale: Mexican Public Health Concerns ............................................. 10  
  1.4 Overview of the Dissertation ................................................................... 17  
Chapter 2: NAFTA’s Impact on Pharmaceutical Patent Law in Canada & Mexico 24  
  2.1 Introduction .............................................................................................. 24  
  2.2 The Pharmaceutical Patent System under NAFTA ................................... 27  
  2.3 Patent Systems in Canada and Mexico under U.S. Pressure ..................... 40  
  2.3.1 Patent Protection Linkage Requirements in Canada ............................... 46  
  2.3.2 Patent Protection Linkage Requirements in Mexico ............................... 55  
  2.3.3 Compulsory Licensing in Canada ............................................................ 61  
  2.3.4 Compulsory Licensing in Mexico ............................................................ 70  
  2.4 Discussion ................................................................................................ 73  
Chapter 3: Impact of Patent System Harmonization on Public Health in Mexico ... 79  
  3.1 Introduction .............................................................................................. 79  
  3.2 Scoping Study Methodology ..................................................................... 81  
  3.2.1 Identifying the Research Question ........................................................ 83  
  3.2.2 Identifying Relevant Studies ................................................................ 84  
  3.2.3 Study Selection ...................................................................................... 87  
  3.2.4 Charting the Data .................................................................................. 88  
  3.2.5 Collating, Summarizing and Reporting the Results .............................. 89  
  3.3 Results .................................................................................................... 90  
  3.4 Discussion ................................................................................................ 125  
  3.4.1 Study Limitations ................................................................................ 130  
  3.5 Directions for Further Research ................................................................. 131  
Chapter 4: Stakeholder Perspectives on Patent System Harmonization .............. 136  
  4.1 Introduction .............................................................................................. 136  
  4.2 Qualitative Methodology ......................................................................... 137  
  4.2.1 Political Economy Paradigm .................................................................. 138  
  4.2.2 Case Study Design ............................................................................... 140  
  4.2.3 Selection of Key Informants ................................................................ 140  
  4.2.4 Data Analysis ....................................................................................... 145  
  4.3 Results .................................................................................................... 147  
  4.3.1 Decreased Access to Medicines ............................................................. 148  
  4.3.2 Increased Access to Medicines .............................................................. 155  
  4.3.3 Increased Pharmaceutical R&D ............................................................. 163  
  4.3.4 Decreased Pharmaceutical R&D ............................................................ 168
List of Tables

Table 1: Scoping Study Criteria .................................................................87
Table 2: Study Disciplinary Category & Research Settings.............................90
Table 3: Summary of Study Designs ...........................................................91
Table 4: Number of Studies for Each Theme .................................................92
Table 5: Exemplary Studies for Decreased Access ........................................93
Table 6: Exemplary Studies for Increased Access ........................................105
Table 7: Exemplary Studies for Increased R&D ............................................112
Table 8: Exemplary Studies for Decreased R&D ..........................................118
Table 9: Summary of Themes ..................................................................148
Table 10: General Elements of Systematic Reviews and Scoping Studies ........249
Table 11: Comparison of Quantitative and Qualitative Research ....................250
List of Figures

Figure 1: Perspectives on Patent System Harmonization ........................................... 5
Figure 2: Development of a Patented Pharmaceutical Product ................................. 10
Figure 3: NAFTA Chapter 17 Articles Impacting Public Health ............................... 28
Figure 4: Scoping Study Search Strategy .................................................................. 88
Figure 5: Scoping Study Conceptual Framework ...................................................... 129
Figure 6: Assessment of Disease Distribution .......................................................... 189
Figure 7: Assessment of Disease Severity ................................................................. 190
Figure 8: Determination of Patent Length .................................................................. 191
Figure 9: Advancement of Scientific Frontier Knowledge Curve ............................. 199
Figure 10: Rate of New Knowledge Curve ............................................................... 200
Figure 11: Phase 3 Clinical Trial Duration ................................................................. 203
Figure 12: Current Patent Term Trajectory ............................................................... 204
Figure 13: Desired Patent Term Trajectory ............................................................... 205
Figure 14: Comparison of Patent Term Trajectories ............................................... 206
Figure 15: Revisiting the Development of a Patented Pharmaceutical Product ....... 207
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANAFAM</td>
<td>Mexican National Association of Pharmaceutical Manufacturers</td>
</tr>
<tr>
<td>APCs</td>
<td>Advance Purchase Commitments</td>
</tr>
<tr>
<td>BRIC</td>
<td>Brazil, Russia, India, and China</td>
</tr>
<tr>
<td>CA4FTA</td>
<td>Canada-Central America Four Free Trade Agreement</td>
</tr>
<tr>
<td>CAMR</td>
<td>Canada Access to Essential Medicines Act</td>
</tr>
<tr>
<td>CIPIH</td>
<td>Commission for Intellectual Property Rights, Innovation and Public Health</td>
</tr>
<tr>
<td>DCs</td>
<td>Developing Countries</td>
</tr>
<tr>
<td>DR-CAFTA</td>
<td>Dominican Republic-Central American Free Trade Agreement</td>
</tr>
<tr>
<td>FDI</td>
<td>Foreign Direct Investment</td>
</tr>
<tr>
<td>FTA</td>
<td>Free Trade Agreement</td>
</tr>
<tr>
<td>GATS</td>
<td>General Agreement on Trade in Services</td>
</tr>
<tr>
<td>GATT</td>
<td>General Agreement on Tariffs and Trade</td>
</tr>
<tr>
<td>GMP</td>
<td>Good manufacturing practices</td>
</tr>
<tr>
<td>IGWG</td>
<td>Intergovernmental Working Group</td>
</tr>
<tr>
<td>IMF</td>
<td>International Monetary Fund</td>
</tr>
<tr>
<td>IP</td>
<td>Intellectual Property</td>
</tr>
<tr>
<td>IPA</td>
<td>Intellectual Property Agreements</td>
</tr>
<tr>
<td>IPR</td>
<td>Intellectual Property Rights</td>
</tr>
<tr>
<td>IPS</td>
<td>Innovation, Policy and Science</td>
</tr>
<tr>
<td>IRDC</td>
<td>International Research and Development Centre</td>
</tr>
<tr>
<td>LATA</td>
<td>Latin American Trade Agreements</td>
</tr>
<tr>
<td>LFPPI</td>
<td><em>Ley de Fomento y Proteccion de la Propiedad Industrial</em> (Law on the Promotion and Protection of Industrial Property)</td>
</tr>
<tr>
<td>MDG</td>
<td>Millennium Development Goal</td>
</tr>
<tr>
<td>MFN</td>
<td>Most Favored Nation</td>
</tr>
<tr>
<td>MSF</td>
<td>Médecins Sans Frontières</td>
</tr>
<tr>
<td>NAFTA</td>
<td>North American Free Trade Agreement</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>OXFAM</td>
<td>Oxford Committee for Famine Relief</td>
</tr>
<tr>
<td>PCT</td>
<td>Patent Cooperation Treaty</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>PDPs</td>
<td>Product Development Partnerships</td>
</tr>
<tr>
<td>PMPI</td>
<td>Patented Medicine Prices Index</td>
</tr>
<tr>
<td>PMPRB</td>
<td>Patented Medicines Prices Review Board</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research &amp; Development</td>
</tr>
<tr>
<td>SPLT</td>
<td>Substantive Patent Law Treaty</td>
</tr>
<tr>
<td>TRIPS</td>
<td>Trade Related Aspects of Intellectual Property Agreement</td>
</tr>
<tr>
<td>USD</td>
<td>US Dollar</td>
</tr>
<tr>
<td>USPTO</td>
<td>United States Patent and Trademark Office</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WIPO</td>
<td>World Intellectual Property Organization</td>
</tr>
<tr>
<td>WTO</td>
<td>World Trade Organization</td>
</tr>
</tbody>
</table>
Acknowledgements

I would like to thank my supervisor, Dr. Jerry Spiegel, for his support through the Global Health Research Program, in the School of Population and Public Health, Faculty of Medicine, UBC. I would also like to thank my committee members, Dr. Patricia Spittal (British Columbia Centre for Excellence in HIV/AIDS), and Professor Ian Townsend-Gault (Faculty of Law, UBC) for their guidance and support throughout the course of my studies. I would like to thank Dr. Steve Morgan at the Centre for Health Services and Policy Research (CHSPR) for his input in the early years of my doctoral work. In addition, during my time as a doctoral student I worked as a graduate research assistant under the mentorship of Dr. Edwin Levy and Dr. Emily Marden, with the Intellectual Property and Policy Group at the W. Maurice Young, Centre for Applied Ethics, Faculty of Interdisciplinary Studies, UBC. I am grateful for the intellectual environment they provided as I grew into an advanced scholar. I would like to thank my editor Kelli McAllister and secondary qualitative data analyst Kim Taylor for their advice and thoughtful comments on my dissertation. I would also like to thank Mr. Cam Mowatt, one of Canada’s most prominent NAFTA lawyers. Without his credentials backing my requests for interviews, I would not have been able to set up interviews with the caliber of respondents who participated in the study. I would like to thank the nineteen high-level key informant stakeholders interviewed in the course of preparing this doctoral dissertation. Many of them provided written materials to supplement the information collected during the interview process. Their contribution in time and support has been essential for the completion of this project.
Finally, I would like to thank the Canadian Institutes of Health Research (CIHR) for funding this research through a three year Canada Graduate Doctoral Award. (The Impact of International Trade Agreements on Health – CGD 80452)

All figures in the dissertation are originals and conceptually designed by the author. Figures 1–9 were created by Kelli McAllister in consultation with myself and are used with permission. Figures 10–14 were created by Stephen Barker in consultation with myself and are used with permission.

Dedication

I dedicate this thesis to my immediate family, all whom work as health professionals. They have been an invaluable source of personal and moral support during the writing of this dissertation.

Dr. Kenneth George Warren, Neurology, University of Alberta
Dr. Sharon Ann Warren, Epidemiology, University of Alberta
Dr. Steven Wells, General Practitioner, My Uncle in Ontario
Dr. Daniel Thomas Warren, Neurosurgeon, Spine Fellow, New York University
Dr. Melina Warren, Radiology Fellow, New York University
And to my lovely fiancé Nicole Thom, thanks for standing by me through the writing of this dissertation.
Chapter 1: Introduction

1.1 Introduction

International trade agreements modify how sovereign countries address issues faced by their populations. In an era of intensifying globalization, the implications of such undertakings on public health have sparked considerable controversy. This dissertation takes up the challenge of investigating this phenomenon. An area of particular relevance for public health is the inclusion of trade agreement provisions that require harmonization. Harmonization is a reduction in variation of national regulatory standards for goods and services. It has been argued that harmonization can lead less-developed countries to initiate standards where none had previously existed. It has also been argued that harmonization can lead to erosion of existing standards. This is because harmonization can tend to require uniform global standards at the level least restrictive to trade interests. An especially contentious debate has raged over whether trade agreements with intellectual property (IP) harmonization provisions create barriers to the access of medicines in developing countries. This dissertation focuses on the impacts of patent system harmonization on access to medicines and pharmaceutical research and development (R&D) in Mexico resulting from the North American Free Trade Agreement (NAFTA). The central research question is: “Does NAFTA patent system harmonization promote access to medicines in Mexico, while incentivizing pharmaceutical R&D?”

NAFTA came into force January 1, 1994 and was the first trade agreement to contain patent system harmonization provisions. NAFTA’s Chapter 17 on Intellectual Property
was largely used as the model for the World Trade Organization’s (WTO) Trade Related Aspects of Intellectual Property (TRIPS) Agreement. Mexico was the first developing country to conform its IP standards to those of a developed country, the United States (U.S.), through its membership in NAFTA. Due to Mexico’s relatively mature experience with these issues, the country is an especially relevant case study for investigating the impact of patent system harmonization on access to medicines.

Understanding global pharmaceutical access is a multi-disciplinary endeavor. The core academic disciplines involved in this dissertation are law and public health. The dissertation examines various critical determinants of health, including those of political and economic natures. Power imbalances, disparities, and health inequities that persist in North America are examined. These factors can influence health conditions, resulting in fewer opportunities for human development and innovation. Continued, renewed efforts are needed to sustain achievements in public health and tackle ongoing and future challenges in regional pharmaceutical/health policy development. An analysis of NAFTA, as the first international agreement to include an IP chapter, provides policymakers with important lessons for future decision-making. It also provides a better understanding of how the creation of the world’s largest economic bloc, as well as its greatest source of innovation in emerging medical technology, continues to impact access to medicines around the globe.

IP is a legal construct that influences pharmaceutical R&D. It affects access to medicines for the prevention and treatment of both communicable and non-communicable diseases.
IP generally includes patents, copyright, trademark, and trade secret law and is applicable to any commercial sector (Cohen & Illingworth, 2003). This dissertation’s focus is on pharmaceutical patents with respect to both pharmaceutical R&D and access. The traditional economic rationale for patents is that they encourage innovation and hasten technological development by providing financial incentive through property protection to patent holders (Sherwood, Scartezini, & Siemsen, 1999). The central idea of all patent systems is that rewarding the creator for an invention provides incentives for the creation of more inventions. This, in turn, benefits society. A second key tenet of this system is that patents not only provide financial incentives for the creation of novel technologies, but also encourage the dissemination of knowledge through disclosure requirements. Under the patent system, the inventor essentially agrees to publicize the invention in exchange for an initial period during which use of the invention is under the inventor’s exclusive economic control. These two functions of patents: (1) to promote innovation through exclusive proprietary incentives, and (2) to disseminate information, ideally serve to advance the development of technology (Merges & Duffy, 2002).

The pharmaceutical industry is characterized by an intense, ongoing conflict between “research-based” and “generic-based” companies, and there are pronounced differences in how each approaches business. Research-based companies place the utmost importance on ensuring that the global patent system is considered “adequate and effective.” Such companies are faced with raising and risking capital for large, long-term clinical trials for novel pharmaceutical candidates (Roffè, Tansey, & Eugui, 2006). Generic-based companies, on the other hand, do not face the large, fixed, upfront costs of
R&D. These companies produce substitute copies of pharmaceuticals once patent terms have expired, based on reverse engineering and bio-equivalency government regulatory requirements. At a social level, this conflict is between two competing interests that require balancing: incentives for private actors to conduct pharmaceutical R&D and public access (affordable and available) to market approved medicines (Hindley, 1971).

Economic theory views pharmaceutical patent protection as the second best way to pay for R&D (Stiglitz, 1991). The best way—a fully efficient outcome—would be for all consumers whose marginal benefit exceeds marginal cost should use the product. Patents, however, permit pricing above marginal cost. This means that some consumers may forego using the product even though their marginal benefit exceeds marginal cost. With large, fixed upfront costs of R&D in clinical trials, the best solution is not currently possible. Government R&D subsidy models have been considered as an alternative approach. The allocation of public funds to clinical trials, however, undermines equity to other important, less risky sectors of the economy. Thus a patent system enables innovator firms to charge prices above marginal cost for a given period of time post-marketing approval is generally viewed as the most pragmatic approach to funding ongoing private sector pharmaceutical R&D (Danzon & Towse, 2003). The most important question, however, still remains: what is the appropriate duration for patent protection?
In the global health context, the debate also focuses on the trade-off between potential benefits of greater pharmaceutical R&D and the potential impact of increased medicine prices on access. Layers of complexity are added to the discussion when we stratify by countries’ economic standing. Patents again are the central concern with regard to IP protection in developing countries, as they allow the holder an exclusivity period with elevated pricing. The HIV/AIDS pandemic spurred the debate over IP rights in international agreements into broader global health policy debates (K. C. Shadlen, 2009).

It is still argued vehemently by many that emerging anti-retroviral pharmaceuticals will not be affordable to patients due to the pricing of products protected by limited term patent monopoly (Chaudhuri, 2005; Varella, 2004).

Proponents of patent system harmonization to a global standard argue that, although prices are a fundamental factor in determining access to medicines, affordable prices can be pursued through multiple mechanisms other than reducing exclusivity rights (Lanjouw
Cockburn, 2000). Bulk procurement, for example, entails pooling medicine orders together to increase purchasing power to negotiate reduced prices (Maskus, 2001). Reduction or elimination of duties and taxes for medicines contributes to price reduction (Mendis, 2007). Local production and distribution of medicines with assured quality can also result in lower prices. The adaptation of differential pricing charged by the manufacturer or seller to countries with different purchasing power is another possible strategy. In IP and health discussions, the focus is usually on pharmaceutical prices (Bettcher, Yach, & Guindon, 2000; Trouiller et al., 2002).

Proponents also argue that trade agreements have sufficient last resort safeguards to protect against the negative impact of pharmaceutical patents on prices and access to medicines. The primary safeguard is compulsory licensing, which requires a pharmaceutical patent holder to allow generic providers to manufacture and distribute a medicine (t’Hoen, 2002). The research conducted in this dissertation examines whether compulsory licensing is adequate to promote affordable access to medicines. Compulsory licensing has seldom been applied and involves complicated implementation and use requirements that result in potentially insurmountable legal procedural and administrative hurdles. A more facilitative patent system model may thus be required. At the domestic level, patent systems should aggressively and simultaneously promote pharmaceutical R&D and access in the most cost-effective and economically efficient way possible without cutting corners on safety and efficacy of the end product. The pharmaceutical sector directly impacts human health, and a rationale exists that it should be regulated as a separate category of economic activity from most other industries. To set the scene,
Section 1.2 of this chapter examines the ongoing global debate concerning IP, international trade agreements, and access to medicines. Section 1.3 presents the public health rationale for the study undertaken in this dissertation. Section 1.4 outlines an overview of the main body of the dissertation.

1.2 The Global Debate

Economists and U.S. policy makers who recognized the importance of IP for technology exporters from knowledge-based economies advanced the integration of IP into trade agreements in the 1980s and 1990s. In 1994, the eighth General Agreement on Tariffs and Trade (GATT) Round, known as the Uruguay Round, created the World Trade Organization (WTO) and formally introduced IP issues into global trade negotiations. The introduction was concurrent with NAFTA negotiations in IP (Doane, 1989). This became the WTO’s TRIPS agreement, and was created to harmonize the global IP system (Lazzarini, 2003a). TRIPS addresses how the principles of GATT should apply to IP and includes provisions for the adequate enforcement of IP rights (Saha, 2009). Most countries have now adopted TRIPS IP standards, however considerable debate has emerged regarding consequences for global health equity (Fink & Reichenmiller, 2006). This is because prior to the signing of the TRIPS agreement, developing countries were free to produce low cost generic substitutes of on-patent medicines in the developed world. It is important to note that novel pharmaceutical compounds are patent protected primarily through domestic law (Mengistie, 2003). If an invention is not protected under a particular country’s national law, it constitutes public domain and can be freely exploited in the country concerned. Pre-TRIPS, seeking patent protection in a foreign country was considered difficult due to the absence of adequate IP legal frameworks in
many countries. In order to mitigate the difficulties of securing a patent in a foreign country, TRIPS was formally set up as a multilateral instrument to include patent system harmonization provisions (Mengistie, 2003). The TRIPS agreement deals with substantive law issues. Another multilateral instrument, the Patent Cooperation Treaty (PCT) intends to harmonize formal procedural law. These agreements, among many other bilateral instruments, attempt to harmonize national patent systems by setting common standards. There is no international patent law that provides for a world patent and the global patent system is still evolving to normative standards. The international patent system harmonization agreements are not meant to replace national patent systems, but rather facilitate the protection of the interests of parties of one member state in another member state that is signatory to the agreement.

TRIPS was designed with the multinational research-based pharmaceutical sector in mind and drafted after extensive lobbying efforts by that industry (Lazzarini, 2003a). Divergent legal interpretations between developed and developing countries, however, combined with significant outcry by civil society advocating for vulnerable populations faced with the HIV/AIDS epidemic and advocating for global health equity have led to a response by the WTO. In 2001, the Doha Declaration announced by the WTO Ministerial affirmed that TRIPS should not act as a barrier to pharmaceutical access in developing nations. It was declared that TRIPS can and should be interpreted and implemented in a manner supportive of WTO members’ right to protect public health and, in particular, to promote access to medicines for all (Abbott & Reichman, 2007a). More specifically, the Doha Declaration reaffirmed certain safeguards, including the following: “Each member has
the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those related to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency” (Roffe et al., 2006). This was considered a victory for developing countries with substantial HIV/AIDS concerns and other public health issues because it re-enforced the importance of health within the context of commercial agreements (Chaudhuri, 2005; Varella, 2004). In 2003, the WTO adopted a waiver as part of the Marrakesh Agreement. The waiver allowed parallel importation: countries could produce generic copies of patented pharmaceutical products under compulsory licenses for export to least-developed countries lacking pharmaceutical manufacturing capacity. Canada was among the first countries to amend its patent law to facilitate the measures and attempt to assist global pharmaceutical access initiatives. This resulted in Canada’s Access to Medicines Regime (CAMR). However, to date implementation of CAMR mechanisms remains almost nil (Cohen-Kohler, Esmail, & Cosio, 2007). It is important to note that most authors do not argue for abolition of the patent system altogether (Correa & Musungu, 2002; Drahos, 2002b). The role of patents in the development of novel pharmaceuticals has been questioned but has not been discarded. The need for and benefit of a patent system is appreciated, yet how global patent system harmonization should proceed and to what standards are still questions open for discussion.
1.3 Rationale: Mexican Public Health Concerns

This research uses NAFTA for analysis, as it was the first IP trade agreement. NAFTA Chapter 17 is based on a draft version of the TRIPS agreement that existed at the time NAFTA was signed. The Uruguay Round negotiations clearly influenced the outcome of NAFTA (Johnson & Ragnar, 1998). Vice versa, the final draft of the TRIPS agreement is largely based on the language used in the signed NAFTA Chapter 17 (Correa, 2004). Both agreements represent the research-based pharmaceutical business agenda for global strengthening of IP law (Fink & Reichenmiller, 2006). The research conducted for this dissertation is in line with the United Nations (UN) Millennium Development Goal (MDG) 8 Target 17. The MDG aims to provide access to affordable, essential drugs in developing countries in cooperation with pharmaceutical companies (Attaran, 2005; Sachs & McArthur, 2005).

This dissertation focuses on NAFTA patent system harmonization obligations not only to simplify the legal analysis but to keep the spotlight on the public health issues faced by Mexico as the developing country of interest. The exception being in Chapter 5 where recommendations for patent system reform across national and global levels are made and their implications for global public health are discussed. Patent system harmonization
measures in trade agreements contain patent protection obligations that may be detrimental to public health, but these agreements also include safeguards to provide governments the ability to protect public health, the primary safeguard being compulsory licensing. Compulsory licensing in trade agreements is considered sufficient by U.S. policy makers to promote pharmaceutical access (Mullin, 2002). Globally, however, opinions differ regarding whether safeguards protect populations from the adverse health effects of patent protection included in FTAs (Singer, 2002). Mexico is used to examine whether the compulsory licensing safeguard is sufficient to protect public health or whether further patent system reform is required to enhance access.

Mexico, as a global health country case study, is in the midst of pronounced epidemiologic transition. Mexico faces both developing and developed world health burdens, known as a double burden of disease (Gutiérrez-Delgado & Guajardo-Barrón, 2009). In 1989, Frenk and colleagues wrote about the health transition in middle-income countries. The authors analyzed the dynamics of the health changes taking place in middle-income countries in the midst of intensive economic transformations (Frenk, Bobadilla, Sepulveda, & Cervantes, 1989). The authors reported that social response to the complex health needs of the future would have to be designed on the basis of scientific research with regard to both the evolving epidemiologic reality and the relative effectiveness of interventions. Both of these response issues are pervasively addressed throughout this dissertation. In Mexico, the general model of epidemiological transition shows the pattern of causes of death has evolved rapidly over the past decades (Omran, 2005). These figures indicate an advanced epidemiologic transition. An analysis of
specific cause of death demonstrates ischemic heart disease, stroke, and diabetes are among the five leading causes of death in all 32 Mexican states (González-Pier, 2007).

Mexico’s health system has not kept up with the pressures of the double burden of disease (Gutiérrez-Delgado & Guajardo-Barrón, 2009). Common infections, malnutrition, and reproductive health problems coexist with chronic disease and injury. This adds new layers of complexity to its patterns of disease, disability, and death. On the one hand, the unfinished agenda of communicable diseases must be addressed; while on the other hand, emerging challenges are represented by chronic diseases. Although this transition is well-advanced, the consequences for a double burden of disease are both complex and protracted. Between 1950 and 2000, the proportion of deaths attributable to communicable disease decreased sharply from 50% in 1950 to 14% in 2000 and is expected to fall further to 10% by 2025. Over the same 50 year interval the proportion of all deaths due to non-communicable diseases has risen from 23% to 75% (González-Pier, 2007). The Mexican health system has been overwhelmed by the need to simultaneously confront common infections, malnutrition, reproductive health problems associated with extreme poverty, and communicable disease burdens of elevated prevalence among certain vulnerable populations (including dengue, malaria, and TB/HIV co-infection), alongside the increasing incidence of chronic disease conditions such as diabetes, heart disease, and cancer which are normally considered more pressing to developed world populations (González-Pier, 2007). The importance of this case study is emphasized by the fact that this dynamic process has become familiar to most developing countries (Frenk, 2006). Conditions faced in Mexico reflect those faced by other emerging
economies such as the BRIC (Brazil, Russia, India, and China) nations that make up a large portion of the world population. Like these countries, Mexico is undergoing interrelated processes of demographic and socio-economic transition, which affect public health.

Twenty years have passed since NAFTA was signed. In Mexico, reform actually began in 1991, but many of the IP legal reforms impacting public health still lack clarity (Baca, 1994). In the early 1990s, considerable IP legal and institutional work was done to enable Mexico to enter NAFTA in compliance with U.S. trade demands with respect to IP rights (Pemberton & Soni Jr, 1992). This preparatory work had an important impact on pharmaceutical procurement in Mexico. Before NAFTA, most of the public sector medicine purchases were generics and even when the pharmaceuticals were on-patent in other countries they were copied and bought by government as generic equivalents in Mexico (Torres Guerra & Gutiérrez, 2009). Pre-NAFTA, the IP system in Mexico was relaxed and domestic pharmaceutical companies produced almost any pharmaceutical in Mexico as long as it could be reverse engineered. If a medicine could be produced and there were no pharmaceutical production technical barriers, then it could be distributed and sold. At that time there was a general market equilibrium and understanding amongst industry players that the national Mexican industry would sell generic pharmaceuticals to the public providers and the international companies would sell brand name pharmaceuticals to the private sector. Before NAFTA, national companies could copy pharmaceuticals legally and sell them to the public sector. The government bought very little from the research-based multinational pharmaceutical companies and the national
Mexican industry sold very little to the private health care providers. That was the equilibrium in the pharmaceutical market.

After NAFTA was signed, international companies started to sell on-patent brand name pharmaceutical generics to the public sector. The market equilibrium that was in place prior to the signing of NAFTA started to break. National companies started selling to the private sector in an attempt to compete. Multinational companies started selling their on-patent pharmaceutical products to the public sector, because the national companies could no longer as easily copy the new pharmaceuticals for fear of patent infringement lawsuits. NAFTA made it more difficult for small pharmaceutical companies in Mexico to compete because import/export tariffs were taken down. NAFTA also introduced strengthened IP protection for multinational company pharmaceutical products, and those companies’ trans-located plants into Mexico (Gasman, 1995).

In Mexico, the Secretary of Economy (Secretaria de economia) is in charge of reviewing the legal implementation of NAFTA obligations among a plethora of other international agreements. To date, there are more than ten FTAs in force that have IP language based on the NAFTA template. The Secretary reviews these instruments to ensure domestic implementation initiatives are consistent with the international agreements. For example, there is a plurilateral Mexico–EU Agreement. There are bilateral agreements with Norway, Iceland, Liechtenstein, Israel, Nicaragua, Costa Rica, Columbia, Chile, Bolivia, Uruguay, and Switzerland. Mexico is also a signatory to a plurilateral agreement with El Salvador, Guatemala, and Honduras as one single regional FTA. Mexico has one bilateral
FTA in Asia with Japan signed in 2004. The Mexico–Japan treaty attempts to meet all the obligations of the past agreements that have been signed at different periods of time. There have been changes in the global political and economic landscape since the early trade treaties, which are referred to as first generation treaties; NAFTA is considered a second-generation treaty. The recent FTAs Mexico has signed with the EU and Japan are usually referred to as third generation agreements. The globalization process through the proliferation of trade agreements is ongoing. The process evolves over time and each agreement can be different in terms of procedural and/or substantive content, but all these FTAs share common basic principles in respect of patent system harmonization. They are based in TRIPS and NAFTA standards (Dahlman & Kuznetsov, 2005).

There is variation because some aspects have to be negotiated anew with different member states. This is country specific, but the fundamental principles found in NAFTA and TRIPS are basically adhered to in next-generation trade agreements. Importantly, there is not a multiplicity of different provisions for patent system harmonization in individual trade agreements; rather, there is a shared standard based on NAFTA. Attempts are made to be consistent with NAFTA’s Chapter 17 mandate. For example, the FTA with Japan basically incorporates the same principles as NAFTA. This is the case even though the IP chapter in NAFTA was written almost three decades ago at a time when there was much less understanding of how patent system harmonization might impact public health in different political and economic settings. Even though there have been many next generation FTAs signed and there is a better understanding of the impact of patent system harmonization on public health, countries, including Mexico, continue
attempts to follow the NAFTA principles.

If our guiding law goes down the wrong road it often becomes very difficult to alter its direction even if many problems arise. This is the opposite of how science works, operationally. In science, by critically examining the currently existing knowledge base to understand what questions to ask, novel approaches to addressing frontier problems emerge. By its nature, law is responsive to new scientific development. This is the reason law always has difficulty keeping up with new social issues in science, from the regulation of the internet to bio-ethical issues in genomics. If trade negotiators made initial decisions in the absence of evidence, the deficiencies present during the original negotiation and drafting of NAFTA/TRIPS are likely to still exist today. There is now a complex interwoven web of international agreements directing global patent system governance under the rule of law. The NAFTA/TRIPS framework imposes international legal obligations over the world’s largest economic trading bloc in terms of GDP (Ayhan Kose, Meredith, & Towe, 2005). North America (the U.S. in particular) is also the largest global supplier of novel pharmaceuticals (Chaudhry & Walsh, 1995). Patent system uniformity that may have been ill-conceived requiring *de jure* harmonization of domestic legal systems to *minimum* standards may well need reform. Making countries NAFTA compliant to a minimum standard leaves considerable room for disharmony given the likelihood of upward pressure placed on government by influential research-based pharmaceutical company lobby groups. This disharmony may be creating significant procedural and substantive barriers to access to medicines. Policy objectives and initiatives of the three NAFTA member states, in fact, at times deviate significantly in
In order to investigate the impact of NAFTA in Mexico, this research was guided by the central question: “Does NAFTA patent system harmonization promote access to medicines in Mexico, while incentivizing pharmaceutical R&D?” This research question was addressed through three distinct yet complementary methodological approaches. First, the way in which NAFTA obligations and safeguards have been implemented was analyzed by comparing the harmonization of the Canadian and Mexican legal systems to NAFTA standards. Second, a scoping study based in a public health research methodology reviewed the existing literature to determine what is known about the public health impact of patent system harmonization in Mexico (Arksey & O’Malley, 2005). Third, qualitative research conducted through interviews of experts and key informants provided primary evidence of the impact of patent system harmonization on public health in Mexico. These methodological approaches not only answer the central research question with regard to Mexico but also provide insight into whether and what type of global patent system reform to the current framework is required and, if required, how success should be measured in the future. Possible avenues for patent system reform are presented with supporting policy recommendations based on the evidence produced by these three methodological approaches.

1.4 Overview of the Dissertation
A complete evaluation of the net effects of the NAFTA/TRIPS agreements in all developing countries requires broad assessment of all the costs and benefits of patent system harmonization and is beyond the scope of this dissertation. This research
concentrates on a circumscribed task: analyzing the effects of pharmaceutical patent system harmonization on public health in Mexico to achieve greater understanding and develop recommendations for reform to the global patent system. This section outlines the structure of the dissertation and introduces the methods used to address the research question. The dissertation is an interdisciplinary multi-method work that begins with legal analysis and then moves on to research methods based in public health.

Chapter 2 presents a comparative legal analysis. This chapter examines how the legal implementation of NAFTA obligations has influenced Canada’s domestic patent system compared to the Mexican system. The question “Has the implementation of NAFTA produced harmonized pharmaceutical patent legislation in Canada and Mexico?” is asked and analyzed. These countries were compared to elucidate discrepancies in law where domestic patent systems were modified to co-exist under a U.S. trade policy regime that focuses on harmonization to a U.S. standard. The implications of NAFTA on new law in accordance with treaty membership allows for interesting cross-country comparisons. Significant disharmony among NAFTA countries’ patent systems still exists. Nuances in the law have both direct and indirect consequences for pharmaceutical access and R&D. The analysis of patent provisions in NAFTA and how they have been implemented into Canadian and Mexican law illuminates differences in government regulatory approach specific to each country’s pharmaceutical needs. Factors that may explain why the patent system is not harmonious to a regional standard are identified. The objective of Chapter 2 is to assess whether the harmonization requirements of NAFTA and subsequent implementation measures have generated domestic legislation in
Canada and Mexico that is harmonious to the benefit of the member states. I conclude that harmonization to an *optimal* standard as opposed to a *minimum* standard would be better for NAFTA countries and would lead to improvements in access to medicines and protection of public health. *Sui generis* patent law based on the current level of economic development of any given country is impractical and increases barriers to access due to the likelihood of litigious conflict. Pharmaceutical trade agreements should work towards a harmonious global system, but significant reform to the current system is required.

Chapter 3 is a scoping study, which moves the legal analysis to a public health discussion. The study assesses the impact of NAFTA on public health in Mexico. The scoping study utilized the methodological framework advanced by Arksey and O’Malley (Arksey & O'Malley, 2005). This entails a comprehensive review of literature from a variety of disciplines and study designs (Levac, Colquhoun, & O'Brien, 2010). Scoping reviews involve the selection, collection, and summary of existing evidence in a broad thematic area for the purpose of identifying subareas where sufficient evidence exists to conduct a full systematic review and subareas where insufficient evidence requires further primary research (Arksey & O'Malley, 2005). The scoping study was undertaken to answer the question, “*What is known from the existing literature about the impact of NAFTA’s patent system harmonization on public health in Mexico?*” The majority of available literature identified was descriptive. Analytical evidence was found to be lacking, but key studies are discussed in detail. An emergent thematic analysis was conducted to summarize and compare research across disciplines and methodological approaches. Studies were thematically categorized by result: positive or negative
consequences of patent system harmonization on access to medicines and pharmaceutical R&D. This is followed by a discussion of net impacts on health.

Chapter 4 presents qualitative research conducted. Key informant stakeholder interviews were conducted to provide primary evidence on the impact of NAFTA patent system harmonization in Mexico. The question, “Are available safeguards in Mexico adequate for promoting access to medicines within a patent system that is set up to incentivize pharmaceutical R&D?” was asked and answered. Mexico was used as developing country case study of interest as Mexico has been a signatory to NAFTA since 1994, whereas other developing countries have only recently signed on to similar FTAs. Thus, by identifying the consequences to Mexico one can foresee and perhaps prevent similar problems in other developing countries. A political economy paradigm was used as a lens to assess the ongoing impact of NAFTA patent system harmonization in Mexico. Chapter 4 provides guidance to other developing countries on what to expect from trade agreements that contain patent system harmonization obligations. Stakeholder perceptions converged with a major finding that the use of compulsory licensing as a primary safeguard for enabling access to medicines is fraught with difficulties and additional options should be explored.

Chapter 5 is an analytical discussion of the evidence provided through the research conducted in the body of this dissertation. The discussion is on what is required to redirect the current global patent system. The chapter presents possible avenues for patent system reform to address the parallel global health issues of how to achieve equitable
pharmaceutical access and maintain incentives for efficient innovative pharmaceutical R&D under a patent system model. These recommendations are based on the conclusion that the current patent systems in Mexico and abroad are not adequately promoting equitable global access to medicines and innovative and efficient pharmaceutical R&D. I present alternatives to the current patent system that only entails slight alterations, but may produce significant results. Section 5.2.1 presents an initial proposal which is discarded in favour of a second proposed alternative in section 5.2.2. It explains a more administratively feasible approach to patent system reform that can foster both access and innovative R&D. Pharmaceutical access and R&D can be made more efficient by patent system reform through flexible patent terms. The concepts presented are analogous to adjusting flexible interest rates to promote economic growth and stability through monetary policy. The approach I present should promote equitable access to medicines while maintaining (if not improving) incentives for efficient pharmaceutical R&D during appropriate periods. Section 5.3 makes suggestions on how to adopt patent system reform into international law. I recommend the separation of pharmaceutical patent law that impacts health into distinct international pharmaceutical sector agreements that supersede the myriad of international agreements on IP that currently exist. The theoretical patent system reform could be applied to any country’s patent law and implemented through a multilateral framework. In Section 5.4, some supporting policy recommendations are made to further achieve intended goals. Section 5.5 concludes the dissertation with some final thoughts.
The law is the most important tool available to government decision makers for the organization and achievement of societal goals. This dissertation takes the view that patent system reform can be used to achieve an adequate balance between the concurrent goals of access and R&D—even though these goals are often considered mutually exclusive and compete with each other in global health policy debates under the current patent system model. Trade agreements that contain IP chapters were intended to spur innovative economic activity and provide embedded safeguards that allow governments the flexibility to protect public health. This dissertation provides evidence that current safeguards are inadequate. It advocates slight but potentially highly effective restructuring of the global pharmaceutical patent system. Simple arguments that trade agreements negatively impact developing countries because of strong pharmaceutical patent protection that results in overpriced medicines is based on a misunderstanding of the nexus between global trade, the patent system, medicines, and public health. The resulting evidence-insufficient debate has stalled many bilateral and plurilateral agreements, as well as multilateral progress within the WTO. This is detrimental to positive global economic development and an epidemiologic transition for developing nations. Developed and developing countries alike are entering into a highly complex web of legal obligations that impact global health, a web that is still not fully understood (Koplan et al., 2009). This study assesses NAFTA’s impact on Mexico and provides input into an assessment of theoretical patent system reform alternatives. Recommendations are made for supporting policy measures to better meet global health interests. This compendium of scholarly work makes a novel and significant contribution to humanity’s most pressing health needs through unique multi-method research,
provision of primary evidence, and the theoretical discussion of reform to the global patent system. The impact of trade agreements are not written in stone, and with sufficient political will, certain aspects can potentially be challenged or better calibrated, especially with respect to patent system harmonization and the protection of public health.
Chapter 2: NAFTA’s Impact on Pharmaceutical Patent Law in Canada & Mexico

2.1 Introduction
This chapter of the dissertation focuses on how patent system harmonization obligations have been written into Canadian and Mexican domestic legislation. Given that each country has distinct ideological characteristics, levels of economic development, health systems, and legal traditions, the impact of harmonized patent system obligations on public health can be diverse. This chapter addresses the question, “Has the implementation of NAFTA produced harmonized pharmaceutical patent legislation in Canada and Mexico?” In 1994, the North American Free Trade Agreement (NAFTA) became the first major trade treaty to include intellectual property (IP) rights. Significantly, the reforms on pharmaceutical patent law that took place during NAFTA negotiations set a model for global IP law harmonization that was subsequently applied during the Trade-Related Aspects of Intellectual Property Rights (TRIPS) negotiations (Cohen, 2003). NAFTA has now been in place for almost two decades, but a number of important legal issues remain to be resolved regarding NAFTA’s impact on public health even today.

Despite the harmonization mandate, many inconsistencies in national IP law exist among the member states. NAFTA establishes minimum standards for IP rights. Parties (i.e., member states) to the agreement may implement in their domestic law more extensive protection than is required (Art. 1701 & 1702). These protective rights include pharmaceuticals patent protection (Art. 1709). The language adopted in the agreement
may lead to a disadvantage for Canada and Mexico. The U.S. is still the dominant developer and supplier of novel medicines to the world. From a U.S. industrial standpoint, this position should be protected. Canada and Mexico both espouse universal health care and give more weight to pharmaceutical policy objectives that focus on access. The privatized U.S. health care system does not place the same importance on equitable access.

In Section 2.2 of this chapter, I describe the pharmaceutical patent protection afforded by NAFTA and the primary available safeguard to protect public health, compulsory licensing, in the context of differences that have evolved through ongoing TRIPS World Trade Organization (WTO) negotiations over the past decade. A compulsory license allows a domestic manufacturer, public or private, to produce and distribute a patented good without the authorization of the patent holder. The rationale for incorporating patent provisions in a trade agreement is to ensure that patent law enforcement is concomitant with free trade principles of market access and non-discrimination. But over-zealous enforcement of IP rights can also inhibit trade by placing importers or exporters at a competitive disadvantage depending on the situation. Whether it is appropriate to include pharmaceutical patent obligations in agreements that require negotiations on a range of industrial sectors in trade and commerce is briefly assessed.

Section 2.3 is a comparative legal analysis that compares the current domestic patent law of Canada and Mexico in response to U.S. trade pressures. Initially, research on the national patent legislation was conducted by consulting the websites for the national
patent offices, Canadian Intellectual Property Office (CIPO) for Canada, and the Instituto Mexicano de la Propiedad Industrial (IMPI) for Mexico. The website of the World Intellectual Property Organization (WIPO) was then consulted as a source of relevant IP legislation. My analysis compared the legal adjustments made by Canada and Mexico to meet NAFTA obligations, and how the special needs of Mexico, as a developing country, were addressed. By 1991, and under U.S. pressure, Canada and Mexico began legislative reform to conform to NAFTA. This section addresses the domestic legal implementation process of NAFTA obligations from 1990 to 2010. Laws are generally made up of two components: (1) general rules, and (2) specific exceptions. In the area of trade agreements, IP, and public health, the legal components are generally: (1) exclusivity protection obligations, and (2) safeguards. Strain is created by governments playing dual roles in health system provision and economic development via international trade negotiations. This strain is analyzed to provide an understanding of Canada’s and Mexico’s relationships with pharmaceutical patent law and response to U.S. interests and pressures. In section 2.4, this tension is discussed in the Mexican context to provide a comparison of how a developing state under the same NAFTA commitments reconciles competing interests. This analysis aims to inform policy makers in Canada, Mexico and developing countries with regard to similar free trade agreements. The comparative legal analysis may also guide representatives from international institutions, such as the United Nations, on how to analyze pharmaceutical patent law. The section offers insight on how access to medicines might be improved for Canada and Mexico, as well as globally, through greater harmonization to an optimal standard as opposed to a minimum standard. Section 2.5 concludes the chapter.
2.2 The Pharmaceutical Patent System under NAFTA

NAFTA came into force January 1, 1994 (Gómez Dantés & Frenk, 1995). It was the first international trade agreement to include obligations to protect IP rights (Torys LLP, 2005). Canada and the U.S. were parties to an earlier free trade agreement (FTA) (Harrison, 2001). At that time Canada, was a developed country much smaller in economic size than the U.S., and by conceding to pharmaceutical policy adjustments, Canada sought to prevent trade conflict with the U.S. that could negatively impact the economy (Cohen, 2003). For Canada, trade concessions made with the U.S. secured access to the U.S. market and obtained U.S. national treatment. For the United States, ensuring protection and enforcement of IP was one of its main concerns. Canada had a strong generics industry and a compulsory licensing system favourable to the production of generics (Corbett, 2000). U.S. concerns regarding IP were due to a necessary shift from a manufacturing-based economy to a knowledge-based one in order to maintain an ongoing competitive advantage. This made the protection of IP through international agreements a priority for the United States Trade Representative (USTR). NAFTA brought Mexico into a new era of economic development with international legal obligations and rights (Moreno-Brid, Santamaria, & Valdivia, 2005). Chapter 17 of NAFTA defines the scope of IP rights broadly and refers to: “[c]opyright and related rights, trademark rights, patent rights, rights in layout and design of semiconductor integrated circuits, trade secret rights, plant breeders’ rights, rights in geographical indications and industrial design rights” (NAFTA Art. 1721 – Definitions). This dissertation is focused on how best to design, implement, and enforce patent law for the pharmaceutical sector (e.g., medicines). There is an ongoing legal discussion in Mexico
about trade secrets and clinical trial data exclusivity. Legal interpretation issues exist regarding the language being used such as the difference between “data protection” and “data exclusivity” and whether the standards involve “non-disclosure” or “non-reliance” of trial data. This discussion is, however, beyond the scope of this dissertation due to the distinct theoretical economic and legal rationales behind such provisions in contrast to patents.

Figure 3: NAFTA Chapter 17 Articles Impacting Public Health

In NAFTA Chapter 1, the objectives deal directly with IP rights. Article 102 (1) (d) states the primary objective of NAFTA is the “adequate and effective protection and enforcement of intellectual property rights in each Party’s territory” (North American Free Trade Agreement Between the Government of Canada, the Government of Mexico, and the Government of the United States, 17 December 1992, Can. T.S. 1994 No. 2, 32 I.L.M. 289 (entered into force January 1, 1994)). Parties to NAFTA must ensure the enforcement procedures set out in NAFTA are available under domestic law so effective action can be taken against infringers. The NAFTA Chapter 17 on Intellectual Property (Art 1701 (1)) establishes a broad obligation for each NAFTA state member to provide nationals of other NAFTA countries with adequate and effective measures to protect and
enforce IP rights while ensuring that such measures do not become barriers to legitimate trade. Article 1701 (2) of the NAFTA establishes *minimum* standards of IP protection, based on the principles set out in the major international IP conventions in existence at the time. NAFTA Article 1702 allows parties to implement *more* extensive protection of IP rights in domestic law than required, provided that such protection is not inconsistent with NAFTA. This article disallows a contracting party to use Chapter 17 as an excuse for creating trade barriers (Goolsby, 1998a). NAFTA Article 1703 requires each party to grant national treatment to nationals of other parties in protecting and enforcing IP rights (Garcia, 1992). A state party cannot grant more favourable IP protection to its own nationals than to nationals of other NAFTA parties (Rein, 2000b). NAFTA Article 1703(1) applies the Most Favored Nation doctrine to IP (Correa, 1992). Thus, subsection (1) requires each party to accord to nationals of another party treatment no *less* favourable than it accords to its own nationals with regard to the protection and enforcement of all IP rights. NAFTA Article 1704 empowers the parties to prevent abuse of IP rights (Chaudhry & Walsh, 1996). The article states that a party may adopt or maintain, consistent with other provisions of NAFTA, appropriate measures to prevent or control such practices or conditions.

Article 1709 outlines NAFTA’s provisions pertaining to patents. Article 1709 (1) requires parties to make patents available for any invention, whether products or processes, in all fields of technology provided that such inventions are; (1) new, (2) result from an inventive step, and are (3) capable of industrial application. The inventive step and industrial application have been deemed synonymous with “non-obvious subject matter”
set out by Canada and Mexico (Shapiro, 2004). In Canada the Patent Act provides,

[t]he subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to (a) information disclosed more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and (b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere. (Patent Act, R.S.C. 1985, c. P-4, s. 28.3)

In Mexico, new uses for existing inventions are protected so long as they are not obvious to one skilled in the art (Farolan, 2001). NAFTA Article 1709 (12) sets out patent term. It deems that “[e]ach party shall provide a term of protection for patents of at least 20 years from the date of filing or 17 years from the date of grant. A Party may extend the term of patent protection, in appropriate cases, to compensate for delays caused by regulatory approval processes.” This extension enables the owner of the patent to recoup time lost in obtaining government approval (Goolsby, 1998b). Thus, this article accommodates both patent term and the requirement of a lengthy government approval process before new pharmaceutical products can be marketed. This language may negatively impact access to medicines in two ways. First, the provision grants at least 20 years, leaving room for parties to extend this time period further. Second, a patent holder may make an application for an extension due to delays caused by regulatory approval process—known as ever-greening of patents. Thus, Chapter 17 regulates patents in a way that allows for prolonged periods of exclusivity (Correa, 2000).
In relation to access to medicines, there are built in safeguards within the NAFTA agreement for the protection of public health. The primary safeguard is compulsory licensing. This safeguard has been identified as an important tool for developing countries to promote access to lower-priced medicines. Whether or not compulsory licensing is an adequate and effective safeguard mechanism, as patents are an enforcement mechanism, is a question open to debate. Compulsory patent licensing was first introduced by the Paris Convention Treaty and allows for each country to legislate measures for compulsory patent licensing. (See Paris Convention Article 5 (A) (2)) International Convention for the Protection of Industrial Property, Mar. 20, 1883, 25 Stat. 1372, T.S. No. 379, as revised at Stockholm on July 14, 1967, 21 U.S.T. 1583 and 24 U.S.T. 2140, TLAS Nos. 6923 and 7727) (Kunz-Hallstein, 1989). Article 5 of the Paris Convention Treaty creates the right of countries to impose compulsory licenses (Julian-Arnold, 1992). This treaty allows governments to compensate for shortcomings associated with not establishing domestic research-based pharmaceutical industry by making it possible for them to reverse engineer pharmaceutical products for their populations (Mossinghoff, 1987a). Pre-NAFTA the Canadian government made substantial use of compulsory licensing in fostering its strong generic-based pharmaceutical sector, in line with its philosophies of universal health care and access (Torremans, 1996).

NAFTA contains provisions for government expropriation of a patent and addresses compulsory licensing in Article 1709 (10) (a)–(l). Any party wishing to infringe on a patent must have domestic law authorizing the infringement. Canada and Mexico both
have compulsory licensing legislation, but the U.S. does not (Creech, 2004). NAFTA Article 1709 (10) states, “Where the law of a party allows for use of the subject matter of a patent, other than that use allowed under paragraph 6, without the authorization of the right holder, including use by the government or other persons authorized by the government” (NAFTA 1709 (10)). Parties are subject to the following guidelines based on NAFTA 1709 (10) (a)–(l):

- (a) Each case will be considered on its own merits;
- (b) A Party is only able to infringe after making efforts to obtain authorization from the patent holder—the exception being in cases of national emergency, or extreme urgency, or other public non-commercial use;
- (c) The scope and duration of such use shall be limited to that authorized;
- (d) such use shall be non-exclusive; and,
- (e) non-assignable;
- (f) Patent infringement by the Party shall be authorized predominately for the supply of the Party’s domestic market on the condition that if the initial reason for allowing infringement ceases and are unlikely to recur, the authorization for the infringement should be terminated (the analogous provision in TRIPS, Article 31 (f), has been the focus of much contention);
- (g) Authorization for such use shall be liable, subject to adequate protection of the legitimate interests of the persons so authorized, to be terminated if and when the circumstances that led to it cease to exist and are unlikely to recur. The competent authority shall have the authority to review, on motivated request, the continued existence of these circumstances;
- (h) When the government is infringing on a patent, adequate remuneration shall be paid to the right holder, taking into account the economic value of the authorization;

- (i) Any authorization to infringe a patent should be accompanied with the ability for the patent holder to seek judicial review or other independent review by a distinct higher authority;

- (j) likewise, any issue regarding adequate remuneration to the rights holder should also be subject to judicial or other independent review by a distinct higher authority;

- (k) The party shall not be obliged to apply the conditions set out in subparagraphs (b) and (f) where such use is permitted to remedy a practice determined after judicial or administrative process to be anticompetitive;

- (l) And, the Party shall not authorize the use of the subject matter of a patent to permit the exploitation of another patent except as a remedy for an adjudicated violation of domestic law regarding anticompetitive practices.

Of particular importance to public health, section 1709 (10) (b) sets out the emergency doctrine that allows a party to expropriate a patent during a national emergency and other cases of extreme urgency. Mexico made use of this provision when faced with the 2009 H1N1 swine flu pandemic. Section 1709 (10) (b) provides:

The requirement to make such efforts may be waived by a Party in the case of a national emergency or other circumstances of extreme urgency or in cases of public noncommercial use. In situations of national emergency or other circumstances of extreme urgency, the right holder shall, nevertheless, be notified as soon as reasonably practicable. In the case of public non-commercial use, where the government or contractor, without making a patent search, knows or
has demonstrable grounds to know that a valid patent is or will be used by or for the government, the right holder shall be informed promptly;

The drafters of NAFTA did not define the terms “national emergency” or “extreme urgency”. Individual states are left to determine what constitutes a national emergency; for instance, the U.S. declared a national emergency during the Anthrax scare in the aftermath of 9/11 (Mullin, 2002). There is nothing, however, in Chapter 17 that can guide a court in the event of litigation, or a dispute settlement panel, in determining if a state wrongfully believed it was being faced with a national emergency. Courts would likely defer to the state on the declaration of a national emergency, provided the state acted in good faith (Shapiro, 2004). TRIPS also grants some basis for compulsory licensing, allowing countries to determine the grounds on which they grant compulsory licenses provided that a set of procedural conditions is met. This is stipulated in Article 31. Akin to the language used in NAFTA, these conditions include, for example, prior negotiations with the patent holder. In instances of “public utility” or “government use” compulsory licenses, countries are released from most of the procedural obligations. Consequently, in times of national emergency or when the compulsory license is granted for public use, countries do not have to abide by most of the ordinary conditions (such as prior negotiations with the patent holder). Because potential delays introduced by negotiations are removed in the case of public utility licenses, they should be easier and quicker to grant (Shapiro, 2004).

The conditions placed on the normal use of compulsory licensing (i.e., not a clear-cut national emergency), means it may be better for governments to negotiate deals (i.e., voluntary licensing) with pharmaceutical companies to purchase bulk quantities at a
discount and avoid use of the emergency doctrine power. This scenario has come to pass in instances where countries have threatened the use of compulsory licenses, most recently in Mexico during the outbreak of H1N1 (Dziuba, 2010). It has been argued that the willingness of governments to negotiate voluntary licenses demonstrates respect of the importance of patent rights to private enterprise (Shapiro, 2004). In practice, compulsory licenses are rarely formally granted (Barton, 2004). The mere threat of compulsory license issuance however has been at times an effective tool. The threat has been used as leverage in the negotiation of price reductions for pharmaceuticals with multinational companies by governments (Barton, 2004). For example, Brazil, South Africa, and Thailand used the threat of compulsory licensing during negotiations to procure HIV/AIDS antiretroviral drugs (Ford, 1999; Kunz-Hallstein, 1989; Lazzarini, 2003b). Similarly, the Mexican government negotiated the procurement of the on-patent pharmaceutical medicine Tamiflu with Roche, but only after threatening use of compulsory licenses during the 2009 outbreak of H1N1 virus (Hodge Jr, 2010b). Thus, although compulsory licensing may not adequately ensure guaranteed flexibility in meeting public health goals, it does grant some developing countries adequate leverage to ensure medicines procurement in non-emergency situations.

NAFTA Article 1709 (10) (f), states a compulsory license shall be authorized predominately for the supply of the domestic market. During TRIPS negotiations, this issue was known as the 31 (f) problem. TRIPS Article 31 discusses the conditions under which a member government may allow for compulsory licensing without the patent holder’s authorization. Subsection (f) limits compulsory licensing to countries with the
capability to produce pharmaceutical products for *domestic* use (Barton, 2004). The 30th of August 2003 WTO General Council decision on the implementation of paragraph 6 of the Doha Declaration (30th of August Decision) addressed the problem of Article 31 (f) in the TRIPS agreement. The Doha Declaration recognized that some WTO members were completely lacking or had insufficient pharmaceutical manufacturing capacity, and therefore would have difficulty making use of compulsory licensing under the TRIPS agreement. Many countries lack pharmaceutical production capacity and would therefore need to import them from countries such as India, an important supplier of affordable generic drugs. Article 31 (f) precluded a country with established pharmaceutical manufacturing, such as Mexico, to produce patented drugs without the patent holder’s permission if those drugs were to be exported rather than sold locally. This is particularly relevant for exports into Central and South America (Zuniga & Combe, 2002). The main destination countries for Mexican pharmaceutical exports have been, and still are, Panama, Colombia, and Venezuela. These countries have little to no pharmaceutical production capacity. In Paragraph 6 of the Doha Declaration, countries focused energy on reaching a solution to this problem by 2002. Prolonged negotiations finally led to an agreement in August 2003. The 30th of August Decision allows any member country to export pharmaceutical products made under compulsory licenses within the terms set out in the Agreement (Barton, 2004). The NAFTA Secretariat has issued no equivalent to the 30th of August Decision. Adoption of a NAFTA-based equivalent to the 30th of August Decision regarding the implementation of paragraph 6 would further promote access to medicines for developing countries. NAFTA is paramount over TRIPS. This means it is of the highest jurisdiction in the event of inconsistencies between the two agreements.
according to Article 103 (NAFTA in Relation to Other Agreements). Thus, although the intention of the 30th of August Decision was to solve the problem posed by Article 31 (f), the same problem is posed by NAFTA Article 1709 (10) (f). The latter article similarly requires that any such use of compulsory licensing shall be authorized predominantly for the supply of the member states domestic market.

Lack of explicit recognition that NAFTA Article 1709 (10) (f) presents members with the same potential restriction that was created by TRIPS Article 31 (f) may analogously negatively impact access to medicines. For example, the U.S., as a NAFTA member, could decide to argue that Canada’s adoption of a licensing system for pharmaceutical exports under the August 30th of August Decision violated Canada’s NAFTA obligations (Roffé et al., 2006). It is, however, hard to imagine that the U.S. would file such a complaint. The U.S. would face international backlash, following their agreement to the prolonged Doha Declaration Paragraph 6 negotiations (Abbott, 2005a). The negotiations were undertaken to address a major global health problem in the trading system. The results of the agreed upon outcome by the WTO member states should not be discarded as non-binding to NAFTA member states due to consistencies between developments over the current understanding of the implications of these treaties. In the unlikely event that a complaint was filed against Canada for violating its NAFTA obligations by acting on the 30th of August Decision, Canada would have a number of positions by which it could respond. The first argument in favour of Canada is that the Doha Declaration extends to NAFTA, as three North American countries are all WTO member states. The language of the Paragraph 6 problem (TRIPS Article 31 (f)) is almost exactly replicated
in the NAFTA agreement. Trade negotiators from the U.S. and Canada could not reasonably have intended to reach agreement in the WTO setting and then effectively rescind the agreement under NAFTA. The Doha Declaration Paragraph 6 Agreement is envisioned to address monumental global health problems and to give force to the rights of WTO developing country member states with little or no pharmaceutical manufacturing capacity. Restrictive measures against Canada as an exporting country would effectively paralyze the Paragraph 6 Agreement. The U.S. would have a difficult time explaining why the member states’ agreement to the Paragraph 6 solution should not be interpreted as an agreement to apply the same terms to NAFTA. In the alternative Canada may be able to rely on NAFTA Article 1709 (6). This article is the general exceptions provision similar to that contained in TRIPS Article 30. NAFTA Article 1709 (6) states:

A Party may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking into account the legitimate interests of other persons.

Canada could argue that its system to implement the WTO Paragraph 6 system was authorized under NAFTA Article 1709 (6). These positions aside, Canada might still reasonably be concerned with meeting its legal obligations under NAFTA. For greater clarity, the NAFTA secretariat should advance a North American Doha Declaration and an equivalent to the 30th of August Decision on the Implementation of Paragraph 6 for NAFTA Article 1709(10)(f). Adoption of this equivalent would help facilitate the use of compulsory licenses for generic producers in North America that could make use of the opportunity to export lower-priced medicines to the developing world.
Following the Implementation of Paragraph 6 of the Doha Declaration on TRIPS and Public Health, Canada amended its patent law and enacted Canada’s Access to Medicines Regime (CAMR). CAMR allows for the production and export of generic drugs to developing countries that lack the manufacturing capacity to undertake a domestic compulsory license. CAMR has been the subject of much criticism, however, for its inability to promote quick access to urgent medicines for countries in need (Goodwin, 2008). In particular, procedural impediments have inhibited its use.

To examine these procedural problems in action, one need only look to the compulsory license sought by Apotex to supply an AIDS antiretroviral combination drug, Apo-Trivair, to Rwanda. After the Canadian legislation passed in June 2004, Médecins Sans Frontières (MSF), the Canadian Generic Producers Association (CGPA), and Health Canada met in round table discussions to explore how Canadian pharmaceutical companies could supply pharmaceuticals to developing countries under CAMR. In August 2004, Apotex, Canada’s largest generic pharmaceutical manufacturer, engaged in discussions with MSF and government representatives to further explore the practical possibilities. Compulsory licenses under CAMR were issued to Apotex to produce and export antiretroviral therapy after prolonged negotiations (Cohen-Kohler, Esmail, & Cosio, 2007). In December 2004, Apotex agreed to produce a three-in-one, fixed-dose antiretroviral, Apo-TriAvir, (zidovudine/lamivudine/nevirapine). At that time, however, the combination antiretroviral was not on the Schedule 1 list of medicines approved for export under the regime appended to Bill C-9. Almost a year later, in September 2005,
the Federal Cabinet followed the recommendations from the Ministers of Industry and Health and approved the addition of this drug to the Schedule 1 list. Apo-TriAvir then went through the Canadian regulatory process and was approved in July 2006. In July 2007, Rwanda notified the WTO of its intent to import, and Canada informed the WTO of its compulsory license in October 2007. A tendering process was held in which Apotex won the successful bid to export the medicine in 2008. To date, this is the sole case of Canadian exportation of generic medicines under the regime and compulsory licensing under CAMR. CAMR reform attempts have proven difficult (Attaran, 2003a). The discussion surrounding CAMR should be elevated to the regional level and considered by the NAFTA Secretariat in the context of ongoing patent system harmonization issues. All three federal governments of the North American trading bloc should be at the table to ensure a harmonized view of how to best develop a coherent strategy on promoting access to medicines in the developing world. Progress would be slow, but discussion is necessary for health-sensitive outcomes. The pharmaceutical patent system under NAFTA makes clear potential safeguards for public health. Difficulties arise not from the lack of available safeguards, but the complexities with using them.

2.3 Patent Systems in Canada and Mexico under U.S. Pressure

The U.S. has pursued an aggressive global policy of patent right protection in order to protect IP resources and maintain its dominance in a knowledge-based economy (Abbott & Reichman, 2007b). In pursuing their aggressive IP rights policy, the U.S. has developed two effective trade-related techniques for dealing with resistance. The first technique relies on paragraph 301 of the 1974 Trade Act (19 USC 2411 et seq., Pub L No. 93-6188). This paragraph authorizes the President to investigate allegations of unfair
trade practices on the part of another country and, if the inequity is not corrected within a designated period of time from its discovery, to retaliate against the country with executive action. This authority has been expanded under the new “Special 301” provision of the 1988 Omnibus Trade and Competitiveness Act (Pub L No. 100-418.), which transferred authority to the United States Trade Representative (USTR). Special 301 also extends the scope of the investigative process, making it possible to deal with trade barriers on a country-by-country basis and establishing a list of “priority countries” whose barriers present major obstacles to U.S. exports (King, 1991). The annual Special 301 Report unilaterally evaluates U.S. trading partners on adequacy and effectiveness of their IP rights protections to combat counterfeiting, internet and digital piracy, and IP as it relates to health policy (Ilias, 2008). In 2009, USTR put 12 countries on the priority watch list, including Canada and Mexico. Canada is on the priority watch list for its ongoing internet pharmacy trade (Pollock, 2005). The U.S. has said Canada failed to accede to and implement the WIPO internet treaties in order to curb the volume of infringing products shipped into the U.S. (Geist, 2007). Patent infringements were the reason behind placing Mexico on the Special 301 Watch List in 2003 (Chaudhry & Zimmerman, 2009). Mexico was on the watch list again in 2005 and 2006. The USTR repeatedly used the issuance of marketing approvals for patent-infringing copies of pharmaceutical products, among other suspected IP shortfalls, to put Mexico on the List of countries in which it suspects piracy is prevalent or tolerated by governments. Mexico remained on the Watch List in 2010 (Flynn, 2010). The U.S. has urged Mexico to devote greater resources to its enforcement agencies and continue to build a consistent record of aggressive prosecution and deterrent-level penalties to enforce IP rights. The U.S. has
also urged Mexico to strengthen its IP regime by enacting legislation to provide *ex officio* authority to law enforcement and customs authorities (Zagaris & Aguilar, 1994). *Ex officio* are powers concomitant with holding a certain office and may be exercised without any further instrument conferring such authority. Recently, the U.S. has encouraged Mexico to provide effective protection against unfair commercial use of undisclosed clinical trial data generated to obtain marketing approval for pharmaceuticals, and to provide an effective system to prevent the issuance of marketing approvals for patented pharmaceuticals, i.e., linkage (Cartagena & Attaran, 2009). Overall, Section 301 issues have a negative impact on regional cooperation and decrease respect for neighbours. The practice should be stopped, but it is unlikely to happen due to ongoing competitive pressures between countries (Duina, 2006).

The second trade-related technique utilized for dealing with resistance to U.S. IP rights policy involves aggressive trade negotiations with countries whose domestic law adversely affects U.S. trade policy objectives. The U.S. has been known to leverage its economic might against a noncompliant country to bar it from entering the GATT or becoming a signatory to a regional free trade agreement such as NAFTA (Abbott, 2005c). This tactic was employed in pre-NAFTA negotiations between the U.S. and Canada. Prior to NAFTA, Canada was pressed to modify its patent law in the area of pharmaceuticals by expanding the life of patents to at least twenty years. Canada was also pressured to abolish the long-standing practice of compulsory licensing which fostered the domestic generic industry. Both demands were consistent with U.S. patent policy direction and harmonization to U.S. standards. This tactic has worked relatively well, as
most countries are not willing to forgo the benefits of international trade with the U.S. in order to maintain lax IP standards at home (Bird, 2006).

It is noteworthy that in the 2001 Doha Declaration, the U.S. affirmed their respect for each country’s right to protect public health (Correa, 2002). The U.S. also supported the TRIPS health solution concluded in August 2003, which permitted WTO member states to issue compulsory licenses to export medicine to countries with little or no production capacity. Further, when the WTO General Council adopted a decision in December 2005 that incorporated this solution into an amendment to TRIPS, the U.S. became the first WTO member to formally accept this amendment (Abbott & Reichman, 2007c). Pharmaceutical compulsory licensing, however, does not take place in the U.S. and is inconsistent with the Patent Act (Ng & Kohler, 2008). The Act imposes no duty on a patent holder to license or use any rights to the patent (35 U.S.C. para. 271 (d) (4) (2004)) (Fauver, 1988a). The government, however, has the authority under the Fifth Amendment to expropriate or take private property provided it gives just compensation (U.S. Const. amend. V. states: “nor shall private property be taken for public use without just compensation”). That being said, the U.S. position continues to be one that advocates for increased strengthening of global IP protection and views international agreements, such as TRIPS, as having sufficient safeguards to enable countries to address public health problems (Abbott, 2005b).

The following subsections comparatively analyze the evolution of pharmaceutical patent law enacted in Canada with Mexican law to understand the differences in how each
country has harmonized to the NAFTA standard. To conduct this comparative legal analysis, research on the national patent legislation was conducted by consulting the websites for the national patent offices, Canadian Intellectual Property Office (CIPO) for Canada, and the Instituto Mexicano de la Propiedad Industrial (IMPI) for Mexico. Following that relevant statutory materials of the two countries were collected from the WIPO Gold Database (http://www.wipo.int/wipolex/en/) which provides streamlined access to reference material of importance for source information on the global IP system. There are comprehensive available legal texts for IP law in both Canada and Mexico. The information found at the websites was verified by the statutory materials collected at the UBC law library.

Comparisons are made between how Canada, a developed country, and Mexico, a developing country, harmonized to the international patent law standard lobbied for by the U.S. government and research-based pharmaceutical corporations. How each country is balancing the sometimes-competing goals of public health protection and economic wealth maximization are addressed. Principles of national treatment, most-favored nation, transparency for eliminating barriers to trade, encouraging fairness, provisions for adequate and effective protection, and enforcement of IP rights might make it seem that harmonization would occur relatively seamlessly among member states (NAFTA, Art. 102 (d)). The same could be argued at the multilateral level under the WTO-administered TRIPS agreement. Interesting differences exist, however, between the two countries’ patent laws despite the mutual goal of advancing harmonization and establishing a framework for further trilateral and multilateral cooperation to expand and enhance the
benefits of NAFTA (NAFTA, Art. 102 (d)).

The analysis conducted in this section suggests that domestic implementation of NAFTA obligations is resulting in each country interpreting obligations in a way that best suits their specific public health needs. They meet NAFTA minimum standards (NAFTA art. 1701 (2)) but do so in a way that best meets each countries’ interests and as such results in a lack of regional harmony. Differences in implementation may lead to an on-going competitive advantage for the U.S., and produce an unacceptably high-risk for costly litigious disputes over unresolved patent law issues. This may have negative implications for each member states’ mutual interest in North America’s economic well-being. This in addition to considerations regarding what would be best from a humanitarian perspective for global access to medicines.

The U.S. international policy position on pharmaceutical patent protection is aggressive persuasive compliance. Issues persist due to inconsistent approaches among countries on how to best implement pharmaceutical patent protection in domestic legislation, protection which would minimize any negative impacts on access to medicines. Uncertainty exists for both how to best implement new law and what constitutes adequate enforcement of that law. The law in each country on controversial subjects, such as linkage requirements between health and patent agencies, or when the doctrine of national emergency may be used to issue compulsory licenses, is still evolving in the context of NAFTA/TRIPS obligations. Member states react to issues surrounding pharmaceutical patent rights and access to medicines with differing degrees of concern
based on their strategic economic positioning. Different approaches to the implementation of linkage requirements and the use of compulsory licensing impacts a government’s ability to adequately procure medicines for its people at a reasonable price as well as to potentially provide support to other developing countries. In order to contextualize the analytical discussion presented in section 2.4, two primary areas are examined. First, patent protection linkage requirements in Canada and Mexico are analyzed as a major NAFTA-plus legal issue. Second, the area of compulsory licensing is analyzed as the primary legal safeguard available to enhance access to medicines.

2.3.1 Patent Protection Linkage Requirements in Canada

Linkage legislation was designed to facilitate market entry for generic pharmaceuticals. Such facilitation has its inception in U.S. case law and is known in IP circles as early working exemptions (Other names include Research Exemption, Waxman-Hatch Exemption or Bolar provision) (Krulwich, 1985). These exemptions are found as U.S. statutory materials in the Drug Price Competition and Patent Term Restoration Act, informally known as the Waxman-Hatch Act (Jones, 2002). The Waxman-Hatch Act attempts to strike a compromise between the interests of the research-based and the generic-based pharmaceutical industry (Corbett, 2000; Dziuba, 2010). Section 156 of the Waxman-Hatch Act is pro-patent holder, allowing a five-year patent extension to compensate for upstream distortion resulting in a shortened patent period due to the delay between filing and having the patent approved. This extension means that if a patent applicant does not have a patent approved shortly after filing, the patent applicant can extend the patent so that the patent is in effect for 17 years (Behrendt, 2002). Section 156 helps generic manufacture by compensating for downstream distortion, allowing generic
manufacturers to start their research prior to the end of the patent so they are ready to manufacture when the patent ends (Jones, 2002). In addition, Section 271 (e) allows an exception to patent infringement for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs (35 U.S.C. para. 271 (e) (1) (2004)) (Engelberg, 1998). Early working provisions allow generic firms to prepare for market entry and expedite competition at the time of patent expiration. Such provisions do not shorten patent terms but rather eliminate the effective extension of patent terms. NAFTA and TRIPS both permit early working provisions (Shadlen, 2009).

The Patent Act of 1923 and its subsequent amendments define patent rights in Canada. Before 1987, IP protection for patented pharmaceuticals was not the strongest among developed countries. Patents had shorter terms and were subject to compulsory license for manufacture and import (since 1923 and 1969, respectively). In 1987, amendments to the Patent Act were introduced (Bill C-22) to enhance pharmaceutical patent protection. The amendments increased protection from compulsory licensing after market approval for patent holding pharmaceutical companies. As well, the patent protection period was extended to twenty years from date of filing instead of the previous granting system of 17 years from the date of the patent’s issue. In 1993, following GATT and NAFTA negotiations, the Canadian government passed Bill C-91, which repealed Canada’s longstanding compulsory licensing regime for patented pharmaceuticals and introduced the early working exception (Paris & Docteur, 2007). The benefits of early working exemptions and quicker generic availability were perceived as a threat to the market
share of research-based pharmaceuticals. As a result, regulations have become stricter over time.

Research-based pharmaceutical industry lobbying efforts highlight inadequacies in Canada’s administrative procedures. These inadequacies have called into question whether Canada meets its NAFTA and TRIPS obligations with respect to pharmaceutical patents based on adequate enforcement obligations (Farolan, 2001). Canada is required under NAFTA and TRIPS to ensure effective enforcement of the standards of patent protection in those agreements. NAFTA Article 1714 and related articles require Canada to:

ensure that enforcement procedures are available under its law so as to permit effective action against any act of infringement of intellectual property rights covered by (these) Agreements, including expeditious remedies to prevent infringements and remedies which constitute a deterrent to further infringements.

The research-based pharmaceutical industry has argued that inadequacies in the law allow generic medicines to be approved by Health Canada while valid patents were still in force (Faunce & Lexchin, 2007). The pharmaceutical industry has maintained that early working regulations failed to provide transparent and equitable consideration of patent holder rights and prevent patent infringement. To prevent abuse by generic manufacturers in selling their approved medicines before patent expiry, Bill C-91 introduced the Patented Medicines (Notice of Compliance) Regulations. The idea behind NOC linkage is that pharmaceutical safety and efficacy regulators at Health Canada cannot issue authorization for market entry of a generic until all of relevant patents on a brand name product have been proven expired (Section 55.2 of the Patent Act, Statutes of
Canada, as enacted by the Patent Act Amendment Act, 1992 (Bill C-91), Statutes of Canada, 1993, c.2.) (Taylor, 2010). This provision requires patentees to provide Health Canada with the list of valid patents linked to any product seeking approval. Generic manufacturers have to check dates of patent expiry of listed patents before marketing or make an attestation, a Notice of Allegation (NOA), explaining why their product is not infringing on current patents. If the patentee disagrees, litigation ensues and an automatic stay is triggered that bars Health Canada from issuing the generic product a marketing authorization for 24 months, until the litigation is resolved or the patent expires, whichever comes first. As such, linkage regulation places an onus on Health Canada to determine whether registered patents would be infringed if approval (i.e., a NOC) was granted for the generic medicine (Rathod, 2010). If a patent is identified, the generic producer is required to issue a NOA of non-infringement to the patent holding research-based company. As a heads up which allows research-based firms time to access judicial procedure to seek a prohibition order and prevent a NOC from being issued by Health Canada to a generic-based firm.

This linkage arrangement has become a basis for effective enforcement of pharmaceutical patent holder’s rights as required under NAFTA. Research-based pharmaceutical industry argues, however, that the manner in which procedures are applied fails to extend protection in a majority of infringement cases. The argument is that the legal burden is on the research-based pharmaceutical company to prove that the generic company’s allegation of non-infringement is not justified as they have patent holder rights. There have been a number of cases since 1993 (when linkage regulations came into effect) in
which patent holders had claimed infringement but were unable to prevent a NOC being issued (Hitchman, 1998). If a patent holder is unsuccessful in preventing Health Canada from issuing an NOC, the next step is to seek relief through an infringement action. A patent holder can apply for an interlocutory injunction to maintain its rights and prevent the infringing generic version from reaching the market (Hussey, 2002b). The Canadian courts, however, apply a very high standard of irreparable harm for an interlocutory injunction. To be successful a patent holder must establish there will be irreparable harm which cannot be compensated by an eventual award of damages (Garland & Want, 2008). The standards applied by the Canadian courts may not be consistent with the standards provided for in NAFTA (NAFTA Article 1701 (1)).

The fundamental private right for patent holders under NAFTA is the exclusive right to prevent the making, use, or sale of a patented product or process that is not authorized by the patent holders (NAFTA Article 1709 (5)). In terms of the enforcement of that right, NAFTA Article 1716 stipulates prompt and effective provisional measures, including interlocutory injunctions, to prevent infringement of any IP right, and in particular to prevent entry into the channels of commerce allegedly infringing goods. The test under NAFTA for provisional measures is whether any delay in the issuance of such measures is likely to cause irreparable harm to the patent holder (NAFTA 1716). This is a lower standard than the irreparable harm test applied by Canadian courts (Garland & Want, 2008). Research-based pharmaceutical companies conclude the availability of injunctions against the marketing of a generic product is insufficient protection as these injunctions are frequently unavailable to the research-based companies. They further argue that
linkage regulations are necessary because generics based competitors are not concerned with being awarded an interlocutory injunction to prevent generic products from reaching the market (Faunce & Lexchin, 2007).

The generic-based sector views these issues quite differently. The Canadian Generic Pharmaceutical Association (CGPA) claims that abuse of regulatory linkage mechanisms results in millions of dollars of losses for the Canadian public due to paying for on-patent versions of pharmaceuticals for extended periods of time. The generic-based industry contends that the linkage regulations are being used for ever-greening. Ever-greening refers to prolonging patent exclusivity through potentially inequitable measures (Hussey, 2002a). In recent years, provisions aiming at protecting patent rights have been used by manufacturers of some top-selling patented pharmaceuticals to delay generic entry. In particular, brand-name companies were suspected of routinely protecting old products by new patents in order to trigger multiple 24-month stay periods against generic market entry. The CGPA maintains that the research-based companies continually list new patents on a given product. This can trigger a new Notice of Allegation to be required and an additional delay on the appearance of a generic (Lexchin, 2005b). The position of research-based companies is that there is always ongoing research into pharmaceuticals. Multiple and broad scoping patents are frequently found on a single medicine in the pharmaceutical sector (Laakmann, 2007). Therefore, they argue, it is natural that new patents will be filed.
In response to the ever-greening attempts by patent holding companies, the Canadian Ministry of Industry and Health developed a joint package of regulatory amendments designed to stabilize the pharmaceutical marketplace by establishing firmer boundaries to the period during which brand-name medicines enjoy market exclusivity. Following consultations with industry stakeholders, a set of amendments came into force on October 5, 2006 and was published on October 18, 2006 in the Canada Gazette, Part II. The new regulations limit the use of ever-greening from follow-on patents into the Notice of Compliance regulations (Rathod, 2010). The regulations prevent any new patents from being filed by a research-based patent-holding company, after a generic company’s submission of an application for market approval of a pharmaceutical to be considered in the NOC regulations process. The freezing of the register prevents any patent arising after the date the generic files its regulatory submission with Health Canada from triggering additional 24-month stays against that generic firm. The new regulations also preclude patents covering areas without direct therapeutic application (such as processes or intermediates) as blocking patents to generic approval (Government of Canada, Canada Gazette Part II Regulations amending the patented medicines (notice of compliance) regulations 2006, 140 (21): 1503–1525). Research-based companies can only protect improvements to the original form of the pharmaceutical that are innovative and therapeutic, known as incremental innovation. The concept of product specificity is the key consideration required of the Minister of Health in applying the listing requirements. This is entrenched in the amendments through more precise language respecting the intended link between the subject matter of a patent in a patent list and the content of the underlying generic submission for marketing authorization. Under the amendments, only
certain clearly defined submission types would present an occasion to submit a new patent list (Paris & Docteur, 2007). These regulations swing the linkage pendulum back towards favouring the generic-based industry.

Thus, linkage regulations are an area where industrial and public health interests compete in some respects and co-evolve in a manner that has direct consequences for access to medicines. An important legal and policy issue is whether, and how, the activities of patent and health officials should be coordinated. Health authorities have become intertwined in the patent system and may be able to influence the prioritization of public health and improve the overall system if the relationship is appropriately structured. Linkage regulations were originally designed to promote entrance of generics into the marketplace by facilitating the process by which a generic-based manufacturer could reproduce an on-patent pharmaceutical prior to the expiration of patent exclusivity. These exemptions allowed generic manufacturers to test generic versions of an on-patent pharmaceutical before the patent expires for the purposes of initiating registry proceedings and interchangeability trials (McPherson, 2006). Without such a provision, the effective life of a patent is extended beyond its original expiry date by the time required to conduct tests on the generic versions for market entry. Research-based pharmaceutical companies are increasingly concerned that NOC regulations cannot provide the basis for effective enforcement of pharmaceutical patent rights as required under NAFTA. These companies claim that Health Canada has been unpredictable in its practices relating to the listing and delisting of patents and in requiring generic-based companies to send a NOA (Faunce & Lexchin, 2007). These issues continue to be the
subject of intense disagreement between Multinational research-based and Canadian generic-based sector companies. Greater clarity is needed. Clarity is unlikely to be achieved in the near future, however, due to the complexity of the issues and ongoing attempts to balance competing, yet equally important, private and public sector interests. Delays caused by needless threats, litigious posturing, and court battles fought over a lack of clarity in the linkage regulations and the *Patent Act* has likely cost hundreds of millions of dollars in wasted resources. This type of unnecessary legal activity results in increased barriers to access to medicines for Canadians. Between 1998 and 2004, out of 138 cases that have gone to court, 12% have taken more than 24 months to resolve. (Office of Patented Medicines and Liaison: Therapeutic Products Directorate statistical report 2004: patented medicines (notice of compliance) regulations. Health Canada 2005.) This situation needs to be remedied.

Many developing countries have also resisted U.S. pressure to proceed with regulatory linkage through their imposition in bilateral trade agreements because it has increasingly favoured patent holders. An objection by health officials is that such linkage places an unwanted administrative and legal responsibility on government health and safety regulation agencies as it transfers the burden of defending a patent from the private rights holder to a public agency paid for by tax dollars. The advanced forms of linkage regulations are not included in NAFTA/TRIPS, but it is a relevant enforcement issue and the next generation of NAFTA/TRIPS plus bilateral agreements. The Dominican Republic Central America Free Trade Agreement (DR-CAFTA) between the U.S. and Central America has linkage provisions (Krikorian & Szymkowiak, 2007; Rajkumar,
Mexico has also introduced linkage regulations into its patent systems as conducive to the global IP law enforcement to an adequate and effective standard found in NAFTA and TRIPS (Shadlen, 2009).

2.3.2 Patent Protection Linkage Requirements in Mexico

Historically, Mexico’s June 1976 Law on Inventions gave relatively low protection to patent rights (Flax, 1999). The Law on Inventions reflected a model of economic development known as import-substituting industrialization (ISI) (Sell, 2004). This protectionist policy and closed-market strategy placed high tariffs on imported goods in order to encourage the production and consumption of national products (Milner, 1999). Laws on private patent rights were weakened in favour of state interests. In 1987 Mexico amended this legal ordinance and added a new law, the Ley de Invenciones y Marcas, or Law on Inventions and Trademarks. Under the new law, patents for pharmaceuticals were to be allowed, but with a ten year transitional period. This allowed producers of copy products time to adjust to the new realities of no longer being able to produce copies of on-patent products. In the 1990s Mexico moved to liberalize their markets to foreign direct investment. Mexico’s poor economic conditions allowed for U.S. leverage in advancing an IP harmonization agenda during the NAFTA negotiations (Sell, 2004).

Meeting trade treaty obligations entails direct domestic costs to countries in the form of legislative changes, new enforcement regulations, and shoring up administrative institutions (Barton, Goldstein, Josling, & Steinberg, 2008). These costs are often disproportionally borne by developing countries (Finger & Schuler, 1999). For Mexico, entering NAFTA required significant patent system reform, but local industry had limited
capacity to generate or capitalize on innovative R&D, and new roles had to be defined for the national pharmaceutical industry and government regulatory institutions as multinational pharmaceutical companies looked south for market expansion.

In order to meet NAFTA trade integration standards, Mexico modernized its IP statutory framework. On 27 June 1991, Mexico enacted the *Ley de Fomento y Proteccion de la Propiedad Industrial* (LFPPI), (Law on the Promotion and Protection of Industrial Property, 27 June 1991) (Troy, 1997). This law renovated the Mexican patent system and pharmaceutical firms were able to patent products in Mexico. The LFPPI provides for pharmaceutical patents for all qualified, new inventions that have an industrial use, as well as improvement patents covering qualified improvements to existing patented inventions. Despite Mexican generic-based pharmaceutical business opposition, the LFPPI changed grant patent protection to twenty years. As a result of the enactment of the LFPPI, starting July 1991 pharmaceutical companies were able to patent products in Mexico as in other countries that explicitly recognized pharmaceutical patents.

The LFPPI also created the mandate for a new administrative body, the *Instituto Mexicano de la Propiedad Industrial* (IMPI), an arm of the Ministry of Economy (Secretaria de Economia), to regulate Intellectual Property in Mexico (Casas & de Gortari, 2001). On November 22, 1993, the Mexican Industrial Property Institute was established by decree. The purpose of IMPI is to foster and protect IP rights and stimulate creativity to the benefit of society. Unlike its counterparts in the Canadian Intellectual Property Office (CIPO) and the U.S. Patent and Trademark Office (USPTO), IMPI has an
active role in patent enforcement. IMPI may conduct investigations, hold hearings, and impose administrative sanctions on patent infringers. IMPI also has search, seizure, and prosecution powers (Farolan, 2001). The Mexican government endowed IMPI with these broad powers as a means of complying with NAFTA Chapter 17 to enforce IP rights (NAFTA—1701). The fundamental reforms to IP law in Mexico under this legislation permitted Mexico to be included in NAFTA. This was not accomplished for other developing countries in Latin America in the subsequent Free Trade Agreement of the Americas negotiations due to disputes over IP chapters (Gasman, 1995).

In 1994, the federal government issued a decree that amended the Ley General de Salud (General Health Law) and the Ley de la Propiedad Industrial (Law on Industrial Property; LPI) that replaced the LFPPI. This was done to establish better coordination between the Ministry of Health (Secretaria de Salud)—the authority responsible for granting pharmaceutical market approval—and the Mexican Institute of Industrial Policy. Prior to this legal amendment, market approvals were frequently granted for patented products to a manufacturer other than the patent holder due to a lack of coordination between the agencies. The amendment required IMPI to publish a special version of the Gaceta de la Propiedad Industrial or Gazette of Industrial Property (Gazette). The special version of the Gazette issues a non-exhaustive list of active ingredients of pharmaceutical products that are under patent in Mexico. The Gazette lists products under patent, International Nonproprietary Names, patent expiry date, patent owner, some technical information, and observations which often includes the current status of any litigation. Second-indication patents and process patents are not included. The purpose of the
Gazette was to provide a link between pharmaceutical patent information that IMPI has granted and the requests for marketing authorization received by the Ministry of Health. Marketing authorization for a pharmaceutical cannot be granted if the active ingredient is listed in the Gazette, except if the applicant is the patent holder. In cases where there is controversy regarding the title of the patent with respect to the substance or active ingredient, there is a provision under Article 227 of the LPI whereby parties may submit their arguments to arbitration. The issuance of the special version of the Gazette has reduced the number of litigious cases, but there are still coordination problems between the Ministry of Health and IMPI that result in marketing authorization being granted to generics firms for producing pharmaceuticals that are still under patent.

At the turn of the millennium, Mexico was placed under further pressure from the U.S. to enhance their linkage system for marketing approval of generic pharmaceuticals despite the absence of this requirement in NAFTA and TRIPS. Mexico has received a considerable amount of criticism for its enforcement policies, including for being too lenient and for favouring generic competitive interest (Farolan, 2001). A much debated aspect of patents is the moment at which a generic manufacturer can reproduce an original pharmaceutical during the patent protection period for the purpose of initiating registry proceedings and interchangeability tests. As mentioned above, this is known as an “early working exemption”. An early working exemption allows generic manufacturers to conduct tests on a generic version of an on-patent pharmaceutical before the patent expires. The effective life of a patent is extended beyond its original expiry date by the time required to conduct tests on the generic versions for market entry.
without such a provision. A related legal issue is the protection of clinical trial data submitted by research-based firms to health authorities for marketing authorization which is covered by NAFTA Article 1711 and TRIPS Article 39.3. This provision protects the original applicant from the “unfair commercial use” of submitted data. In order to comply with the provision, countries allow for a protection period during which generic-based firms are prohibited to use these data for the market approval of their generic versions. There is currently an intense ongoing legal discussion in Mexico about NAFTA trade secret obligations and data exclusivity. As mentioned, however, this discussion is beyond the scope of this dissertation.

Article 22 of the LPI allows scientific experimentation with original pharmaceuticals by entities without commercial aims other than the patent holder. More importantly, recent reform to Article 167 of the Reglamento de Insumos para la Salud (Regulation of Health Inputs) allows generic producers to ask for registration of a generic for the purpose of conducting corresponding studies, tests, and experimental production three years prior to the expiration of the patent. This is the early working exemption or “Bolar exemption” for Mexico. As previously mentioned, even though market approval is only granted once the patent expires, the objective is to allow the time required for preparation of the generic product for market entrance (Moise & Docteur, 2007).

Mexican commentators have said the three year time period is too short and that the time period for the purpose of conducting corresponding studies, bio-equivalency tests and experimental production should not be limited as long as market approval is not granted
until expiration of a patent (Key Informant Interview). According to the USTR, the Mexican Ministry of Health (Secretaria de Salud) has regularly granted marketing approval to medicines where patents existed. Responsibility for licensing pharmaceuticals for market approval in Mexico resides with the Comision Federal para la Proteccion contra Riesgos Sanitarios (COFEPRIS). COFEPRIS is a semi-autonomous department of the Ministry of Health and is the Mexican equivalent to the FDA or Health Canada (Therapeutic Products Directorate). The USTR has claimed that Mexican public health providers have purchased non-patented products on more than one occasion (USTR 2003 and 2004). In September 2003, the Mexican government introduced an enhanced linkage system. Accordingly, COFEPRIS is now strictly required to consult with IMPI and cannot grant marketing authority to pharmaceuticals with current patents (Farolan, 2001).

The IMPI is an administrative government body and not an independent civil tribunal, as is the case in Canada where patent infringed parties seek redress. IMPI may apply several administrative remedies under a declaration of infringement, including inspection, impoundment of equipment, fines, closure of facilities, and administrative arrest (Serrano, 1998). IMPI may also use certain provisional measures that offer a relatively weak form of injunctive relief for the patent holders. These include ordering the withdrawal of infringing goods from the market and ordering the violator to cease infringing actions (Bacalski, 2005). In general, however, there is no private right to injunctive relief for patent infringement. Despite significant enforcement strengthening measures of the national patent system, such weaknesses have lead to continued efforts by the research-based pharmaceutical sector to have the linkage regulations strengthened.
Enforcement and injunctive relief differences between Mexico’s IMPI and the Canadian civil court system provides a key example of NAFTA member states patent system disharmony. Using the administrative agency IMPI to examine, issue, and enforce patents creates a potential conflict of interest (Serrano, 1998). A conflict of interest occurs when an entity is involved in more than one related party interests, one of which could corrupt the motivation for an act in the other (Angell & Relman, 2002). Such a situation occurs when IMPI is asked to invalidate a patent by a generic-based party that IMPI itself granted to the current patent holder. When an administrative agency registers patents and civil courts enforce patents, as in Canada, conflicts of interest are avoided. This procedural disharmony between the three NAFTA member states leads to increased uncertainty for private and state actors operating in the pharmaceutical patent space across jurisdictions. Mexico should consider transferring enforcement of patents to the judicial system independent of IMPI as is done in Canada. Enforcement by the courts would avoid IMPI’s current position of conflict. This would also provide a more objective forum for patent holders to pursue infringement actions. The subordination of COFEPRIS to the Ministry of Economy and IMPI has resulted in calls by civil society for public health reform and changes to its association with the patent system. These calls have not been well received by government and the pharmaceutical industry as industrial goals continue to outweigh the prioritization of public health (Shadlen, 2007b).

2.3.3 Compulsory Licensing in Canada

A major source of friction between the U.S. and Canada during NAFTA negotiations was in the area of compulsory licensing on pharmaceuticals for domestic consumption. Pre-
NAFTA reform, Canada used compulsory licensing to encourage the development of its generic pharmaceutical sector, to encourage lower prices, and to foster its principles of universal access to health care (Rein, 2000a). Canada adopted compulsory licensing for the pharmaceutical industry in 1923 following the British practice in its original patent legislation (Lybecker & Efgeby, 2009). From 1919 to 1977, British law permitted compulsory licensing either when the owner failed to make use of a patent within a specified period or at any time if the patent covered a substance capable of being used as food or medicine or in the production of food or medicine (Klitzke, 1959). This is an interesting *sui generis* rule to silo pharmaceutical patents. Concern over the growth of a healthy competitive pharmaceutical sector affected the direction British patent law took as it sought to stimulate local generics manufacture. This allowed for the application of compulsory licensing. In contrast, the U.S. sought principally to stimulate independent R&D—emphasizing the importance of innovation. Therefore, the U.S. has not traditionally, nor recently, permitted the use of compulsory licensing. Both systems were intended to reward the entrepreneurial process, but each had a different focus (Corbett, 2000). The United States focused on growth through innovation incentivized by exclusivity rights, whereas Britain focused on entrepreneurism through the allowance of competitive markets.

Canada’s universal health care system, more focused on access to affordable medicines, has sought to balance the competing interests of the original patent holder and the public interest. The “public interest” was taken to mean provision of pharmaceutical products to Canadian consumers at the lowest possible costs (Corbett, 2000). As such, all
prescription pharmaceuticals in Canada were subject to compulsory licensing. This requirement facilitated the growth of generic pharmaceutical companies that paid only minimum royalties to patent holders. The Canadian Commissioner of Patents was authorized to determine the amount of royalty the licensee was required to pay to the original patent holder (Chromecek, 1987). Generics-based industry in Canada flourished because the policy reduced upfront licensing expenses. By driving down the cost of pharmaceuticals, the government reduced its spending because the provincial governments were, and continue to be, major buyers of certain pharmaceuticals as part of the Canadian publicly-funded healthcare system. Canada’s historical approach to pharmaceutical patent protection largely stems from its mandate to provide universal health care as opposed to the more market-based approach espoused by the U.S. This enabled Canadian domestic access to generics through compulsory licenses and cost-containment for the overall health care system.

As a result of facilitating domestic access to generics, the U.S. pharmaceutical industry believed the Canadian patent system was the weakest of any industrialized country and sought the termination of compulsory licensing. The compulsory licensing issue became a principal topic of the trade negotiations between the two countries prior to the enactment of NAFTA. The Canadian legislature eventually amended the Canadian Patent Act (R.S.C. 1985, c. P-4.) to eliminate its compulsory licensing system for pharmaceuticals with the introduction of new regulations in 1987 (Reichman & Hasenzahl, 2002). There continues, however, to be a modified compulsory licensing system in place (Atkinson, 2002). The Canadian Patent Act has an appropriations
provision to allow for the practice of compulsory licensing. Section 19 of the Patent Act permits the government to make an application to the Commissioner for use of a patented item (R.S.C. 1985, c. P-4, s. 19.). The Commissioner has the ability to grant the application and limit it based on scope and duration. The Commissioner must notify the patent holders and pay him adequate remuneration (R.S.C. 1985, c. P-4, s. 19 (3)). The patent holder can apply to the Commissioner to terminate the government’s use of the patent if the purpose of the authorization has ceased to exist (R.S.C. 1985, c. P-4, s. 19 (4)). Section 19.1 lists the two conditions for government to grant a compulsory license for a patented item. First, the government must have made efforts to obtain authority to use the patented invention from the patent holder on reasonable commercial terms. Second, its efforts must not have been successful within a reasonable time. The statute does not require those conditions in times of national emergency or extreme urgency or where the use of which the authorization is sought a public non-commercial use, giving the government some flexibility (R.S.C. 1985, c. P-4, s. 19.1 (2)). The authorized use must be non-exclusive and predominately for domestic purposes (R.S.C. 1985, c. P-4, s. 19 (2)). The statute also gives the Federal Court of Appeal jurisdiction to review the Commissioner’s decision (R.S.C. 1985, c. P-4, s. 19.2). The language is remarkably similar to the language subsequently adopted by NAFTA and TRIPS, although it was written into Canada’s 1985 law.

In general, Canada’s public policy for pharmaceutical patents has trended towards tighter enforcement of patent law, more limitations on generic-based competition, and the imposition of standards that are consistent with WTO policy since the implementation of
NAFTA and TRIPS (Barton et al., 2008). Concerns about global access to medicines for developing countries aside, rising pharmaceutical costs mean the Canadian government will have to devise creative policy solutions to promote continued access to affordable medicines for its population (Blouin, Foster, & Labonte, 2002).

Canadian examinations, however, of the effects of compulsory licensing on the pharmaceutical industry and pharmaceutical prices have concluded that there is little positive support for access in their application (Cohen, 2003). Researchers have examined the impact of Bill C-22 (passed on 7 December 1987 in the context of the Canada-US FTA negotiations) and Bill C-91 (passed on February 4, 1993 in the context of the NAFTA negotiations) (Harrison, 2000). Both pieces of legislation dealt primarily with limiting compulsory licensing in Canada. Research has found that larger generic companies are prospering despite passage of the Bill C-22, but the effect on smaller companies is unknown. In terms of impact on prices and provincial pharmaceutical costs, however, it has been noted that the lack of generic price competition as a result of Bill C-22 may have adversely affected provincial pharmaceutical procurement efforts (Lexchin, 2005a). Other commentators have discussed the political context of the pharmaceutical patent environment in Canada, including compulsory licensing, and the historical events leading up to the passing of Bill C-22 (Harrison, 2001). Most argue that the U.S. multinational firms were very successful at influencing various parties to make changes in patent legislation favourable to research-based industry. This creates a less favourable environment for Canadian generic firms and leads to a less competitive environment.
Recent reform to the compulsory license regime in Canada has taken place in the context of Canada’s Access to Medicines Regime (CAMR) (Ravvin, 2008). In November 2001, the Doha Declaration on TRIPS and Public Health was passed to address complaints from WTO developing country member states (Dinwoodie & Dreyfuss, 2004). The Doha Declaration was, in part, an effort to interpret article 31 (f) of TRIPS, which states that compulsory licensing shall be predominately for the supply of the domestic market (Abbott, 2002). That means, under WTO rules, countries with a public health crisis are able to infringe on a patent through the issuance of a compulsory license to a local manufacturer. Given that the majority of developing countries have insufficient or no domestic capacity to manufacture on-patent pharmaceuticals, however, the interpretation of this terminology is crucial for ensuring access to medicines for many least-developed countries (Cohen, 2003).

TRIPS Article 31 (f) was ultimately interpreted to allow for compulsory licenses for the production of generics for exportation to developing countries in 2003 (Correa, 2004). Canada was the first country to amend its domestic patent law in response. On November 7, 2003, the Canadian Government approved Bill-56. It was later renamed Bill C-9 or the Jean Chretien Pledge to Africa. This amended Canada’s Patent Act to allow for limited compulsory licensing related to the exportation of pharmaceuticals. Bill C-9 was passed on May 14, 2004 (Penner & Narayanan, 2005). The amendments permit Canadian generic-based manufacturers to produce and export patented medicines to developing countries deemed, by the WTO, to have insufficient local manufacturing capabilities (Bill C-9, An Act to amend the Patent Act and the Food and Drugs Act, 3rd Sess., 37th Parl.,

The law allows the Canadian government to issue compulsory licensing to generics-based manufacturers for exporting a listed number of medicines to WHO listed countries. The government retains the right to add or subtract countries from the WHO list of developing countries. When Canada receives a request from a listed country, it is required to ask the patent holder to satisfy the order. If the patent holder refuses, the government can seek a generic manufacturer to fill the order with strict limitations on quantity and destination. The legislation also allows Canada to issue compulsory licenses to export generic pharmaceuticals to developed countries during a time of emergency (Elliott, 2006). Deficiencies of CAMR have been emphasized by the generic-based and research-based industries in Canada alike, primarily relating to costs of the requirement to first negotiate a voluntary license with patent holders within the legislative context of CAMR. Generic-based pharmaceutical companies may be required to negotiate a voluntary license with multiple patent holders pursuant to the law in order to provide a platform of medicines (Attaran, 2009a). This is a complex and costly process (Hestermeyer, 2007). Another disincentive is that, if a generic-based company is committed to proceed with a compulsory license, it is limited to two years subject to a one year renewal. The quantity of the license is limited to the country’s original application (Elliott, 2007). Given the heavy front-end pharmaceutical production fixed-capital investment demanded by generic-based companies, these limits do not provide any prospect for long-term market gains. The limits offer generic-based companies little incentive to engage in activities under CAMR. This is particularly the case if a company needs to adjust and/or increase
their manufacturing infrastructure for products not already part of their portfolio (Goodwin, 2008). CAMR has proven fraught with operational difficulties as a workable legal framework (Attaran, 2010). Only one company has supplied pharmaceuticals and only one country has obtained a fixed-dose, triple combination HIV/AIDS pharmaceutical (TriAvir) from Canada under the regime, when Apotex Inc shipped TriAvir to help 21,000 people in Rwanda (Attaran, 2010). Negotiations were convoluted and protracted between the Canadian Government, the Government of Rwanda, Apotex, and the three patent holders, GlaxoSmithKline, Boehringer Ingleheim Canada, and Shire BioChemical, Inc. (Rimmer, 2008). The compulsory license regime is so complicated by legal and administrative hurdles that it does not function appropriately. The administrative hurdles are burdensome for recipient states, such as Rwanda, and for potential generic suppliers (Kohler, Cosio, & Yeh, 2010a). Apotex has claimed it will not attempt to use the framework again given its operational difficulties. Multiple Bills have been proposed that would amend the Patent Act in an attempt to fix CAMR (Kohler, Cosio, & Yeh, 2010b). Most recently this push to reform CAMR resulted in Bills S-232 and C-393, which were introduced on 31 March 2009 and 25 May 25 2009, respectively. Both aimed to streamline the legislation (Kohler, Lexchin, Kuek, & Orbinski, 2010b). Bill C-393 received a second reading on December 5, 2009 and was proceeding through Parliament promisingly until Parliament was dissolved in March 2011 (Kohler, Lexchin, Kuek, & Orbinski, 2010a). These political developments have stalled CAMR reform and this bill did not become law.

To date, CAMR has proven largely ineffective. Consequently, there is insufficient
information to analyze to provide guidance for policy-makers. Some commentators suggest that the 30th of August Decision and CAMR are workable frameworks that simply require reform. A complicated process for all countries involved, a limited list of eligible medicines, and restrictions that prevent re-exportation to facilitate bulk procurement has discouraged generic-based companies from using the CAMR framework (Kohler, Cosio, & Yeh, 2010a). In addition, other facilitative possibilities to promote access to medicines may attach conditions for procurement. Such possibilities can be negated by use of CAMR. For example, the World Bank donations typically require countries to undertake international competitive bidding for the purchase of pharmaceuticals. CAMR does not fit within these requirements and does not provide an alternative arrangement sufficient to justify breaking these donor agreements (Attaran & Sachs, 2001). In the long term, developing countries will need sustainable solutions to meet their health needs. Many developing countries, despite economic costs, want to build their capacity to produce medicines and develop local pharmaceutical industries in order to assure national medicine supply. CAMR does nothing to promote such action. The process of building the infrastructure necessary for local pharmaceutical supply and delivery requires a certain amount of technology transfer. A balance, however elusive, needs to be struck between sustainable access to medicines from exporting countries, and the development of the necessary foundations for technology transfer and domestic pharmaceutical manufacturing capacity. All these issues raise questions for Canada as to whether the CAMR’s failure is a precedent for a shift in pharmaceutical patent policy. Serious questions about the value of a regime that has failed to improve access for developing countries based on the compulsory licensing of patented medicines for
exportation must be asked and answered prior to any further progress being made (Kohler, Cosio, & Yeh et al., 2010b). Not long after Canada enacted CAMR to give effect to the WTO’s compulsory licensing decisions, other countries did likewise. Currently China, the European Union, India, Korea, Norway, and Switzerland among others (32 countries in all) have such laws. Mexico does not. Yet none of those 32 countries’ laws have ever been used (Attaran, 2009b). Canada’s regime, with all its deficiencies, has done more to implement the WTO decisions than all other countries in the world combined. This does not imply, however, that this regime can be considered a success.

2.3.4 Compulsory Licensing in Mexico

A similar scenario to the Canadian one, followed in Mexico post-1991 and post-NAFTA in that significant restrictions to the use of compulsory licenses were imposed into the national legislation. Authority to manufacture generic copies of patented medicines in Mexico can be granted through compulsory licenses, which are possible in Mexico under Articles 70 and 77 of the LPI. Under LPI Article 70, the Ministry may issue compulsory licenses to a third party when the technology within the patent claim is not being worked on within three years from the date of patent granting or four years from the date the patent application was filed by the Ministry (priority date). If, however, the patent holder is importing the product or a company licensed to do so is importing the pharmaceutical (i.e., not originating within Mexico) then no compulsory license can be granted. Thus, although compulsory licensing under Article 70 is theoretically possible, these two waivers make it extremely difficult to obtain a license under this provision. Ultimately, the Ministry will hold a hearing between the applicant and patent holder to decide
whether to grant a compulsory license. Under Article 72 of the LFPI, in order to obtain a compulsory license, an applicant must have the technical and economic capacity to efficiently work the patented invention. If the Ministry grants a compulsory license, it will set out the duration, conditions, field of application, and amount of royalties to be paid to the patent holder. Under Article 73, compulsory license royalty payments cease when a patent lapses. Under Article 75, a compulsory license may be revoked if a licensee fails to work a patent within two years, unless “justified reasons exist in the opinion of the Ministry” to continue the license. Under Article 76, in accordance with the Paris Convention, a compulsory license under the new law may not be exclusive. With the Ministry’s authorization, a recipient of a compulsory license may only assign a license together with the part of the business in which the licensed patent is worked. At the request of either the patent holder or licensee, the Ministry may decide, after a hearing, to amend the conditions of a compulsory license when supervening causes so justify, particularly when the patent holder has granted a contractual license more favourable than the compulsory license.

A compulsory license can also be granted under LPI Article 77. Article 77 provides for the grant of a compulsory license under certain conditions. Article 77 states that a license to produce a pharmaceutical under patent may be granted to another laboratory for reasons of emergency or national security. This would include a shortage of medicines or a health crisis. The law provides for compulsory licensing based on adequacy of supply where the production, supply, or distribution of basic commodities for the people would be impeded or rendered more difficult or expensive. Compulsory licensing based on the
adequacy of supply doctrine occurs when a patent holder is unable to meet the market demand under the patent holder’s exclusive right to manufacture and sell the product. Due to the fact that compulsory licenses are less favorable to a patent holder than a voluntary license, governments have often threatened the use of compulsory licenses based on adequacy of supply. This is done as an incentive for patent holders to negotiate voluntarily with a potential licensee (Fauver, 1988b). No compulsory license has been granted in Mexico in the last twenty years. Several attempts have been made however, to obtain compulsory licenses for HIV/AIDS drugs under Article 77 (Sykes, 2002; von Schoen Angerer, Wilson, Ford, & Kasper, 2001). The Mexican health authorities have also used the threat of compulsory licenses during the 2009 H1N1 pandemic (Condon & Sinha, 2009; Hodge Jr, 2010a). These Article 77 attempts have inevitably faltered on the basis of what constitutes a shortage or health crisis and have ended in negotiated solutions and voluntary licenses with the patent holder (Bacalski, 2005). A patent holder under the LPI may contest the grant of a compulsory license based on justified or economic reasons pursuant to the Paris Convention or alternatively by proving that the licensee has been carrying out the import of the patented product or product of a patented process into Mexico (Industrial Property Law, at art. 70).

Norway, the Netherlands, India, China, and the European Union have followed Canada’s lead and amended their legislation to allow the export of medicines under compulsory licenses (Kohl er, Lexchin, Kuek, & Orbinski, 2010b). As of 2011, Mexico has not made such amendments. A review of the use of compulsory licensing in the LPI, written and implemented through the demands required for inclusion into NAFTA, indicates that
compulsory patent licensing is used as a last resort in Mexico. The LPI, along with NAFTA, has resulted in greater multinational business activity without the protectionist restrictions instituted by previous Mexican governments, but it does little to promote access to medicines. The LPI has restricted when the Mexican government can impose a compulsory patent license to flagrant patent abuse, and has relegated compulsory licensing as a tool to promote access to medicines to the background.

2.4 Discussion
This chapter has considered the current dimensions of pharmaceutical patent systems in Canadian and Mexican contexts. In answering the question, “Has the implementation of NAFTA produced harmonized pharmaceutical patent legislation in Canada and Mexico?”, the comparative legal analysis conducted in this chapter demonstrates that an extremely complex pharmaceutical patent protection legal landscape exists in North America. This landscape is anything but harmonized. In particular, Canada and Mexico have developed distinct patent systems to best suit their particular economic and ideological positioning. Overall, Canada and Mexico have demonstrated similar desires to act in accordance with trade demands put forward unilaterally by the U.S. Both countries have put in place patent law consistent with the international standards under NAFTA. Arguably, both countries modified their patent law to ensure they made gains in other areas of the regional trading system. The governments of both Canada and Mexico were compelled to reform their pharmaceutical patent law as a result of external U.S. pressure. Nevertheless, important differences exist in how Canada and Mexico have responded to those pressures. Canada has strengthened its linkage regulation in favor of improved patent protection, but implemented CAMR as a measure to allow Canadian
companies to provide greater access to medicines externally through compulsory licensing and exportation to developing countries. Mexico has demonstrated greater resistance to the strengthening of its patent law in the patent/health system coordinated regulatory linkage framework, protecting access to medicines and competitive generic markets internally. In addition, Mexico has not yet advanced its domestic legislation to address the Paragraph 6 and Article 31 (f) decisions of Doha and TRIPS. These differences between Canada and Mexico arise from their differing economic and developmental positions on the global stage. Mexico, as a developing country, has had to come farther in its reform to be compliant with instituting stronger patent law than Canada to be included in NAFTA. Mexico, however, has done so with a protracted approach in an effort to protect its national generics pharmaceutical industry. Mexico’s weaker negotiating position as a developing country during NAFTA negotiations, in combination with its lack of a previous bilateral free trade agreement with the U.S. (as Canada had with the Canada–U.S. FTA), has resulted in the slow implementation of international obligations. This has also reduced the capacity to be as concerned with promoting access to medicines for populations outside its own national borders (Harrison, 2001).

The trend of strengthening international patent law in the 1990s in Canada and Mexico may be now swinging back toward loosening systems due to international pressure from public health activists. Exclusivity rights from patent protection over pharmaceuticals undeniably lead to higher prices for medicines, thus altering market structure. The patent systems of these two countries will continue to evolve as pressure continues for both
increased and decreased regulation by advocates for competing sides of the pharmaceutical sector (research-based versus generic-based). These potentially conflicting interests become even more confused when considering consolidation of the research-based and generic-based sectors through merger and acquisition activity in recent years (Roffe et al., 2006).

The first article of Chapter 17 on Intellectual Property (Art 1701 (1)) establishes a broad obligation for each NAFTA state party to provide nationals of other NAFTA countries with adequate and effective measures to protect and enforce IP rights while ensuring that such measures do not become barriers to legitimate trade. Article 1701 (2) of NAFTA establishes minimum standards of protection for IP, based on the principles set out in the major international IP conventions in existence prior to NAFTA. NAFTA Article 1702 allows parties to implement more extensive protection of IP rights in its domestic law than is required, provided that such protection is not inconsistent with NAFTA. This article disallows a contracting party to use Chapter 17 as an excuse for creating trade barriers (Goolsby, 1998a). The language of these articles, however, may be what is leading to disharmony in the patent systems between countries and a lack of international optimal harmonization standards for pharmaceutical patent rights. The language used in NAFTA 1701 by the original drafters, and which has found its way into subsequent trade agreements, likely would have better served both pharmaceutical R&D and access to medicines if the word optimal as opposed to minimal was used. NAFTA Article 1701 (2) and Article 1702, as provisions that allow parties to the agreement to implement into domestic law as minimum standards and more extensive protection of IP rights than is
required under this agreement should be eliminated. This results in the establishment of a floor below which none of the parties can fall, but it does not require them to carefully consider what normative standards would best balance the competing interests at issue.

In addition, newer generation agreements, such as the European Community (EC)-Mexico FTA, provide examples of bilateralism and how a different standard of patent system harmonization might be applied. Article 12 of the Agreement commits both parties to providing adequate and effective protection to the highest international standards. What is meant by highest international standards is open to interpretation, yet the next generation EC-Mexico FTA contains a Unilateral Declaration by the Community and its Member States on the Intellectual Property Conventions referred to in Article 12 that sets up institutional framework to deal with IP issues. This framework makes it clear that the meaning of highest standard is not confined to standards prevailing at the time of the FTA but may include subsequent standards that emerge (Drahos, 2001). The impact of the EC-Mexico agreement will only be known in time, but the language used in the next generation agreement is promising. This is a good step forward.

The primary safeguard in trade agreements to protect public health and promote access to medicines is the compulsory license. This safeguard, however, is inadequate in an international system that has not been harmonized to the optimal standard. More fundamental changes to the patent system are needed to facilitate access. Compulsory licenses are cumbersome and difficult to apply, as illustrated by legislative efforts like Canada’s Access to Medicines Regime to export to those in developing countries and
Mexico’s attempts to satisfy domestic demands for HIV/AIDS or H1N1 medicines. That being said, compulsory licensing or the threat of compulsory licensing may be useful to increase access to patented pharmaceuticals. The option should not be abandoned entirely. Compulsory or negotiated lowering of pharmaceutical prices, while less significant to people in developed nations, are not negligible for developing country health systems facing significant budgetary constraining realities. This comparative legal analysis has demonstrated, however, that in practice the use of compulsory licensing is a laborious downstream process from a procedural perspective and results in significant back-end distortion to access.

Disharmony of the regional patent system and pharmaceutical patent law may be leading to decreased access to medicines and R&D due to the pronounced possibility of long, costly, litigious disputes created by an uncertain and disjointed patent law landscape. Available safeguards in NAFTA and TRIPS present governments attempting to use them with many hurdles that must be overcome. In principle, compulsory licenses, which are at the heart of safeguards to encourage a reduction in barriers to access, should be a relatively simple mechanism to apply. In practice, the opposite is true. Ultimately, pharmaceutical prices remain higher than necessary due to prolonged periods of patent rights that are aggressively protected, both systemically and on a case-by-case basis, by research-based firms. If properly attenuated with sound law reform and appropriate guiding public policy measures, the current norms for protecting technology and granting patents could lead to the achievement of both more equitable short-term access and long-term encouragement of innovative activity in pharmaceutical R&D. These changes, if
made, could better meet the needs of both the developed and developing world’s populations and begin to reduce the dichotomous perceptions that currently polarize the debates over these issues.

This comparative legal analysis provides health stakeholders with information that can be used to improve their ability to act regarding government decisions. Furthermore, this information may promote exchanges between countries that can assist health sector decision makers who are involved in providing input to those actors who negotiate and implement free trade agreements. The next chapter presents a scoping study based on public health methodology that was conducted to analyze what is known about how patent system harmonization has positively or negatively impacted public health in Mexico.
Chapter 3: Impact of Patent System Harmonization on Public Health in Mexico

3.1 Introduction
Although NAFTA was signed in 1994, IP legislation in the three signatory countries is still being implemented and amended as new issues emerge. IP reform, accordingly, continues to be a lobbying priority for the multinational pharmaceutical industry in Mexico. Recognizing the public policy challenges associated with this fluid situation, this chapter shifts the discussion away from legal issues presented in Chapter 2 to an examination of “What is known from the existing literature about the impact of NAFTA’s patent system harmonization on public health in Mexico?” A full understanding of the impact of patent system harmonization on public health draws on literature from legal, economic, medical, and public health fields. Due to the diverse disciplines that contribute to this literature, there is a lack of cohesive research. In order to synthesize these seemingly disparate fields, an understanding of the themes and gaps in the available literature must be identified in order to move toward an integrated view of appropriate health policy measures.

A scoping approach was undertaken in order to accommodate the different methodologies used across disciplines. The Canadian Institutes of Health Research (CIHR) funded the present study, and advocate for the use of a scoping study approach for information synthesis across disciplines (http://www.cihr-irsc.ca/e/29914.html). Given the research aims of this dissertation and the CIHR position, a scoping study was chosen over a narrative review. Scoping studies are often preliminary to full syntheses,
undertaken when feasibility is questionable, either because the potentially relevant literature is thought to be vast and diverse (varying by theoretical orientation, discipline and/or methodologies) or because there is reason to believe that not enough quality literature exists. In this instance both concerns were justified, making a scoping review the appropriate methodological choice. Scoping studies aim to overcome the restrictions associated with systematic review that require similar study designs for data extraction and synthesis of information (Dixon-Woods, Agarwal, Young, Jones, & Sutton, 2004).

Thus, a scoping approach involves identification of prominent themes in the literature from a range of research methodologies and can inform policy and practice in the area (Hearn, Feuer, Higginson, & Sheldon, 1999; Pope, Ziebland, & Mays, 2000). The scoping study presented in this chapter presents a numerical summary and qualitative thematic analysis of available studies. This approach enabled integration of findings across research disciplines to fully assess the current state of knowledge in the area (Levac et al., 2010). Pharmaceutical patents can impact public health in two principal areas. First, there is the issue of access, which includes links between patents, the exclusion of competitors, monopoly pricing, and the availability of new medicines. Second, there is the issue of promoting innovation that includes the role of patents in motivating discovery and development of new pharmaceuticals and the affect of exclusivity rights on allocation of R&D expenditure across diseases, countries and organizations.
This scoping study is timely, as the Mexican national pharmaceutical policy recently identified improved access to medicines as a critical priority (Wirtz, Reich, Leyva Flores, & Dreser, 2008). In a recent background document (2005) considering a new national pharmaceutical policy, the Mexican government highlighted the importance of generics to lower pharmaceutical expenditures (Enríquez Rubio, Frati Munari, & González Pier, 2007). Pharmaceutical R&D and subsequent access issues in the North American context have also recently received more attention due to increased recognition of the importance of regional cooperation during communicable disease outbreaks – most recently with the H1N1 swine flu pandemic (Das, 2009; Fraser, 2009; Perez-Padilla et al., 2009).

This chapter will present the rationale, methodology, and results from the comprehensive scoping study to assess the impact of NAFTA’s patent system harmonization provisions on public health in Mexico. Section 3.2 describes in detail the specific methods used in this scoping study including analysis and integration of the findings. Section 3.3 presents the results of the literature review. Section 3.4 discusses the major findings through thematic analysis including consideration of the broader implications for research, policy, and practice. These considerations subsequently guided the qualitative research undertaken in Chapter 4 (starting on page 136). Section 3.5 provides a discussion of the conclusions based on the scoping review including directions for future primary research.

3.2 Scoping Study Methodology

The scoping study has begun to appear more often in public health research as it presents an increasingly popular option for synthesizing evidence. It is important to recognize that rapid growth in literature reviews has resulted in varied terminology to describe
approaches that share certain essential characteristics, namely collecting, evaluating, and presenting available research evidence. There are no agreed upon definitions for these review approaches, although significant efforts by Cochrane and Campbell Collaborations have been made to formalize reviews in health care (Egger, Smith, & Altman, 2001). As a consequence of differing definitions, researchers may use labels loosely and apply different standards to their reviews. For example, reviews defined by their authors as systematic may not at all times embrace the same high standards in terms of quality assessment and minimizing bias when selecting literature. Given these differing standards, I have chosen to follow the approach published by Arksey and O’Malley (Arksey & O'Malley, 2005). This is the landmark article on the conduction of scoping studies. This approach has been refined via further recommendations by Levac and colleagues, which I have chosen to incorporate here (Levac et al., 2010). Table 10 in the Appendix (page 249) summarizes the differences between systematic and scoping reviews.

Scoping studies aim to thoroughly map the literature in order to clarify boundaries and identify gaps in the evidence where further primary research is needed. This scoping study was conducted in a rigorous and transparent manner, with the explicit intention of documenting it in sufficient detail to enable replication and to increase the reliability of the findings (Egger et al., 2001). Arksey and O’Malley (2005) suggest the methodological framework for conducting such a review is as follows:

Stage 1: Identifying the research question

Stage 2: Identifying relevant studies
Stage 3: Study selection
Stage 4: Charting the data
Stage 5: Collating, summarizing and reporting the results

3.2.1 Identifying the Research Question

The search results in a scoping study should achieve sufficient depth and breadth in the literature. The scoping method is guided by a prerequisite to identify all pertinent literature regardless of study design. This in turn leads to more focused research questions for investigation through an iterative process (Arksey & O'Malley, 2005). The overriding research question for this scoping study was, “What is known from the existing literature about the impact of NAFTA’s patent system harmonization on public health in Mexico?”

As recommended by Levac et al., the research question should be clearly articulated to guide the scope of the inquiry (Levac et al., 2010). The concept, in this instance patent system harmonization, and target population, Mexico, clarified the focus of the scoping study. The study began from this question with a search for relevant peer-reviewed journal articles and grey literature. Every identifiably relevant database was searched. Titles of articles resulting from the search were checked first for relevance. If the titles were relevant, abstracts were retrieved. Hard copies of all articles considered appropriate for inclusion in the review based on their abstracts were obtained for analysis and are available from the researcher.
3.2.2 Identifying Relevant Studies

Feasibility required judgments be made at the outset about what would be covered in the scoping review (Arksey & O'Malley, 2005). The purpose of a scoping study is to be as comprehensive as possible. This review is limited to documents published between January 1989 and March 2010. Prior to 1989, the literature on negotiations resulting in the NAFTA Agreement is sparse. Papers published in English and Spanish language studies were reviewed. Material published in other languages was excluded due to the cost and time involved in translating material. The scoping study was conducted in consultation with the Centre for Health Services and Policy Research (CHSPR) research librarian and other reference librarians at the University of British Columbia. Studies were searched for using the keywords: “NAFTA”, “intellectual property”, “pharmaceuticals”, “patents”, “public health”, “Mexico” and the exact phrases “patent system harmonization” and “access to medicines”. To limit the research studies reviewed to those that focused on the research question, NAFTA without TRIPS was used as a keyword. Refworks Version 2.0 was used to manage collected references and citations. Refworks is an online research management and writing tool designed to help researchers gather, organize, store and share all types of information. The tool generates citations and bibliographies. Refworks proved invaluable for managing records and keeping track of articles throughout the application of inclusion and exclusion criteria. Consistent with the methods established by Arksey and O’Malley, the methodological quality of the studies was not evaluated (Arksey & O'Malley, 2005; O'Malley & Croucher, 2005; Roland et al., 2006).
The following databases were initially searched in consultation with the CHSPR librarian (number of publications identified follow in brackets):

1. Pubmed – U.S. National Library of Medicine, National Institutes of Health (7)
2. LILACS – Virtual Health Library, BIREME/PAHO/WHO – Latin American and Caribbean Center on Health Sciences Information (8)
4. LexisNexis (16)
5. INSP – Mexican National Institute of Public Health Database (0)

These searches identified 32 relevant articles. Next online databases of the following organizations were searched for relevant publications (number of publications identified follow in brackets):

1. World Trade Organization (16)
2. World Bank (11)
3. International Monetary Fund (3)
4. United Nations Conference on Trade and Development (UN) (2)
5. Organization for Economic Co-operation and Development (7)
6. World Health Organization (UN) (19)
7. Pan American Health Organization (UN) (1)
8. North American Free Trade Agreement Secretariat (0)
9. World Intellectual Property Organization (UN) (4)

These searches identified 63 relevant articles. A catch-all search was then conducted using Google Scholar to protect against inadequate collection and identify any previously
unidentified relevant articles. Google Scholar identified 368 relevant articles. To ensure all relevant articles had been included, bibliographic citations of studies found were checked for any additional articles. During the process of conducting these searches, a saturation point was reached where no new studies were being identified.

As recommended by Arksey and O’Malley (2005), an iterative consultative exercise with the key informants interviewed during the qualitative research was conducted subsequent to the initial draft of the scoping study (Arksey & O'Malley, 2005). This is presented in the subsequent chapter. Levac et al. also include an optional consultation exercise as stage 6 of the methodological framework for a scoping study (Levac et al., 2010). Levac et al. recommend that consultation should be an essential part of the scoping study methodology and should incorporate opportunities for knowledge transfer and exchange with stakeholders in the field (Levac et al., 2010). Key informants were asked to provide any reference materials they thought might be essential to obtaining a complete picture of the patent system harmonization/public health situation in Mexico. In return, key informants were provided with materials that might be of interest to them in their particular positions or if requested. Two rounds of interviews conducted with stakeholders in Mexico City in December 2008 and November 2009 produced 13 additional relevant articles not identified during the initial searches. Additional articles were included as they were identified throughout the research process. The final thematic analysis presented in this chapter was conducted using an ongoing iterative process, with the search protocol repeated on more than one occasion up to and inclusive of March 2010.
3.2.3 Study Selection

Of the 476 studies initially identified, inclusion and exclusion criteria were applied to eliminate studies that did not address the research question. Due to the multi-disciplinary nature of the subject area, relevant studies were included from any theoretical orientation or discipline. Studies included papers that offered descriptive accounts without an explicit study design. Full text articles were obtained for those studies that appeared to best fit the research question. If the relevance of a study was uncertain from the abstract, the full article was obtained.

Table 1 lists the scoping study criteria used to identify and eliminate studies. The process and studies identified at each stage of study selection is shown in Figure 4 (on page 88).

Table 1: Scoping Study Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Topical relevance from any research tradition or discipline</td>
<td>• Published in language other than English or Spanish</td>
</tr>
<tr>
<td>• Published in English or Spanish (for Spanish language articles the English version was found and collected where possible)</td>
<td>• Published before 1989</td>
</tr>
<tr>
<td>• Published January 1989 – March 2010</td>
<td>• Study did not include issues directly related to Mexico</td>
</tr>
<tr>
<td>• Addressed primarily Mexican issues</td>
<td></td>
</tr>
</tbody>
</table>
After screening titles and abstracts, 358 articles of the 476 articles initially identified were excluded because they did not meet all the inclusion criteria or because they met the exclusion criteria.

**Figure 4: Scoping Study Search Strategy**

Full texts of the remaining 118 papers were read and on this basis a further 37 were deemed irrelevant and excluded. In total, 81 articles met the specified criteria and were included in the scoping study for analysis.

### 3.2.4 Charting the Data

Based on recommendations by Levac et al., a data charting form was developed to extract variables that would help to answer the research question (Levac et al., 2010). Key information obtained from the articles reviewed was charted next. Charting is a technique for synthesizing and interpreting qualitative data by sorting material according to key
themes (Ritchie, Spencer, Bryman, & Burgess, 1994). A master workbook spreadsheet in Microsoft Excel (Version 14.0.2) was developed and used to produce the tables presented throughout this chapter. The data charting exercise organized documents by year, disciplinary approach, author/editor, journal/book, title, research settings, study question, study objective, study design/methodology, participant/data characteristics, data collection methods/instruments, summary of results and discussion, and thematic headings for extracted data. The Microsoft Excel master workbook allowed for cross-referencing information and comparative thematic analysis. A uniform approach to information extraction for all 81 studies was adopted. The master workbook is available as an electronic appendix to this dissertation upon request. In order to ensure sufficient rigor in data extraction, the data chart was continually updated, and articles read and re-read multiple times over the five years of my doctorate. Although Levac et al., also recommend an additional researcher when conducting a scoping study, this was not implemented as the research was conducted as part of a doctoral program and therefore needed to represent individual scholarship.

3.2.5 Collating, Summarizing and Reporting the Results

The final stage of the scoping study involves collating, summarizing and reporting the results. Section 3.3 of this chapter, provides a descriptive numerical summary and thematic analysis as recommended by Arksey and O’Malley. The numerical summary includes the following characteristics: studies by disciplinary category and research setting, overall number of studies by study design, and number of studies by thematic category. In the current scoping study, the literature was organized thematically as four identified major themes emerged during the course of the study.
3.3 Results

What emerged from the scoping study was a discussion of benefits and detriments of patent system harmonization on access to medicines and pharmaceutical R&D. All 81 articles included in the final review were trans-disciplinary in terms of the content under discussion, each was categorized by one of three primary disciplinary categories: health policy, health economics, and health law. Thirty-seven papers fell into the health policy category, 20 into the health economics category, and 24 into health law. The research setting for the majority of the literature reviewed was specific to Mexico for 48 papers. There were 12 regional papers. There were 21 international studies that included Mexico as a comparator country. Table 3 below summarizes the number of studies in each disciplinary category and setting.

Table 2: Study Disciplinary Category & Research Settings

<table>
<thead>
<tr>
<th>Primary Disciplinary Category (n)</th>
<th>Health policy (37)</th>
<th>Health economics (20)</th>
<th>Health law (24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Setting (n)</td>
<td>Mexico (48)</td>
<td>Regional (12)</td>
<td>International (21)</td>
</tr>
</tbody>
</table>

A complete literature map shows that a variety of study designs have been used in attempt to understand and analyze the subject area. Approaches were primarily descriptive in nature, likely due to the complexity of studying a distal determinant of health such as patent system harmonization. There were 16 papers that strictly applied a descriptive report of the area under study with no further analytical design. The other types of study (number) included in the review were: comparative legal analysis (16); comparative policy analysis (9); econometric (8); qualitative (5); critical legal analysis (5); innovative quantitative approaches to studying legislation and policy (5);
comparative price level data analysis (5); cross-sectional (5); evaluative (3); epidemiologic (2); longitudinal (1); and finally, a relevant literature review (1) on access to medicines which did not cover the issue of IP. The descriptive numerical summary of this information is found in Table 3, below.

**Table 3: Summary of Study Designs**

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptive</td>
<td>16</td>
</tr>
<tr>
<td>Comparative legal analysis</td>
<td>16</td>
</tr>
<tr>
<td>Comparative policy analysis</td>
<td>9</td>
</tr>
<tr>
<td>Econometric</td>
<td>8</td>
</tr>
<tr>
<td>Qualitative</td>
<td>5</td>
</tr>
<tr>
<td>Critical legal analysis</td>
<td>5</td>
</tr>
<tr>
<td>Innovative quantitative approach to legislation and policy</td>
<td>5</td>
</tr>
<tr>
<td>Comparative price level data analysis</td>
<td>5</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>5</td>
</tr>
<tr>
<td>Evaluative</td>
<td>3</td>
</tr>
<tr>
<td>Epidemiologic</td>
<td>2</td>
</tr>
<tr>
<td>Longitudinal</td>
<td>1</td>
</tr>
<tr>
<td>Literature Review</td>
<td>1</td>
</tr>
</tbody>
</table>

The studies varied in quality but, as mentioned above, quality assessment is not a central objective in scoping studies. The following section presents tabular results of the studies reviewed. An expanded discussion of exemplary studies is provided within each theme identified. A qualitative thematic analysis of findings that have been used to address the question of how patent system harmonization has impacted public health in Mexico is provided in section 3.4. As mentioned, the scoping study illuminated a discussion of the benefits and detriments of patent system harmonization on access to medicines and
pharmaceutical R&D. My analysis has lead to a thematic breakdown of this discussion as follows (the number of studies under each theme is shown in Table 4):

1. Decreased access to medicines – Due to higher prices (less affordable) of on-patent medicine and decreased generic availability from the implementation of a stronger patent system.

2. Increased access to medicines – Due to improved availability from the presence of multinational firms in Mexico and safeguards available within NAFTA to facilitate access.

3. Increased pharmaceutical R&D – Due to improved national innovation systems and the economic incentives resulting from stronger patent legislation.

4. Decreased or negligible pharmaceutical R&D – Due to decreased incentives to conduct innovative R&D in Mexico.

**Table 4: Number of Studies for Each Theme**

<table>
<thead>
<tr>
<th>Theme</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased access to medicines</td>
<td>53</td>
</tr>
<tr>
<td>Increased access to medicine</td>
<td>28</td>
</tr>
<tr>
<td>Increased pharmaceutical R&amp;D</td>
<td>17</td>
</tr>
<tr>
<td>Decreased pharmaceutical R&amp;D</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>116*</td>
</tr>
</tbody>
</table>

* Some studies contained more than one of the four themes, which lead to a total number greater than 81.

I will now address each theme in turn.

**Decreased Access to Medicines**

This first major theme that emerged in the scoping study was that patent system harmonization had negative impacts on access to medicines in Mexico. These issues were neglected and important considerations regarding patent system harmonization and
pharmaceutical access in Mexico were relegated to the background due to commercial pressures. The potential impact of NAFTA on medical care and health services in Mexico was cursorily assessed by academics at the time in order to identify internal measures to increase the benefits and minimize risks (Frenk et al., 1994). NAFTA was expected to offer opportunities for positive developments in Mexico, with the caveat that these positive developments would depend on Mexico’s ability to apply preventative measures to avoid negative impacts on the health system. The potential negative impact of pharmaceuticals on population health in Mexico was identified. Potential risks included possible strengthening of the role played by curative medicine, accompanied by an increase in the cost of care and irrational use of pharmaceutical products. Studies have found that pharmaceutical prices in Mexico are higher than in many developed countries when adjusted for income (Danzon & Furukawa, 2003). Inequities in access to medicines in Mexico have also been reported for vulnerable populations who spend proportionally more out-of-pocket on medicines than individuals with higher income (Nigenda, Orozco, & Olaiz, 2003). Table 5 shows the exemplary studies.

**Table 5: Exemplary Studies for Decreased Access**

<table>
<thead>
<tr>
<th>Date Published &amp; Author</th>
<th>Title</th>
<th>Disciplinary Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995 – Gasman, N.</td>
<td>Drifting through time - Pharmaceutical policies in Mexico</td>
<td>Health policy</td>
</tr>
<tr>
<td>2003 – Homedes, N. &amp; Ugalde, A.</td>
<td>Globalization and health at the United States-Mexico Border</td>
<td>Health policy</td>
</tr>
<tr>
<td>2003/2008 – Danzon, P.M. &amp; Furukawa, M.F</td>
<td><em>Two Articles</em> (1) Prices and availability of pharmaceuticals: evidence from nine countries; (2) International prices and availability of pharmaceuticals in 2005</td>
<td>Health economics</td>
</tr>
<tr>
<td>Date Published &amp; Author</td>
<td>Title</td>
<td>Disciplinary Approach</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>2004 – Oliveira, M.A. et al.</td>
<td>Has the implementation of the TRIPS agreement in Latin America and the Caribbean produced intellectual property legislation that favours public health?</td>
<td>Health policy</td>
</tr>
<tr>
<td>2005 – Homedes, N. et al.</td>
<td>The World Bank, pharmaceutical policies, and health reforms in Latin America</td>
<td>Health policy</td>
</tr>
<tr>
<td>2005 – Waitzkin, H. et al.</td>
<td>Global trade, public health, and health services: stakeholder’s constructions of the key issues</td>
<td>Health policy</td>
</tr>
<tr>
<td>2007 – Barraza, M. &amp; Campos, A.</td>
<td>Improving pharmaceutical regulation in Mexico: the British experience</td>
<td>Health policy</td>
</tr>
<tr>
<td>2009 – Shadlen, K.C.</td>
<td>The politics of patents and drugs in Brazil and Mexico: the industrial bases of health activism</td>
<td>Health policy</td>
</tr>
</tbody>
</table>

A landmark article was written by Gasman in 1995 on pharmaceutical policies in Mexico and the potential influence of NAFTA (Gasman, 1995). Gasman noted that, in NAFTA negotiations, the effects of the treaty on health were not specifically addressed. She attributed the absence of health issues on the NAFTA agenda to complex differences among the health systems of the North American region and lack of interest in or understanding of the issues. The article describes issues related to the pharmaceutical sector that were relevant during the NAFTA negotiations and identifies how IP became a global issue in the mid-1980s when the United States stressed the need to protect R&D investment by improving the global IP system. Larger developing countries, including Mexico, argued against this shift in the global IP system due to their incapacity to expand domestic pharmaceutical R&D. Gasman described the pharmaceutical sector’s active involvement in consultations and negotiations on NAFTA Chapter 17. Patents were seen
as a prerequisite for any negotiation since they would ensure the protection of future products and prevent massive losses due to counterfeiting. The article identified a potential risk resulting from Mexico’s integration into NAFTA as getting U.S. novel technology that would involve having to pay large amounts for licenses and on-patent products (Gasman, 1995). Gasman considered Mexico an excellent example of an imperfect market in which policy actions are required both in economic and health arenas to promote access to medicines and prevent market distortions.

A 2001 study by De Lima et al. analyzed the legal regulations for opioid availability in five Latin American countries, including Mexico. This was done so in the context of WHO criteria for opioid access (Liliana De Lima, Sakowski, Stratton Hill, & Bruera, 2001). Mexico failed to meet WHO criteria for adequately regulating access to these products and was ranked the country with the lowest number of international standards on opioid availability. Overall the study reported significant problems in access. The study was not patent issue specific, but its main observation was the numerous barriers found in the laws and regulations that interfere with access to opioids for Latin American and, in particular, Mexican patients. The study found that all countries studied have restrictive laws that combined with the presence of over regulations results in reduced access. Legislation was not found to be the only barrier to access. Factors such as poverty, health care education, cultural issues, and advocacy were also major contributors. The authors concluded that the laws and regulations of the five countries studied with reported availability problems failed to meet WHO standardized principles and showed multiple barriers to opioid access. These legislation barriers are at least
partially responsible for decreasing opioid access for, in particular, cancer patients in these countries. A main lesson learned from this study was that patents are not the only subject of concern when trying to improve access to medicines for patients. It was also important to note that the WHO has standardization or harmonization policies in the regulation of pharmaceuticals and it is not just a WTO framework for organization.

In 2003 Homedes et al. examined globalization and health at the U.S. and Mexico border as a case study of the impact of globalization on health policy decision-making (Homedes & Ugalde, 2003). NAFTA was used as a marker to assess the effects of economic interdependence on health cooperation along the border area. The study concludes that if international health problems are to be solved, political, cultural, and social interdependence need to be built with the same effort by which policy makers promote international trade. The study affirmed that NAFTA has succeeded in creating bureaucratic norms that place additional burdens on trans-border health programs. Interviewees reported that as a result of NAFTA the federal level was giving more attention to the border. For border residents wishing to access health services, this meant more rigidity that had been reduced and in many cases eliminated through informal mechanisms of cooperation that existed before NAFTA. One interviewee mentioned the increasing amounts of administrative red tape required in moving equipment and biological samples across the border for the implementation of bi-national priority TB programs. It was concluded that, while there has been some success in the creation of legal structures to facilitate integration, NAFTA has created bureaucratic norms that
place additional burdens on trans-border health programs subsequently reducing access to medical supplies including pharmaceuticals.

In 2003 Danzon and Furukawa compared pharmaceutical prices in nine countries; Canada, Chile, France, Germany, Italy, Japan, Mexico, the United Kingdom, and the United States (Danzon & Furukawa, 2003). The authors found that overall prices in Mexico were about 80% of U.S. prices, lower than prices in Germany, Italy, and the United Kingdom, but higher than prices in Canada and France. Surprisingly, prices of generics in Mexico were greater than in the United States and on-patent pharmaceuticals were priced about 30% lower. Danzon and Furukawa found that differences in pharmaceutical prices among countries roughly reflect income differences, with the exception of Mexico and Chile where the level of prices for pharmaceuticals is more than five times the level of income-adjusted prices in the United States. They pointed out that, to the extent income can be considered a proxy for the price elasticity of demand for pharmaceuticals, Mexicans are paying a far higher price for their pharmaceuticals than would be expected, given their relatively low level of average income. The authors noted that, in Mexico’s case, price levels may reflect manufacturers’ decisions not to offer prices more in line with Mexico’s per capita income, for fear of parallel importation into the United States. The use of income as a proxy for the price elasticity of demand is questionable given the many prospective determinants of demand elasticity (income distribution, consumer preferences, and level of out-of-pocket payments for pharmaceutical purchases are among them).
In 2004 Oliveira et al. conducted a unique study in which legislation in 11 Latin American and Caribbean countries was analyzed (Chaves & Oliveira, 2007). The variables considered were: the term of patents issued, patentable subject matter, transition periods from signing of the TRIPS agreement (i.e., time until international legislation was enacted domestically), reversal of the burden of proof of patent infringement onto the alleged generic infringer, exhaustion of rights, compulsory licensing, and early working exceptions that allow a company to complete all requisite procedures to register a generic pharmaceutical for market approval before the original patent expires. This study was more specific to TRIPS than NAFTA. It did address how Mexico has responded to implementation obligations. The study noted that Mexico did not utilize provisions allowing for compulsory licensing of a patent when it is dependent on another patented technology. Mexico also does not have explicit legislation that allows parallel importation or exhaustion of rights principles (Oliveira, 2004). A distinct difference between the NAFTA and TRIPS models is their approach to exhaustion of rights. NAFTA does not include exhaustion of patent rights principles, meaning that parallel importation is prohibited in North America. TRIPS includes such principles, which allow for parallel importation of pharmaceuticals in other regions of the world. The study concluded that the countries involved, including Mexico, did not incorporate all of the safeguard mechanisms to promote access allowed by the TRIPS agreement. The authors noted that the situation may deteriorate further for developing countries if other bilateral TRIPS plus Agreements establish more restrictive rules for IP rights.
In 2005 Homedes et al. wrote on World Bank pharmaceutical polices and health reforms in Latin America (Homedes, Ugalde, & Forns, 2005). The only pharmaceutical intervention included in a World Bank loan to Mexico’s Seguro Popular, the federal universal health insurance scheme for the poor that began in 2003, is the free distribution of pharmaceuticals needed to deliver a basic package of health services in hard-to-reach areas such as the southern most state of Chiapas. World Bank support has been scaled back due to Mexico’s position as a middle-income country in the midst of economic transition. One key feature of Seguro Popular is the provision of free medications to those insured under the program. If fully implemented, 40 million or more Mexicans would be entitled to the insurance. This goes far in meeting the pharmaceutical demand of the overall population and health coverage can be a key component of access. Regrettably, assessments of the universal insurance program indicate that the federal government does not have the resources to finance the scheme. Organizational and logistical problems were also identified as formidable. While the authors noted the World Bank recommended pharmaceutical policies that coordinated with the needs of the region, fieldwork and a review of the literature suggested that the recommended pharmaceutical interventions were left out of implemented health reforms. The authors noted that the utilization of public health services depends on the availability of medicines. Global health equity needs to start with the provision of free medicines for particularly vulnerable populations. In Mexico three health reform policies have been implemented. The first policy is decentralization. Administrative duties have been dispersed from the federal health secretariat to the state health secretariats and, in some states, to the local administrative level. This move was geared towards improving availability and
accessibility. Case studies in several states identified by the authors indicate that decentralization had some indirect positive and some negative consequences for access. Transferring some decision-making to the states has improved availability in health centres. The fragmentation, however, makes the procurement of medicines more expensive. The decentralized units cannot achieve the economies of scale through bulk procurement of a larger buying authority. The states do not have the human capital or technical expertise to prepare international or national tenders. The second policy is the delivery of a package of free basic interventions to the entire impoverished population. The third policy is the Seguro Popular, Mexico’s effort at the provision of universal health care. The Homedes et al. article clearly demonstrated that the World Bank believes patents create monopolies that drive pharmaceutical prices up. The authors indicate that large savings can be accrued by purchasing generic pharmaceuticals. The choice between medicines that are therapeutically equivalent should be based on cost reduction strategies that involve competitive bidding.

In 2005 Waitzkin et al. used a qualitative analytical methodology to identify the perceptions held by major stakeholders participating in policy debates about global trade, and public health in the Americas (Waitzkin, Jasso-Aguilar, Landwehr, & Mountain, 2005). Interviews were conducted with key representatives of major organizations participating in these debates. Several types of organizations were targeted: government agencies, international financial and trade organizations, international health organizations, multinational corporations, and advocacy groups. The researchers determined that organizational stakeholders held widely divergent viewpoints regarding
the interconnections between trade, public health and health services. Respondents believed that trade agreements and IP protection would likely improve health conditions worldwide through global economic development. All respondents were optimistic that economic globalization will foster public health and access to health services worldwide, except one from Mexico who gave no reason.

A 2007 study by Barraza and Campos, members of the Economic Analysis Unit of the Mexican Ministry of Health, observed that, although prices in Mexico are lower than those observed in other countries, once income level is taken into account, prices in Mexico are on average 2.4 times higher than those of the United States (Barraza & Campos, 2007). They concluded that price regulation in the public sector consists mainly of the negotiating power exerted through large public health care institutions, which purchase medicines associated with health care services provided. This type of regulation is known in the literature as indirect price regulation. The report was a pharmaceutical regulation comparative analysis in the context of the United Kingdom and Mexican health systems. The most relevant issues about pharmaceutical regulation in the United Kingdom were assessed for information that could be potentially useful to improve pharmaceutical regulation in Mexico. Regulation of the pharmaceutical field in Mexico has been traditionally aimed at guaranteeing safety and efficacy of the products available in the market. The report suggests important progress has been made to regulate available products. Measures adopted have been focused on the definition of basic pharmaceutical formularies for the public institutions providing health care and the application of mechanisms to enhance public sector pharmaceutical purchasing and supply. Important
changes to the regulation have taken place regarding patent rights. The introduction of innovative products into the market has been sought through patent awards improving availability of novel products. The need for adopting a broader focus regarding pharmaceutical regulation analysis has been recently identified. The researchers reported that price regulation in the public sector consists mainly of the negotiating power exerted through large public health care institutions. All public health care institutions acquire medicines dispensed in their hospitals, clinics and pharmacies. The lack of universal access to medical insurance coverage combined with procurement problems however has forced the Mexican population to use private pharmacies to obtain their medicines. The private market represents slightly more than 80% of the Mexican pharmaceutical market value. This situation generates unmet health needs for those who do not have the resources to purchase the medicines in the private market and subjects them to potentially catastrophic out-of-pocket expenditure.

For private market patented products a direct price regulation scheme is applied in an effort to keep prices reasonable. The Ministry of Economy operates this scheme and it covers only patented medicines since 2005. The participation of pharmaceutical companies is voluntary. Price control is based on the fact that for each product the maximum retail price cannot exceed an international reference price estimated from the average prices observed in the six major markets, plus a commercialization factor. This scheme is in line with an approach towards price regulation that considers the presence of fixed upfront R&D. The need to pay a higher price than the marginal production cost is acknowledged, so that companies can recover the R&D costs related to the clinical trial
process required to achieve regulatory approval. The report suggests that the adoption of this scheme in 2005 permitted deregulation of generic pharmaceuticals for which there are no economic arguments nor observed market conditions that would justify the use of price controls.

A 2008 literature review by Wirtz et al. demonstrated that published, peer-reviewed research on pharmaceuticals in Mexico has significant limitations in terms of breadth and specificity of health issues addressed (Wirtz et al., 2008). Regarding health problems the review identified four areas where there is little available scholarly evidence: (i) major causes of mortality in Mexico, (ii) causes and consequences of irrational use of medicines, (iii) use of medicines in secondary care and rural areas, and (iv) access to medicines. Wirtz et al. suggested strategies for making private market pharmaceuticals more affordable to people from low-income groups, including price regulation, generic use and competition stimulation. The authors reported that the studies reviewed on access indicate pharmaceutical prices in Mexico are higher than in many developed countries relative to income. They also reported that people from lower income groups spend proportionally more on medicines than individuals with higher income and an inability to access medicines is the main reason people do not return to public health care services.

In 2009 Shadlen wrote about the politics of patents and pharmaceuticals, using the comparator cases of Brazil and Mexico (Shadlen, 2009). Shadlen argued that, since Mexico’s introduction of IP law reform in the 1990s, government response to public health concerns has been thwarted by industrial activism through powerful
pharmaceutical lobby groups. The ability to domestically address public health interests is at odds with international obligations and the interests of the multinational research-based pharmaceutical sector. Shadlen concluded that the subordination of the Health Ministry to the Economic Ministry and the diminished ability of the Mexican national generic sector post-NAFTA meant that calls for patent system reform that prioritized public health concerns were not answered in Mexico. The patent law reform complicated the process by which compulsory licenses could be issued. Shadlen argued this ultimately had the perverse effect of strengthening the pharmaceutical patent system against the interest of public health. Evidence to support this conclusion was derived from analysis of relevant documents. Shadlen comparatively analyzed reforms specifically in the context of NAFTA and TRIPS obligations, and concluded that Mexico did not simply fail to emulate Brazil’s IP systemic moves away from TRIPS plus measures over the past decade, but rather moved to an extended version of TRIPS plus. He presented a political economy explanation for Brazil and Mexico’s divergent trajectories, focusing on the actors pushing for reform and identifying patterns of political mobilization. High prices yielded initiatives for health prioritized pharmaceutical patent reform in both countries. The important actors, however, led these initiatives and the extent to which leaders in local pharmaceutical sectors were available as partners for health oriented reform. In Brazil, a more autonomous local pharmaceutical sector and a significant incidence of HIV/AIDS throughout the country’s population allowed the Ministry of Health to build an alliance that supported patent system reform which prioritized health. Shadlen concluded that in Mexico, fundamental transformations of the new pharmaceutical sector, catalyzed by the signing of NAFTA, meant that patent system reform became directed by
multinational companies locating in Mexico. In Shadlen’s view, this ultimately had the perverse effect of reinforcing a challenged system.

**Increased Access to Medicines**

The second major emergent theme that resulted from the scoping study was that NAFTA patent system harmonization obligations may have a positive impact on access to medicines. Although several authors have concluded that NAFTA has resulted in decreased access, others mention that trade integration seems to have had an impact leading increased pharmaceutical access in Mexico. Trade liberalization (with patent system harmonization) has indirect and direct effects on health services, including the provision of medicines. The indirect effects are related to NAFTA’s influence on economic development. Higher individual income increases purchasing power, as well as the demand for, and ability to purchase, quality medicines. Direct effects stem from changes in the trade flow of goods in health, including more available pharmaceuticals. Opportunities for NAFTA-driven improved access presented in the literature include increased access to novel technology (through improved availability of high quality pharmaceutical products) and tariff elimination on those pharmaceuticals. Table 6 presents exemplary studies for increased access.

**Table 6: Exemplary Studies for Increased Access**

<table>
<thead>
<tr>
<th>Date Published &amp; Author</th>
<th>Title</th>
<th>Disciplinary Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997 – Gomez-Dantes, M. et al.</td>
<td>Commerce in health services in North America with the context of the North American Free Trade Agreement</td>
<td>Health policy</td>
</tr>
<tr>
<td>Date Published &amp; Author</td>
<td>Title</td>
<td>Disciplinary Approach</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>2004 – Shapiro, R.</td>
<td>Patent infringement during a time of national emergency: Are Canadian, American, and Mexican governments permitted to do so under their domestic law, NAFTA and TRIPS; If so at what cost?</td>
<td>Health law</td>
</tr>
<tr>
<td>2005 – Bacalaski, J.</td>
<td>Mexico’s pharmaceutical patent dilemma and the lesson of India</td>
<td>Health law</td>
</tr>
<tr>
<td>2007 – Chaves, G.C. &amp; Oliveira, M.A.</td>
<td>A proposal for measuring the degree of public health-sensitivity of patent legislation in the context of the WTO TRIPS agreement</td>
<td>Health law</td>
</tr>
<tr>
<td>2009 – Gutiérrez-Delgado, C. &amp; Guajardo-Barrón, V.</td>
<td>The double burden of disease in developing countries: the Mexican Experience</td>
<td>Health economics</td>
</tr>
</tbody>
</table>

The 1997 article by Gomez-Dantes et al. investigated how NAFTA created benefits and risks for Mexico’s national health care system (Gomez-Dantes, Frenk, & Cruz, 1997). The article discussed increased commercial trade and accessibility in personal health services in North America. It also analyzed elements of NAFTA that affect the delivery, regulation, and financing of health care services in Mexico. The article identified risks posed by NAFTA including possible strengthening of the role played by curative medicine escorted by increasing costs and irrational use of medicine. The article also noted that, through trade integration, increasing contact with highly technology-dependent medical cultures (such as those in Canada and the U.S.) necessitates flexible mechanisms and networks that make it possible to evaluate not only the safety and efficacy of technological innovations entering the marketplace, but also their cost-effectiveness.
Shapiro’s 2004 health law article conducted a comparative legal analysis to assess the consequences of patent infringement under the doctrine of national emergency for Canadian, U.S., and Mexican governments under their domestic law, NAFTA, and TRIPS (Shapiro, 2004). The author presented the viewpoint that public safety should be the main concern and, if the government can save even one life by overriding a patent, then overriding is worth it. A total disregard for patents, however, removes the incentives for pharmaceutical companies to engage in R&D. The author concluded the ideal situation is for governments to negotiate voluntary license deals with pharmaceutical companies, to purchase bulk quantities at a discount in order to increase access and avoid using their emergency doctrine power. These voluntary license deals would demonstrate a respect for patent rights. U.S. and Canadian domestic law both have provisions allowing for the expropriation of patents to promote pharmaceutical access during times of national emergency, with the requirement of providing compensation. Because of the provisions in their respective constitutions and distinct ideological differences, the U.S. and Canadian governments may have the responsibility to pay higher levels of compensation than what NAFTA or TRIPS require. The author concludes that all this at the very minimum means that access during times of national emergency should be assured one way or the other. The question of what constitutes a national emergency has been the subject of much academic discussion, as it is not defined in the domestic legislation of the three countries nor the International Agreements.

A 2005 study by Bacalaski examined the current state of Mexico’s pharmaceutical industry to demonstrate how Mexico can improve that industry through the application of
reasonable patent protection (Bacalski, 2005). The more mature Indian pharmaceutical industry was examined as a comparison model for Mexico’s industry. Questions were asked about the current state of Mexico’s nascent pharmaceutical industry and how it may be improved to balance competing interests of pharmaceutical patent rights and the protection of public health. The article demonstrated many parties are concerned that high patent protection results in poor access to medicines. A reasonable fear exists that as developing countries strengthen their patent regimes, there will be a concomitant rise in pharmaceutical prices that will disproportionately affect marginalized populations. Bacalski argued that, while this concern is valid, it is mitigated by a general rise in overall economic well-being that accompanies the institution of stronger patent protection as industry grows and unemployment falls. The author suggested acceptance that many other factors, besides patents, affect pharmaceutical prices and availability. This is particularly true in the developing world where government procurement and supply programs may be deficient. Bacalski further argued that signatories to international agreements like TRIPS and NAFTA demonstrate that legislators are resolute in making patent rights a strong, enforceable incentive for innovation and that Mexico is on the right course by strengthening its patent laws. This bodes well, as fostering technological growth in the pharmaceutical industry may help Mexico to become an important and competitive player in the world market. There would be a greater availability of innovative pharmaceutical products. The author concluded that trade integration leads to an increased GDP, and potentially, to increased purchasing power for consumers.
In 2007 Chaves and Oliveira conducted a unique study measuring public health sensitivity of patent legislation (Chaves & Oliveira, 2007). While not specific to NAFTA, the article drew relevant conclusions for Mexico. This study proposed a framework for quantitatively measuring public health sensitivity of patent legislation implemented in various countries after the WTO’s TRIPS agreement entered into force. The methodology for establishing and testing the proposed framework involved content validation through consensus techniques, and an analysis of patent legislation from 19 Latin American and Caribbean countries. The framework was developed, tested, and validated using an adapted Delphi method consensus technique. This did not require all participants to meet face-to-face, rather each responded to e-mailed questionnaires. The first step was to select participants. The study sought professionals (lawyers, medical doctors, economists, and activists) who had experience dealing with patent legislation and access to medicines. Content validation consisted of verifying that the framework generated incorporated all aspects related to the concepts used in the study. Selected professionals who performed a sequential process with feedback achieved this through a consensus. This back and forth procedure allowed participants to include and/or exclude legal provisions and attribute scores for each, as well as to reach a consensus on incorporating all aspects relating to the concept of health sensitive patent legislation. The authors argued that the framework’s usefulness arises from its clear parameters for measuring patent legislation health sensitivity. They noted, however, it could be improved by including indicators related to government and organized society initiatives that minimize negative effects on access to medicines. This clearly indicates that the researchers recognize that many factors exist beyond the realm of IP. The results demonstrated that the framework detected relevant
differences in country patent legislation. Mexico was ranked fourth in terms of health sensitive patent legislation; its patent legislation does not include data exclusivity, yet protects data for five years as established by NAFTA, Article 1711, Trade Secrets. This benefits access by allowing generic substitutes market approval with fewer regulatory hurdles to jump through. Data exclusivity’s impact on pharmaceutical R&D and access is another area of academic analysis, but it is beyond the scope of this dissertation. Chaves and Oliveira conclude that none of the 19 countries studied are taking full advantage of the right to incorporate all TRIPS flexibilities to protect public health as stated in the Doha Declaration. Nevertheless, it is clear there are safeguards in place that may be used to increase access.

A 2009 article by Gutiérrez-Delgado and Guajardo-Barrón focused on the challenges arising from a double burden of disease in developing countries, examining the case of Mexico. Specific examples of the pressures faced by the Mexican public health services, to provide and finance treatment for communicable diseases and non-communicable diseases, are used to illustrate the extent of such challenges in the context of a country with limited resources. The study observed that public competition over resources for treating different diseases and conditions results in requisite trade-offs between equity and efficiency goals. The authors concluded that the implications of addressing the challenges presented by a double burden of disease require a multi-disciplinary approach to develop and strengthen the policymaking process. Analytical tools should be applied in each stage of the policy planning cycle and explicit priority setting processes should be used together with monitoring and assessment to strengthen decision-making under
limited resources. Most developing countries are already advanced along the epidemiological transition toward an increasing non-communicable disease burden that generates increasing pressure on the limited resources available for their health care systems. The importance of this study is that it forces developed countries to shift their perspective on how to best assist developing countries in tackling disease burden and access to medicine issues when making decisions regarding resource allocation. New technologies in the treatment of chronic diseases place pressure on the limited resources available in the health system. Examples of the pressure on financial resources are provided by chronic patients living with HIV/AIDS on sustained highly active anti-retroviral (HAART) treatment, novel pharmaceutical interventions against various forms of oncological disease and renal replacement therapies. This article reported that in 2008, the Mexican Ministry of Health (2008) negotiated with pharmaceutical suppliers for price reductions on patented anti-retroviral treatment to address an average cost disparity compared to other Latin America countries. In parallel, the Ministry decided not to purchase the most novel expensive patented anti-retroviral medicines until a cost-effectiveness analysis could be performed. The result of these cost-control measures was improved access in the medium term.

**Increased Pharmaceutical R&D**

The third major emergent theme that arose from the scoping study was that patent system harmonization improves incentives for pharmaceutical R&D. Some authors included in the scoping study have concluded that strengthened IP rights would lead to an increase in resources used for pharmaceutical R&D in Mexico (Gutterman, 1990). Some propose that strong patent rights may provide incentives for R&D collaborations addressing the
needs of Mexico (Frenk et al., 1994). Given the limited evidence available, the causal link between patent rights and pharmaceutical R&D for neglected diseases of relevance to Mexico is weak. It was interesting to note that American authors wrote most of the studies that advocated NAFTA as being positive for pharmaceutical R&D in Mexico. The scoping review suggests that more comprehensive innovation policy efforts are needed in areas other than those that focus on patents, but there may have been some positive aspects for pharmaceutical R&D in Mexico due to patent system harmonization. Exemplary studies are shown in Table 7.

**Table 7: Exemplary Studies for Increased R&D**

<table>
<thead>
<tr>
<th>Date Published &amp; Author</th>
<th>Title</th>
<th>Disciplinary Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999 – Flax, R.H.</td>
<td>NAFTA &amp; the patent systems of its members: is there potential for a unification of the North American patent systems?</td>
<td>Health law</td>
</tr>
<tr>
<td>2003 – Kravzov-Jinich, J. et al.</td>
<td>Rx price control methods in Mexico</td>
<td>Health policy</td>
</tr>
<tr>
<td>2007 – Zuniga, M.P. et al.</td>
<td>Technology acquisition strategies in the pharmaceutical industry in Mexico</td>
<td>Health economics</td>
</tr>
<tr>
<td>2008 – Santiago-Rodriguez, F.</td>
<td>Two Articles – (1) Policy responses to the internationalisation of clinical trials to developing countries: exploring the case of Mexico; (2) Facing the trial of internationalizing clinical trials to developing countries: with some evidence from Mexico</td>
<td>Health policy</td>
</tr>
</tbody>
</table>

In 1995 Berg wrote about what she viewed as converging views in IP among the NAFTA parties. The author studied the barriers to trade presented by inadequate protection of IP rights and how developing countries, which have traditionally argued against providing
such protections, were beginning to recognize a need for stronger protections (Berg, 1995). Through legal analysis, she argued that the most significant detriment of inadequate protection of patent rights is the creation of a major non-tariff barrier to trade. This barrier was due to companies’ uneasiness towards entering markets that do not provide the appropriate level of legislative patent protection and enforcement mechanisms. She also disagreed with some studies that had attempted to prove that shorter periods of patent protection may actually be optimal in terms of national welfare. Berg contended that such studies must be qualified, that any type of country can benefit from adequate protection of patent rights and that there is no strong a priori evidence that these countries will necessarily benefit or lose from a reform of their patent systems. The author concluded that Mexico’s attempt to achieve an industrialized level of technological competence would fail until its national innovation system adapted to better apply the benefits of strong patent laws. Since that time, Mexico has moved towards a developed view of patent protection and an increased potential for economic growth through innovative efforts is incipient inside Mexico.

A 1999 article by Flax presents a historical description of the development of patent law that leads into an overview of the three distinct patent systems of the United States, Mexico, and Canada to demonstrate how they have been changed by NAFTA (Flax, 1999). Flax also presents an overview of the patent system in the EU to exemplify a regional attempt to unify patent systems and establish a free trade zone. This system is compared to North America’s, and explores how their patent systems could be further unified. Analysis in the article suggests that, although the NAFTA countries have made
great strides towards toppling barriers inhibiting free trade, IP protection differences offered remain. Due to three distinct patent systems in the NAFTA countries, the inventor of a new product possessing commercial opportunities may not be afforded equal protection from infringement in each of the NAFTA countries. Though some issues have been resolved, other areas of disagreement still exist. Nevertheless Flax concluded that, even in light of remaining differences, NAFTA’s patent provisions represented a major signpost as each country moves towards the provision of adequate and effective enforcement of patent rights. Flax is decidedly pro-IP, justifying the international protection of IP on three key principles: (1) IP protection stimulates technological innovation, (2) technological innovation contributes beneficially to economic growth, and (3) development through economic growth is desirable throughout the continent.

A 2003 article by Kravzov-Jinich et al. focused on an evaluation of pharmaceutical price control methods in Mexico (Kravzov-Jinich, Altagracia-Martínez, Yamasaki-Lopez, Salgado-Schoelly, & Cardona-Carlfn, 2003). Some interesting conclusions for improved R&D efforts were drawn. The article described how until the mid-1980s Mexico had an economy based on protectionism, with little exposure to the international markets. In 1986 it became a member of GATT in order to liberate its economy. Mexico negotiated special conditions for some sectors, including pharmaceuticals, recognizing them as strategically vital to the country’s development and to the preservation of its sovereignty. Pharmaceutical patents and biotechnology patents derived from plants or animals were not recognized by Mexico at that time. NAFTA negotiations with the U.S. and Canada in 1994 revealed that the Mexican pharmaceutical sector had excessive protection from
international markets. Mexico suffered from a poor application of the Good Manufacture Practices (GMP) set out by the U.S. FDA, little pharmaceutical R&D, poor investment in the field and the nonexistence of pharmaceutical patents.

A 2007 article by Zuniga et al. examined technology acquisition strategies in the Mexican pharmaceutical industry and the use of in-house R&D and technology transfer between 1994 and 2000 (Zuniga, Guzman, & Brown, 2007). The authors used two econometric models to (1) study the factors which determined technology acquisition strategies in the Mexican pharmaceutical industry, and (2) evaluate the complement between internal R&D and technology transfer. They presented the theoretical debate between companies’ technological strategies and the results of earlier empirical work and also explored international and Mexican pharmaceutical industries technology acquisition strategies. The article presented their econometric model results and recommended innovation stimulation policies. Their study indicated that, unlike the pharmaceutical industries of other major developing countries in economic transition, such as India and China, there was a low probability of complementarities between R&D and technology transfer in the Mexican pharmaceutical industry. Their analysis demonstrated that significant segmentation exists among national companies. Primarily there are companies that have based their development of generic pharmaceuticals on a closed economy, with lax IP protection and a niche relationship of public sector procurement. A much smaller group of companies created an innovation strategy focused on the production of new products so there have been some increased efforts towards pharmaceutical R&D. According to these companies, innovation has been mainly limited due to a lack of adequate financing.
and an absence of public policies that support the industry in countries like India and Brazil. The authors suggest that strengthening of the patent system facilitates technology transfer, leading to greater domestic pharmaceutical R&D and potential inception of innovative products. The study further suggested increasing innovative capacities in industrial productivity could be achieved by strengthening the liaison between the industry and scientific activity conceived in public universities. Co-operation should include collaboration in ongoing product innovation development in such novel areas as biochemistry and biotechnology, and also process upgrading geared towards higher-quality pharmaceuticals through plant modernization. The value reverse innovation in Mexico was not discarded. If a firm licenses a patented pharmaceutical and produces it under the patented brand name, it was considered important that such a firm possess the technological capabilities linked to R&D investment in order to produce a generic substitute on patent expiration to enhance access.

Two articles by Santiago-Rodriguez in 2008 on policy responses to the internationalization of clinical trials to developing countries focused on Mexico. The first paper discussed some minimum ethical principles to be observed for trial performance, and those principles’ relevance for developing countries (Santiago-Rodriguez, 2008). Santiago-Rodriguez uses the case of Mexico to illustrate challenges in conditioning public policy to ensure adequate observance of ethical requirements. Primary data were gathered through semi-structured interviews carried out in Mexico during 2007. Informants included representatives from multinational subsidiaries operating in Mexico, national pharmaceutical firms, local trade organizations, (CANIFARMA and AMIIF), the
Mexican regulatory agency (COFEPRIS), and the coordinating body for public health research centres (CCINSHAE). Secondary data sources included presentations by sector experts and documents from both academic and industry sources on the structure, size, and overall environment of clinical research in Mexico. These sources were used to triangulate information obtained through interviews. Particular attention was paid to the regulatory clinical research environment and the structure and function of bodies involved in the ethical evaluation and monitoring of clinical trials. The study concludes that, while relevant government regulatory agencies seem to be adjusting to growing clinical trial activities, insufficient resources and actual endowment of powers to enforce regulations has hindered efforts. The study demonstrates a definite upward trend in clinical trial activity in Mexico. The author’s analysis of the secondary data sources led to the conclusion that interactivity among heterogeneous Mexican and foreign agents may underpin adequate performance of innovation systems. Interaction provides opportunities to learn from counterparts’ experiences in dealing with explicit tribulations during the innovation process. Santiago-Rodriquez’ second article analyzed recent developments in markets for clinical trials in Mexico. The article brings together literature on internalization of R&D and ethical implications and regulation of clinical trials. It characterizes clinical trials within the broader innovation process in the pharmaceutical industry, including some detriments of their internalization and location to developing countries. The author drew the following conclusion: weak enforcement of inadequate regulations and incomplete reform processes support concerns about how well potential benefits of initiating domestic clinical trials may surpass the inherent risks. The author
concluded that the creation of ad hoc regulatory agencies is insufficient if those agencies are not properly endowed and empowered.

**Decreased Pharmaceutical R&D**

The fourth major theme that emerged from the scoping study was that patent system harmonization in Mexico may lead to decreased pharmaceutical R&D. The scoping study revealed a number of authors who concluded that patent system harmonization under NAFTA led to decreased or negligible change in pharmaceutical R&D in Mexico. Existing evidence on pharmaceutical R&D in Mexico indicates that NAFTA might have helped spur trade, foreign direct investment, and economic growth, but reallocation effects and not regional patent system harmonization mainly drove these benefits. NAFTA has not necessarily led to enhanced learning capacity in Mexico’s private pharmaceutical sector. It seems that Mexico needs to do more to stimulate innovative research in pharmaceutical R&D.

**Table 8: Exemplary Studies for Decreased R&D**

<table>
<thead>
<tr>
<th>Date Published &amp; Author</th>
<th>Title</th>
<th>Disciplinary Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995 – Gasman, N.</td>
<td>Drifting through time - Pharmaceutical policies in Mexico</td>
<td>Health policy</td>
</tr>
<tr>
<td>2000 – Cimoli, M. &amp; Gonsen, R.</td>
<td>Developing innovation systems - Mexico in a global context</td>
<td>Health economics</td>
</tr>
<tr>
<td>2002 – Zuniga, M.A. &amp; Combe, E.</td>
<td>Introducing patent protection in the pharmaceutical sector: a first evaluation of the Mexican case</td>
<td>Health economics</td>
</tr>
<tr>
<td>2003 – Lederman, D. et al.</td>
<td>Lessons from NAFTA for Latin America and Caribbean (LAC) countries: a summary of research findings</td>
<td>Health economics</td>
</tr>
<tr>
<td>2008 – Kuznetsov, Y.N. &amp; Dahlman, C.J.</td>
<td>Mexico’s transition to a knowledge-based economy: challenges and opportunities</td>
<td>Health economics</td>
</tr>
</tbody>
</table>
Returning to the landmark Gasman article (1995) on pharmaceutical policies in Mexico, mentioned above; Gasman predicted that NAFTA would improve the position of the U.S. multinational pharmaceutical industry but not that of the Mexican national pharmaceutical industry. It was expected that greater patent system strengthening in Mexico would result in increased foreign direct investment in Mexico by U.S. multinational firms (Gasman, 1995). This would result in a positive economic effect for Mexico that might help to improve the overall health of the population but was not considered promising in terms of Mexico building a sustainable, national, innovative pharmaceutical sector. Gasman argued that Mexican firms would face great difficulties competing. The most probable scenario was that multinational companies would increasingly dominate Mexico’s pharmaceutical sector. It was predicted that most national companies would go bankrupt and surviving firms would merge or be sold to the multinationals in an increasingly consolidated pharmaceutical sector. This turned out to be true in the research-based sector. However the Mexican generic-based sector has increasingly strengthened its competitive efforts in response through a market demand that serves a largely low income population (Hayden, 2007). Gomez-Dantes et al. echoed this sentiment in 1997, when writing about Mexico’s national health care system and the risks posed by NAFTA (Gomez-Dantes et al., 1997). That article identified the threat of liberalized trade leading to fewer stimuli for national research development as a consequence of increased access to and reliance on North American scientific centres. This possibility seemed especially noteworthy in light of the enormous power and resource asymmetry existing between the countries in the region.
In 2000, Cimoli and Gonsen published a significant work on developing Mexican innovation systems in the global context. Two chapters of a larger book are dedicated to the Mexican pharmaceutical and biotechnology sectors. The first chapter examines the role of the pharmaceutical industry in the context of national innovation systems (Cimoli, 2000). It presents an economic characterization of the pharmaceutical sector, the role of government as the institutional framework, and a characterization of technological capabilities of the pharmaceutical industry. It also includes a discussion of public research institutions that establish linkages with pharmaceutical firms and the knowledge flows that occur between them. The chapter describes how the market structure of pharmaceuticals in Mexico is delineated into two distinct groups. The first group is oriented towards government service and consists of mainly mature generic products. Domestic companies satisfy government demand for the generic products (public market cost-containment approach). The second group is oriented towards private sector consumers and is characterized by differentiation of products through brand names and higher value-added arguments. This private market is more dynamic since it has larger profit margins due to differentiation and patent protection. The authors note that, with the liberalization of the Mexican economy, laws concerning patent rights were brought into conformity with international standards and agreements, but that patent protection has not encouraged local innovative R&D activity as is usually the case in more developed economies. They report that after 1991, patenting activity by Mexicans diminished in relation to foreigners from 7.5% in 1980–91 to 2% in 1992–96. Usually, innovative multinational companies have their novel medications, formulations, or production processes already patented elsewhere before their application to IMPI. The authors argue
that the current patent system has been useful to foreign entities for commercial strategies and has not acted as an incentive for invention within Mexico. The second chapter in Cimoli and Gosnen’s book examines the potential of biotechnology in Mexico through analysis of the relevant institutions, human capital formation, and the technological regime that characterizes biotechnology. The chapter argues that, in the international context the relevant knowledge base for biotechnology involves tacit aspects related to firms’ idiosyncratic capabilities with regard to frontier scientific knowledge. Advances in disciplines, including but not limited to molecular biology, cellular biology, and molecular genetics, provide the sources of knowledge for products being developed in high science. The authors suggested that knowledge generation is stunted in Mexico due to the lack of an industry capable of incorporating advanced biotechnology development into its operations, either by conducting its own R&D or by complementing its capabilities through alliances with public or university-based research institutes. The few companies created in Mexico to exploit the advanced techniques of biotechnology at the industrial level have not succeeded. In Mexico, despite the fact that biotechnology was recognized in government programs as a priority area, there has not been an explicit policy in support of biotechnology. The authors mention that there are some excellent biotechnology research groups in Mexico but, in the most advanced scientific areas, like molecular biology, there is no transmission of knowledge to industry because of the lack of R&D capacity possessed by Mexican firms.

In 2002 Zuniga and Combe wrote about the introduction of pharmaceutical patent protection in Mexico (Zuniga & Combe, 2002). Their article surveyed studies evaluating
the impact of patent system harmonization in southern countries on consumer welfare and economic activity. The article provides an analysis of the pharmaceutical industry in Mexico before and after patent reform. The paper described technological creation in the Mexican pharmaceutical industry as being negligible in the past decade since the introduction of the Law for the Promotion and Protection of Industrial Property in June 1991. They recognized feasibility constraints in undertaking analysis due to the obscurity of accessing detailed data for both multinational and domestic firms. The authors did, however, identify some trends that have important implications for the current competition between multinational and domestic firms. This article suggests that dynamic gains are still far off and a more active public policy is needed to stimulate R&D efforts. Strengthening patent protection will not automatically change ways to finance R&D projects, nor will it change the technological capacity to develop new medicines by domestic firms in the short term. Zuniga and Combe concluded that it remains to be seen (a decade out) to what extent patent reforms stimulate or deter faster commercialization of pharmaceutical innovations in Mexico. They concluded that patent protection seems to have strengthened foreign direct investment since the number of multinationals localized in Mexico increased after the patent reform. They indicate, however, the impact this has had on increased Mexican innovation in pharmaceutical R&D is not well understood and needs more study.

In 2003 Lederman et al. wrote about lessons from NAFTA for Latin America and the Caribbean (Lederman, Maloney, & Serven, 2005). This was a comprehensive report published by the World Bank. The report aimed to provide guidance to countries on what
they can expect from trade agreements analogous to NAFTA such as the DR-CAFTA. It identified that NAFTA is a treaty that has helped Mexico approach the level of economic development of its partners, but has not been enough to ensure equal technological capacity with the U.S. and Canada. The report concluded that NAFTA’s main contribution to Mexico’s innovation effort has been its Chapter 17 on IP rights and requisite harmonization measures. The existing evidence, however, on the association between Mexico’s patent system and its ability to innovate remained unclear. The analysis did suggest that stronger patent protection was associated with higher levels of R&D spending relative to GDP. The report recommends that Mexico still needs to make substantial policy improvements to catch up with the pace of innovation in the U.S. and Canada. The report concluded that key constraints result from institutional gaps and deficiencies in education and innovation policies. According to the authors, the liberalization of trade and efforts towards patent system harmonization are necessary measures but are not sufficient to spur an innovative environment alone. The inefficiency of Mexico’s innovation systems is reflected in the level of patents received for each dollar invested in R&D. This number is significantly below the OECD average. These authors, like others, noted that Mexico’s inefficiency seems to be associated with the lack of constructive linkages between universities/public research institutes and industry. This deficiency does not provide incentives for its researchers to participate in productive long-term R&D relationships. It is also reflected by the private sector’s perceptions concerning the quality of the research conducted in the universities and their lack of maintaining collaborative projects with public research institutes. Mexico’s innovation lag is further illuminated in the number of U.S. patents granted to Mexican researchers.
The number of patents is significantly below what should be expected relative to GDP, labor force, and exports to the U.S. The report concluded that innovative capacity is essential to exploit the potential of NAFTA and the Mexican government needs to intensify its progress in education and innovation spending. The authors recommended this be accomplished by overhauling what is considered to be a dysfunctional national innovation system.

The World Bank published another paper in 2008 by Kuznetsov and Dahlman on Mexico’s transition to a knowledge-based economy (Kuznetsov & Dahlman, 2008). Econometric methods with panel data analyzed Mexico’s challenges and opportunities using Korea, Finland, China, Ireland, and others as comparator countries. The study applied the Knowledge Assessment Methodology (KAM), which includes 76 quantitative and qualitative variables for assessing a country’s position on the four pillars of the knowledge economy framework. Mexico fared poorly compared to many of its main competitors in Innovation. In Latin America, Mexico falls behind Brazil and significantly behind Argentina, Costa Rica, and Chile. The report’s main recommendations included that the NAFTA agenda needs to be deepened and that Mexico should create institutional capabilities through innovation upgrading. Improving education and updating Mexico’s infrastructure for information and communications technology were seen as essential aspects of an upgrade. It was also noted that alliances among dynamic agents throughout North America are fundamental to benefiting from new opportunities. The report concluded that to improve incentives for innovation, linkages between public research institutes and industry can be strengthened in a number of ways. Public institutions
should reward researchers that generate productive research projects and create linkages with the private sector. Rules for funding for R&D should be introduced that favour collaborations between universities and private firms. Finally, funding should be targeted to sectors known for strategic value. The report concluded that while first-generation NAFTA-related reforms were based on low-cost labor in Mexico, second-generation reforms will be based on lower-cost skilled labor. R&D links with the U.S. and Canada in innovative efforts is at the centre of knowledge-based, second-generation NAFTA reforms. The authors noted that reforms within the NAFTA agenda must focus on improving national capacity to generate knowledge, which can be transformed into wealth. The authors clearly called a second-generation NAFTA agenda, a knowledge economy agenda for Mexico.

3.4 Discussion
This scoping study is useful for public health professionals who seek to provide international trade negotiators and national decision-makers with information on the public health implications of patent system harmonization. Although NAFTA is no longer a front-page topic, its controversial nature is still a live issue for a number of reasons. The U.S. government response to the global financial crisis of 2008 has brought NAFTA issues back to the forefront of discussions. Trade issues have again become important in repairing regional economic health as governments reassess polarizing measures of further trade integration or protection. The recent emergence of H1N1 in Mexico, and SARS transmission through Mexico, has made regional communicable disease outbreak response, and access to on-patent medicines in the case of national emergency, a prominent issue in the media and among public health professionals.
Finally, Mexico is facing an advanced epidemiologic transition and double burden of disease, meaning it increasingly faces similar health burdens to our own (Gutiérrez-Delgado & Guajardo-Barrón, 2009).

A key strength of this scoping study is that it has provided a rigorous and transparent method in mapping a complex multidisciplinary area. It has identified the volume, nature, and characteristics of the literature in this field of interest. This scoping review has identified common themes emerging from previous research in the study area. The majority of studies included in this review found that increased patent protection negatively impacts access through increased prices for the consumer. The literature suggests that the innovative effects of a stronger patent system on pharmaceutical R&D in Mexico have been at best minimal.

By addressing the question “What is known from the existing literature about the impact of NAFTA’s patent system harmonization on public health in Mexico?” The scoping study found two primary thematic effects on public health of Mexico harmonizing its patent system to NAFTA standards.

1. Patent system harmonization has a net impact on pharmaceutical access in Mexico.

2. Patent system harmonization has a net impact on pharmaceutical R&D in Mexico.

The impacts are considered net because there seems to be positive and negative implications for both pharmaceutical access and R&D. Understanding the magnitude of
these effects becomes important. Under these two primary thematic effects, the scoping study identified four thematic areas of potential net public health impact in Mexico. The scoping study concluded that:

1. *Decreased pharmaceutical access* exists through higher prices. Patents result in higher prices due to prolonged periods of exclusivity rights on pharmaceuticals. This leads to greater barriers to access due to questions of affordability. There are significant obligations to implement legislation to enforce patents under NAFTA.

2. *Increased pharmaceutical access* exists through increased on-patent pharmaceutical availability through increased FDI and multinational presence and trade flows. In addition, many safeguards exist within trade regimes (NAFTA and TRIPS) to promote access, however, findings suggest that significant barriers exist due to the complexities involved in making use of given safeguards.

3. *Increased pharmaceutical R&D activity* exists through obligatory NAFTA patent law reforms. The number of multinationals in Mexico increased after patent system harmonization. It is difficult, however, to say whether this is a factor leading to increased pharmaceutical R&D in Mexico. There is potential for increased local pharmaceutical clinical trial R&D in areas such as diabetes, which is highly prevalent in Mexico.

4. *Decreased pharmaceutical R&D activity* exists due to reliance on U.S. R&D and a failure to develop, fund, and maintain domestic innovation systems. Since patent system harmonization has been introduced to Mexico, increases in innovative R&D in the pharmaceutical industry can be described as negligible.
These derived themes can be presented as a conceptual framework for understanding how patent system harmonization impacts the two principal areas of public health. First, is the issue of pharmaceutical access, where discussion focuses on the links between patents, competitive exclusionary measures, and the affordability of novel medicines. Second, there is the issue of incentivizing pharmaceutical R&D. This discussion focuses on the role of patents in motivating the discovery and development of new pharmaceuticals, and the effect of these rights on R&D expenditure and its allocation across diseases. The framework can be used as a generic tool for analyzing the impact of patent system harmonization provisions in trade agreements on health. It can also be used as a guide for decision makers to understand the policy formulation processes that occur in analogous future scenarios, guiding decision-makers in developing appropriate patent/health system policy. The framework could be applied to answering research questions in the area for different countries as signatories to other trade agreements requiring patent system harmonization. Although the nature of the various components of patent system harmonization and its different impacts will vary across countries at different times in their economic development, the framework provides a useful model for conceptualizing potential effects.
Figure 5: Scoping Study Conceptual Framework

The framework illustrates the trade-offs in the international harmonization of patent systems between access to novel medicines and the incentives considered a necessary condition for R&D of novel pharmaceuticals. Net health impact is a result of patent law implementation and pharmaceutical policy decisions as harmonization proceeds. Trade-offs need to be optimally and iteratively balanced and re-balanced to maximize net public health benefits of harmonization (i.e., green arrows should be maximized). This requires the development of effective global and domestic mechanisms that resolve current patent system structural problems, problems which lead to economic inefficiencies detrimental to global health equity. While health is a complex outcome and determinants of health are multi-factorial, an explicit framework for further decision-making can advance the formulation of appropriate health policy. This conceptual framework provides a basis for developing appropriate pharmaceutical policy in national decision-making and
international negotiations on trade for the benefit of public health. By providing a basis for decision-makers to trace through the potential impacts of a particular patent system reform on health, the framework encourages decision-making that takes explicit account of the net benefit health implications of trade agreements containing patent system harmonization obligations. This will help in the resolution of disharmony in the patent system in North America and may be generalized to create better cooperative conditions between states throughout the world. This is particularly true when looking at analogous situations of neighbouring states where power imbalances exist. The conceptual framework is a meaningful contribution to future empirical research by providing a basis for analysis of patent system harmonization scenarios on health.

### 3.4.1 Study Limitations

Scoping studies provide a comprehensive descriptive account of available research. They do not provide a quantitative synthesis of the research. This could be seen as a limitation. Systematic review, however, as it is understood in health research with statistical meta-analysis is not appropriate for this area of inquiry, given the varying study designs found in the literature that address the research question (Egger et al., 2001). It is not feasible to quantitatively synthesize pharmaceutical access and R&D studies that are conducted using different methodological approaches and stem from different academic disciplinary traditions (Kleijnen & Antes, 2002). The studies included in this scoping review focused on the impact of NAFTA in Mexico. The questionable applicability of the study’s findings to other countries facing analogous trade-related patent system harmonization is another important limitation of this scoping study. The findings are most suitably generalized to the signatory countries of other low/middle income countries in Central
America (e.g., recent signatories to DR-CAFTA). These countries have cultural, economic, and epidemiologic profile similarities to Mexico in the mid-1990s. Any generalization to these countries, however—especially to developing countries in other parts of the world—should be done with caution and the understanding that each country’s health situations are unique.

3.5 Directions for Further Research
The overall state of the evidence is weak. There is an abundance of material, but only a few primary research studies exist. The reasons for this are likely multi-factorial. First, insufficient monitoring within Mexico is a problem. Obtaining pharmaceutical data from private firms can be difficult. Second, appropriate study design is complex when assessing the impact of a distal determinant of health. Third, feasibility and resource constraints in Mexico for research are also identifiable problems. This scoping study found divergence in the literature about the impact of patent system harmonization on access to medicines in Mexico. Some researchers suggested that the current NAFTA-based regional patent system seems to have had negative effects on access to medicines, primarily in terms of pricing. In addition, there is considerable evidence that regional patent systems are fraught with high costs of administration and dispute resolution that further delay access. The adequacy of current available safeguards to promote access, such as compulsory licensing, is under question. Patent system harmonization, however, may have some positive effects in terms of novel medicines made available in Mexico at an improved pace due to increased confidence in the patent enforcement mechanisms.
From a review of the available literature, there is also no conclusive agreement regarding the impact of NAFTA’s patent system harmonization obligations on pharmaceutical R&D in Mexico. Some researchers argue that the absence of patent protection encourages technology transfer and technological innovation through reverse engineering of imitator products (Mengistie, 2003). Others argue that patent protection is a mechanism, which encourages technology transfer through foreign direct investment or licensing, and the indirect results are effective means of technological learning (Drahos, 2002a). Those who support the existence of a positive relationship between patent protection, foreign direct investment, and technology transfer argue that without protection, decision-making on investments would be difficult. Most authors maintain that stronger patent rights alone are a necessary yet not sufficient condition to stimulate pharmaceutical R&D. IP rights are only one of the factors influencing innovation. Other factors relate to a country’s educational infrastructure, pharmaceutical R&D costs, market structural conditions, organization of the pharmaceutical sector generally, and its ability to appropriate returns from ongoing research efforts. From the pool of evidence analyzed in this scoping study, it seems that a strengthened system of patent protection has had limited effectiveness in stimulating innovation in pharmaceutical R&D in Mexico, and that supplemental government policies are required to enhance R&D efforts. A stronger patent system does seem to have enhanced the conduct of clinical trials in Mexico, likely enhancing the global process of pharmaceutical development (Santiago-Rodriguez, 2008).

There is insufficient available evidence to support research-based recommendations in Mexico on how to best further balance the often described competing policy goals of
ensuring access to medicines while promoting pharmaceutical R&D. The literature that does exist on the impact of patent system harmonization in Mexico to U.S. standards on access and R&D is divergent. Published opinions are somewhat polarized at opposite ends, much like the global debate. The actual impact on public health is difficult to determine from the literature available to date.

Determining whether and how existing evidence in a certain area is deficient are important objectives of scoping studies. The findings of this scoping study served as a stimulus for conducting further primary investigation that is both appropriate and necessary. Based on the findings of this scoping study, further research was considered necessary to understand the current state of Mexican patent system harmonization and its important impacts on public health. Further research might help to develop patent system reform and policy recommendations to improve access to medicines within a patent system that incentivizes domestic pharmaceutical R&D. Most of the currently available literature concerning NAFTA, patent system harmonization, and public health in Mexico consists of polemical debate, without empirical evidence to substantiate claims made for or against increased patent system harmonization. Nevertheless there is an immediate need to minimize risks stemming from trade integration on health. Rather than advocating the abolition of trade agreements, which would compromise health, government-guided fair trade free market advantages should be sought. An evolutionary understanding of how to achieve these advantages is necessary. Focus should be maintained on strategies to ensure that the opportunities for improving public health through trade are maximized (Smith, 2006). Economic development generally leads to
health system improvements that facilitate access to health services, including the provision of pharmaceuticals.

Other than elevated prices of pharmaceuticals due to upholding patent rights, there may be very few other detrimental impacts of being a signatory member to a trade agreement requiring patent system harmonization. Procurement, supply availability, and distribution conditions seem to improve with trade integration and globalization. More effort is needed, however, to understand how to implement policies that aim to promote access to medicines that address the price conditions caused by limited term, yet prolonged, periods of market exclusivity. Compulsory licensing as the primary legal safeguard available for the promotion of access must be examined further. The movement towards an ongoing and unnecessary strengthening of international patent law through the proliferation of U.S. multinational pharmaceutical trade interests in bilateral agreements may be effectively muffled through the provision of sound objective evidence in the interest of achieving greater global health equity. Ultimately, evidence-based research and advocacy must aim to change the ways patent system harmonization is written into next-generation trade agreements. This may include amendments to NAFTA/TRIPS and how those amendments are implemented into domestic law. Such changes require that governments and pharmaceutical companies be held responsible for commitments to the common good.

Through the scoping study the following focused research question was formulated for the primary research conducted in the next chapter: “Are available safeguards in Mexico
It is possible to provide reasonable empirical evidence that answers the research question through a qualitative analysis of stakeholder perspectives. This task has been undertaken in the next chapter of this dissertation. This research is needed to address the complex implications of requiring Mexico to continue reforming its patent system in order to meet international treaty obligations that were signed when public health impacts were not well considered, almost two decades ago.
Chapter 4: Stakeholder Perspectives on Patent System Harmonization

4.1 Introduction
This chapter analyzes stakeholder perspectives on the impact of patent system harmonization on public health in Mexico. Qualitative research was conducted to examine Mexico as a single country case study. Mexico’s Plan Nacional de Desarrollo 2007–12, set out by Presidential Decree, identified improving access to medicines as one of the strategic priorities for the current administration in the Programa Sectorial de Salud (www.presidencia.gob.mx). The research question addressed in this chapter is “Are available safeguards in Mexico adequate for promoting access to medicines within a patent system that is set up to incentivize pharmaceutical R&D?” Post-NAFTA political and economic processes were analyzed through in-depth, semi-structured interviews with key informant stakeholders in Mexico City.

The scoping study in Chapter 3 determined that the impact of NAFTA Chapter 17 patent system harmonization provisions on public health is an unsatisfactorily studied area of global health research. Available evidence is divergent and polarized. In this chapter, the convergent thematic perspectives that emerged through a triangulation of responses from different stakeholders were categorized to allow for evidence-based conclusions.

The complexity of analyzing the impact of patent system harmonization requirements based in trade agreements on public health made qualitative research an appropriate methodological choice. The research required an approach that elicited in-depth
perceptions and experiences in order to lead to theory construction. Qualitative research is increasingly applied in the public health field. Qualitative methods allow for construction of theory relevant to public health outcomes developed from stakeholder perspectives (Ulin, Robinson, & Tolley, 2005). One of the primary goals of this dissertation was to determine whether patent reform is necessary to improve public health outcomes, not only in Mexico but also globally. Another goal was to construct a model for appropriately responsive patent system reform. By studying in-depth patent system harmonization and medicines in Mexico, I was able to achieve this goal and develop a globally applicable model of patent system reform.

Data on access to medicines and pharmaceutical R&D is not readily available in Mexico (Barraza & Campos, 2007; Lozano et al., 2006). Improved data collection systems are needed in order to rigorously assess the impact of patent system harmonization on pharmaceutical access and R&D. These deficiencies in the available data all but precluded the use of quantitative methods and led to the current exploratory qualitative study. This chapter is organized in the following sections: Section 4.2 presents a detailed description of the methodology chosen and research methods applied; Section 4.3 lays out the results of the qualitative data collection exercise; Section 4.4 is an analytical discussion of the data collected; Section 4.5 draws conclusions on stakeholder perspectives on patent system harmonization in Mexico, and generally.

4.2 Qualitative Methodology

Qualitative and quantitative researchers are both concerned with developing solid theories as research outcomes. Their approach to this task is somewhat different however,
as qualitative research is inductive (Patton, 2002). Qualitative research emphasizes construction of theory or hypothesis generation (Eisenhardt, 1989; Punch & Punch, 2005). Once generated, a theory may be used further in quantitative research to generate and test hypotheses. In part, qualitative research was chosen for this dissertation because of the goal of developing theoretical patent system reform. Table 11 in the Appendix (page 250) is based on the work of Morse and Field and compares the approaches taken to quantitative and qualitative research (Morse & Field, 1995).

### 4.2.1 Political Economy Paradigm

Qualitative research is conducted through a paradigm by which the researcher has chosen to view the study (Creswell, 2007). A paradigm or worldview is a basic set of beliefs that guide action (Guba, 1990). This dissertation works from the paradigm of the political economy. Political economy was a term originally used for studying markets and their relation to law and government (Bevilacqua, 1968). The term political economy is now used more broadly and refers to interdisciplinary studies drawing upon economics, law, and politics in explaining how political institutions and the economic system influence each other (Bortis, 1997). In this study the focus is on the various functions of the Mexican Ministry of Health (Secretaria de Salud) and the Ministry of Economy (Secretaria de Economia), and their interactions with the pharmaceutical sector as a major part of the economic system. The role and influence of the public research institutes within this political economy are also part of the analysis. Political economy can be used as a paradigm to analyze and explain the impact of political factors and economic factors on certain outcomes, in this case public health outcomes, and how a system might be changed to improve those outcomes (Phelps, 1985). The political
economy of public health is concerned with how political decision-making and state economies influence population level health (Szreter & Woolcock, 2004). National strategies for patent and health system governance influence capacities to address public health concerns through access to novel pharmaceuticals, as well as trajectories of economic development through the commercialization and provision of newly available medicines (Shadlen, 2007a). This political economy of public health paradigm can be used to situate the effect of various institutions, political processes, and economic interests on pharmaceutical access and R&D policy. This makes the paradigm ideally suited to answering the research question asked in this chapter (Lienhardt & Ogden, 2004).

The wave of international patent system reform that occurred during the negotiation of NAFTA was concluded before the relationship between patents, access to pharmaceuticals, and public health became a prominent global political issue. A profound effect of NAFTA with regard to this relationship was how it catalyzed pharmaceutical sector industrial change in Mexico. NAFTA has affected government policy choice, leading to a shift in focus in this chapter from NAFTA as an international trade agreement to NAFTA as political economy (Shadlen, 2007a). Rather than focusing on the implementation of domestic legislation as in Chapter 2, this chapter focuses on analyzing distinct stakeholder responses to opportunities and challenges presented by patent system harmonization based in a political economy of public health paradigm. The perspectives of different major stakeholder groups are explored, including those of government, pharmaceutical industry, and research institutes.
4.2.2 Case Study Design

A case study approach, with Mexico as the country of interest, was chosen (Creswell, 2007). One purpose of case studies is to identify and answer research questions that stem from concerns about the implications of new policies or the actualization of such policies. Case studies can also be used to examine the implementation of policies over a period of time (Pope & Mays, 2004). Pollit et al. have advocated for the use of case studies to identify the impact of government policies on health systems (Pollit et al., 1990). Case studies have been described as a better methodology than other qualitative designs for documenting processes of market innovation, competition, collusion, equilibration, institutional change, regional integration, and disintegration (Odell, 2001). For these reasons, the case study was the most appropriate method to examine the political economy of NAFTA implementation on public health in Mexico. As previously mentioned, Mexico represents a unique situation amongst developing countries having been exposed to, and harmonized its patent legislation with, developed countries via NAFTA since 1994.

4.2.3 Selection of Key Informants

Purposive sampling was used to recruit participants who met the study criteria, as is the standard for qualitative studies. The researcher selects individuals and sites for study because they can purposefully inform an understanding of the research problem (MacDougall & Fudge, 2001). Key informants were selected based on their expertise in areas relevant to the case study. The process began by identifying individuals to interview for key stakeholder perspectives on the impact of patent system harmonization in Mexico. A list of potential interviewees was developed via three methods: (1) exploring
the Internet for websites addressing the issues to be investigated, (2) discussion with academics in several disciplines, and (3) discussion with my network of legal professionals who are among the top NAFTA lawyers in Canada. Subsequent sampling by referral occurred as individuals who were interviewed identified colleagues and other relevant stakeholders. Thus, there was some degree of referral sampling, which is also used in qualitative research (Biernacki & Waldorf, 1981). As recommended by methodological guidelines for qualitative research, the sampling process initially diverged as many valuable sources were mentioned and then converged as key names were identified (Marshall & Rossman, 1995). Individuals identified by this process were contacted with an interview request via email (see Appendix A.1, Initial Contact Letter for Subject Recruitment on page 250).

**Data Collection**

Semi-structured interviews were conducted in person, in an office setting of the informants’ choice in Mexico City or the surrounding area. Interviews were conducted in two rounds, December 2008 and November 2009. Previous research shows that key informants respond best to inquiries about broad areas of content and to intelligent, provocative, open-ended questions that allow them to use their knowledge base (Marshall & Rossman, 1995). The interview consisted of 44 open-ended questions and allowed for follow-up questions, clarifications, or probes. The interview questions were provided to informants in advance, if requested. Interviews were conducted with the goal of reaching theme saturation (Glassman, Reich, Laserson & Rojas, 1999). Respondents were recruited until the responses became redundant and additional information was not elicited (Patton, 1987). By these criteria 19 open-ended, in-depth interviews were
conducted with key informant stakeholders from three different groups:

- Mexican government – health and economic ministries
- Pharmaceutical industry – primarily research-based companies
- Research institutions

Government agencies are stakeholders as they regulate, procure, and provide medicines to the population through various institutional mechanisms. The pharmaceutical industry is a stakeholder as it conducts R&D, manufactures, and distributes pharmaceuticals. Research institutions are stakeholders because of their advisory role to government and industry, in terms of pharmaceutical R&D and access to medicines. Research institutions also play a role in basic science research, which is fundamental to discovery. They have the special role of training physicians, pharmacists, and other public health practitioners for the national health infrastructure. Of the 19 key informants interviewed, nine were government officials, five were representatives from the pharmaceutical industry, and five were representatives from research institutions.

The interview script consisted of two parts (see Appendix A.3 Interview Script on page 256). Part A of the script was based on the WHO Conceptual Framework for Collective Action to Address Access to Essential Medicines (Everard, 2004). The information collected via Part A helped the researcher acquire a greater understanding of the Mexican health care system and access to health services. The results of the Chapter 3 scoping study were used in the development of Part B of interview script (Appendix A.3 on page 256). They were specifically developed to collect information and answer the Chapter 4
research question, “Are available safeguards in Mexico adequate for promoting access to medicines, within a patent system that is set up to incentivize pharmaceutical R&D?” Interview questions were based on the thematic constructs of the Chapter 3 scoping study. The questions in the interview script were written in non-leading, neutral language to minimize the potential for bias and in order to collect data on two major public health topics of interest: (1) access to medicines, and (2) pharmaceutical R&D.

In December 2008, an initial ten interviews were conducted and further eleven interviews were conducted in November 2009. Two of the interviews were follow-up interviews, due to the amount of information garnered in the short time frame of the original informant interview. In the first round, questions in both Part A and B were posed to the stakeholders. Data from Part A was collected but not further analyzed because the information garnered was outside the scope of the research topic’s focus on the impact of international trade agreements on health. In the second round, only Part B of the interview script was used in order to focus on the research question. Every interview, in both rounds, was digital audio recorded. Interviews were sixty to ninety minutes in duration. Allwest Reporting Ltd of Vancouver, British Columbia, transcribed the interviews.

**Ethics Approval**

Ethics approval for the qualitative study was received from the University of British Columbia Research Ethics Board on 8 September 2008 (File No. H07-01972 - LATA Study). The Behavioral Research Ethics Board (BREB) at the University of British Columbia approved the study under the minimal risk category (Reid & Krahn, 2007).
Minimal risk is defined in the Tri-Council Policy Statement as involving potential subjects who can reasonably be expected to regard the probability and magnitude of possible harms implied by participation in the research as being no greater than those encountered in his or her everyday life (Christie, Wood, Schechter & O'Shaughnessy, 2004). Study participants were at senior administrative levels and understood that certain information may be sensitive to their respective organizations, and had the choice not to disclose any such information. No unforeseen ethical issues arose while conducting the interviews. All key informants signed an informed consent form indicating that they understood the purpose of the research study, the nature of their participation in the study and were aware of any potential risks or benefits of participation (see Appendix A.2, Informed Consent on page 253). Participants were guaranteed anonymity and assured that any report of the project results would be generic and not reveal any identifying information without their explicit permission. Participants were informed that qualitative data garnered might eventually be used in published papers, participation was voluntary, and information collected would be confidential. Some participants were indifferent about having their comments attributed to them in literature; most chose to remain anonymous. Signed consent forms and hard copies of data have been stored throughout the study period in locked filing cabinets. Data stored on the computer was password protected. Data de-identification was undertaken for write-up; however, a small risk remains that subjects may be unintentionally identified through recognition of their more distinct viewpoints. For ethical rigor, key informants were asked to review drafts from the interview transcripts for accuracy and, if necessary, to revise or include additional data. Earlier drafts of this chapter were also sent to selected participants as a member
checking exercise. I solicited several participants’ views of the credibility of the findings. According to Stake, participants should be asked to examine rough drafts of the researcher’s work and to provide critical observations or interpretations to assess credibility/internal validity (Stake, 1995). None of the key informants chose to make any changes.

4.2.4 Data Analysis

The core elements of qualitative data analysis are: (1) preparing the data; (2) reducing the data into meaningful segments called codes; (3) combining the codes into broader categories or main themes; and (4) presenting and comparing the data across themes in data graphs, tables, or charts (Creswell, 2007). The raw data was approximately 23 hours in digital audio format stored as MPEG files and 800 pages of transcribed material in Microsoft Word. NVivo8, a qualitative data analysis software program, was used to facilitate interview data analysis.

Each transcript was read five times and a priori or “prefigured” coding was conducted on the transcripts using the four a priori themes that were developed from the scoping study. I understood that through a thorough analysis of these themes the research question could be effectively answered. The a priori themes were:

1. Decreased access to medicines
2. Increased access to medicines
3. Decreased pharmaceutical R&D
4. Increased pharmaceutical R&D

Using *a priori* codes often from a theoretical model or the literature is popular in the health sciences, but they did serve to limit the analysis rather than opening up the codes to reflect stakeholder perceptions in a traditional qualitative way (Crabtree & Miller, 1992a; Crabtree & Miller, 1992b). As such, emergent codes were then identified within each interview and aggregated into categories. These categories were then placed under the *a priori* themes by analyzing where transcript data overlapped. The quantity or caliber of data content being assigned to each theme was entirely emergent based on the data.

The emergent coding followed a process in which transcripts were coded by labeling each sentence, paragraph, or section with a code name representing an idea with which that section of the data was associated. Repeated coding on previously coded transcripts was performed to ensure consistency and to review interpretations until no new insights were illuminated. Once completed the codes that had common elements were merged to form categories. This is a constant comparative technique (Glaser, 1965; Hewitt-Taylor, 2001). The transcripts were revisited multiple times after the initial coding until it was clear no new codes were emerging that could be substantially categorized and placed into the *a priori* themes. When no new codes emerged from revisiting the transcripts, saturation in analysis was achieved. During coding, memos were made in NVivo about how certain decisions were reached and how the coding process was conducted for subsequent reference. Definitions for codes were recorded for reference and each transcript was read and coded with this standard coding process in mind. The meticulousness with which this process was undertaken was part of establishing an audit
trail for reliability.

Categories that had sufficient data were further analyzed for convergent stakeholder perspectives or distinct areas where the stakeholders found agreement. Categories that did not converge were ultimately put aside from further analysis. Understanding the convergence in perspective across stakeholder groups is crucial to theory development on the public health impact of patent system harmonization in Mexico. This type of analysis is a form of triangulation where different sources of data provide corroborating evidence to shed light on a theme (convergence across stakeholder groups). Triangulation of the different sources of data contributes to the trustworthiness, authenticity, or external validity of the results (Creswell, 2007). Credibility and internal validity were enhanced through inter-coder agreement. A secondary data analyst was used to code raw transcript data, to seek agreement on code names, and to verify if passages were being coded the same way. Prior to secondary data analyst review, raw data was stripped of contact name identifiers to ensure confidentiality of the key informants. The results of this analytical process are presented in the next section.

4.3 Results

This section presents the results regarding the stakeholder perspectives (government, pharmaceutical industry, and research institutes) on the impact of Mexico’s compliance with NAFTA patent system harmonization on public health. The converging categories that emerged from the interviews and were inserted into each of the broad a priori themes are presented. These results are summarized in Table 9, below, and then discussed in detail.
Table 9: Summary of Themes

<table>
<thead>
<tr>
<th>Decreased Access to Medicines</th>
<th>Increased Access to Medicines</th>
<th>Increased Pharmaceutical R&amp;D</th>
<th>Decreased Pharmaceutical R&amp;D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linkage requirements</td>
<td>Availability</td>
<td>Classical economic rationale for patents</td>
<td>Intellectual resources Misdirected</td>
</tr>
<tr>
<td>Litigation potential</td>
<td>Bolar provisions</td>
<td>Institutional support</td>
<td>Lack of IP culture</td>
</tr>
<tr>
<td>Prices affordability</td>
<td>Compulsory licensing</td>
<td>Greater clarity in the law</td>
<td>Lack of resources</td>
</tr>
<tr>
<td></td>
<td>Inter-ministerial cooperation</td>
<td></td>
<td>Reliance on North American R&amp;D</td>
</tr>
</tbody>
</table>

*Note: A priori themes are across the top row in grey and emergent categories are in each column.*

### 4.3.1 Decreased Access to Medicines

The problems with access that Mexico has seen in recent years relate to newer on-patent pharmaceuticals, not those of traditional concern to a developing country. The prominent convergent perspectives that arose under the *a priori* theme “decreased access to medicines” included the categories: linkage requirements, litigation potential, and price affordability. All of these issues directly relate to the enforcement of on-patent novel pharmaceuticals, and I discuss each in turn below.

**Linkage Requirements**

Stakeholders provided some background information relevant to their perspective on linkage requirements. In Mexico generic-based companies submit an application to the health authority, COFEPRIS (in the Ministry of Health), to obtain marketing approval for a new pharmaceutical. COFEPRIS then runs a formal check with the patent office, IMPI (in the Ministry of Economics), to determine whether the pharmaceutical or a substance (active ingredient) used in the pharmaceutical has a patent. Only after IMPI
verifies the pharmaceutical product is not patent protected can COFEPRIS issue a notice of compliance and generic-based producers market their product. This form of linkage is not required under NAFTA or TRIPS, but stems from early working provisions and the adequate and effective enforcement of IP rights. Mexico has chosen to adopt linkage requirements into its system as a TRIPS plus measure. All stakeholder groups felt ambiguities in linkage regulations contribute to access problems.

Although most government stakeholders supported a role for IMPI in awarding patents, they noted that linkage requirements generate considerable polarized debate over whose responsibility it is to check for patent protection. They often expressed the viewpoint that checking for patent protection was an undue burden on the government health office COFEPRIS. One informant noted:

> It is a cost that I don’t know if we should have, because then we are not only committed with guaranteeing the safety, efficacy and quality of drugs. I am not sure if our mandate is to check if the things that we are approving have patent protection, or are not patent protected.

In addition, government stakeholders noted that there had been much discussion over what should be checked for patent protection. Mexican legislation clearly establishes that linkage requirements apply to patent protection on active principal ingredients, but their application to other constituent ingredients is not specified. Research-based pharmaceutical companies pressure COFEPRIS, however, to have ingredients in addition to active ingredients searched for patent protection. One such stakeholder noted that there is disagreement among the parties involved on whether patent searches for other constituent ingredients is warranted, as it places additional responsibility on an already overburdened regulatory body. IMPI keeps a registry of patents to refer to when
approached by COFEPRIS, meaning that COFEPRIS could review for additional constituent ingredient patents if inclined. COFEPRIS government stakeholders, however, do not view this as part of their current mandate and object to how research-based industry has attempted to force the issue, as one stakeholder noted:

The research-based industry has found a legal way to include not just active ingredient patents but other kinds of patents in this journal. So a lot of laboratories have come here to tell us that we are not doing what the law tells us to do because we are not reviewing these kinds of patents, which are already included in the journal.

Pharmaceutical sector stakeholders emphasized that Mexican legislation needs to be revised to ensure all ingredient patents are searched for in the IMPI registry. These informants were concerned that infringing generic submissions for market approval were not sufficiently assessed under the linkage requirements by COFEPRIS, because COFEPRIS was only required to check for patents on active, and not constituent, ingredients. Pharmaceutical sector stakeholders thought that the law should be modified to include all ingredients. They admitted, however, that this would impede the production and marketing of generic substitutes. The sentiment of research institute informants was that the linkage requirements on only active ingredients rule is likely decreasing access to generic substitutes due to administrative confusion and procedural delays.

**Litigation Potential**

All stakeholder groups were of the view that access is impeded where legal uncertainty exists and pharmaceutical production may be stalled due to the threat of litigation. Government stakeholders were especially concerned that in Mexico, companies may sue the health agency directly over patent infringement. In Mexico, as a potential subject to time consuming and expensive litigation COFEPRIS role in verifying patents is extended
upon and taken very seriously. As one stakeholder mentioned:

If a laboratory [of a generic company] gets a license and if you think the laboratory [of the generic company] is violating a patent you have, then why, as in the U.S., you don’t sue the laboratory [of the generic company] instead of suing us for having granted the license?

This means that the review process to verify if patents are in existence takes longer. This leads to delayed access. The possibility even exists that at times COFEPRIS may choose to err on the safe side and not allow a generic substitute to enter the market if the patent status of a given product under consideration is unclear. Pharmaceutical sector stakeholders were more concerned that companies in Mexico had avoided clinical research in certain areas, fearing potential litigation because of the restricted review undertaken by COFEPRIS for patents. These stakeholders repeatedly placed the responsibility for litigation on the government for only assessing active ingredients for patent protection. Research institute stakeholder perspectives converged with the government and industry stakeholder perspectives that litigation or the threat of litigation was a potential impediment to access to both new products and generic substitutes.

**Prices/Affordability**

All stakeholder groups viewed the high price of patented medicines as the primary barrier to medicine access. Government stakeholders were of the view that reasonable prices have been achieved through central price negotiation for on-patent medicines, generic procurement first policies and the competitive bidding process for interchangeable generics. They recognized, however, that granting exclusive patent rights kept the prices of medicines elevated, as long as those pharmaceuticals were patent protected. They repeatedly noted the distinct impact of the Mexican epidemiologic transition on the
government’s ability to contain costs. As a Ministry of Health (*Secretaria de Salud*) informant stated:

Access is still a concern to the very poor South American countries, yes, but in the more developed countries in Latin America, most of the essential medicines you have [are] on the list of [the] WHO, they’re pretty much available. What is complicated now is the more expensive drugs for chronic diseases not communicable diseases. Those are the issues for Mexico.

A Ministry of Economy (*Secretaria De Economia*), key informant noted:

If we look at the Health Ministry’s reports, you will see how the proportion of expenditure in medication really went up in the last fifteen years because of the change in the epidemiological profile.

Government stakeholders also noted that, even though generic substitutes bring the price of Pharmaceuticals down, this mainly benefits people covered under the public health system. Many factors will affect the demand for pharmaceuticals. The prevalence of various health conditions, the breadth of insurance coverage for pharmaceuticals and pharmaceutical prices are the most obvious examples. As one government stakeholder stated:

I think the problem, more than a price problem, [gets] down to a problem of a lack of universal access to health care. So if patients are not having access to drugs, obviously it is because they are expensive if they have to purchase them directly.

All three stakeholder groups recognized that lack of available pharmaceuticals is one of the areas of greatest dissatisfaction amongst patients in public state health services clinics and hospitals. Lack of pharmaceutical availability is the key reason for high out-of-pocket spending by low-income groups. Government stakeholders perceived problems of supply to have arisen from inefficient and overly centralized arrangements for the purchase and distribution of pharmaceuticals handled by the federal Ministry of Health.
Recent decentralization may have improved the situation in some states, but, this reduces negotiating and purchasing power of government health agencies. Many hospitals and primary clinics still do not always have the needed pharmaceuticals in stock to treat their patients (Organization for Economic Co-operation and Development, 2005). Stakeholders in general also recognized there was a limit to how much the cost of generics could be reduced in light of government policies requiring improved quality standards for them.

Pharmaceutical sector stakeholders understood that elevated prices of on-patent pharmaceuticals could reduce access to medicines. They expressed concern, however, that cost containment had been pushed too far by the government and that some companies were not profitable enough to remain in business. One such stakeholder felt that private sector profit motive should be kept in mind by the government. This stakeholder expanded upon their perspective by arguing that the government should not simply press for lower and lower cost medicines, thinking only about access, because this leads to reduced R&D and thus has the potential to impede the development and availability of future novel pharmaceuticals. In addition, the pharmaceutical sector stakeholders noted that sometimes the government’s aggressive cost-containment policies resulted in choosing generic substitutes for patients in the public health system instead of the best available new medicine. This stakeholder thought that the government should balance benefits to the public with benefits to pharmaceutical companies better:

If we don’t work in a set of policies that help us together with a win/win approach, in which one you win, in which one I win . . . I have to lose something, we will sacrifice sustainability in the pharmaceutical business.

Another pharmaceutical sector stakeholder felt aggressive government cost-containment
policies through the procurement of generic substitutions had not yet come to companies going out of business, but it had the potential to do so. This stakeholder further questioned the point of having wonderful new lifesaving medicines if companies cannot afford to produce them and conduct further R&D. Research institute stakeholders asserted that prices for medicines may have come down in Mexico but they were still high relative to per capita income and higher than in some other Latin American countries. One stakeholder mentioned that government had asked for help from the research institutes in negotiating prices with companies who had exclusive patent rights:

They told us that they were negotiating with companies which have a monopoly, which have patents, so they ask us for help in the institute and say, look we want your help because you are analyzing [the] prices, you can help us to do a better negotiation, which is very difficult anyway because we are dealing with a monopolist. So how can I achieve a lower price of something if there is only one provider?

Price affordability is an ongoing problematic issue and it is one that does not look likely to be resolved any time in the near future.

**Summary**

Overall, the three stakeholder groups agreed that, decreased access to medicines is in part due to delays in producing generic substitutes. This delay is because of disputes between the government and pharmaceutical industry over what should be included in patent linkage requirements. Fear of litigation over patented infringement also contributed to decreased access to medicines. The cost of on-patent medicines remains high and creates a barrier to access. Epidemiological patterns indicate an ongoing transition in Mexico whereby chronic conditions are replacing infectious diseases as the most frequent causes of mortality and incapacity. One consequence of this changing epidemiology is the need
for higher cost pharmaceuticals. Health agency officials believe that had purchasing patterns not changed due to the epidemiological transition, much less would be spent on medicines because the bulk of purchases would be for relatively lower cost products. In other words, the traditional health problems of infectious diseases are treated with single-dose, generic medicine but increased prevalence of chronic diseases leads to ongoing medication with newer treatments that are often on-patent and therefore have a higher cost. Generics prices can only be reduced so far through competition, but government requirements to improve quality have led to increased production costs.

### 4.3.2 Increased Access to Medicines

One of the objectives of Mexico’s national development program, published every six years, is to advance the accessibility of medicines for Mexicans. The prominent convergent perspectives that emerged and categorized under the *a priori* theme “increased access to medicines” include: availability, Bolar provisions, compulsory licensing, and inter-ministerial cooperation. Each category is discussed further below.

**Availability**

One factor that the stakeholder groups consistently identified as increasing accessibility was the greater availability of novel medicines in Mexico due to strengthened patent protection. This protection provides research-based pharmaceutical companies the comfort to launch novel products on the market without fear that IP will be immediately expropriated and products reverse engineered and sold as generic substitutes in the market. Government stakeholders felt there was no problem with availability of new
pharmaceuticals in the market. They also reported that, with regard to on-patent pharmaceutical availability, there does not seem to be a delay in the launching of new products in Mexico brought on by greater confidence in patent protection for novel product providers. Pharmaceutical sector stakeholders also held the view that there was not an availability problem in Mexico for novel pharmaceuticals. They indicated that Mexico is sometimes one of the first countries to have new pharmaceuticals, not only in Latin America, but in the world. These stakeholders pointed out that Mexico is sometimes the first to commercialize new medicines because of company confidence that they can operate in Mexico and that their rights will be respected through patent protection harmonized to NAFTA standards. One stakeholder indicated that increased foreign direct investment by multinational companies has drastically shortened the wait time for state of the art medicines since the introduction of NAFTA in Mexico:

Before NAFTA we [had] to wait about 5 or 6 years to have the new molecules on the market and after NAFTA we had state of the art medicines in Mexico including some cases the first launch of the medicine in the worldwide market in Mexico.

Another pharmaceutical sector representative stated:

I must say that I’m convinced that the strong IP system is good for the nation . . . it has fostered investment in the country and we have the best medicine in the shortest time and if you compare the current experience with probably 10 years ago, it’s completely different.

Research institute stakeholders also concluded that availability has improved due to increased patent protection. They mentioned that primary care, particularly in cities, has extensive programs that work very well to provide novel medicines. For example, in Mexico City the local Minister of Health implemented a program to provide all the necessary medicines for individuals with HIV/AIDS. The stakeholders’ view was that
considerable attention has been paid to HIV/AIDS in Mexico. Moreover, the stakeholders expressed the sentiment that Mexico has had more success in addressing the HIV/AIDS epidemic than Brazil or other Latin American countries. One research stakeholder believed that the situation was even better than in the United States. Overall, stakeholders agreed that the harmonization to NAFTA standards has led to greater confidence in Mexican protection of patent rights, and thus, greater availability of novel pharmaceutical treatment options.

**Bolar Provisions**

Stakeholders provided some background information relevant to their perspectives on Bolar provisions. Bolar provisions or early working exemptions allow generic-based companies to begin a process for approval to produce generic substitutes up to three years prior to patent expiration. Government stakeholders supported Bolar provisions for improving access, but suggested that the point in time when companies begin preparing for submission of a generic substitute dossier should be greater than three years prior. For example, one stakeholder referred to how in the U.S. a generics application can be started as early as desired prior to patent expiration. The policy in the U.S. is informed by the understanding that a generic medicine can only be approved for market once the patent has expired. This informant felt that for chemical entities three years is fair but for other kinds of products, such as biologics, more time is probably needed to allow the product to be on the market the day after patent expiration. Pharmaceutical sector stakeholders viewed Bolar provisions as good for generic-based companies since they allow for generic company registration prior to patent expiration and launch of their generic the
day the patent expires. Research institute stakeholders felt that Bolar provisions facilitated early entry of generic substitutes, but that there have been some difficulties in their efficient implementation, due to a cumbersome application process. In summary, the opinion on Bolar provisions was that they were helpful in promoting access, but that there should be no restriction on how early prior to patent expiration a generic company can begin preparing for product launch so long as COFEPRIS does not consent to market approval.

**Compulsory Licensing**

Stakeholders provided some background information relevant to their perspective on compulsory licensing. Compulsory licensing is the primary legal tool available to promote access and protect public health. Mexican patent legislation provides for compulsory licensing to facilitate access to on-patent medicines. Perspectives from the three stakeholder groups converged on the point that compulsory licensing could improve access but it was never used. Different stakeholders provided different reasons as to why compulsory licensing was underutilized. Government stakeholders emphasized that, although compulsory licensing is permitted, it has been never used, even in the recent H1N1 epidemic. The most ‘use’ compulsory licensing has received has been threatened use. Government stakeholders identified a number of explanations for compulsory licensing not being used as an effective tool to promote access. The most notable reason being a lack of guiding principles to define ‘national emergency,’ for which the use of compulsory licensing is primarily intended for in the case of pharmaceutical patents in both international and national law. Government stakeholders felt that the legislation on
compulsory licensing should clarify the definition of national emergency and establish a more transparent process to ensure the ability of generic companies to provide extra medicine when necessary, while still respecting patent holder rights. A second important reason was the fact that reduced prices could usually be negotiated quickly through a voluntary license with a patent holder. It was noted that companies would agree to produce as much medicine as needed if the conditions are warranted and they as well believe it is a national emergency. More generally, government stakeholders accepted compulsory licensing’s ability to promote access but noted that alone, it is insufficient.

As one government stakeholder commented:

I think [with] mechanisms to safeguard public health [you] have to look not only at IP and tools like compulsory licensing. That’s one tool. But you cannot see it in isolation from the rest of—all other things that the public sector, our public health sector needs to do in the light of fragmentation, decentralization. I mean, fragmentation between institutions, and then decentralization you have multiple dimensions of basically a mess. So before even thinking about compulsory licensing, you need first to put some order in the house.

Pharmaceutical sector stakeholders recognized the intent of compulsory licensing to promote access to on-patent medicines under certain circumstances, but perceived the Mexican compulsory license mechanism to be very ambiguous and should be clarified. They also felt it would seldom happen that a company holding a patent for a certain pharmaceutical would not be able to produce enough product and be able to negotiate a reasonable price in warranted cases. Essentially this negates the need for compulsory licensing. One pharmaceutical sector stakeholder noted that the provisions for compulsory licensing in Mexico are not consistent with the TRIPS Doha Declaration provisions because they do not meet the minimum requirements on notifying the patent holder and how the patent holder is going to be compensated. Research institute
stakeholders agreed that the government basically does not use compulsory licensing even though it is allowed. One alluded to the recent health crisis of H1N1 when the people needed Tamiflu. The government did not use the safeguard because sufficient stock was provided by the multinationals through negotiation prior to issuance of a compulsory license.

**Inter-ministerial Cooperation**

Stakeholders provided relevant background to their perspectives on inter-ministerial cooperation. The Mexican government now has common ground for talking about IP topics. Regular inter-ministerial policy meetings for improvement of the pharmaceutical sector are currently being held. The Ministry of Health, COFEPRIS (which is part of the Ministry of Health), the Ministry of Economy, IMPI (which is part of the Ministry of Economy), the Treasury Department (which is part of the Ministry of Economy), and COFECO (*Comisión Federal de Competencia*—the Federal Competition Commission) all participate. Different interests are taken into consideration as these entities move forward. All three stakeholder groups perceived that inter-ministerial cooperation benefited access, especially through negotiating the price of medicines.

Government stakeholders supported inter-ministerial cooperation, for example, between the Ministries of Health and Economics by presenting a united front to pharmaceutical industry stakeholders regardless of the issue. One such stakeholder commented:

> I think that [inter-ministerial cooperation] was a good decision because for government what the research-based industry used to do was try to advance their topics individually with whoever gave them audience so they
went to the Ministry of Economy, they went to the Ministry of Health, they went to IMPI, they went to a lot of important actors inside government. So it has been interesting because we are now seated in the same table and trying to get a conclusion as a whole government. So we have closed the holes, the potential penetration. Industry is quite aware that they have to come to us in this group to be listened to and that no one is going to take any decision on their own.

Another government stakeholder referred to how committees consisting of the Ministry of Health, Ministry of Economy, and IMPI now negotiate pricing of medicines for public institutions, with each bringing their special knowledge to the negotiating process. He referred to the fact that Mexico has established a commission for the negotiation of prices in patented medication for public health institutions when generics are not available. For generic substitutes, price competitive bidding and tendering is required for government procurement by NAFTA Chapter 10. Mexican law stipulates that international bids must be used if an international treaty to which Mexico is a signatory obliges it to do so. As such generics-based companies have to bid to supply public health institutions with medicines and the bidding process has been used with Mexico’s NAFTA partners, Canada and the U.S., to increase competition.

Pharmaceutical sector stakeholders were less enthusiastic about both price negotiations and competitive bidding because of the implication for profits. They acknowledged it, however, as a process requisite. They recognized the advantage in terms of cost containment that inter-ministerial cooperation gave to the government in on-patent pharmaceutical negotiations and being better able to steer the international bidding process for generic procurement.
Research institute stakeholders pointed out that price competition only applies to generics and mostly helps people accessing the public health system. There is a big markup on pharmaceuticals that have a patent and are more typically sold and bought in the private, rather than the public, system. This means that patients using the private system do not benefit from price competition. One commented:

> Only half the population has access to the social security system and can benefit from generics policies. [People in the private system may have problems accessing generic products because] even if in the paper there is a revelation that all doctors should prescribe in a generic form, it has never been enforced, so everybody would prescribe it in the private sector. It is just by commercial name, and because the generic substitution is not allowed in drug stores. So if you got this prescription of the very expensive antibiotic that you go to the drugstore and they can’t tell you to get the generic.

Research institute stakeholders recognized that the prices for on-patent medicines had come down through negotiating processes in the public health system, but as with the generics prices, they were still high in comparison to other Latin American countries. One such stakeholder commented that the government did not seem to have a negotiating strategy of incorporating evidence of prices from other places into its procurement efforts.

Convergence arising among the three stakeholder groups could be summarized as follows. Patent protection has encouraged multinationals to open branches in Mexico, reducing the wait time for new pharmaceuticals to become available. Bolar provisions also improve access by fostering transition to generic substitutes. Compulsory licensing has the ability to increase access but has never been used in Mexico. It is more aimed at
communicable than non-communicable diseases through the national emergency doctrines found in NAFTA/TRIPS. Government emphasis on generic substitutes in the public system has reduced prices and improved access but mostly for those who are covered under the public system.

4.3.3 Increased Pharmaceutical R&D

It should be noted that there are now a number of sources for funding R&D in Mexico. Basic scientific research is funded through public sources. In addition, more money for basic research is becoming available from international agencies such as the Gates Foundation. Multinational pharmaceutical companies increasingly sponsor clinical trials to be conducted in Mexico. The convergent perspectives that arose under “increased pharmaceutical R&D” included: classical economic rationale for patents, institutional support, and greater clarity in the law. Each is discussed below in turn.

Classical Economic Rationale for Patents

The classical economic rationale for patents is that by giving inventors exclusive property rights to an invention, and the potential for reaping economic reward, this incentivizes innovation. Stakeholder perceptions converged on the belief that NAFTA membership has affected the science and technology sector in Mexico in a positive way. Most attributed this to the legal IP framework established in Mexico as part of its membership in NAFTA. One government stakeholder commented:

I think it has provided a strong legal framework that allows for an environment to make more investment. I mean we have the same
discussion at international level whether the industries that conduct research regarding medicines are going to be more attractive for those counties that have a legal framework that protects that research. In the case of Mexico, I think we have strong IP law, and our international commitments are reflected in those laws.

Other government stakeholders mentioned that there had been an increase in the number of patents approved, although one noted that the number was still low in comparison to Asian countries but second highest in Latin America after Argentina. Another noted that the impact on patents was relatively recent and suggested that patent system harmonization had a delayed yet positive effect for pharmaceutical R&D prospects in Mexico.

Pharmaceutical sector stakeholders also felt that strengthening the patent system in Mexico had led to more R&D because that strengthening protects developers. As mentioned by one such stakeholder:

> It allows companies and industry to have a business case to conduct research, to invest in research, to keep promoting new medicines, to keep the wheel going. If you spend millions of dollars in developing medicines and the next day another people can copy that medicine and you cannot even recover that investment, I mean, you lose the incentive to produce those new medicines.

One pharmaceutical sector stakeholder mentioned that innovative basic research was less common than clinical trials for pharmaceuticals being developed by multinationals in Mexico. The perspective was that this is a benefit nonetheless through prolonged learning processes leading to innovation and capacity-building. Another stakeholder mentioned that patent system harmonization had significantly increased the number of clinical trials being conducted in Mexico:

> We have had more investment in the sector, in clinical trials, it was very
good for Mexico. I mean we have quintupled the investment in clinical trials, phase III mainly but phase II as well.

Research institute stakeholders felt that patenting had also benefited the universities. Domestic R&D companies now tried to work with them for the development of innovations since universities were starting to encourage patenting innovations by their faculty members. Research institute stakeholders also emphasized the importance of multinational pharmaceutical companies in funding clinical trials. One such stakeholder referred to a database kept of clinical trials, which listed funders:

So I think in the list, in the top 10 is Merck, Lilly, Sanofil, and Roche, these big national, trans-nationals are in the list of the top leading pharmaceutical companies doing clinical trials in Mexico. And my feeling is that [the government] is not amongst this top 10 funders of clinical trials in Mexico.

Overall, the stakeholder perspectives indicate a recent positive trend towards Mexican involvement in and initiation of clinical trials despite a lack of government involvement. This trend may have R&D spillover effects for the larger innovation system in terms of technology and knowledge transfer and increased learning capacity for parties involved in early stage research. However, the country still faces many obstacles in reaching the levels of pharmaceutical R&D found in the U.S. and Canada.

**Institutional Support**

Background information relevant to institutional support was also analyzed. The research granting council that promotes early stage research in Mexico is the Consejo National de Ciencia y Technoloiga (CONACyT). Universidad Nacional Autonoma de Mexico (UNAM) is the main national public university where most of Mexico’s basic research is
conducted. Perceptions converged from the three stakeholder groups that patent system harmonization was having a positive effect on institutional support for pharmaceutical R&D.

Government stakeholders reported that CONACyT, the authority for research and innovation policy, had recently changed to better support innovation in Mexico. One informant mentioned that other government authorities were also gaining better awareness and understanding of patent law in Mexico and were improving the enforcement of law. This informant felt that a spillover effect of these changes was government improvement of quality measures in Mexico:

I mean today if you go to an industrial plant in Mexico you will have exactly the same technology as in the U.S. or Canada. The same. Nobody in his right mind would open a factory in Mexico with second-rate technology because you’d lose.

Pharmaceutical sector stakeholders saw patent protection through government involvement as fostering innovative pharmaceutical R&D because it encourages multinational companies and private granting agencies to place confidence in the system without risking their capital. This R&D usually addresses pharmaceuticals that have broader application than to the population of Mexico, but the spirit of innovation has spilled over into Mexican industry. One pharmaceutical stakeholder mentioned:

We have a firm that was very successful because they make things that multinationals are not interested in because there are some. Orphaned medicines where the multinationals are not interested in developing because there are only small markets. For example, they developed vaccines against scorpion, spider and snakebites . . .

Research institute stakeholders appreciated that CONACyT has a specific section on promoting innovation and protecting patents. They were concerned that not enough
innovation was occurring because domestic industries were serving multinationals attracted by NAFTA instead of focusing strictly on innovative efforts to meet Mexico’s needs. As one such stakeholder noted:

To absorb the extra knowledge, to absorb the spillovers, the right of foreign investment, the technology transfer and all these things, it only happens if the local firms invest in R&D.

**Greater Clarity in the Law**

Stakeholders perceived greater clarity in the law to be a factor in increasing R&D. Government stakeholders felt that NAFTA had both fostered domestic innovation and attracted more pharmaceutical R&D foreign investment through greater clarity in the patent law. One commented:

I think they have created more certainty and of course the legal framework became clearer, more advanced . . . In that sense, it seems positive. It is a positive impact, and it is an impact in infrastructure in the sense that you have a set of rules that are clear and identifiable to follow up on these issues.

Pharmaceutical sector stakeholders agreed with government stakeholders but felt that legal protection could be further improved to encourage more innovation by multinationals located in Mexico, possibly by clarifying debate over what COFEPRIS reviewed. The sentiment was generally that innovation could be encouraged further if better and clearer legal protection could be obtained. Research institute stakeholders also perceived the value of greater clarity in the law but seemed concerned about the transparency of decision-making negotiations between government and industry.
Overall, stakeholder perspectives converged that patent system harmonization has provided a framework whereby respect for patent rights exists and the classical economic rationale for patents flourishes. Institutional support for R&D has improved prospects for basic research through increased funding opportunities. Further legal clarification of patent system law may encourage even more R&D.

### 4.3.4 Decreased Pharmaceutical R&D

The number of domestic research-based pharmaceutical firms in Mexico has not increased due to patent system harmonization. This dearth is possibly the legacy of the lax patent laws that existed until the early 1990s. A benefit of the previously lax patent system was that it may have helped foster the growth of a domestic generic-based pharmaceutical industry, but with patent system harmonization there is currently a lack of R&D taking place in Mexico. The prominent convergent perspectives categorized as emergent themes that arose under the *a priori* theme “decreased pharmaceutical R&D” included: intellectual resources misdirected, lack of IP culture, lack of resources, and reliance on North American R&D. I will now consider each theme, below, in detail.

**Intellectual Resources Misdirected**

All stakeholder groups viewed the Mexican pharmaceutical industry as too focused on generics with not enough focus on innovative R&D. The perception was that patent system harmonization had not changed this imbalance in Mexico. The government stakeholder perspective on this issue was that great efforts have been made by the
generic-based sector in Mexico to compete. Unfortunately, efforts to compete in the generic industry are unlikely to lead to innovative capacity in R&D. Pharmaceutical sector stakeholders expressed concern that not enough R&D was undertaken by domestic companies to address Mexico’s specific needs, instead focusing on reverse engineering products from foreign companies. The focus on reverse engineering misallocates intellectual resources in Mexico as it occurs at the expense of otherwise innovative R&D activities. As one such stakeholder mentioned:

We have a lot of, like, intellectual people worthy of getting enrolled into a perfect research and development project concerning an illness like diabetes. We have the natural resources, we have, I mean, all these rich natural minerals and all the things that are there, but I don’t think—it’s not properly addressed.

Another pharmaceutical sector stakeholder felt that the lack of innovative R&D was regrettably due to the fact that it is simply easier to copy than innovate. Research institute stakeholders agreed with this assessment, pointing to the lack of coherent national strategy for innovation in Mexico as another contributing factor. One mentioned a debate witnessed at a pharmacology conference:

The national association of pharmacologists, they were talking about pharmaceutical policies and they were addressing many of these issues and there was like two groups saying—one of them said, well, we should forget about innovation in Mexico, we don’t have the tools, we don’t have the knowledge and we should forget about that . . . and there was another big group that said, well no, we are pharmacologists, we are supposed to work towards [the development of] medicines.

Thus, it appears there may be more than one factor contributing to the ongoing paucity of innovative R&D in Mexico.
**Lack of IP Culture**

The three stakeholder groups did not perceive public research institutes and universities as fostering pharmaceutical R&D through effective patent right management. Government stakeholders felt that improvements in pharmaceutical R&D have been slow in materializing and one cause is the lack of IP culture in universities. Universities in Mexico have basic and applied research centres of excellence. Although these centres have the potential for R&D, they do not recognize the importance of patent rights for protection or development of their innovations. The centres also lack knowledge on how to use patent rights. Universities primarily aim to publish research results for academic recognition. Any consideration of patent rights as a tool for economic support of research is, at best, fleeting. The lack of awareness of IP rights in universities is negatively impacting the potential for R&D.

Pharmaceutical sector stakeholders agreed that the lack of IP culture in universities contributed to a lack of R&D. Stakeholders cited examples of university researchers who tried to get patents several years after they had published innovations, when it was not only too late because the innovations were in the public domain, but also because other parties outside Mexico had taken up their work in various forms. One such stakeholder commented that there have been some very sad cases in Mexico in which inventors lost their innovations because they were unaware of how and when to protect their work. This stakeholder recommended that there should be more education about IP from public school to professional schools, noting that IP law has only recently been offered in Mexican law schools. Another pharmaceutical sector informant noted that not only do
universities fail to provide education on IP issues, they also fail to provide economic incentives for innovations to university researchers and inventors.

The law in Mexico says that if you work for a university, everything you do, it is going to go to the university. So a lot of researchers are more interested in being published because it gives them more prestige. Because, I mean, it doesn’t matter how many patents they get, all of them are going to the university. So they don’t really care.

Research institute stakeholders, however, felt that the profit motive was not always that important to university researchers, since they were often interested in researching pharmaceuticals that might be useful to Mexico but not widely marketable in other countries. One stated:

I think the researchers I am working with are very, very interested in doing research, which is particularly useful for their context. So I know people here in the institute and also in other institutions are very concerned [with] and want to do research on these specific needs for Mexico. I don’t see a link that they argue and say we do not—or do this research because of an intellectual profit sharing protection . . . because for me personally, this can result in a huge economic benefit . . . . [The] majority probably thinks, okay, for my promotion it is important to have such and such articles, and these journals . . . [its] not like thinking of a spin-off company or where I can be financially involved.

The majority of research institute stakeholders were more interested in being promoted than economic gain through commercialization activities. Another research institute stakeholder pointed out that in reality publishing might bring researchers more economic gain, even if they could profit from patents, because patenting was prohibitively expensive both for them and for their universities. This informant provided further insight into the economic realities for researchers with the following comment:

The system here gives you extra money—for publications and [you gain] status for publications . . . you don’t have $20,000 U.S. to make a patent in one European country or more.

This informant provided further insight into the economic realities for researchers
considering a Patent Cooperation Treaty (PCT) application.

For the PCT, you pay $7000 dollars, and then after you have the PCT agreed, and then you have to go to Spain, to EU first, to every country, making, you know, a patent [application] for every country. That’s ridiculous . . . researchers do not have that money, so we – let’s leave it. Even though our university covered one – if our patent makes the PCT, and the other patents in Europe and South America, well, we’re stopping, and we won’t go through the process in the United States, not at all. Let them take it. What’s the use? We cannot cover all those bureaucratic [fees] and huge amount of money [involved].

To summarize, stakeholders agreed that a lack of IP culture contributed to decreased pharmaceutical R&D. However, they differed on views of whether it was realistic to expect university-based researchers to be motivated to seek patents for their innovations within the harmonized patent system.

**Lack of Resources**

All stakeholder groups viewed the government as dedicating insufficient resources for domestic innovation efforts, particularly for the foundational science that precedes pharmaceutical R&D. Stakeholders agreed that there is not a prioritization or focus from the government to promote innovative pharmaceutical R&D. Government stakeholders themselves recognized that government did not provide enough funding to support domestic innovation in the pharmaceutical sciences. Pharmaceutical stakeholders agreed, with one stating:

> I will tell the government, “Create programs, promote, establish serious projects, long-term programs to get domestic innovation in place, or get it to run, at least.” Perhaps at the end it will fail, but at least try to get it to run, and this is where there is no programs. Or, [they are] very rare, and they’re in theory, and only a few people know about it. But not like a very strong campaign, national-wide, as I would like to recommend for it to be
launched, so that we can get some research done, some research . . . to
development . . . [which] translates into economic activity and growth.

Research institute stakeholders likewise felt the government should provide more funding
for universities to support innovative research. One such stakeholder commented,

There is the lack of resources, the lack of labs. Okay, they give you 5,000
pesos extra every month to have a degree. So for four years, you have the
degree. Well, now, what you do with the degree? There is no reagents, no
instruments, no laboratory . . . most faculty here don’t have little offices
to work. It’s not a—you know, it’s a lack of general policy for research
and development. In Mexico, it goes back to the first point I said. We
don’t have [a] national pharmaceutical policy.

This stakeholder quoted statistics illustrating low government investment.

In 1976, for example, you have 0.3% of the national gross product go into
Whatever. Let’s say the ‘80s . . . have at that point, 0.2, with that . . . the
President said last week that we have 0.4. [That is] a fairly level
percentage going into research and development.

**Reliance on North American R&D**

All stakeholder groups agreed patent system harmonization did not change the lack of
multinational pharmaceutical company support for pharmaceutical research in Mexico.
Multinational research companies continue to conduct research in U.S. and European
labs.

Government stakeholders were of the position that, while multinational companies had
located production plants in Mexico, this presence did not necessarily mean they were
encouraging domestic pharmaceutical R&D. The government stakeholders also
mentioned that trade integration, and therefore competition, with the U.S. seemed to be a
disincentive for Mexican companies to innovate in the pharmaceutical sector.
Increasingly, Mexican companies seemed to have become more reliant on North American R&D.

Pharmaceutical sector stakeholders generally concurred with government stakeholders that multinational corporations do not encourage national R&D. However, one stakeholder felt that national companies should not blame their problems on the companies that NAFTA had attracted. Pharmaceutical sector stakeholders felt that the influx of multinationals after NAFTA was signed encouraged the government to rely on these foreign multinationals to innovate rather than to promote pharmaceutical R&D among Mexican companies. One particular informant placed the blame on domestic companies because of their focus on copying pharmaceuticals. This informant further commented that government facilitated this focus since it helped to keep pharmaceutical costs down in Mexico. This stakeholder characterized national companies as follows:

There’s statistical information that proves that, yes, trans-nationals at the moment that the TRIPS or any other treaty, international treaty, were implemented—free trade agreements—they did come and [they] brought their technology and transfer technology and research-based sites, and all the things that you can imagine. Yes, that’s true. I do believe that . . . when NAFTA was implemented, you just saw a powerful stream of companies, trans-national companies in every sector. And opening of public sectors also, and a lot of economic growth, and yes, that part, it is true. But the part that because of this entering of foreign investment and foreign companies into a country weakening the potential strong based nationals, I think that’s just too philosophical, or just too, like, bad luck statement that these people, that the nationals suffer. I don’t believe that. How would they—how [would] the entering of these companies threaten or weaken national industries?

Research institute stakeholders are concerned that the government has not made it a policy priority to build a strong domestic research-based pharmaceutical industry—at least in part because medicines can be supplied from multinationals. They also believe
that multinationals do not support innovative R&D in Mexico. One cited a study documenting that, while the number of patents had increased in Mexico since NAFTA, they were primarily patents applied for pharmaceuticals developed by multinationals. To quote one stakeholder:

The multinationals are simply here to produce their products. They don’t make research here. And they don’t prepare research. It’s against policy. [There is] no head-to-head [clinical trials] research. I went to the top of [Company A], and to the top of [Company B] for that support, and they said no. “No.” You know, my corporation will fire me. The main corporation will fire me if they know I’m [pursuing] head-to-head investigations.”

Research institute stakeholders also felt that Mexico had become more reliant on North American R&D post-NAFTA. One stakeholder commented:

The government, they have not built an idea to have a strong pharmaceutical industry. You know, Mexico produced before local vaccines. Mexico was getting into that. But since . . . we adopted NAFTA, the government [has said], “No, we don’t need to work in this field anymore because [the] United States is going to provide.”

Another such stakeholder agreed, adding that there had been an impetus to develop a national pharmaceutical policy in the 1980s but, after NAFTA, this policy was seemingly abandoned. The same stakeholder felt that NAFTA partners had supported the Mexican government in abandoning a national pharmaceutical R&D policy, attributing this to a preference by multinational pharmaceutical companies for established R&D programs in their own countries.

In summary, convergent perspectives were that domestic R&D is stagnant and has declined since the introduction of NAFTA due, in part, to government purchasing policies that strongly favour generic substitutes and cost containment. This policy,
combined with a lack of established R&D industry, results in Mexican pharmaceutical companies focusing their innovative efforts on reverse engineering techniques, resulting in a misallocation of intellectual resources. In spite of patent system harmonization, the lack of IP culture in public research institutes and universities; insufficient government funding; and a reliance on North American R&D are all contributing factors that work against any impetus to innovate.

4.4 Discussion: Achieving Balance

The research in this chapter has examined the views of stakeholders on how patent system harmonization has impacted access to medicines and pharmaceutical R&D in Mexico. The results indicate that the answer to the research question “Are available safeguards in Mexico adequate for promoting access to medicines within a patent system that is set up to incentivize pharmaceutical R&D?” is that safeguards are available but inadequate to achieve the goals of promoting access to medicines and improving health outcomes. The stakeholder groups uniformly agreed that compulsory licensing, as the primary tool to protect public health, is inadequate to promote access to medicines within the current patent system, which is set up to incentivize pharmaceutical R&D. Overall, with respect to patents as an incentive for pharmaceutical R&D innovation, stakeholders were of the view that Mexico has not become more innovative since NAFTA implementation and, if the country has, any increase in innovation has been delayed and negligible.

There was much debate in Mexico during the early nineties over how to best implement a NAFTA-compliant patent system into domestic legislation. One unplanned benefit of this
research is that it gave stakeholders the opportunity to consider and discuss a range of significant public health issues. At the time, and even today, the relationship between access to medicines and patents in trade agreements is not well understood by key informants from government who primarily work in public health policy. Key informants from the economic ministry and the pharmaceutical industry better understood the relationship between patents and access to medicines. Generally, stakeholders demonstrated an understanding of trade agreement/IP issues or pharmaceutical access issues (price being only one component of access), but lacked specific understanding of the component parts linking the two.

In Mexico, key organizational stakeholders have recently begun to engage in round table discussions while continuing to negotiate behind closed doors about patent system harmonization policies that impact public health. Meaningful policy that strikes an appropriate balance between (1) promoting access to medicines and (2) patent protection for pharmaceutical R&D is difficult to achieve. Effective policy requires strong political will to create market conditions that facilitate the achievement of both health and economic goals. In response, the government has created inter-ministerial working groups to better inform decisions on patent system harmonization issues, including early working provisions and linkage requirements. These working groups have shown themselves to be more responsive to public health issues and meeting presidential mandates on improved access to medicines. Pharmaceutical companies are no longer able to exploit differences between bureaucratic departments to achieve their goals. Much work, however, is still needed. Mexico’s pharmaceutical policy challenge for ongoing
patent system harmonization focuses on how to respond to the urgent social need of access to affordable medicines, without curtailing the industrial goals of incipient national research-based and larger generic-based pharmaceutical sectors.

The main benefit of the qualitative research reported in this chapter is the provision of primary evidence. This can further inform public dialogue and the development of health and pharmaceutical policy in NAFTA member states and abroad. When perceptions stemming from different stakeholder groups converge in agreement, a triangulation of sources provides reasonable evidence of the impact NAFTA’s patent system harmonization process on access to medicines and pharmaceutical R&D. The results of qualitative analysis are different from those resulting from observational quantitative study. Quantitative analysis aims to examine the relationship between dependent and independent variables, while controlling for intervening (confounding) variables in order to draw conclusions and generalize findings to a larger population. The end product of qualitative analysis is the development of mid-range theory that can be applied to a larger population—in this case, other countries in the developing world. Stakeholders agreed that access to the most expensive medicines, especially those for chronic diseases such as cancer and diabetes, presents a problem. Access is limited by elevated pricing of on-patent pharmaceuticals. Stakeholder perceptions converged on the point that the primary safeguard of compulsory licensing is inadequate to promote access. Compulsory licensing has never been used in Mexico—even in the recent H1N1 emergency. In addition, given the pronounced epidemiologic transition in Mexico access to medicines for non-communicable diseases is a problem that the safeguard of compulsory licensing
does not address. Such licenses, as the international law is written are primarily applied in instances of national emergency or public health urgency, not for prolonged chronic disease conditions faced by an increasing number of people. These provisions are limited by the legal language of the current trade agreements, which provide compulsory licensing for unexpected events such as pandemic outbreaks—rather than the somewhat predicable, but ever increasing burden of non-communicable chronic disease in the developing world.

The mid-range theory I developed is that a blanket twenty-year patent term impedes access and R&D. Therefore, I propose that if we alter the granting of patent terms from a fixed twenty year life period to a flexible and adjustable term based on health and economic conditions that exist during any given time period, we will improve both global equity in access to medicines and reduce economic inefficiencies in our current model for pharmaceutical R&D. This position is based on the convergence of stakeholder perspectives evidence that compulsory licensing, as a downstream post-market approval safeguard and as an economic/legal tool, is inadequate to promote access to medicines and that prolonged periods of patent exclusivity do not enhance pharmaceutical R&D efforts. Greater government decision-making power needs to occur upstream at the patent application stage, with patent terms approved by patent authorities in conjunction with health authorities.

### 4.4.1 Study Limitations

There are limitations to the study presented in this chapter and the results should be
considered with these in mind. First, as in any research using qualitative methods, sampling and data analysis does not lead to quantifiable findings. This study focused on perspectives of stakeholders but did not evaluate the application of NAFTA’s Chapter 17 in a quantitative way. The aim was to capture a multiple stakeholder critique of NAFTA’s implementation, by analyzing perspectives on access to medicines and pharmaceutical R&D in Mexico from those familiar with patent system harmonization issues. Second, the results are based on interviews with a circumscribed number of key informants. Interviews were conducted with the goal of theme saturation. Sample size, however, was limited by project feasibility constraints (e.g., travel, available funds, logistics). Third, data was only gathered in Mexico. Although the study was conducted such that the results could be generalized, they remain most informed and applicable to Mexico.

4.5 Conclusion
The policy-making process necessary to mitigate negative consequences of patent system harmonization in Mexico is complicated. It has been hampered by a shortage of human and financial resources, and negatively affected by administrative barriers and a lack of inter-ministerial cooperation. Mexico has undergone pronounced epidemiologic transition from economic development. Access to the most expensive pharmaceuticals for chronic diseases such as cancer and diabetes has become a prominent issue. Some scholars have argued that most pharmaceuticals on the WHO essential medicines list are off patent (Attaran, 2004). Pharmaceutical needs, however, vary depending on the epidemiologic profiles of developing countries. This is a crucial point when analyzing how to address the global problem of access to medicines. In Mexico, the positive economic
development has improved the social and environmental health conditions and thus reduced the burden of communicable disease. The result is a population with increased life expectancy and an increase in non-communicable diseases, which have different treatment needs. Novel, on-patent pharmaceuticals to treat chronic diseases—such as cancer, diabetes, cardiovascular, and respiratory illness—present issues of access. That being said, the availability of medicines obtained through government procurement and distribution mechanisms has improved. The newest on-patent pharmaceuticals arrive on the market early because of an increased multinational pharmaceutical sector presence confident in the patent enforcement system. Affordability issues remain, but since the implementation of NAFTA, Mexico’s health system has undergone a swift evolution from one that is typical of a developing country to one that values universal coverage for its people, though this goal has yet to be fully achieved.

The current safeguard mechanism of compulsory licensing to promote access has its place in the global patent system. The threat of compulsory licensing has been a useful bargaining tool in national public health emergencies such as SARS and or H1N1 (Bird, 2009). Compulsory licensing will likely continue to be a tool in future national emergencies and pandemics. The compulsory licensing approach seems to promote accessible medicines to vulnerable populations in the short term, but if used regularly it risks undermining incentives to develop new pharmaceuticals in the long term (Danzon & Towse, 2003). Compulsory licensing has rarely been used. Given the complications inherent in compulsory licensing, it seems that an alternative approach of flexible patent terms determined upstream, during the pre-commercialization process, may be a better
long-term tool for reducing prices and enhancing affordability downstream, while maintaining a patent system that incentivizes pharmaceutical R&D. This proposal is elaborated upon in the final chapter of this dissertation.
Chapter 5: Possible Avenues for Patent System Reform

5.1 Introduction

Law and policy stemming from international trade agreements and patent system harmonization have been examined in this dissertation with particular regard to their impact on access to medicines, pharmaceutical R&D, and determinants of health. Ideally, free trade agreements positively impact the economic development of developing countries, thereby generating health system improvements. From this perspective, the best way to reduce the demand for communicable disease medications in developing countries is through continued economic development. As the epidemiologic profile of developing countries shifts toward developed world health burdens, we are increasingly faced with solving what become global problems with respect to access to medicines. The question then becomes how to mitigate the potential negative impact of patent system harmonization as diverse populations’ health burdens converge. The world’s current patent system has supported the researched-based pharmaceutical industry. This is a relatively efficient method for bringing novel pharmaceutical compounds to market. The central research question was, “Does NAFTA patent system harmonization promote access to medicines in Mexico, while incentivizing pharmaceutical R&D?” The research undertaken has provided an answer to that question: the Mexican patent system is an operational and representative system of the larger global system, but it is in need of reform to promote greater access to medicines and better satisfy the aim of encouraging pharmaceutical R&D. Based on this case study, the patent system could be reformed to better meet the health needs of the global population. Almost every country via the WTO is now facing similar patent system requirements, and thus similar access to medicine
issues. Once signed, international agreements such as NAFTA and TRIPS are binding legal contracts at the international level and cannot be altered unless changes are agreed to by all parties involved (Clarkson, 2002). One of the major problems of the global patent system is that bilateral agreements subsequent to NAFTA and TRIPS have followed the same basic model despite our advancement in understanding the implications for public health. This results in the entrenchment of legal norms that were founded on lack of available evidence in the 1990s.

Numerous reform proposals to improve either equitable access to medicines or efficient pharmaceutical R&D have been suggested as solutions to the current global debate on the substantive patent framework under TRIPS. For access, some authors suggest that rather than relying on law reform, it would be easier to bring targeted relief to the few cases where medicines are patented in urgent areas (Attaran, 2003b; Attaran, 2004). Differential pricing, one of the most prominent approaches discussed in the literature, may help make novel pharmaceuticals developed for high income markets affordable in developing countries. The price-differential solution is not considered to be ideal, however. Manufacturers are reluctant to grant low prices in low-income countries because pharmaceuticals are likely to find their way to higher-income countries through parallel trade. Sustainable price differences require that higher income countries forego importing low priced medicines from low-income countries. In addition, differential pricing cannot fully resolve affordability problems for existing medicines if they have high marginal costs due to high production distribution costs, or retail markups. For a vulnerable person there may not be an appreciable difference between $100/day or
$10/day for a medicine when their income is $1/day—both prices are equally unaffordable. Medications for chronic conditions, especially those that are costly to produce such as anti-retrovirals, may be not be affordable for vulnerable populations even at prices close to marginal cost. In such circumstances, differential pricing may reduce, but not eliminate, the problem of access to pharmaceuticals for developing country populations. Other suggested reforms have proposed reducing patent terms. These proposals feature patent ladders where minimum patent protection length varies according to level of per capita income in a geographic region (Hoekman, Maskus, & Saggi, 2005). The lower level of per capita income, the shorter the patent term would be, and the sooner generic competition would be available in those markets. Patent ladders avoid a uniform approach to harmonization of patent systems. De La Calle suggests that patent terms should have different lengths for developing countries based on market size. The implication of such a reform is that the larger the country (in population), the shorter the patent period because less time is required to recoup front-end investment and achieve a reasonable financial return (personal communication).

In this chapter, patent system reform is recommended based on my qualitative research findings that the current global patent system (with Mexico as the representative model) does not adequately promote access to medicines, while incentivizing pharmaceutical R&D. In section 5.2, I introduce possible avenues for patent system reform. I present two approaches that attempt to advance equitable pharmaceutical access and efficient R&D aims simultaneously, instead of pitting these goals against one another as mutually exclusive (Hertz, 1997). I will discuss in a step-wise manner how patent systems could be
reformed to reduce inequity and inefficiency. In this discussion, I will present two possible approaches for reform. In section 5.2.1, the first reform applies different patent term lengths to different inventions based on a non-biased scalar approach. I developed this approach prior to undertaking my qualitative research and it was based on my understanding of the problem and the literature I had reviewed up to that time. Through the course of my research dissertation, I subsequently discarded this approach as being too *sui generis* and fear that, while it may be beneficial in terms of pharmaceutical access and R&D, it would ultimately lead to administrative red tape and a high potential for conflict between competing interested parties. In section 5.2.2, I introduce a second approach to patent system reform, which was developed during and following my qualitative research. This approach is based on flexible and adjustable patent terms akin to interest rates. Section 5.3 then presents some thoughts on how theoretical patent reform could be adopted into the international legal framework. In Section 5.4, two major supporting policy recommendations are made and justifications are given for each. These are elaborated upon in subsection 5.4.1, Support Epidemiologic Transition through Further Economic Development and subsection 5.4.2, Strengthen Developing World Innovation Systems. Both of these recommendations require cooperation from stakeholders at all levels of government and should be backed by reiterative evidence provisions through knowledge translation from ongoing trans-disciplinary monitoring and evaluative research. In addition to the usual intellectual goal of deeper understanding, this dissertation aims to make a practical contribution to policy debates and guides decision-making for reform in this area. Section 5.5 concludes this dissertation with some final thoughts.
The sole exception to the general economics rule that monopolies are bad for competition and lead to price fixing is the area of patents. Pharmaceutical patents have been deemed necessary to incentivize an innovation process that involves large, up-front R&D costs. From the outset I wish to make clear that I do not advocate for their abolishment altogether. However, I will present substantive reforms to the pharmaceutical patent system. The current principal safeguard to facilitate access of compulsory licensing is inadequate. Upstream reform at the patent approval stage is advocated for to provide solutions and improve health outcomes. During NAFTA negotiations, a major source of friction between Canada and the U.S. was the length of pharmaceutical patent term (Cohen, 2003; Hore, 2000). I present in the subsections below two possible options to curtail the negative effects of limited, yet prolonged periods of patent protection. It is an unresolved question as to what is an adequate term to achieve a reasonable return on investment for innovative pharmaceutical firms. The length of a patent term must balance the rights of private sector patent holders with the ability of public health care providers to procure and distribute medicines for its population.

5.2.1 Patent Term Determination Scale
At an early stage of my research, I had concluded that patent term length should be based on how the novel scientific information in patent claims (found in the patent application) is to be applied in the industrial (pharmaceutical) setting to different disease burdens. This was an attractive approach initially. Terms could be determined through a patent office assessment of applications by examining the utility claims found in those patent applications (Fitt & Nodder, 2010; Michaels, 1994). In essence, patent terms would be
based on prioritization of health care interventions. It is common practice in government to evaluate the value of health care programs and interventions when making funding decisions (Field & Lohr, 1992; Mitton & Donaldson, 2004). Funding priorities for both health research and programs are often informed by disease burden measures (Gillum, 2011). In a similar vein, metrics could be incorporated by patent offices into decision-making on how long a given patent term should be based on a scalar formulaic approach. I have termed this approach the “Patent Term Determination Scale”. It includes a three-step approach to determining patent term, which eschews the current twenty year term for patent protection.

**Step 1 – Assessment based on Disease Distribution**

The first reform that could be implemented is patent term stratification according to the proportion of disease or by prevalence. This reform circumvents a blanket twenty-year term of patent protection for every application that comes across the patent office’s desk; instead, it sets patent terms based on consideration of disease distribution. Patent officials could assess disease distribution by examining WHO generated prevalence statistics or similar data. Patent terms would be shortened where there was a demonstrable need, indicated by prevalence of disease, for affordable access to large quantities of novel medicines, as shown in Figure 6.
Adoption of the patent term determination scale would lead to an inverse relationship between patent term available for a particular novel pharmaceutical innovation (discussed in its patent claim upon application) and its utility to a particular disease (based on prevalence). Thus, patent term would be scaled based on general principle that the higher the global prevalence, the shorter the approved patent term, and the lower the global prevalence, the longer the approved patent term.

**Step 2 – Assessment based on Disease Severity (Cause Specific Mortality Rate)**

The second step of the patent term determination scale reform is for variable patent terms to be classified by a patent claim’s applicability to address disease severity (cause-specific mortality rate), as shown in Figure 7. Terms would be determined by review of the patent application utility claims in order to assess the potential benefits of a new pharmaceutical innovation for patients. Decisions would be legitimized through the government’s mandate to act in, and protect, the public’s best interest. Thus, patent law would be reformed to allow for shorter patent terms for innovations that dealt with serious health conditions. The upshot of shorter patent terms would be that generic substitutes become accessible sooner. In a similar vein, longer patent terms would be granted for health products addressing non-life–threatening health conditions.
Figure 7: Assessment of Global Disease Severity

This proposal can also be understood in terms of price elasticity of demand: the percentage change in the quantity demanded of a good divided by the percentage change in its price. Pharmaceuticals for life-threatening illnesses are demand price inelastic. In other words, prices for medicines that treat life-threatening illnesses will be paid for at any price, if possible. Therefore, shorter patent terms to allow generic substitutes sooner are favourable, to reduce prices through market competition. Pharmaceuticals for non-life threatening illnesses are demand price elastic because patients will tend to forgo discretionary medicines if prices increase. These pharmaceutical products can therefore have longer patent terms. Implementation of this reform would stratify the available patent term protection and consequently mean shorter patent terms for diseases with high severity, for example, cancer-based medicines. Thus, this step of the patent term determination scale would rest on the basis that the higher the global cause specific mortality rate for a health condition in a patent’s utility claim, the shorter the approved patent term; similarly, the lower the cause specific mortality rate for a health condition in a patent’s utility claim, the longer the approved patent term.
Step 3 – Average the two measures to determine patent term length

Equipped with the above metrics (disease distribution and severity), the patent office would average these measures to produce a suitably responsive patent term. The basic formula would be:

\[
\text{Patent Term Life} = \frac{\text{Distribution (prevalence)} + \text{Severity (morality rate)}}{2}
\]

Figure 8 illustrates how these measures would be combined to determine patent length.

Figure 8: Determination of Patent Length

Industry would then decide whether further R&D is warranted and a sufficient market opportunity exists for the commercialization process. From the perspective of research-based pharmaceutical companies, this means the potential for return on investment, and thus strategic decision-making, would be based (in terms of time remaining to patent expiry in forecasting analysis) on the average life years of the entirety of its patent product portfolio.

In the present system, patents are reviewed and approved by patent offices on the basis of novelty, inventive step, and utility (industrial application) criteria. It should be possible to implement a reform that requires review by patent/health offices that assesses how the
patent application applies to human health with respect to disease distribution and severity and subsequently determine patent term based on this assessment. The use of such metrics for patent offices in determining a term length for different patent applications would likely be an onerous task. Law reform could, however, acknowledge a relationship between these variables as part of the requirement in securing patent exclusivity. It is important to keep in mind, of course, the assumption that patents (proprietary rights) are needed to incentivize private sector pharmaceutical development and should not and cannot be eliminated entirely given our current scientific knowledge frontier.

One prominent real world example exists for patent system reform based on determination of health priorities. It exemplifies how government patent and health agencies can work in conjunction to improve public health. The reform occurred in Brazil during the late 1990s and was catalyzed by the backlash to HIV/AIDS by civil activists. The reform required all patent applications for pharmaceutical products, once approved by the patent examiners in the Brazilian Patent Office (Instituto Nacional da Propriedade Industrial, INPI), be passed along to the health ministry (Agencia Nacional de Vigilancia Sanitaria, ANVISA) for review. A patent was issued only after ANVISA offered consent. This reform was introduced to make it more difficult to obtain economic exclusivity rights over certain pharmaceuticals (Shadlen, 2007a). Brazil’s government health agencies were given a crucial role in determining the outcome of any given patent application. This example buttresses my suggestion that we could base patent term on
health/disease condition. Brazil went one step further than my proposed reform and simply disallows patents on certain pharmaceutical products.

A patent application review by health agencies would be facilitative for the successful execution of my scalar approach to determining patent term length. In Brazil, the requirement that ANVISA grant prior consent to pharmaceutical patents formally subordinates the patent agency to the health agency. This system has proven successful in Brazil and remains in place. In Canada and Mexico, the requirement that health authorities consult with patent offices to determine if patents exist based on linkage requirements prior to granting market approval for generics makes the health agency subordinate to the patent agency. With a better understanding of the importance of patents on public health outcomes, health ministries can play a partnership role in the approval of patent applications. This partnership between patent and health offices would also likely have the collateral effect of making patent drafters more selective and specific about patent claims, instead of attempting to be as broad as possible.

This first approach to patent system reform would increase access, getting the most important medicines to patients faster at a lower cost, while leaving economic incentives in place by lengthening the patent term on other pharmaceuticals of less importance from a medical and public health perspective. Private sector R&D activity needs to be encouraged, while at the same time quicker access at a better price is promoted by ensuring the most important medicines for severe diseases are off-patent earlier if
beneficial for larger populations and society as a whole. This approach allows longer protection for patent applications that involve science and technology and address disease and health conditions with low distribution/low severity. It concurrently allows for a system with the structural flexibility to improve access. The net effect should be improved access and R&D, through shorter patent terms and fast-track development for more important innovations.

It should be possible to develop a non-biased system because decision-making would be based on scientific statistical measures determined by the WHO, or another independent global health authority, outside the influence of domestic government opinion. I am, however, hesitant to conclude any system that involves human decision-making to be totally free of bias. A major positive tenet of this solution is that it incorporates variability. Not only can this solution adapt to different medical advances, it can also change to accommodate population and epidemic changes. As conditions change, the values of each variable will change, while the overall equation for determining patent term remains constant.

However, after my qualitative data analysis and contemplation of the evidence provided in Chapter 4, I realized this approach would result in a complex burden placed on patent and health offices within and across countries. This burden would potentially lead to severe legal, administrative, and political discord between government patent offices, patent applicants, research-based firms, and generic-based firms alike. This makes this
approach impractical. Further impracticalities arise due to the overlapping nature of scientific knowledge, incremental innovation and its application, and the likelihood of major stakeholder arguments based on perceived inequalities. All of these factors would most likely lead to significant waste of resources, delayed pharmaceutical R&D, and decreased access due to upstream disputes over what patent term should be awarded to a particular patent application. The patent term determination scale accounts for complexity in a system that involves many competing factors, and a multiplicity of stakeholder perspectives and needs, however, it would ultimately introduce too much contention and delay—thus leading to my second reform possibility: flexible patent terms.

5.2.2 Flexible Patent Terms

The second reform possibility involves flexible patent terms also by focusing on upstream reform, but simplifies the administrative issues of dealing with multiple stakeholders. Each individual patent application, however, would not be assessed and awarded a different term. In this approach, government patent officials would cooperate with health officials to decide the current patent term to be awarded to all patent applicants. This patent term would be based on an assessment of relevant global health and economic conditions. The concept is similar to the idea of flexible interest rates that are adjusted by a country’s central bank in monetary policy decision-making to stabilize the economy as according to the Keynesian feedback rule. As a flexible patent term, the length of time patents grant exclusivity rights to their holder would be adjustable as relevant global health and economic conditions change. This reform if properly
implemented may address the market distortion created by twenty-year monopoly patent terms that often extend well beyond the successful market approval date of pharmaceuticals. This is explained further below.

As mentioned, there is a competitive market distortion problem in the pharmaceutical industry created by the current standard twenty-year monopoly patent term. Moreover, this distortion will likely only increase as patent term lengthsens under international trade regimes that set out minimum levels of IP protection. The twenty-year patent term extends well beyond the successful market approval date for most novel medicines. It is difficult to estimate the effects of this distortion, and thus solutions to minimize it are less than forthcoming. In order to resolve this problem, there needs to be an answer to the question of how to provide an adequate term of proprietary protection to private actors involved in commercialization. The longer the term, the more valuable the patent to its owner, but what is the appropriate balance between patent holder rights and those of consumers of novel pharmaceutical products? The current static approach to patent terms does not strike an appropriate balance. A flexible patent term would add some much needed dynamism in this area.

In order to develop a system with adequate protections for private actors and consumers, we need a nuanced understanding of what each stakeholder requires. Private actors that would like ever increasing patent terms cannot solely define adequate pharmaceutical protection. Those with economic interests at stake, however, fiercely oppose any
arguments for any reduction in patent protection (i.e., research-based pharmaceutical companies). In 2003, the Mexican government considered a reform to the patent law that would have reduced patent terms to ten years in the case of serious health situations (Shadlen, 2010). This is the only recent attempt to scale back patent terms in North America. The original initiative for patent term reduction to ten years was sponsored by Farmacias Similares, a branded generics enterprise, and was clearly contrary to Mexico’s NAFTA and TRIPS obligations (Hayden, 2007). Unsurprisingly, the reform was not implemented into law as originally envisioned. In March 2003, the Chamber’s Science and Technology Commission (CCyT) passed a modest reform that increased the capacity of the Health Secretariat to issue compulsory licenses in the case of health emergencies (Shadlen, 2009). It is worthwhile to note that upon the introduction of patent reform, the transnational pharmaceutical sector sought to secure reform favourable to their interests, which would make compulsory licensing provisions less deployable (Shadlen, 2009). Such demonstrable resistance to reform measures means that sound rationale backing any patent term reform must be presented in order to bring the pharmaceutical sector onside.

The need for patents is predicated on attracting the enormous financing necessary for conducting large-scale clinical trials, yet it is clear that reform to our existing patent system is needed. At some point scientific knowledge will likely advance to a point where large-scale clinical trials are no longer needed to prove safety and efficacy of new therapeutic candidates and it is foreseeable that someday we will no longer need patents. When this level of scientific knowledge is reached, there will likely no longer be a need to allocate large amounts of capital resources for such efforts, up-front fixed costs will
become negligible, and patents will no longer be necessary. I will now describe in detail the concomitant parts necessary to understand why the flexible patent term approach improves upon the market distortion presented by the current system. This possible avenue for patent system reform has three concomitant parts:

1. Understanding the advancement of the scientific frontier;
2. Determination of average clinical trial length; and
3. Determination of flexible patent term.

Part 1: Understanding the Advancement of the Scientific Frontier

The global patent system is about managing the world’s scientific frontier (Figure 9). As science evolves it introduces new issues to society, and the law must respond accordingly to the benefit of the public. In this way, patents play an important role in humankind’s evolutionary process. In other words, frontier scientific achievement that form the basis of patent claims become subject to proprietary rights that allow for economic development through innovation and further scientific development. Frontier knowledge is drafted in patent claims and through the patent approval process that requires novelty, non-obviousness, and utility. That frontier is verified and documented. In the early years of medical science discovery and invention, humankind knew little and the knowledge applied to invention required only short development times. The exclusivity periods needed to develop innovative products was minimal. Over the years, our scientific knowledge frontier has advanced and innovations became increasingly complex.
Figure 9: Advancement of Scientific Frontier Knowledge Curve

As shown in Figure 9, initially, total knowledge was low. As a result, we did not need long patent terms. As history progresses, our total knowledge is increasing (K), and the rate of new knowledge accelerates. As such, we needed longer patent terms. Eventually, however, there is an inflection point where the rate of new knowledge (K/t) meets a maximum even though total knowledge is still increasing. This is shown as the inflection point in Figure 9, which is also the maximum point in Figure 10; this is where we should find a maximum patent term. Past the inflection maximum point, the rate of new knowledge slows down and patent term can also begin to decrease. As we move further along in time and the rate of new knowledge curve’s horizontal limit approaches zero, patents can be shortened until capital no longer needs to be allocated for development because safety and efficacy can be proven without clinical trials; our total knowledge frontier moves towards infinity. As previously mentioned, the point in time where the
maximum point in the rate of new knowledge curve is reached in Figure 10 is the point in time where patent term should also meet its maximum.

**Figure 10: Rate of New Knowledge Curve**

Support for a decreasing rate of new knowledge can be assessed, albeit indirectly, by examining the rate at which new patents are issued. Patents are granted for exclusive protection on new medicines. Patents represent new knowledge by their granting requirements of novelty, non-obviousness, and utility. However, it is important to note that the actual number of patents per annum obtained for distinctly new pharmaceutical products is declining. Thousands of patents are granted for pharmaceuticals, but the majority of these cover minor modifications of older existing pharmaceuticals. The National Institute for Health Care Management in the U.S. reported that from 1989–2000, 153 (15%) of all new pharmaceutical approvals were medicines providing a significant clinical improvement (Correa, 2007). The number of new molecular entities (NMEs)
approved by the U.S. FDA has drastically declined since the mid-1990s (from 53 in 1996 to 17 in 2002) (Lexchin, 2006; Roffe et al., 2006). Thus, while the pharmaceutical sector is the major user of the patent system only a small—and in fact declining—number of new chemical entities are approved annually. A decline in innovative productivity has been apparent since the mid-1990s (OECD Health Policy Studies, 2008). This data analysis buttresses the view that while total knowledge is still increasing, the rate of new knowledge is diminishing and patent term could begin to decrease. Recognition of this trend suggests that longer patent terms are not necessarily leading to increased innovation of new pharmaceutical candidates. Today’s patent term is twenty years, which is longer than necessary. The decrease in issuance of patents for novel pharmaceutical products, combined with increased efficiency in clinical trials assessing efficacy and safety, are two strong factors that advocate for shorter patent terms. In summary, in spite of an increasing patent term the output of new pharmaceuticals has declined. Most pharmaceutical innovation has proven to be incremental in recent years—factors which support shorter patent protection, not longer.

**Part 2: Determination of Average Clinical Trial Length**

Ever-increasing amounts of new knowledge are created as the scientific frontier expands. However, as science advances, so does the scientific process. We reach a level where clinical trials should become shorter; safety and efficacy, can be demonstrated faster. This is linked to Part 1 in that the rate of new knowledge being created decreases as our knowledge base expands to infinity. Clinical trials should become shorter because the slower we learn new things, the less time it takes us to prove the old things we already
know a lot about. This is buttressed by our knowledge that, as is true in other industries, most pharmaceutical innovation in recent decades has been incremental rather than radical. Most such innovation has little or no added therapeutic value over existing treatments (OECD Health Policy Studies, 2008). Average time to completion of clinical trials for market approval of new candidates over time is illustrated in Figure 11. Figure 11 is analogous in shape to the rate of new knowledge curve shown in Figure 10, as its horizontal limit approaches zero as time goes to infinity. The average clinical trial time to completion curve horizontal limit approaches zero and with that patent term can be shortened. Eventually patent terms should decrease to zero as they are rendered obsolete. Figure 11 is also supported by undeveloped literature on the subject. The average length of a clinical trial increased by 21% from 1999–2001, but companies under pressure to reduce pharmaceutical development costs are intensively searching for efficiencies in their product development process (Vogelson, June 2011). A number of reasons for this phenomenon have been identified. For example, pharmaceutical companies are outsourcing their clinical research to contract research organizations (CROs) due to knowledge specialization capacities. Studies have shown that CROs are able to complete pharmaceutical development faster than the pharmaceutical companies (Getz, 2006). Other ways to increase the speed of new pharmaceutical development is to adopt information technology to manage the enormous amount of clinical trial participant information collected and streamline patient recruitment (Brooks, May 2006; Etheredge, 2007). These trends all suggest that the average time for a new pharmaceutical candidate, from clinical trial to market approval, is decreasing.
Part 3: Determination of Flexible Patent Term

As discussed above, patent terms have increased globally to the current standard of twenty years, aided in part by the proliferation of trade agreements. It seems likely that this trend will continue unless prudent analysis presents feasible options. Average patent terms should be able to slowly decrease with a decreasing rate of new knowledge and improvements to clinical trials that reduce inefficiencies and the time required for development of novel pharmaceutical products. This with the option to adjust a flexible patent term longer again if we notice our innovation processes faltering. Figure 12 is a rudimentary representation of the time trajectory we are facing for current patent term. As time has progressed we are almost exponentially increasing our patent term, based on a justification that this lengthening is necessary to recoup the heavy upfront fixed R&D costs of high risk large scale clinical trials.
Figure 12: Current Patent Term Trajectory

As discussed in Part 2, the average time to complete clinical trials should be decreasing based both on my theoretical analysis and a brief empirical analysis of the data presented in some undeveloped available literature on otherwise hard to obtain information. This means patent terms should run concomitant and only slightly higher than the curve that represents average time to complete clinical trials in order to sufficiently satisfy the economic rationale behind their existence. This is demonstrated in Figure 13 as the green line (desired patent term).
Figure 13: Desired Patent Term Trajectory

Figure 14 combines the previous two figures (Figure 12, Figure 13) to illustrate the economic inefficiency created and pronounced market distortion to access incurred. This market distortion is representative of continued patent term expansion, which is based on the argument that increasingly complicated trials are necessary to develop pharmaceutical treatments for complex chronic diseases. The argument that patent terms must be longer as trials become longer and more expensive—with the recruitment of growing numbers of patients to increase statistical power—is misguided and results in a misallocation of valuable resources. This is because the desired trajectory of patent terms is represented by the green curve and should only be sufficiently longer than the time it takes for a pharmaceutical candidate to achieve market approval. The rate of new knowledge being achieved is diminishing and our ability to run successful trials on incrementally inventive pharmaceutical candidates—which we already have some degree of understanding of—
should be improving (i.e., shorter and less resource intensive).

Figure 14: Comparison of Patent Term Trajectories.

Patent terms will only ever reach zero if science advances to a level of understanding where trials are no longer needed (i.e., technology development time approaches zero). Until science advances to such a level, patents are necessary for pharmaceutical development. Even with the theoretical analysis presented here, it is hard for us to determine exactly where we are on this timeline, or what the ideal patent term should be at any given time period. I would argue that we have already passed the maximum point in the curve and that patent term should be trending downward. This is, in large part, exactly why the patent term must be flexible as opposed to fixed. Our goal should be to keep the length of patent terms aligned with the average length of clinical trials to promote access while still incentivizing private sector pharmaceutical R&D. This can be understood by re-examining Figure 2, from Chapter 1, reproduced below.
The patent system needs the flexibility of adjustable patent terms to attempt to minimize the time period represented by the red arrow, where pharmaceuticals are both on market and on patent. Our goal is to keep this time period as short as possible to promote access, while still incentivizing private sector pharmaceutical R&D. Patent offices in coordination with health ministries will have the ability to adjust a flexible term in attempting to achieve this aim. This discussion only applies to pharmaceutical patents that have human medical/health applications/consequences that require safety and efficacy to be demonstrated through clinical trials. An economic argument for patents that need twenty year exclusivity periods as having any a value for incentivizing innovation not directly related to the conduction of large scale clinical trials to prove safety and efficacy for human health benefit is highly debatable.

Public health office involvement in patent review is not a new concept, but flexible patent terms based on ongoing assessments by the government agencies’ coordinated efforts is an approach not yet adequately explored by academics or practitioners. The government could begin to allow for a flexible, as opposed to fixed, patent term that could be adjusted upon yearly review (or as necessary based on surrounding public health and economic
conditions). At initiation of reform, I would suggest starting with the current twenty-year patent term award as a baseline term for incoming patent applications, but with the understanding that this is now a flexible and adjustable term. We are looking for away to balance, and in fact improve upon, our current trade-off between promoting access to medicines within a patent system that incentivizes R&D for novel pharmaceuticals. The best way to achieve gains in satisfying both goals is to adjust a flexible patent term based on surrounding conditions. Ideally, we should see a trend towards the shortening of number of years awarded, but this cannot be achieved overnight given our current and necessary clinical trials based model. We must be sensitive to the economic rationale behind patent exclusivity. Ongoing evaluation of the implications of the theoretical patent system reform presented here is an exercise beyond the scope of this dissertation. Future large-scale empirical research collaborations in the area in the context of the impacts of patent system harmonization on global public health will provide more evidence and enable decision-makers to be more enlightened when contemplating appropriate patent term.

5.3 Adoption of Reforms by the International Legal Framework

If adopted, my suggested reforms in Section 5.2.2 would need to be written and implemented into national law through a new multilateral, but not multi-sector, pharmaceutical trade agreement. This trade agreement would cover both substantial and procedural global patent system law to an optimal level. Reforms to national pharmaceutical patent systems should be directed from the international level in order to achieve equitable harmonization of global patent law. This is a requisite, no matter how difficult consensus at the multilateral level may be to achieve. Uniformity would be key
to diminishing controversy, because the rules would apply equally to all. Future
generations deserve our careful consideration of current issues in an increasingly
interconnected world.

As discussed in the North American context (Chapter 2), despite overarching goals of
international patent system harmonization significant disharmony exists. At the global
level, the European Patent Office (EPO) has partnered with the USPTO, Korean
Intellectual Property Office (KIPO), Japan Patent Office (JPO), and State Intellectual
Property Office of China (SIPO) with the aim of improving cooperation (Drahos, 2010;
Mabey Jr, 2010). A current international priority of these offices is WIPO Patent
Cooperation Treaty (PCT) reform (DeBeer & Bannerman, 2010). The Patent Cooperation
Treaty is a procedural agreement concluded in 1970, amended in 1979 and further
modified in 1984 (Nanda, 2004). The objective of the PCT was to deal with the problem
of filing applications in several countries within the period of time prescribed by the Paris
Industrial Property Convention (Kuanpoth, 2011a). The treaty provides the basis for
filing a single application, performing an international prior art search and is considered
the most advanced mechanism in international cooperation in the field of patents since
the conclusion of the Paris Convention (Alikhan, 2000; Asami, 2002; Ruiz & Musungu,
2002). Greater procedural harmonization between NAFTA member countries could draw
from the PCT model. It is important to recognize that although the PCT focuses on
harmonizing patent law procedure such as shared databases, in the long run it may lead to
similar results in substantive patent examination and global patent term setting. A group
such as this could lead globalized efforts in the determination of what is the appropriate
patent term to award patent applicants given current global health and economic conditions. A draft Substantive Patent Law Treaty (SPLT), although not specific to the pharmaceutical sector, has been organized by WIPO in an attempt to deal with controversial issues that do not have global consensus and are not covered under the PCT as procedural issues (Takenaka, 2002). As mentioned, the multilateral TRIPS agreement deals with patent law substantive requirements (Duffy, 2002). TRIPS, however, left significant legal issues to be dealt with by national patent authorities (Sabatelli, 1994). The SPLT aims to further harmonize formal requirements for granting and maintaining patents (Kuanpoth, 2011b). Whereas the TRIPS agreement provides for minimum requirements under the WTO, the SPLT, in contrast, would aim to establish best practices at the international level (Correa & Musungu, 2002). Somewhat akin to my suggestion of optimal requirements for patent protection in Chapter 2, a best practice requirement would be a good step forward. This agreement could also include provisions regarding a flexible and adjustable patent term.

The international patent system has evolved to deal with difficulties arising from the territoriality of patents under domestic law with a certain amount of disregard for the protection of public health (Holbrook, 2004). Good global health governance is needed to bring the global patent system back on track. Patent protection is domestic law by nature; a Canadian patent affords inventors protection in Canada only while a Mexican patent only affords inventors protection in Mexico (Keon, 1986). Patent applicants must seek comparable protection from each country in which they are likely to use their patents (Wasserman, 2007). There is little or no protection for those who fail to do so or who
operate in a country that has laws very different in scope or duration. This explains the past, current, and ongoing attitude of multinational pharmaceutical companies towards the protection of IP in international trade agreements (Mossinghoff, 1987b). International law can be a powerful instrument for improving the health of the world's population if used properly (Ruger, 2007). Participants in the development of global public health law require expert knowledge of global disease distributions and epidemiologic transition, the inner workings of modern international structural institutions of high relevance to health, and the global health economics of medicines and pharmaceutical R&D (Gostin, 2008).

The suggested reforms should be incorporated into a new multilateral treaty amalgamating the procedural and substantive issues into one treaty advanced by joint efforts of the WTO, WIPO, and the WHO. The PCT harmonizes formal standards and procedures, while NAFTA and TRIPS cover substantive issues. The patent system harmonization principles of these treaties should be amalgamated. The treaty should be specific to the pharmaceutical industry and supersede existing treaties, as opposed to the current complex web of legal instruments covering IP over a range of technological products. This treaty would include provisions on current pharmaceutical patent law for the protection of novel inventions, the pharmaceutical patent system reform recommended in section 5.2.2, and other R&D treaty issues. It would also contain other safeguards for access, including compulsory licensing provisions that address the inadequacies identified throughout the dissertation. This would add clarity to the current landscape that exists for participant stakeholders.
Pharmaceutical sector segregation, and all the pharmaceutical patent system harmonization issues, could have been achieved during the original drafting of the NAFTA/TRIPS agreements—although no attempt was made at the time. For instance, under NAFTA, there are separate sub-agreements on Labor and the Environment (Viju, Kerr & Mekkaoui, 2010). This should have been applied to the pharmaceutical sector given its unique commercial and trade activity and impact on human health. Excessive and complex overlapping IP obligations across sectors less relevant to public health have generated significant uncertainty and indirect costs due to the length and time spent on legal activity. Pharmaceutical patent issues should not be bundled into one package under a trade agreement IP chapter within a larger commercial trade agreement.

Extracting pharmaceutical patent system issues into a separate trade agreement approach would also benefit negotiations for expanding positive guided free trade. The efforts by many groups to stall or permanently dismantle the proliferation of other liberalizing free trade agreements, such as the Free Trade Area of the Americas (FTAA), were largely due to the controversial nature of the IP chapters, pharmaceutical patents, and their implications for public health (Imam, 2003). This is a negative outcome since trade integration, which might have had many other positive economic benefits for developing countries experiencing epidemiologic transition fails to occur (Lippert, 1998). The inclusion of pharmaceutical patent system harmonization obligations under larger trade agreements that encompass all sectors of economic activity results in a confusing and conflict-enhancing landscape where resources that could be spent on pharmaceutical discovery, development, and delivery are lost due to time spent on deliberations over
interpretative legal advice or even litigation.

The complexity of the legal landscape needs to be simplified and strong political will is needed to achieve a new multilateral agreement that covers the pharmaceutical sector for the benefit of global health. The WTO TRIPS agreement is the current global standard for the substantive protection of IP. The picture that materializes is an ever-increasing standard of global pharmaceutical patent protection. This standard makes little or no attempt to include real and adequate provisions for the protection of public health or transfer of technology requirements that would facilitate growth for developing country R&D or generic pharmaceutical sectors. In those cases where public health is protected, it is usually done as an afterthought as was the case of the Doha Declaration (Lalitha, 2009). Technology transfer requirements in international conventions are framed in soft language (Glowka, Burhenn-Guilmin, & Synge, 1994). Continued focus is needed on reducing discrepancies between national pharmaceutical patent systems that persist despite harmonization obligations in international treaties. Critics of substantive IP harmonization required by TRIPS argue that agreement restricts the freedom of developing countries to evolve national patent systems in line with their level of technological capacity and economic development (Secretariat, 1996). This may be true yet the implementation of the TRIPS agreement involves the strengthening of patent system administration and enforcement capacity through improvements to the legal framework. This entails a large upfront fixed cost to the developing countries, but is necessary regardless. In the long run, the harmonization process contributes to improved legal infrastructure and economic development and most importantly national and global
patent systems governed by the rule of law.

In summary, a new global agreement is needed that specifically covers the pharmaceutical sector. This would include the development of a new framework for regulating R&D and contain clear safeguards on access including the avenues I have suggested for reform in this final chapter. Such an agreement would supersede and be implemented as a substitute for the PCT and NAFTA/TRIPS frameworks. Academics have an evolving understanding of how patent system harmonization impacts public health issues in the unique area of pharmaceutical commercial activity. A new agreement and coinciding institutional framework would apply to all pharmaceuticals, which then could be extended to a larger universe of health care technologies. The focus, however, must stay on commercial and economic aspects of the global landscape that cover human health and medical technology.

5.4 Policy Recommendations
In addition to the intellectual goal of deeper understanding, this dissertation aim to make a practical contribution to global policy debates and help guide decision making in this area. All countries should work towards the fulfillment of equitable access to medicines necessary for the prevention of transmission and the treatment of disease. There may be many avenues for enhancing the reforms recommended in this chapter. A global strategy for implementation should be developed that includes input through joint coordination between the WTO TRIPS Council, WIPO, and WHO. In addition, WTO could create a working group on health, whose recommendations would be based on WHO guidelines (Westerhaus & Castro, 2006). These institutions have advanced other important public
health-related IP initiatives and play an important role (Matthews, 2004). In the Americas, the Pan American Health Organization (PAHO) should have a role in providing input in trade negotiations to ensure public health is a priority and developing countries are not taken advantage of at the negotiating table. Reforms will also need to be accepted by U.S. and EU sovereign governmental bodies. They are home to the many head offices of the multinational research-based pharmaceutical sector and face massive lobby pressure (Vogel, 1998). At the domestic level, health ministries and patent offices that handle pharmaceutical patent applications should be better coordinated to consider pharmaceutical patent applications. They should set the current available patent term through assessment of prevailing public health and economic conditions, with guidance from the international level. Traditionally, patent offices are appendages of economic ministries and focus primarily on the interest of industry. Attempts are underway, however, to achieve better synergies across ministries (Everard, 2004; Reichman & Dreyfuss, 2007).

In the next two sub-sections, two major supporting policy recommendations are made and justifications are given for the importance of each: (1) support epidemiologic transition through further economic development, and (2) strengthen developing world innovation systems. There is a need for interventions that guide epidemiologic transition in order to augment patent system reform thereby maximizing global public health efforts. It is misguided to view access to medicines from developed/developing or north/south world dichotomies when dealing with the global problem of access to medicines. A more holistic approach is required that deals with the issues through
transnational policy, taking into account epidemiologic transition in developing countries. Innovation system strengthening in developing countries is also required; it will be positive if resources are allocated appropriately. Both of these recommendations require cooperation among relevant stakeholders and policy measures should be backed by reiterative evidence provision through knowledge translation provided from evaluative trans-disciplinary research.

5.4.1 Support for Epidemiologic Transition

Research on patent system harmonization has emphasized identifying the negative political, economic, and structural challenges that arise for developing countries when they are negotiating and enter into trade agreements (Cameron & Tomlin, 2002; Jawara & Kwa, 2004; Laun, 2007; Orme, 1996). There is an equally strong argument that economic development results in health system improvements and an epidemiologic transition, as has been seen in Mexico, which reduces the burden of communicable diseases in a population. This reduces the requisite demand for access to medicines that have been the subject of the literary debate. The focus has been on access to HIV/AIDS anti-retrovirals, anti-tuberculosis, anti-malarial agents, and pharmaceutical interventions for other neglected diseases of relevance primarily to the developing world.

Pharmaceutical needs at the population level vary depending on the epidemiologic profiles of a given country. As a country’s economic position improves, its population has an increasing life expectancy. Chronic degenerative disease burdens increase, involving different treatment needs. Demand grows for cancer medicines and pharmaceuticals to treat other degenerative diseases—diabetes, respiratory illnesses, and
so on (Cohen-Kohler et al., 2007). Epidemiological transition puts strain on developing countries’ health budgets as they move to procure these medicines. As a global community we move to a more holistic approach in solving access problems as our disease burdens converge. This is a positive on one hand, and a negative on the other. Unlike analyzing the problem from a north/south dichotomy, the demand for pharmaceuticals to treat communicable diseases decreases and we start addressing the same issues. Policy measures are needed to better influence this epidemiologic transition towards chronic conditions in developing countries, alongside current efforts to scale up prevention of communicable disease transmission. The lack of evidence in the debate surrounding trade agreements and their impact on access to medicines and public health has caused other FTAs to stall or fail (Vivas-Eugui, 2003). This probably results in delayed economic development in developing countries and a delayed epidemiologic transition towards developed-world disease burdens. The exact disease burdens that are the focus of major research efforts by scientists in the developed world—and therefore command the most financial attention—are our best chance for global advancement.

Mexico has undergone an advanced epidemiologic transition towards developed world health burdens (Gakidou et al., 2007). It has moved away from WHO Type III and II classified diseases and towards Type I diseases. Type III are neglected diseases and overwhelmingly or exclusively found in developing countries. The majority of the burden of Type II diseases is found in developing countries, for example, HIV/AIDS or tuberculosis. Type I diseases have large burdens of disease in developed countries and increasing burdens in developing countries. This is also a representative epidemiologic
profile of the other large developing BRIC nations. This type of epidemiologic transition will be seen in many developing countries of Central America as greater economic integration with the U.S. and Canada is achieved. This presents opportunities and challenges in the area of promoting access to medicines. Opportunities because the demand for medicines that address communicable diseases such as HIV/AIDS, tuberculosis, and malaria are reduced as incidence rates decrease and prevalence levels are reduced due to economic development and improvements in the social and environmental determinants of health found in these countries. Challenges are created, however, as greater demand for access to medicines for non-communicable chronic diseases—such as heart disease, diabetes, and cancer—are created through advanced epidemiologic transition. This transition is good in the sense that most pharmaceutical R&D efforts are focused on developed world diseases burdens, but challenging in the sense that budgetary allocations need to be continually expanded to procure more expensive medicines. A major UN initiative has recently been launched to address the issue of an elevating non-communicable disease burden in the developing world (Sridhar, Morrison, & Piot, 2011).

Global policy should be directed towards encouraging the shift in the epidemiologic profile among developing countries towards those of developed countries. Mexico has become very efficient at alternative methods to improve overall public health. Emphasis has been placed on interventions related to the Millennium Development Goals involving maternal and child health (Gakidou et al., 2007; Horton, 2006; Sepúlveda et al., 2007). Continued and ongoing focus on targeted interventions that shift epidemiologic transition
towards developed world health burdens—and away from communicable disease burdens—is needed (Spiegel et al., 2010). Focused economic development that benefits public health is essential. Social determinants of ill health interventions need to be more vigorously applied that may eliminate the onset and spread of disease. Inappropriately investing scarce financial resources in large scale clinical trials for low burden, neglected diseases should be avoided. These resources could be used to improve public health through socio-economic and environmental interventions, but do not carry the same potential for return on investment. A public health and economic development strategy of guided epidemiologic transition would further decrease demand for pharmaceuticals required for treating communicable diseases. This subsequently reduces the need for R&D resources to be allocated in that direction. In addition, economic development increases vulnerable lower socio-economic populations’ purchasing power and ability to afford existing medicines. This reduces the chance of catastrophic out-of-pocket health expenditure on pharmaceuticals where health care coverage is not yet universal (Knaul et al., 2007). Such a strategy also addresses the lack of motivation pharmaceutical companies have to conduct R&D in neglected diseases because demand moves towards addressing diseases as a global population concern, as opposed to the current developed/developing dichotomy. Enhanced effects could occur through economic development that is specifically directed towards improved infrastructure in national pharmaceutical sectors which address developing countries’ lack of pharmaceutical production capacity. This may have the concomitant effect of addressing developing countries’ current lack of larger innovation systems infrastructure. Resultant knowledge transfer should promote improvements in this sector through the development of local
pharmaceutical production capacity iteratively. This knowledge can be further used to address health concerns specific to developing world countries if so desired at the local level.

The stifling of proliferating trade agreements by anti-globalization movements, and those parties concerned, over access to medicines based on patent system harmonization is founded in weak evidence about how to best address the developing world’s health burden. The multilateral FTAA was largely halted due to complications with the negotiations of the IP Chapter (San Sebastián & Hurtig, 2004). The stalled agreements may have contributed to increased burdens of ill health due to inhibited economic development of developing countries. It is my position that the benefits of economic integration and business development between countries outweigh the detrimental effects and fair trade agreements should be encouraged. This, of course, is with the aforementioned caveat that IP issues relevant to pharmaceuticals should be considered separately from current blanket trade agreements. These issues should be inserted into new pharmaceutical sector specific agreements, for clarity and prioritization of public health due to the sector’s particular importance to human health.

5.4.2 Strengthen Developing World Innovation Systems

It has been identified that through NAFTA, the amount of time required for Mexican manufacturers to adopt U.S. technological innovations was halved (Lederman et al., 2005). This has benefits in terms of increased availability of locally produced novel medicines of assured quality. However, these benefits are difficult to measure, and have a
detrimental impact on Mexico’s ability to self-innovate due to a passive reliance on U.S. and Canadian R&D efforts. The ability to self-innovate is essential for a country intending to compete in the global market place. NAFTA has provided new opportunities for Mexico, yet significant political reforms are still needed to put in place an innovation system capable of fostering technological advancement. An adequate innovative capacity is essential for Mexico to fully exploit the potential of belonging to a global patent system. Mexico needs to intensify its educational programs to promote a culture of understanding the importance of IP. Policy that supports scientists who actively wish to pursue patent applications should be encouraged. Establishing a national plan on science, technology and innovation may boost competitiveness. This needs a renewed commitment and budgetary funding.

To date, it seems most developing countries, Mexico included, have not benefited as much as was hoped from patent system harmonization and the use of patents as a tool for economic development and wealth creation (Idris, 2003). From the knowledge garnered from the scoping study (Chapter 3) and my qualitative research (Chapter 4), this is largely due to the absence of complementary supportive policy measures. Based on these findings, my view is that in most cases, patents are a necessary but not sufficient condition for incentivising research-based pharmaceutical R&D in developing countries. Appropriate policy measures need to be taken to complement the patent system and catalyze innovative efforts of developing nations. In developing countries, comprehensive technology enabling policies that encourage innovative activities are often lacking (Mani, 2004). Critical structural elements for innovation are weak and
appropriation arrangements public research institutes and the private sector are lacking (Cimoli, 2000). Quality researchers are often sparse and research facilities are often ill-equipped due to limited available funding (Horton, 2000). Further, an environment for change should be fostered and developing countries should not be reliant on more powerful neighbours, which can lead to decreased self-sufficiency.

Developing countries should not simply sit back and let other nations advance the pharmaceutical R&D agenda. As an example, Mexico is a technologically advanced developing country and with a fairly robust economy. In addition, Mexico has close economic ties to the United States, the result of both geographic proximity and the common market created by NAFTA. By developing talent and managing its own research base and innovation systems, Mexico may be better able to serve its own market. It may even be able to expand to supply novel pharmaceutical products to markets in other countries as well (Ernst & Center, 2000). To accomplish this objective, Mexico must implement and enforce patent protections in a way that balances the competitive interests of research-based multinational pharmaceutical companies and innovators located in Mexico. It must do so in a way that specifically addresses the Mexican public’s need for accessible medicines (Lesser, 2001). At present, local companies also operate in an environment where the government upholds international standards of patent protection as signatories to both TRIPS and NAFTA. Mexico should encourage the development and maintenance of a strong national innovation system that encourages companies to proactively compete in the global market (Sell, 2003). Multinational companies in developed nations spend a great deal on R&D to assemble competitive patent portfolios.
In order to compete effectively in the globalized market, pharmaceutical companies in developing nations that already have a strong generic manufacturing production base should also invest in basic science R&D and build their own patent portfolios. They otherwise risk competing essentially empty-handed against multinational firms that have had years to develop their pharmaceutical candidate pipelines. An innovative pharmaceutical industrial base in developing countries facilitates service to their own people. It contributes to the global pharmaceutical field at large through innovation, generated by home grown scientists and start-up companies that may enter into strategic alliances with the multinationals (Hu, Schultz, Sheu, & Tschopp, 2007). Mexico needs to focus on building their own science and technology infrastructure by partnering with high-income country university and research institutes. Public universities should work with global partners to develop innovative products that can reach the international market. Mexico needs to study and learn from the university industry liaison business models employed by developed country enterprises that have succeeded in advancing technology. Public-private partnership models (PPPs) can be an efficient model for bridging the translational research gap between basic research and clinical development by bridging together expertise from academia in public research institutes with the pharmaceutical industry (Brown & Frame, 2009; Bull & McNeill, 2007; Moran, 2005). In the more technologically advanced developing countries, such as Brazil and India, meaningful pharmaceutical research is being initiated (Mathur, 2007; Riche, 2006).

Mexico can act by establishing its own innovation agenda that truly reflects its needs and conditions. Gains may be achieved by using its respective strengths to encourage
collaboration with research institutions from developed countries, and by developing local business models that bring local innovation to those who need it. Patent system reform must be integrated into and supported by corollary domestic economic development and innovation policies, in Mexico and in other countries. Further innovation system infrastructure should improve developing countries’ pharmaceutical production and delivery capacities to get medicines to those most in need.

5.5 Conclusions
The debate over the length and scope of patent rights is largely between the American research-based multinational pharmaceutical companies and generic substitute firms. The American multinational pharmaceutical companies have successfully lobbied the U.S. government to advance their strong patent protection position through the proliferation of international trade agreements with patent system harmonization chapters. On the other side of the debate are generic substitute firms, which are more closely aligned with governments that prioritize universal access to health care (for example, Canada and Mexico). This position is also backed by non-governmental organizations, such as Médecins Sans Frontières, acting for severely marginalized populations in the least developed countries. Patent system harmonization has become a major sticking point in international trade negotiations with the lines drawn so clearly. Trade is hampered by the arguments of some social organizations, without sufficient supportive evidence. This is a detriment to economic improvements in developing countries. This, in turn, has a negative impact on the health of vulnerable populations and individuals within those countries.
The negative impacts of patent harmonization on public health must be assessed in light of the positive impact of trade on economic development. Economic development has a direct impact on health (Sachs, 2005). It lowers the environmental and social determinants of communicable disease, leading to reduced prevalence and lower incidence rates, as well as to epidemiologic transition towards chronic non-communicable diseases (Sachs & Malaney, 2002). Early academic papers written on the impact of pharmaceutical patents on access to essential medicines emphasize that for communicable diseases of high burden to the developing world may be unaffordable. This is correct, but the overall picture needs to be further developed with energy directed towards economic development actions that minimize the incidence of communicable diseases in a given population. Existing literature has, in large part, inadequately addressed the larger epidemiologic transition catalyzed by trade integration on health outcomes in developing countries. My analysis of the importance of understanding how epidemiologic transition impacts the aggregate demand profile of global pharmaceutical needs makes a significant contribution to the available academic literature.

My in-depth multi-method research has provided greater understanding of the impact of international trade agreements on public health. Evidence was provided that compulsory licensing as a safeguard is inadequate as a downstream measure in the promotion of access. The results of the comparative legal analysis in Chapter 2 found that international trade agreements should be drafted with optimal pharmaceutical patent protection standards in mind. The scoping study conducted in Chapter 3 found patent system harmonization results in a net health benefit for Mexico that can be further maximized
through feedback evidence to decision-makers. The qualitative research conducted in Chapter 4 concluded that the granting of patent terms from a fixed twenty-year period to a flexible and adjustable term would improve both global equity in access to medicines and reduce economic inefficiencies in our current model for pharmaceutical R&D, while maintaining adequate incentives to conduct pharmaceutical R&D. All of these findings suggest that a global patent system must be developed with law and policy making in mind responsive to health and economic conditions during any given time period. Capacity and consensus building in legal, regulatory, and pharmaceutical patent system management across multiple stakeholders is an important first step towards improving pharmaceutical access and R&D. Effective use of global trade safeguard mechanisms, for example in compulsory licensing by governments, may facilitate pharmaceutical access but are inadequate. Consequently, the patent system reform recommended in this final chapter and supporting policy measures address a complex equation that requires ongoing evaluation for global patent and health system improvements. A flexible and adjustable patent term, if yielded wisely, would lead to greater global health equity in access to medicines and reduce market distortion and economic inefficiencies currently found in the pharmaceutical sector in Mexico and worldwide. The positive and negative aspects of patent system harmonization must be continually assessed by further research in all countries to determine the best course of action to maximize human benefit.
References


Love, J. P. Recent examples of the use of compulsory licenses on patents. *KEI Research Note 2007, 2*


MacDougall, C., & Fudge, E. (2001). Planning and recruiting the sample for focus groups and in-depth interviews. *Qualitative Health Research, 11* (1), 117.


Ruiz, M., & Musungu, S. F. (2002). The international debate on traditional knowledge as prior art in the patent system: Issues and options for developing countries South Centre (Independent Commission of the South on Development Issues).


Secretariat, U. (1996). The TRIPs agreement and developing countries.


Vogelson, C. T. (June 2011). We are the world? *Modern Drug Discovery*.


Appendix

Table 10: General Elements of Systematic Reviews and Scoping Studies

<table>
<thead>
<tr>
<th>Systematic Reviews</th>
<th>Scoping Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typically focuses on a well-defined question where appropriate study designs can be identified in advance.</td>
<td>Tends to address broader topics where many different designs might be applicable.</td>
</tr>
<tr>
<td>Aims to provide answers to questions from a relatively narrow range of quality assessed studies.</td>
<td>Less likely to neither address specific research questions, nor assess the quality of included studies.</td>
</tr>
<tr>
<td>At a general level, scoping studies might aim to map rapidly the key concepts underpinning a research area, and the main sources and types of evidence available.</td>
<td>The definition draws attention to the need for comprehensive coverage of the available literature. There may be different degrees of depth (amount of information extracted from studies and subsequently reported) covered in different kinds of scoping studies. The extent to which a scoping study seeks to provide in-depth coverage of available literature depends on the purpose of the review itself.</td>
</tr>
<tr>
<td>A mechanism is needed to eliminate studies that do not address the central research question – systematic review methods develop inclusion and exclusion criteria, based on a specific research question, at the outset of the project to ensure consistency in decision-making.</td>
<td>A scoping study adopts similar methods – although criteria may be devised post hoc, based on increasing familiarity with the literature, that we could then apply to all the citations to determine their relevance.</td>
</tr>
<tr>
<td>Data Extraction – in the case of meta-analysis it might involve specific statistical techniques.</td>
<td>Charting - describes a technique for synthesizing and interpreting qualitative data by sifting, charting and sorting material according to key issues and themes.</td>
</tr>
<tr>
<td>The process of collecting and reviewing studies for a full systematic review may require researchers to read and review a large number of studies and only a small percentage may be included in the final report. Evidence or findings from studies not included in the review may consequently remain hidden from publication.</td>
<td>A scoping study seeks to present an overview of all material reviewed and consequently issues of how best to present this potentially large bodies of material are critical.</td>
</tr>
<tr>
<td>Unlike a systematic review the scoping study does not seek to ‘synthesize’ evidence or to aggregate findings from different studies.</td>
<td></td>
</tr>
</tbody>
</table>
A scoping study will need some analytic framework or thematic construction in order to present a narrative account of existing literature, but there is no attempt made to present a view regarding the weight of evidence in relation to particular interventions or policies. This is because the scoping study does not seek to assess quality of evidence and consequently cannot determine whether particular studies provide robust or generalizable findings.

<table>
<thead>
<tr>
<th>Systematic Reviews</th>
<th>Scoping Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A scoping study will need some analytic framework or thematic construction in order to present a narrative account of existing literature, but there is no attempt made to present a view regarding the weight of evidence in relation to particular interventions or policies. This is because the scoping study does not seek to assess quality of evidence and consequently cannot determine whether particular studies provide robust or generalizable findings.</td>
</tr>
</tbody>
</table>

### Table 11: Comparison of Quantitative and Qualitative Research

<table>
<thead>
<tr>
<th>Quantitative Research</th>
<th>Qualitative Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphasis is on testing a theory</td>
<td>Emphasis is on construction of a theory</td>
</tr>
<tr>
<td>Quantitative researchers establish a theory which seeks to identify all constructs, concepts, and hypotheses before beginning data collection. Concepts are operationalized so the hypothesis may be tested. Concerned with rigor and replication, the researcher ensures that the measurement instruments are reliable and valid. Data are collected and the statistical relationships between the variables are established.</td>
<td>A good theory should be testable. Although testing theory is normally outside the realm of qualitative inquiry, qualitative theorists play an important role in theory construction. These theories should be significant enough and polished enough for subsequent quantitative testing.</td>
</tr>
<tr>
<td>Bias is controlled by randomly selecting a representative sample from the total population.</td>
<td>Purposive or theoretical sampling is conducted and the researcher must be aware of their own cultural, perspective, bias, or agenda.</td>
</tr>
<tr>
<td>The techniques for research design and analysis are prescribed a priori in the research proposal, and acceptable, tested, and appropriate written steps or guidelines assist the researcher throughout the process.</td>
<td>If an extensive library search reveals very little previous information about the research topic, the topic is probably not developed enough to use quantitative methods, and an exploratory, descriptive study using qualitative methods should be conducted.</td>
</tr>
<tr>
<td>The goal of quantitative research is to test the theory deductively by systematically testing the hypothesis.</td>
<td>The goal of qualitative research can be the inductive development of theory in areas where available evidence is limited and generation of hypotheses for further quantitative testing.</td>
</tr>
<tr>
<td>If the research question is stated as a hypothesis seeking to demonstrate a relationship between two or more variables, then enough is probably known about the variables to use quantitative methods. (How much? How many?)</td>
<td>Qualitative research questions are probably exploratory, seeking to describe a situation or understand a person or an event (i.e., “What is__?” or “How does__?” types of questions).</td>
</tr>
<tr>
<td>It is invalid to use deductive research design and quantitative methods when too little is known about the topic.</td>
<td>It is inappropriate to use inductive research design and qualitative methods when a considerable amount is known about the topic.</td>
</tr>
</tbody>
</table>
A.1 Initial Contact Letter for Subject Recruitment

The Impact of International Agreements on Health
Patent System Harmonization and Medicines in Mexico

Date

Subject: Request for academic interview

Dear [NAME],

I am a graduate student at the University of British Columbia, Canada. I received your name from [NAME]. I am currently conducting a research project to study international evidence on the impact of international trade agreements on health. The study is supported by a Canada Doctorate Graduate Scholarship from the Canadian Institutes of Health Research. As part of this study, I am interviewing stakeholder representatives of government agencies, pharmaceutical corporations, and research institutes in Mexico.

The research project examines the question, “What is the Impact of International Trade Agreements on Health?” By focusing on the case study of international trade agreements affecting Mexico, this research will examine the concern that international directives with beneficial intention may often turn out to have a detrimental impact at the national and local level. The focus area of the research is on procurement of access to essential medicines and developing nations’ capacity to build and maintain autonomous pharmaceutical R&D systems. Governance issues associated with patent system harmonization will be explored.

The result of this study will benefit both the Mexican and Canadian public health agenda by identifying a framework for the evaluation of policy decisions that examine implications for future international agreements. The research will also critically assess how evidence related to such impacts is being incorporated into the negotiation and evaluation of these agreements.

The research focus and methodological approach will be of interest to researchers and policy makers in the region looking at the area of how we apply evidence to develop international agreements as well as how to analyze the consequences of those in place or being considered.

I will be in Mexico City from [Date]. If you are willing and available, I would very much like to meet with you to interview you regarding your organization’s activities and any involvement you have had with the aforementioned research question.

If you agree to be interviewed, you may choose to either have your name and organization mentioned in publications that result from the study, or to have your name and/or organization remain anonymous in connection with any statements you make.
during the interview. The duration of the interview will be approximately [30-60] minutes and I can schedule it for a time that is convenient for you.

The results of this study will be published eventually as part of my Ph.D. dissertation at the University of British Columbia.

If you are able to make time for an interview, kindly contact me at [Email]. I will contact your office shortly to set up an appointment.

Thank you for your time, and please feel free to contact me if you have any additional questions about the study or the interview.

Yours sincerely,

Benjamin Warren, LL.B., LL.M.  
Ph.D. Candidate, Department of Health Care and Epidemiology  
Faculty of Medicine  
Global Health Research Program, University of British Columbia  
2206 East Mall, Rm. 433A  
Vancouver, BC, Canada, V6T 1Z3
A.2 Informed Consent

The Impact of International Agreements on Health
Patent System Harmonization and Medicines in Mexico

Co-Investigator
Benjamin Warren, LL.B., LL.M., Ph.D. Candidate
Faculty of Medicine, Department of Health Care and Epidemiology

Principal Investigator
Dr. Jerry Spiegel
Associate Professor, Department of Health Care and Epidemiology, UBC

Informed Consent: Expert Interview

Please read all sections of this form carefully. In order for your responses to be included in the analysis phase of this research project you will need to sign this form at the beginning of this interview.

Informed Consent

This project is called the Impact of International Agreements on Health.

This study is being carried out by health researcher Benjamin Charles Warren, Doctoral Candidate, from the Department of Health Care and Epidemiology, Faculty of Medicine, UBC. This study is supported by a Canadian Institutes for Health Research Doctoral Graduate Scholarship.

Information garnered may eventually be used in published papers. You understand that your participation is voluntary and any identifiable data collected from you will remain strictly confidential and will not be attributed to you without your permission.

What does consent mean?

Your consent means that you understand what participation in the study will involve and agree to participate in the study of your own free will. In-depth semi-structured interviews will be conducted and interviews will utilize a number of open-ended questions.

The information may be used as support in a variety of accounts the researchers may present. You understand that the interviews may be digital audio recorded and material will be managed to ensure appropriate confidentiality of sources. The information provided to the interviewer is considered confidential. Interviews will be approximately one hour in length.
**What is the study about?**

You have been asked to participate in this project as you have expert knowledge in the area of international trade agreements and/or access to medicines. In addition to our discussions with you, we will consult with other experts. In using the gathered information, our aims include discerning the health implication of IP provisions contained in numerous international agreements. In doing this, the study aims to provide a useful framework for global health researchers in the North American region.

**Why is your participation important?**

International trade agreements are having a profound and far reaching impact on public health. The original assessment of negative health impacts from such agreements was inadequately considered. The research proposed will provide a framework for those negotiating such agreements to better identify the potential outcomes of their decisions that affect everyone in developed and developing nations. As an expert interviewee you are in a position to provide a factual account of an event, a procedure, a process, a historical account, and so forth.

**What will happen in the interview?**

In the interview you will be asked to discuss a predetermined subject of which you have specific knowledge. The interview will be informal with open-ended questions and may last up to one hour. The discussion will be recorded. Information about you will not be associated with the data, and you will be asked to help construct how any references to you or this interview may be described. Once the interview is completed, the information you provide will be analyzed, compared and supported by information received in other interviews. Information provided will not be attributed to you unless requested. The information will then be presented in a doctoral thesis and publications in several scholarly journals.

**Who will get to see the information and what will they get to see?**

Only the doctoral candidate (co-investigator), the principal investigator, and project specific transcribers will ever see the raw data. Un-linkable and aggregated data will be retained for further analysis; however, all audio recordings and original data will be destroyed after five years.

**Who can you contact for more information?**

Please feel free to contact the above if you desire any additional information about your participation in the project.
If at any time you have concerns about your rights or the way in which your research is being carried out, you may contact UBC Office of Research Services and Administration, at [Phone Number].

I understand that my participation in this expert interview is voluntary and any information I provide will be considered confidential. That means my name will not be associated in any way with the results of this research without my consent.

Please attribute comments to myself in publications that use information from this interview.

Initial – Yes  Initial - No

By signing below, I agree to participate in the expert interview.

_________________________________
Printed Name

_________________________________
Signature of Participant

_________________________________
Date

You will be given a copy of this consent form for your records. Please retain that copy and refer to the contact information if you have further questions.
**A.3 Interview Script**

The Impact of International Agreements on Health
Patent System Harmonization and Medicines in Mexico


This script will guide the discussion of the impact of international trade agreements on access to medicines & public health. The interview will be conducted with key informants from three identified stakeholder groups:

1. Government Agencies (public health & economic);
2. The Pharmaceutical Industry (research-based & generics); and,
3. Non-governmental organizations and Academic institutes.

A number of thematic categories of inquiry have been identified that the research seeks to address. This was achieved through a WHO Framework and a Scoping Study.

Improving access to medicines is perhaps the most complex challenge for all actors involved in the field of medicines supply. They must all combine their efforts and expertise, and work jointly towards solutions. Many factors define the level of access, such as financing, prices, distribution systems, and appropriate dispensing and use of essential medicines. WHO has formulated a four-part framework to guide and coordinate collective action on access to essential medicines: Rational Selection & Use, Affordable Prices, Sustainable Financing; and Reliable Supply Systems.

NAFTA was the First International Trade Agreement to include obligations to protect Intellectual Property (IP) Rights. The WTO subsequently adopted the TRIPS agreement, but the IP provisions of the NAFTA remain an important source of obligations for the three NAFTA state parties having potential impact on access to medicines.

The interview questions have been divided into these thematic categories. Information will be collected and analyzed on the following themes as guided by the research questions and study objectives.
<table>
<thead>
<tr>
<th>Part A. Questions based on the WHO Equitable Access to Essential Medicines Framework</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Rational selection and use of essential medicines</strong></td>
</tr>
</tbody>
</table>
| 1. In your opinion, have national treatment guidelines in Mexico been developed based on the best available evidence concerning efficacy, safety, quality, and cost-effectiveness? Are they adequate and clear?  
2. Has a national list of essential medicines based on national treatment guidelines been developed?  
3. Is a national list of essential medicines for procurement, reimbursement, training, donations and supervision used? |
| **2. Affordable Prices – Most Relevant to Trade Agreements and IP Issues** |
| 4. From your perspective, is available and impartial price information used?  
5. Is price competition allowed in the local market?  
6. Is bulk procurement promoted?  
7. Are procurement of generic policies implemented?  
8. Are equitable pricing mechanisms and agreements for newer essential medicines for priority diseases negotiated?  
9. Is price negotiation for newly registered essential medicines undertaken?  
10. Are duties, tariffs, and taxes on essential medicines eliminated?  
11. Are mark-ups through more efficient distribution and dispensing systems reduced?  
12. Is local production of essential medicines of assured quality when appropriate and feasible encouraged?  
13. Are NAFTA and WTO/TRIPS compatible safeguards adopted into national legislation? |
| **3. Sustainable Financing** |
| 14. From your perspective, has public funding for health, including for essential medicines been increased since the implementation of NAFTA?  
15. Has out-of-pocket spending, especially by the poor been reduced?  
16. Has health insurance through national, local, and employer schemes been expanded?  
17. Has external funding been targeted - grants, loans, donations - at specific diseases with high public health impact?  
18. Have other financing mechanisms, such as debt-relief and solidarity funds been explored? |
| **4. Reliable supply systems** |
| 19. From your perspective have access to essential medicines in health sector development been integrated?  
20. Have efficient public-private-NGO mix approaches in supply delivery been created? |
21. Has quality of medicines through regulatory control been assured?
22. Have various purchasing schemes: procurement co-operatives been established?
23. Are traditional medicines in the provision in health care considered?

**Part B. Questions based on Results of a Scoping Study**

**1. Policy Formulation and Implementation Pre/Post NAFTA**

1. What was your role during the negotiation and implementation of NAFTA?
2. What are the attitudes, decisions, and actions expressed by this organization regarding NAFTA and Access to Medicines in Mexico?
3. Did this organization consider the public health consequences (benefits/detriments) of NAFTA Chapter 17 patent provisions prior to treaty ratification?
4. How much were these considerations driven by evidence?
5. Do recent policies that comply with NAFTA IP obligations mitigate the potential detrimental public health impact?
6. Is evidence-based consensus on these polices being achieved by Stakeholders?

**2. Access to Medicines Impact**

7. How has the legal implementation of NAFTA’s domestic IP obligations impacted public health and the accessibility of pharmaceuticals in Mexico?
8. What domestic legislation or policy instruments have been developed to harmonize with or circumvent IP provisions that may (beneficially/negatively) impact access to medicines?
9. Are available flexibilities (including compulsory licenses) adequate and appropriate for protecting public health?
10. If not, what different measures necessary and what new flexibilities might be implemented?
11. Have indicators with which to assess domestic policy effectiveness on access to medicines been established?

**3. Pharmaceutical R&D Impact**

11. How has the implementation of NAFTA impacted domestic innovation systems?
12. How has NAFTA affected the Science & Technology sectors of Mexico?
13. Has stronger intellectual property protection in Mexico led to more research on drugs to address developing countries (Mexico) needs?
14. Do you think clinical research in urgent areas (ex. Multi-drug Resistant TB) have been avoided by researchers by the exercise or threatened exercise of IP rights?
15. What were the processes by which post-NAFTA policies pertaining to innovation system development, maintenance, and health impact formulated and approved?
16. What are the key conditions influencing the formulation and approval of policies pertaining to innovation system development, maintenance, and health impact?

**4. Regional Guidance & What should Mexico do next?**

19. Has a balance been met in the policy development of meeting short-term goals of ensuring access to medicines with longer-term innovation system goals?
20. What lessons can you provide for decision and policy makers in developing countries in Central America as recent signatories (2003) to the DR-CAFTA?
21. Do you think NAFTA needs to be revisited to strengthen co-operation & economic integration between the Member States and encourage a more level playing ground?

End of Interview