

DISCUSSION PAPER

68357

**PUBLIC AND PRIVATE SECTOR APPROACHES
TO
IMPROVING PHARMACEUTICAL QUALITY
IN
BANGLADESH**

**Janet Bumpas
Kees Kostermans
Dinesh Nair**

South Asia, Human Development Department

THE WORLD BANK

August 2007

Table of Contents

Acknowledgements.....	v
Foreword	vi
Summary	vii
1. Introduction	1
1.1 Background	1
1.2 Objective	1
1.3 Methodology	1
2. The Global Pharmaceutical Industry.....	2
2.1 R&D Based Pharmaceutical Firms.....	2
2.2 Generic Pharmaceutical Firms	2
2.3 Manufacturing Process	3
3. Pharmaceuticals in Bangladesh	5
3.1 Pharmaceutical Manufacturing Firms in Bangladesh	5
3.2 Drug Quality.....	5
3.3 Domestic Drug Distribution	6
3.4 Export Market.....	8
3.5 Partnerships with Global Firms.....	12
4. TRIPS and Bangladesh.....	14
4.1 The WTO and TRIPS	14
4.2 TRIPS' Implications for Bangladesh	15
4.3 Bangladesh Patent Law	17
5. Benchmarking the competitiveness of Bangladesh's pharmaceutical sector .	18
5.1 Manufacturing Cost.....	19
5.2 Workforce Skills.....	22
5.3 Government and Regulatory Environment.....	22
5.4 Drug Legislation.....	23
5.5 Drug Directorate Administration.....	24
5.6 Drug Testing Laboratories.....	25
5.7 Bioequivalence Laboratories.....	25
5.8 Manufacturing Certification	26
5.9 Macro Factors.....	27
6. Potential Approaches to Improving Quality of Pharmaceuticals in Bangladesh	29
.....	
7. Conclusions and Next Steps.....	31
7.1 Improving Price and Quality on the Domestic Market	31
7.2 Improving price and quality on the export market.....	34
7.3 Taking advantage of TRIPS	35
Endnotes.....	41

List of Tables

Table 1: Bangladesh's Pharmaceutical Exports in USD millions.....	8
Table 2: Recent Exports by Some Bangladeshi Pharmaceutical Firms	9
Table 3: Square and Beximco expenditures	22
Table 4: Gross Enrollment Ratios in Selected Countries	22

List of Figures

Figure 1: Annual Growth Rates of the Bangladesh Pharmaceutical Sector.....	5
Figure 2: Pharmaceutical manufacturing cost driver	19
Figure 3: Scale Economy Curves	21
Figure 4: Local Production and Tertiary School Enrollment.....	27
Figure 5: MNC's R&D Activities in India.....	38

List of Boxes

Box 1: Case Study Beximco.....	9
Box 2: Case Study of Incepta.....	11
Box 3: Case Study of Square Pharmaceuticals	12
Box 4: Lessons Learned from India and China.....	18
Box 5: Medicines Transparency Alliance (MeTA).....	33
Box 6: China.....	37
Box 7: India.....	38

List of Acronyms

Acronym	Definition
API	Active Pharmaceutical Ingredient
BAPI	Bangladesh Association of Pharmaceutical Industries
BMA	Bangladesh Medical Association
cGMP	Current Good Manufacturing Practice
DCO	Drug Control Ordinance (Bangladesh)
DCC	Drug Control Council (Zimbabwe)
DDA	Drug Directorate Administration (Bangladesh)
DTL	Drug Testing Laboratories
FDI	Foreign Direct Investment
GAAP	Generally Accepted Accounting Principles
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
GSK	Glaxo Smith Kline
HIV/AIDS	Human Immunodeficiency Virus / Acquired Immune Deficiency Syndrome
HVAC	Heating, Ventilation and Air-Conditioning
ICDDR,B	International Center for Diarrhoeal Disease Research, Bangladesh
IFC	International Finance Corporation
IPR	Intellectual Property Rights
LDC	Least Developed Country
KWH	Kilowatt Hours
MNC	Multinational Corporation
MSF	Médecins Sans Frontières
MVA	Manufacturing Value Added
Nafdac	National Agency for Food, Drug Administration and Control (Nigeria)
NDP	National Drug Policy
NGO	Non-Governmental Organization
NOC	No Objection Certificate
PP&E	Plant Property & Equipment
R&D	Research and Development
QA	Quality Assurance
RS	Indian Rupee
TGA	Therapeutic Goods Administration (Australia)
TLC	Thin Layer Chromatography
TRIPS	Agreement on Trade Related Aspects of Intellectual Property Rights
UK	United Kingdom
UKMHRA	United Kingdom Medicines and Healthcare Products Regulatory Agency
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Development Organization
USA	United States of America
USFDA	United States Food and Drug Administration
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Acknowledgements

This report has been prepared by a team of World Bank staff and consultant led by Kees Kostermans (Task Team Leader). The team members included Janet Bumpas, Dinesh Nair and Iffat Mahmud. Administrative and logistical support was provided by Aynul Haque and Shahadat Chowdhury.

The study has been financed by the United Kingdom Department for International Development (DFID), Delegation of the European Commission (EC), the Embassy of the Kingdom of the Netherlands (RNE), the Swedish International Development Cooperation Agency (Sida) and the World Bank through the Bangladesh Health, Nutrition and Population Sector Program (HNPSP). We thank all the pool financiers of HNPSP for supporting this assignment.

We are grateful to Ehsanul Fattah, the then Secretary of Ministry of Health and Family Welfare (MOHFW), for his support and interest in this work. We are grateful to all the officials of MOHFW, Directorate of Drug Administration and the Bangladesh Association of Pharmaceutical Industries (BAPI). During the preparation of this report, we had discussions with people in the Bank and various stakeholders involved with the pharmaceutical industry. We acknowledge the contribution of all of them. We would also like to thank our peer reviewers for their constructive comments on the draft report – Andreas Seiter, Ramesh Govindaraj, Syed Mahmood, and Monique Mrazek. We are grateful to our World Bank colleagues: Robert Floyd, Thomas Buckley, Eric Manes, Vinaya Swaroop, and Mohammed Alhousseyni Toure.

Finally we appreciate the support of the Country Management Unit of the World Bank Office Dhaka for the publication of this report.

Foreword

Pharmaceuticals are an extremely important part of the Bangladesh health expenditures. Almost one-third of total annual per capita health-care spending is on pharmaceuticals. The domestic pharmaceutical market in Bangladesh is cost-sensitive, protected from imports, and has a loose regulatory environment. While some domestic manufacturers produce pharmaceuticals of world-class standards, others can and do flourish with a lower quality product.

Previous efforts to improve access to drugs, their pricing, and quality have focused on tighter regulation of the market. The efforts have not been very successful. However, the pharmaceutical business sector and the Bangladesh population have a joint interest in accessing pharmaceuticals of good quality and at a competitive cost. This paper explores new ways to address the issue through the private sector.

The preparation of this report was made possible through the collaborative efforts of the Government of Bangladesh and the World Bank. We hope that the findings of this report will provide useful institutional suggestions for the Government to improve the price and quality competitiveness of Bangladesh's pharmaceuticals.

Xian Zhu
Country Director
World Bank Office Dhaka

Anabela Abreu
Sector Manager
South Asia Human Development Sector

Summary

Low-cost high-quality drugs benefit society and improve pharmaceutical companies' competitive edge. This study presents the issues that must be considered to achieve these common objectives in Bangladesh. This is not a policy paper outlining exact recommendations, rather it is a discussion paper which explores the field and points towards options for Government and the local industry.

Previous efforts to improve the drug quality in Bangladesh focused without much success on stricter regulation of the public market. This paper addresses this issue from a more private sector approach. The existing quality and price of pharmaceuticals are analyzed and alternative mechanisms are explored to improve the quality and cost competitiveness of Bangladesh's pharmaceuticals domestically and internationally.

Pharmaceuticals are an extremely important part of the Bangladesh health expenditures. In 1997, more than \$3.50 of a total annual per capita health spending of \$10.60 was for pharmaceuticals.ⁱ The domestic pharmaceutical market in Bangladesh is cost-sensitive, protected from imports, and has a loose regulatory environment. While some domestic manufacturers produce pharmaceuticals of world-class standards, others can and do flourish with a lower quality product.

Four factors drive the price and quality competitiveness of pharmaceuticals.

1. **Manufacturing Cost.** While Bangladesh has several advantages due to lower cost labor and power, it is at a disadvantage with regards to the largest cost drivers, i.e. Active Pharmaceutical Ingredients (APIs) and scale.
2. **Workforce Skills.** Although Bangladesh's pharmaceutical labor costs are approximately 30% less than India's, the industry faces challenges in the technical training required because Bangladesh's educational system lags behind global levels.
3. **Government and Regulatory Environment.** The current regulatory environment is protected and under-regulated. Importing drugs is difficult, allowing domestic firms to dominate the market. Due to the power of these firms and the government regulatory agencies' weakness, quality control laws are not strictly enforced.
4. **Macro Factors.** Countries tend to have stronger domestic industries when the following characteristics are present: high levels of secondary and tertiary educational enrollment; GDPs greater than \$100 billion; populations greater than 100 million; a high manufacturing value added score by the United Nations Industrial Development Organization (UNIDO); and a net positive pharmaceutical balance of trade.

While Bangladesh's base for pharmaceutical manufacturing is strong, some structural constraints prevent firms from meeting global standards for price and quality competitiveness. Institutional and policy measures can address some of constraints. Others will require longer term capacity building, and some will remain a competitive challenge for firms to overcome.

Five potential mechanisms have been identified to improve the quality of drugs available in Bangladesh.

1. ***Export-led improvement.*** Quality improvements in drugs made by firms to export may affect the domestic market. But because firms tend to segment production for the different markets, with higher quality drugs going to export markets and lower quality drugs remaining in the less-regulated domestic market, the domestic industry only benefits indirectly.
2. ***Regulatory-led quality improvement.*** A strict regulatory environment does result in higher drug quality but significant political will is required to enforce the regulations. The domestic regulatory institutions are not currently able to effectively manage quality issues. The public is therefore at risk.
3. ***Competition-led improvement.*** There is widespread agreement that firms in economies with liberal trade policies and greater openness show stronger economic growth and overall development performance in the long run. Bangladeshi pharmaceutical firms operate in a closed protected market. Moves to open the economy and increase competition will most likely lead to cost and quality improvement but such changes will also cause some hardship for Bangladeshi firms, primarily those operating at a sub-competitive level.
4. ***Private sector-led improvement.*** In many industries and countries, the private sector has played a role in maintaining and monitoring quality. Leaders in Bangladesh's domestic pharmaceutical industry are interested in raising product quality levels and could play a role in this regard.
5. ***Knowledge-transfer-led improvement.*** Most firms in Bangladesh want to provide the highest quality drugs possible. Government and donors should work with firms producing at less than Good Manufacturing Practices (GMP) levels to raise their standards to a minimum acceptable level. For firms striving toward higher levels of quality improvement, working with the global industry through some form of joint venture, licensing agreement, or contract manufacturing situation is the best mechanism.

This paper also examines two external forces currently impacting Bangladesh's pharmaceutical sector which can provide opportunities for change. The first is WTO's Trade Related Aspects of Intellectual Property (TRIPS), which grants Bangladesh domestic manufacturing opportunities and limited export advantages. Pursuing TRIPS' opportunities must be carefully considered for the following reasons: they are time-sensitive, require up-front investments, are likely influenced by international political pressures, provide unclear benefits, and China and India, the world leaders in low-cost pharmaceutical manufacturing, are still extremely competitive. If Bangladesh decides to invest in pharmaceutical manufacturing to take advantage of TRIPS, it should strive to create a sustainable and growing industry after 2016, when the TRIPS' flexibilities are scheduled to end. To compete in the long run, Bangladeshi firms will have to excel based on the price and quality of their drugs.

The second force affecting the industry is the rapidly changing international marketplace. Globalization has resulted in an extremely competitive international market with firms seeking low-cost manufacturing sources. Multinational corporations (MNCs) are closing expensive excess capacity and searching for new, less expensive suppliers of active pharmaceutical ingredients (APIs) or for developing countries in which to undertake the

entire manufacturing process. Due to cost constraints in the European and US health markets and a narrow product pipeline from innovative firms, generic drug companies are growing faster than innovative research companies.

This paper concludes with policy and institutional suggestions for Government to improve the price and quality competitiveness of Bangladesh's pharmaceuticals. The recommendations are targeted at improving the domestic market, increasing export potential and taking advantage of TRIPS. The conclusions are preliminary and more analysis is suggested.

Introduction

Background

Bangladesh has a highly protected pharmaceutical industry coupled with a weak regulatory mechanism. Therefore the quality of pharmaceuticals on the local market is highly variable. This poses a public health risk. Previous efforts to improve access to drugs, their pricing and quality have focused on tighter regulation of the market. The efforts have not been very successful. However, the pharmaceutical business sector and the Bangladesh population have a joint interest in access to pharmaceuticals of good quality and at a competitive cost. This paper explores new ways to address the issue through the private sector.

Objective

This study's analysis will identify specific policy and institutional options to improve the cost and quality of pharmaceuticals produced in Bangladesh and its competitiveness in the global market. The terms of reference for this study can be found in Appendix 1.

Methodology

The authors conducted in-depth interviews in Bangladesh with representatives from government, industry, NGOs, international organizations and pharmacists and completed a review of existing literature. As a result, some of the study's conclusions must be considered preliminary, since they are based on anecdotal evidence which was not validated by systematic surveys. Because this report is intended to raise issues and provoke debate and not to provide definitive conclusions and recommendations, this methodology was chosen to provide an initial rapid assessment of this complex and dynamic sector. Throughout the study, several subjects are highlighted requiring further study. A list of interviewees can be found in Appendix 2.

The Global Pharmaceutical Industry

Pharmaceutical manufacturing is a technically challenging but potentially financially rewarding industry. From 1993-1997, the average return on assets for the industry globally was 10.96%.ⁱⁱ In 2006, the industry was estimated at \$643 billion.ⁱⁱⁱ Large research-based multinational corporations (MNCs) dominate the industry in revenue, whereas generic firms are starting to dominate in volume.

R&D Based Pharmaceutical Firms

The short-term product pipeline for global pharmaceutical MNCs is thin and niche. The absence of new blockbuster drugs in the near term forces MNCs to focus on the following to maintain profit growth:

1. **Patent extensions.** The National Institute for Health Care Management estimates that from 1989-2000, only 153 (15%) of all new US drug approvals were for medicines providing significant clinical improvements.^{iv} The rest were for minor modifications of existing medicines.
2. **Scale.** MNCs seek to rationalize both research and development (R&D) and manufacturing. R&D facilities are increasingly based on “centers of expertise,” where resources for a single disease are assembled in one physical location. Pfizer, for example, consolidated its R&D operations from five to three sites. Large-scale pharmaceutical manufacturing lowers the costs per unit as a result of the following: allocation of fixed costs to more units; larger equipment which tends to result in increased volume and lower costs per unit; fewer product changeovers; less analytical testing; and, more streamlined inventory management. Manufacturing facilities must balance the available economies-of-scale at one large, low-cost facility located in a logistically well-placed area with a company’s need to be close to markets as well as comply with a government’s regulations for local production. Seven or eight years ago, Pfizer had approximately 120 manufacturing sites; they now have approximately 70.^v
3. **Cost cutting.** MNCs cut costs by outsourcing parts of their manufacturing and by moving to lower-cost contract manufacturers. This trend is therapeutic area-specific, and differences in this tendency exist by therapeutic category.^{vi} MNCs are also migrating from the small number of suppliers, with whom they have traditionally worked, to active pharmaceutical ingredient (API) manufacturers, often in India or China, which can reliably supply lower-cost bulk ingredients.^{vii}
4. **Mergers.** Pharmaceutical firms are turning to strategic acquisitions to improve sales and profits.

Generic Pharmaceutical Firms

Generic pharmaceutical sales are predicted to grow 13% to 14% in 2007 or \$65 billion, almost 10% of projected worldwide drug sales. Compared with a predicted 5% to 6% increase in the global pharmaceutical market, the generic drug sector shows the fastest growth.^{viii} The sector is expected to be highly competitive as firms acquire scale through

many mergers and acquisitions. Generic firms' core competencies lie in the following areas:

1. **Reverse engineering.** A manufacturer typically develops a generic drug by reverse engineering to discover the chemical composition of a patented drug invented by another firm. The manufacturer then creates its own drug based on the same chemical composition. To complete the process from drug creation to regulatory approval requires approximately 24 months in the United States. The steps required include performing the reverse engineering of the drug, designing and implementing the product manufacturing processes, completing the drug stability testing (i.e., if the product is stated to have a shelf life of two years, it must be shelved for two years and then demonstrate the same efficacy), and receiving regulatory approval for the generic drug.^{ix}
2. **Manufacturing high-quality drugs at a low cost:** Generic firms are also moving production to India and China to reduce costs.^x
3. **Branding.** In strictly regulated markets, all generic drugs have the same quality. In countries with looser drug regulatory environments, quality of generics can vary widely. In such markets, pharmaceutical manufacturers brand their drugs to try and differentiate products for the consumer. However, generic equivalent brands, of equal or lesser quality, are often priced at considerable and unjustifiable premiums.^{xi}
4. **Managing patent expirations.** Generic firms are adept at challenging patents and managing the approval process. When a drug patent expires, a generic firm is usually ready with a generic brand of the drug and all the required approvals to put it on the market the day following the expiration date. Generics are the most profitable pharmaceuticals, with returns sometimes up to 20%, particularly if only one generic is on the market.^{xii} Over time, other firms enter the market, drug prices drop toward marginal costs along with the high profit margins. TRIPS' Bolar Exemption allows firms to conduct research on patented drugs and prepare for regulatory approval of generics before a patent's term ends. Because of this, firms begin to prepare generic products early, sometimes years in advance. Ivax, Reddy-Cheminor and Par, for example, started to file for US regulatory approval approximately 10 years prior to the 2011 patent expiry for Olanzapine.^{xiii} Generic firms may not merely wait for a patent to expire; they may aggressively challenge them. The Indian firm Ranbaxy was involved in 14 patent suits in the US from 2000-2003, which were discussed in an article entitled "In India a Little Lab Work and Lots of Lawyers."^{xiv}

Manufacturing Process

There are generally two steps to pharmaceutical manufacturing. First, active pharmaceutical ingredients (APIs) are manufactured. API production is a highly sophisticated, technically demanding chemical and biochemical fermentation and synthesis process. In 2004, the API market was \$69 billion.^{xv} APIs are a significant manufacturing cost of a drug. For example, on average, 40-50% of the cost of goods sold for generic oral solids comes from APIs.^{xvi} Commodity API manufacturing tends to be a high-volume, low-margin business based extensively on scale economies and large dedicated manufacturing lines. Smaller manufacturers therefore have limited

opportunities to compete globally. The average commodity API margin of profit is less than 10%. In fact, many large bulk API exporters from India work with a 3% margin on exported products.^{xvii} Firms can either manufacture their own APIs or purchase them on the open market.

The second step in pharmaceutical manufacturing is the drug's final formulation. Unlike the chemical business of API production, final formulations belong to the manufacturing sector. During this process, firms mix APIs and excipients (other non-active ingredients), press the mixture into pills, tablets, or solutions, and then package the product for the consumer market. Final formulations are as equally complex as API manufacturing but require different skills. Because firms can produce fifty or more products in a single plant with adaptable equipment, economies of scale are less important for final formulations than for API manufacturing. Profit margins for final formulations average 20-30%.^{xviii}

Pharmaceuticals in Bangladesh

Pharmaceutical Manufacturing Firms in Bangladesh

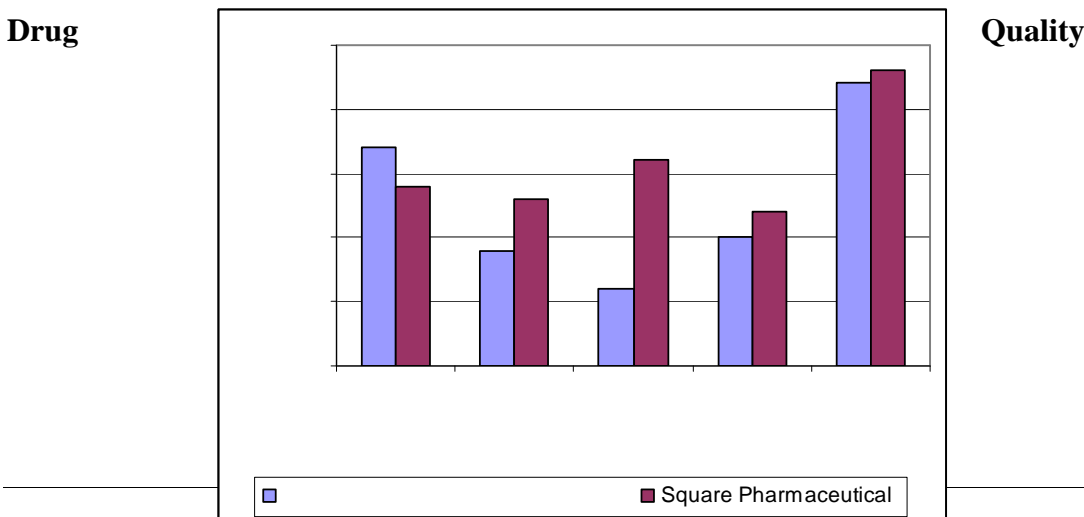
Bangladeshi pharmaceutical firms focus primarily on branded generic final formulations using imported APIs. About 80% of the drugs sold in Bangladesh are generics and 20% are patented drugs.^{xxix} The country manufactures about 450 generic drugs for 5,300 registered brands which have 8,300 different forms of dosages and strengths. These include a wide range of products from anti-ulcerants, flouroquinolones, anti-rheumatic non-steroid drugs, non-narcotic analgesics, antihistamines, and oral anti-diabetic drugs. Some larger firms are also starting to produce anti-cancer and anti-retroviral drugs.^{xxx}

Domestically, Bangladeshi firms generate 82% of the market in pharmaceuticals; locally based MNCs account for 13%, and the final 5% is imported. Although 235 pharmaceutical companies are registered in Bangladesh, only about 85 are actively producing drugs. The top 30 to 40 companies dominate almost the entire market; the top 10 hold 70% of domestic market share; and the top two, Beximco and Square, capture over 25% of the market.^{xxxi} The industry structure is relatively concentrated. In comparison, the top ten Japanese firms generated approximately 45% of the domestic industry revenue in 2006, while the top ten UK firms generated approximately 53%, and the top ten German firms generated approximately 60%.^{xxxi}

Because Bangladesh API capacity is insignificant, API firms import approximately 80% of their APIs. Fifteen to seventeen Bangladeshi firms are involved in the manufacture of about twenty APIs, but they usually run the final chemical synthesis stage with API intermediaries, instead of the complete chemical synthesis. The other 1,000 required APIs are imported.^{xxxiii} Approximately 75-80% of the imported APIs are generic.^{xxxiv}

In 2005, the size of the Bangladeshi pharmaceutical market was \$500 million, and it is expected to grow at 10% per annum.^{xxxv} In Figure 1 (data taken from the Square Annual Report 2005–2006), the industry's annual historical growth rate is compared with Square Pharmaceutical's, the largest domestic firm.

Figure 1: Annual Growth Rates of the Bangladesh Pharmaceutical Sector



For generic pharmaceutical products, quality is defined as the generic drug having the same active ingredients as the original formulation and being bioequivalent to the brand name counterpart with respect to pharmacokinetic and pharmacodynamic properties (equivalent absorption rates, elimination rates, and other in vivo effects). By extension, therefore, generics are assumed to be identical to the original product in dose, strength, route of administration, safety, efficacy and intended use.

While some Bangladeshi pharmaceutical products on the market are of world-class standards, others are less so. Medical professionals and pharmacists interviewed voiced strong opinions on the quality levels of different brands. Although further comprehensive and systematic analysis is required to assess Bangladesh's pharmaceutical quality, some anecdotal reports exist of lower quality drugs.

- The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) tested the zinc content in 20 zinc-syrup formulations marketed in Bangladesh. The samples were purchased from local pharmacies in Dhaka. Only two of the tested products contained zinc concentrations within 5% of the stated content. The rest contained zinc, just not enough. The problem could have originated from either poor manufacturing or poor product handling in the distribution channel, because zinc degrades if exposed to light.^{xxvii}
- Of eleven drugs UNICEF sent for testing to a laboratory in Australia, two had substandard results. When the manufacturers were informed, one company immediately stopped production until it found the problem—a very good response. The other company however, refused to address the problem, claiming that the test was in error. UNICEF sent the drug for a second testing to a lab in Denmark where the drug was also found substandard. The company still refused to address the issue.^{xxviii}

Some Bangladeshi firms have invested in quality raw materials, manufacturing processes and environment, and technical know-how. However, a “perverse incentive” exists against upgrading due to the weak regulatory structure. Firms that have invested minimally in quality continue to sell drugs alongside those that have invested substantially. Because of weak regulations, the consumer cannot determine quality differences and select for purchase the superior product. As a result, firms that have invested in quality manufacturing and quality processes are in a sense penalized.

Domestic Drug Distribution

Bangladesh's drug distribution marketplace is composed of small independent pharmacies. This structure combined with an under-regulated industry, few firms manufacturing pharmaceuticals, and companies competing to sell branded generics based on brand names provides ample opportunity for the sale of low-quality drugs at higher prices.^{xxix} That the quality of drugs available for sale varies significantly in Bangladesh is therefore no surprise!

Pharmaceutical firms can sell their products to private sector pharmacies, the government and its public health care facilities, or to international organizations operating in Bangladesh (e.g., UNICEF). Government sales are not as profitable as private sector sales because the government pays less, on consignment, and at times, after considerable delay. Pharmaceutical firms nevertheless still target public facilities because doctors become acquainted with the firms' drugs and then prescribe them in their private practices. And, because drugs are not readily available at public facilities, patients receiving treatment there may still go to a private pharmacy to procure the required drugs. Without these public sector connections, many firms would turn more attention to the private sector.^{xxx}

Although there are approximately 200,000 private pharmacies in Bangladesh, the government lists officially only 76,000 pharmacies.^{xxxii} The rest are illegal, without a license or a licensed pharmacist on staff. Pharmacists have varying education levels and many lack adequate training. For example, a visit to four pharmacies in Dhaka and ten pharmacies in the bordering Gazipur, Narayanganj, Keranigonj and Manikgonj Districts revealed that each had one professional pharmacist (with four years of coursework); while the two medium-sized pharmacies visited had one person with a year's training and several untrained coworkers all working as pharmacists. Rural pharmacies may have pharmacists with high school educations and approximately two weeks training. The Bangladesh Pharmacist Society is currently implementing the first phase of a three-phased program to improve pharmacists' skills. The program should be completed in seven to eight years.^{xxxiii}

Most pharmacies are individual shops, though some chains are starting to develop, especially in urban areas. Large pharmacies visited reported buying medicines according to sales trends, e.g., what sells the most. The medium and small pharmacies visited reported linkages with a medical doctor. Their sales were therefore usually skewed towards that medical professional's preferences.

Several brands of each drug, with variable quality levels, are on the market. In urban areas, the visited pharmacies tended to sell higher quality brands, whereas in more rural areas, pharmacies visited tended to sell lower quality, lower cost brands. This may be due to a district's political sway influencing brand selection. The pharmacies visited tended to have brands associated with people who held power in that district. Those more distant from the city center also had increasingly more ayurvedic and herbal medicines.

The top twenty pharmaceutical manufacturing firms have established extensive sales and distribution networks. Each pharmacy visited has 10-50 pharmaceutical firms supplying their medicines daily. For example, Beximco Pharmaceuticals has 1,200 representatives visiting pharmacies daily to take drug orders. Each pharmacy receives approximately 12-15 Beximco shipments per month. Acme Pharmaceuticals has 1,100 representatives and Square Pharmaceuticals has 950 representatives visiting pharmacies.^{xxxiii} None of the pharmacies visited restock any medicine that does not sell well. The small pharmacies report only keeping a medicine for a maximum of six months.

A significant number of drug consumers obtain drugs without a prescription. When a consumer lacks a prescription, s/he will either ask a pharmacist for a specific drug or describe his/her ailment to a pharmacist who diagnoses the problem and recommends a drug on the spot. Popular products include a variety of antibiotics, painkillers, and gastric remedies. Consumers purchase one to ten tablets or capsules at a time. The quantity of drugs purchased often depends more on the consumer's finances of than on the required dose of medicine.

Export Market

Pharmaceutical firms in Bangladesh export approximately \$27.54 million in products to 68 countries.^{xxxiv} Bangladeshi firms can export to the following markets:

- **Regulated:** Square Pharmaceuticals, the only Bangladeshi pharmaceutical firm accredited in a regulated market, received the UK's regulatory approval in May 2007. Other firms' biggest barriers to regulated markets are manufacturing facilities (at a cost of at least \$50 million) and know-how.
- **Moderately Regulated:** Some markets, such as Tanzania and Malaysia, are moderately regulated. While countries do not always require stringent certification, a certification from a regulated market signifies quality and provides a firm with a competitive advantage.
- **Unregulated:** Most Bangladeshi pharmaceuticals are exported to less than fully regulated markets such as Bhutan, Pakistan, Sri Lanka, Nepal, Vietnam and Myanmar.^{xxxv}

Bangladesh's exports are growing rapidly, as shown in Table 1.

Table 1: Bangladesh's Pharmaceutical Exports in USD millions^{xxxvi}

	1975	1980	1985	1990	1995	2000	2002	2003	2004	2005	2006
Pharmaceutical Exports	0.37	0.15	0.04	0.12	2.74	5.61	6.6	9.05	12.69	21.26	27.54
Pharmaceutical Exports less Novartis/Sandoz [i]							4.09	6.03		10.37	14.74
Total Exports	382.6	749.3	934.4	1,524	3,428	5,752	5,986	6,548	7,603	8,652	10,514
Pharmaceutical exports as a % of total exports	0.1	0.02	0.01	0.01	0.08	0.1	0.11	0.14	0.17	0.25	0.26
Pharmaceutical exports growth rate (%)		-59	-73	200	2183	105	18	37	40	68	30

The majority of Bangladesh's pharmaceutical exports are from Novartis/Sandoz, as shown in Table 2. Novartis/Sandoz, an MNC operating in Bangladesh, has approximately 25 manufacturing sites globally. Bangladesh is one of its smaller sites. The Bangladeshi manufacturing site is an EU certified plant which produces about 500 million tablets a year and generates about \$35-\$40 million in sales. It has been growing rapidly—15-18%

per year—and is responsible for a significant portion of Bangladesh’s pharmaceutical export growth. It imports APIs, acquires packaging domestically, and manufactures final formulations in Bangladesh for export (\$12 million) or for sale to the domestic market (\$23-\$28 million).^{xxxvii}

Exporting a pharmaceutical product is challenging. Each country has its own product regulations, registration requirements, language requirements, cultural preferences, national packaging requirements, and industry protection mechanisms. Sales on the global market are quite competitive with firms from around the world vying for business. Furthermore, initiating exports requires a significant investment in money, time and paperwork to register the product in the target country. As generic products are branded in less regulated markets, pharmaceutical firms also need to make significant investments in sales and marketing to create product demand. All these investments are made without a guarantee of future sales.

Table 2: Recent Exports by Some Bangladeshi Pharmaceutical Firms^{xxxviii}

Company	Export (USD)	Year of Export
Novartis / Sandoz	12,820,162	2004-2005
Beximco Pharmaceuticals	1,400,000	2004
Square Pharmaceuticals	1,200,000	2004
Jams Pharmaceuticals	633,721	2000-2004
Jayson Pharmaceuticals	626,546	2004
The Acme Laboratory Co	600,000	2004
Eskayef Bangladesh	331,876	2004
Aristopharma	305,648	July 2004 – June 2005
Renata	281,788	2004
Navana Pharmaceuticals	240,175	Sept 2003 – June 2005
Aventis	223,999	2004
ACI	156,392	2004
Essential Drug Co	124,687	2004
Globe Pharmaceuticals	68,410	2005-2006
Opsonin Pharmaceuticals	34,109	2004

Most pharmaceutical firms are family owned. While many have the capacity to export, some do not have the in-house expertise.^{xxxix} As a result, approximately only sixteen firms export products. There are no “majority exporters,” e.g., companies that sell more than 50% of their output in export markets.^{xl} Beximco, for example, is one of the leading exporters. Its 2005 exports were \$1.3 million or 2.7% of total sales.^{xli} (see profile in Box 1). However, many companies initiated the process of product registration in international markets only in the last two to three years.^{xlii} The export situation is evolving. For example, Square Pharmaceuticals increased exports by 34% from 2004-05 to 2005-06.

Box 1: Case Study Beximco

Beximco is one of Bangladesh's largest pharmaceutical exporters. It began exporting to Russia in 1992. Learning how to register products in foreign markets was a challenging experience for Beximco, but it proved profitable. Export profits were 37% higher than from domestic sales. After Russia, Beximco expanded to other markets.⁴⁵ It is currently registered to export to 23 countries: Botswana, Cambodia, Georgia, Ghana, Hong Kong (China), Kenya, Iran, Malaysia, Mozambique, Myanmar, Nepal, Pakistan, The Philippines, Russia, Somalia, Singapore, South Korea, Sri Lanka, Taiwan, Ukraine, Vietnam, and Yemen.⁴⁶ In the early 2000s, Beximco started to upgrade its facilities to obtain export certification to more regulated markets.

Bangladeshi firms that export are 9-10% more productive than non-exporting firms, according to a recent World Bank study. Some possible reasons for this advantage may be due to:

1. Technological lessons learned from foreign buyers.
2. Exporters improved their own technological capabilities to exploit profitable opportunities in export markets. For example, exporters need to adopt stringent technical standards to satisfy more sophisticated consumers, and/or they are under more pressure to fill orders in a timely fashion and to ensure product quality for export markets which are more competitive than domestic market.
3. Better firms self-selected to enter export markets rather than the effects of exporting necessarily improving the firms.

The pharmaceutical industry in Bangladesh has been aggressively investing in infrastructure. An analysis of capital stock growth rates reveal that firms over invested in the 1990s and then slowed their investments from 1999 to 2002. Over this period, increased capacity utilization rates imply that firms were more intensively using their existing machines instead of purchasing new ones.^{xliii} From 2002 onwards, firms invested approximately \$250 million—most likely to upgrade their facilities to obtain international export certifications. The top ten firms accounted for 70% of the investments.^{xliv}

Firms have several potential sources for new investment capital. In 2004, 35% of new pharmaceutical investment financing came from the sale of stock (twelve firms are listed in the stock exchanges in Dhaka and Chittagong); 33% came from domestic commercial banks; 14% was from the firm's own internally retained earnings; and 2.5% was from international commercial banks.^{xlv} Incepta, profiled in Box 2, has primarily used retained earnings for its impressive growth. The International Finance Corporation (IFC), the private sector arm of the World Bank, identified a "financing bottleneck" in mid-size, life-sciences companies to invest in innovation. The IFC has not as yet made an investment in the Bangladeshi pharmaceutical sector.^{xlvi}

Box 2: Case Study of Incepta

Incepta was founded in 1999. It wants to position itself as a research-based dosage form manufacturing firm with a global presence. It currently focuses on more technologically advanced products such as sustained-release tablets, quick mouth dissolving tablets, barrier-coated delayed-release tablets, etc. Incepta is interested in adding API production and reverse engineering capabilities to its business.

Incepta has grown rapidly. Within five years of its establishment, it became the third largest Bangladeshi pharmaceutical firm. By 2004, Incepta's turnover stood at 1.2 billion Taka and a product portfolio of 125 brands and almost 1,500 employees. A young and entrepreneurial management team, which gained its experience in international, regulated markets such as Europe and the United States, is credited with much of its success. To fund this growth, Incepta did not use bank financing, except for a small amount during the first two years. The start-up team initially capitalized from family and friends and has funded expansion through annual earnings.⁵²

Bangladeshi pharmaceutical firms need to make significant investments to meet international manufacturing standards. Typical capital improvements to raise existing Bangladeshi pharmaceutical facilities to international standards include the following:

- **Heating, ventilation and air-conditioning (HVAC) systems to ensure no cross-contamination.** Most Bangladeshi firms use bag-filters (97% efficiency), whereas many international standards require hepa filters (98-99% efficiency). To install these, a facility would have to shut down for approximately six months.
- **Warehouse.** International standards dictate that warehouses must maintain the environmental standards stated on the product insert. If the insert indicates that the item must be stored "at less than 25 degrees Celsius," the warehouse must also maintain the required temperature. Bangladesh's warehouses are not air-conditioned and temperatures from May through July can reach 30 degrees Celsius, and higher.
- **Validation documentation.** While the Government of Bangladesh does not require validation documentation, international certifications demand extensive documentation of procedures. The cleaning validation is the most important and challenging validation to achieve. It documents equipment and factory cleaning procedures before changing the drug being produced on the production line to prevent any cross-contamination.

Building a new facility may be easier than attempting to upgrade an existing facility to meet GMP or other international standards. To build a new high-quality facility requires at least \$50 million, two years, and available land. In 2000, for example, Square Pharmaceuticals spent \$50 million on its new plant designed to meet UK certification, which they received in May 2007. (It took three years to complete the regulatory certification process.) To construct this plant, Square hired a British firm to design the plans, and then a 250-member team from Thailand worked onsite to interpret the plans and build the appropriate facilities. Skilled workers were imported because these skills

did not exist in Bangladesh. Building an equivalent plant would be much more expensive today due to the Taka's decreasing value.^{xlvii} Beximco recently invested \$65 million in a new plant to pass GMP and US certification, but it has yet to start the registration process.^{xlviii}

Partnerships with Global Firms

MNCs can operate in a country in multiple ways, including foreign direct investment (FDI), contract manufacturing, joint ventures and strategic partnerships or licensing. Each arrangement varies in terms of which partner contributes more resources and technical knowledge, which partner assumes more risk, and which partner accrues more benefits and profits.

Due to cost pressures, MNCs increasingly seek to manufacture pharmaceuticals in developing countries. Pharmaceutical contract manufacturing and research services is a large and growing business. Worldwide revenues totaled \$100 billion in 2004. With a predicted average annual growth rate of 10.8%, revenues are estimated to reach \$168 billion by 2009.^{xlix}

Contract manufacturing is a good business opportunity for Bangladeshi firms, and if well done, it can enable technology transfers to domestic firms. As a result, they can acquire world-class experience in finished dosage manufacturing, APIs or other aspects of pharmaceutical manufacturing. Square Pharmaceuticals, one of Bangladesh's largest pharmaceutical firms, attributes much of its success to what it learned by working with an MNC. Its experience is detailed in Box 3.

Box 3: Case Study of Square Pharmaceuticals

Square was founded by Chairman Samson Chowdhury and three friends in 1958. Today, Square is the largest Bangladeshi pharmaceutical firm with net revenues of 6.09 billion Taka (86.6 million USD) and profits of 1.17 billion Taka (16.6 million USD).⁵⁷ In 1974, Square entered into a third party licensing agreement with Jansen Pharmaceuticals (a subsidiary of Johnson & Johnson) to manufacture and sell five Jansen patented products in Bangladesh. Square was presented with a business opportunity that significantly changed it. With Jansen's name on the product as well as Square's, Jansen had a vested interest to ensure product quality. Jansen therefore trained the local staff and Square sent staff to Belgium for more training with Jansen. The collaboration also exposed Square to international standards of quality manufacturing. The relationship had a profound affect on Square's executives and how they approached business. Chairman Chowdhury attributes much of Square Pharmaceuticals' success to this initial licensing arrangement. The arrangement ended in 1982 with the new Drug Control Ordinance that prohibited this type of arrangement.⁵⁸

Bangladeshi pharmaceutical firms can make several types of contract manufacturing arrangements with MNCs, including:

- ***Contract manufacturing with the product intended for export to a regulated market.*** The current National Drug Policy (NDP) permits this. Contract manufacturing for export is a significant financial opportunity, but challenging. The domestic pharmaceutical firm must have a facility accredited by a regulated market. To date, Square Pharmaceuticals is the only such Bangladeshi firm with a qualified facility. It is currently initiating a contract manufacturing arrangement with a British firm.
- ***Contract manufacturing with the product intended for the domestic market.*** The Drug Control Ordinance (DCO) prohibits foreign firms from selling products in Bangladesh unless they have a manufacturing presence in the country. Thus, Bangladeshi firms can only contract manufacture for domestic distribution with MNCs that already have a presence in Bangladesh. An example of this arrangement is Beximco contract manufactures Ventolin (an inhaler) for GlaxoSmithKline.^{lii}

TRIPS and Bangladesh

The WTO and TRIPS

The WTO's Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) requires all signatories to legislate twenty-year patent protection for pharmaceutical products into their domestic law. TRIPS is not a uniform international law, but a framework for intellectual property protection with minimum agreed standards. While signatory countries must meet its requirements through legislation, TRIPS provides significant flexibility.

The following transition periods were established for TRIPS compliance:

1. **January 2000.** Developing countries with patent protection had to bring their patent law into compliance with TRIPS' standards (Article 65.2). Countries without patent protection had to create a "mailbox" to receive patent applications. During this period, the country would then receive the "mailbox application" for products previously patented in another country must grant exclusive marketing rights during this transitional period (Article 70.8 and 70.9). Thirteen countries notified the WTO that they were using this transition period. But a number of them implemented full TRIPS' patent protection before the 2005 deadline to do so. In 2003, six members were still using the transition period: Cuba, Egypt, India, Pakistan, Qatar and the United Arab Emirates.^{liii}
2. **January 2005.** As of this date, all WTO countries, except the 49 least-developed countries (LDCs), had to ensure that their national laws fully conformed to the TRIPS' provisions. If a pharmaceutical product was in the mailbox program, the country must continue to grant exclusive marketing rights to that product. Although January 2005 marked a landmark in intellectual property protection for the pharmaceutical industry, TRIPS' full effects will be phased in over time due to:
 - Natural product migration. As new patented drugs are developed, they will gradually tend to replace older generic drugs.
 - Countries processing their mailboxes. Although no official figures are available, Médecins Sans Frontières estimates that India received over 9,000 mailbox applications.^{liv} But to date, India has granted only one patent to Hoffman La Roche for its hepatitis C therapy, Peginterferon Alfa-2A.
 - "Grandfather clauses." India's Patent Act does provide protection for existing generic manufacturers in the form of "automatic compulsory licenses" or "prior use rights." Generic versions of patented medicine can continue to be manufactured in India provided that: (1) the generic manufacturer was producing and marketing the product prior to January 1, 2005; (2) the generic manufacturer made significant investment in the production and marketing for the product; and, (3) a reasonable royalty is paid to the patent holder.
3. **January 2016.** The 49 LDCs are not obligated to legislate patent rights for pharmaceutical products until 2016. (The United Nations defines a LDC based on

criteria of low-income, human resource weakness and economic vulnerability.) LDCs are not required to participate in the mailbox program or give exclusive marketing rights for any drugs during the period that patent protection is not provided. Therefore, until 2016, LDCs need not provide any patent protection, or they may choose to provide less patent protection than required by TRIPS or patent protection equal to or greater than TRIPS requires. Many LDCs have implemented full TRIPS patent protection or expanded TRIPS-plus patent protection in advance of the 2016 deadline (which may possibly be extended).

TRIPS significantly changed the international pharmaceutical world. Before the TRIPS negotiations began, more than 50 countries did not grant pharmaceutical product patent protection at all and some also excluded process patents.^{lv} In general, when countries are building their pharmaceutical industry, local firms benefit from a loose patent environment. Once the industry advances and local firms start producing innovative new drugs, the interests of the country's domestic firms are served by having patent protection in place.

Implementing TRIPS presents a challenge for many developing countries. They may lack the technical expertise required to implement TRIPS, or bilateral and other pressures may be imposed to prevent a country from using TRIPS' flexibility and the country may instead adopt TRIPS-plus standards. Other issues regarding TRIPS' implementation involve voluntary licensing by MNCs, which may sometimes provide an attractive alternative to pursuing a compulsory license, when existing conditions cause difficulty in regulating anti-competitive practices, abuse of intellectual property rights, and problems assessing pricing and patent status information. The US government spent \$1.5 billion to maintain its patent office in 2006,^{lvi} an enormous sum that few other countries can afford. Furthermore, much of the international assistance for TRIPS' implementation has been focused on enforcing patent-holders rights instead of assisting countries in taking advantage of the flexibilities TRIPS offers.^{lvii}

TRIPS' Implications for Bangladesh

Until 2016, TRIPS provides Bangladesh with domestic, patent-free production rights and limited exporting advantages. Bangladesh imports approximately 80% of its APIs for domestic production, 20-25% of which are patented. These API costs will most likely rise as TRIPS phases in.

Bangladesh enjoys some export advantages from TRIPS. But these advantages are somewhat offset by the pace and competitiveness of the Indian and Chinese generic markets. In both markets, companies can produce drugs at highly competitive pricing—even with higher costs associated with buying patented APIs or paying royalties. Bangladesh will have to rely on the standard business practices of producing the highest quality product at the lowest price to compete on the international market. Until 2016, however, Bangladesh has the following export advantages under TRIPS:

1. ***Export to any country if the drug is not under patent.*** Any firm in any country can benefit from this stipulation. For example, most drugs on WHO's Model List of Essential Drugs are not patented, as affordability is one of the criteria used in designating medicines as "essential."
2. ***Export to another LDC or non-WTO country that has not implemented product patent protection.*** It seems that most LDCs have instituted patent protection. Only two African LDCs have not provided for TRIPS-compliant intellectual property protection, one of which was not yet a WTO member, according to a 2001 Intellectual Property Rights (IPR) Commission study. In Asia, Myanmar, which is engaged in the WTO accession process, is perhaps the only country that has not yet put in place a patent protection regime.^{lviii} TRIPS' Article 65.5 states that any country using the transitional flexibility period shall not change its laws to result in a lesser degree of consistency with TRIPS. However, Bangladeshi firms are exporting generic versions of patented drugs to many LDCs without a problem.^{lix}
3. ***Export to a country where the patent holder has not filed for patent protection for the drug.*** Companies do not file drug patents in all countries, particularly where sales and profit prospects are low or there is no meaningful judicial patent protection. These gaps in patent coverage can be exploited.
4. ***Export to a country that has issued a compulsory drug license and awarded the production contract to Bangladesh.*** TRIPS' Article 31 grants governments the right to issue a compulsory license for public health purposes, which occurs when a government overrides a patent and grants another entity the right to produce the patented product. Although Canada, Japan, the United States and the United Kingdom have all issued domestic compulsory pharmaceutical licenses, very few developing countries have done so. The expense and time of litigation with developed countries can act as a deterrent. Governments must also balance fully exploiting TRIPS flexibilities while maintaining good relations with MNCs, which often use domestic firms for outsourcing or manufacturing.^{lx} Thailand, for example, is at the center of an international legal dispute for issuing a compulsory license in November 2006 for Merck's Efavirenz, an HIV/AIDS drug. The case is being closely watched around the world.^{lxi}

The December 6, 2005 WTO decision gives countries without adequate manufacturing capacity the right to import the drug for which it issues a compulsory license. Thirty-three countries have declared they will not use TRIPS flexibility to import and eleven countries announced they would use it only in a national emergency.^{lxii}

Before 2005, many countries could fulfill a compulsory license importation request because many were manufacturing patented drugs off patent. As of 2005, Bangladesh will be one of the few countries in the world where firms are legally producing newly patented drugs off patent whereas India and China, the world's largest suppliers of generic drugs, will no longer be able to engage in this practice for any drug patented

after 2005. Because firms require two to three years to reverse engineer and start producing a specific drug of quality, if any country issues an import request for a compulsory license for any drug patented after 2005, Bangladesh will have an advantage if it is already manufacturing the drug domestically. However, TRIPS has clearly stated that export for compulsory licensing is intended for health policy not industrial policy.

Bangladesh Patent Law

Bangladesh's patent law is based on the Patent and Designs Act of 1911 and the Patents and Designs Rules of 1933. The law grants both process and product patent rights for pharmaceutical products. The Patent Office has issued approximately 40 drug formula patents. It issues approximately 300 patents in total per year, 90% of which are held by MNCs.^{lxiii}

The patent law in Bangladesh is inconsistent with TRIPS in many ways, the most basic of which is Bangladesh is not required to enact patent legislation of any kind until 2016. The Department of Patent, Designs and Trademarks, within the Ministry of Industries, is preparing a Draft Patent Act since 2006. This draft law, written with the assistance of the World Intellectual Property Organization (WIPO), excludes pharmaceutical patents and includes the Bolar Provision^{lxiv} and parallel importation.^{lxv} The current 1911 law already provides a process for compulsory licenses but the option has never been used.^{lxvi} The current compulsory license legislation is extremely cumbersome; a verdict must be obtained from the appellate court, which is a challenge. UNDP's 2001 Human Development Report recommends a streamlined and procedural approach to compulsory licenses.

A recent Dutch study (we were provided with a draft copy) of Bangladeshi patent law concluded that the current draft law still needs work. The study also concluded that it is not likely to be passed by the current government in the foreseeable future. Thus, the study recommends implementing minor legislation declaring TRIPS to be applicable in Bangladesh.

Benchmarking the competitiveness of Bangladesh's pharmaceutical sector

The ability of Bangladeshi firms to compete on the global market is uncertain. Overall, Indian and Chinese companies are ahead of Bangladesh in such areas as technological and management skills, scale and backward and forward linkages. Box 4 highlights some lessons learned from India and China. More information on these two countries can be found in Appendix 3.

Box 4: Lessons Learned from India and China

1. Scale matters. When firms produce for a large population, they invest in scale manufacturing facilities which can produce drugs at a lower cost.
2. Backward integration into solvents and other starting materials has a significant impact on final cost.
3. Access to talent matters. India has strong ties with the US and Europe for training PhDs; whereas in China the government finances universities and R&D.
4. The government can set regulations to stimulate an industry to grow in a given direction.
5. Government intervention in the pharmaceutical sector can lead to private sector firms making desired changes.

Bangladesh's pharmaceutical industry will find it difficult to compete with China or India, but its successes will be product and niche dependent. Bangladeshi firms are unlikely to excel in petroleum-based pharmaceuticals because China has access to low-cost Siberian crude making it very cheap for them to manufacture these products.^{lxvii} Other products are heavily dependent on scale and have manufacturers already producing at scale.

A pharmaceutical sector's international competitiveness is determined by four factors: manufacturing costs, workforce, business environment, and market, as shown in

Figure 2. A preliminary analysis of these four quadrants indicates that Bangladeshi firms have obstacles to overcome to become globally competitive. Some manufacturing costs are less than world averages, but some are higher. The workforce significantly lags global averages and pharmaceuticals are a "brain-intensive industry." The government and regulatory environment do not appear to be conducive to producing the safest, most effective and accessible drugs. Some macro factors favor success while others are less decisive. This does not mean Bangladesh's pharmaceutical sector cannot be successful. Rather, it means that some factors are not working in its favor. To successfully proceed into the global marketplace, industry and government must plan strategically.

Figure 2: Pharmaceutical manufacturing cost driver

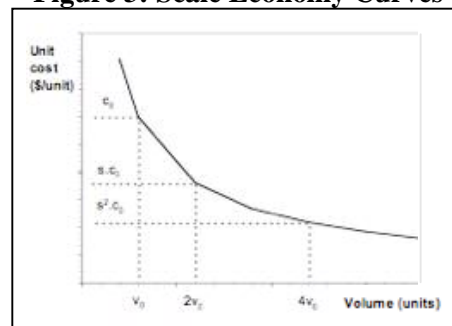
Manufacturing	Manufacturing Costs	Workforce skills	Cost
<p>A conclusive manufacturing analysis of costs, by a more in-examination of industry value chain supply and chains). To internationally, also have to and other trade potential quality differential requirements and impacts of patent protection in different countries. The analysis should also be product-specific and export market-specific. The main cost drivers of this analysis include:</p>	<ul style="list-style-type: none"> • Raw Materials • Labor • Transportation • Capital • Energy 	<ul style="list-style-type: none"> • Technical Manufacturing • Reverse Engineering • Quality Assurance • API Production • Innovative Research 	<p>analysis of costs requires an factory gate complemented depth the existing structure and its (including both distribution benchmark this the study would consider tariffs barriers, differences, packaging</p>
	<p>Government & Regulatory Environment</p> <ul style="list-style-type: none"> • Government Policy • Regulatory Institutions • Tax and Other Benefits • Tariffs and Other Barriers 	<p>Macro Factors</p> <ul style="list-style-type: none"> • Education Levels • GDP • Population Size • Manufacturing Competitiveness • Pharmaceutical Balance of Trade 	

requirements and impacts of patent protection in different countries. The analysis should also be product-specific and export market-specific. The main cost drivers of this analysis include:

1. **Cost of raw materials.** Globally, firms either purchase APIs on the domestic or global market or manufacture them in-house. Bangladesh does not have significant domestic API production capacity, so firms purchase most APIs on the global market. Factors that determine API prices include:
 - **Product differences.** APIs are sold on the global market, but are not quite a commodity. Firms' products vary in sales price and quality. Perceived product quality differences mean APIs cost more from a facility certified for a regulated market than from a facility without the certifications.
 - **Scale.** APIs are more scale-dependent than final formulations, so scale matters. Some very large Indian and Chinese firms are in the API business.
 - **Tariffs.** API tariff costs vary by country. In Bangladesh, tariffs vary from 0% for cardiovascular and life-saving products to 7.5% for vitamins. Thus, Indian and Chinese final formulation firms may have an advantage due to their own domestic API industry.
 - **Transportation.** Transportation both to the port of Dhaka and then to the manufacturing site impact price.

Domestic API production in Bangladesh is hampered by the following:

- ***Lack of production facilities.*** Initial plans exist to develop an API park which should greatly address the industry's infrastructure problem when completed. API production requires expensive water effluent treatment plants and other infrastructure that an API park could provide to firms as a common good. Some firms are still investigating building their own API facilities, mainly because of the slow progress toward establishing the park. Building a functioning API plant will take approximately 18 months after a site is approved.
 - ***Lack of scientific know-how.*** Skills to build and run an API plant would have to be imported because they currently do not exist in the country. In the time required to develop skills locally, firms can use consultants from India or China, for example. In addition, because India and China may be consolidating API production due to phasing in TRIPS, a surplus of these skills in the region may result.
 - ***Shipping and import costs for the raw solvent are currently too high.*** By operating within a network, the Indian pharmaceutical industry has a competitive advantage. All the support industries needed for manufacturing are located on-site in India whereas Bangladeshi firms pay for international transportation for solvents and, unless located at Chittagong, also pay for domestic transportation. Square Pharmaceuticals estimates that domestic transportation would increase raw solvent costs 5-6%, a significant cost in this low-margin, high-volume business.^{lxviii} Bangladesh needs to consider how to facilitate cheaper importation of raw solvents or create backward linkages and develop this industry as well.
2. ***Labor costs.*** Labor costs also drive efficiency. Formulation manufacturing costs in the United States are typically \$18,000 per million tablets while in India, they are only \$8,000 per million tablets. Cooney, at MIT, estimates that assuming equivalent scale in factories, labor accounts for approximately 60% of India's cost advantage, packaging for another 20%, and facilities and other costs are the final 20%.^{lxix} The Bangladesh Association of Pharmaceutical Industries (BAPI) estimates that Bangladesh's labor costs are approximately 20-30% lower than in India.^{lxx} This advantage is diminished, however, because Bangladeshi firms have to import some APIs and reverse engineering talent until these areas are more fully developed domestically.
3. ***Fixed costs of machines and factories.*** Four factors drive this cost.
- ***Scale:*** All manufacturing is dependent to one degree or another on scale. Figure 3 shows a generalized scale curve. If a Bangladeshi firm builds capacity at a scale that is too far to the left, for example, all the TRIPS patent exemptions may not be enough to counter its higher manufacturing costs. Square, one of the largest manufacturers in Bangladesh, currently has capacity for 2.1 million tablets per year from three facilities,^{lxxii} which is considered small- to mid-size. In comparison, a single tablet press in a major European or US manufacturing facility can produce 250,000 tablets an hour.^{lxxiii}

Figure 3: Scale Economy Curves

- *Plant construction costs:* In the developing world construction costs are lower. Indian plant construction costs are estimated to be less than 30% of US costs.^{lxxiv}
 - *Equipment cost:* Facilities targeting accreditation in a regulated market need equipment with full quality assurance (QA) functionality, which is usually procured from Europe. Facilities targeting less regulated markets can use less expensive equipment without such features.
 - *Land cost:* Land is very expensive in Bangladesh and difficult to procure. While land in rural areas is less expensive and easier to procure, fewer talented staff will want to live there.
4. **Power Costs.** Bangladesh's power costs are approximately 2 Taka per KWH for self-generation while government costs are 3.5 Taka per KWH in rural areas and 5.5 Taka per KWH in cities.^{lxxv} This is less than in India, but more than in China.
 5. **Tariff, taxes and other trade barriers.** When a country imports a pharmaceutical product from Bangladesh, it can apply a tariff and tax to the product. While tariffs and taxes directly increase the imported drug's price, other trade barriers can indirectly impact the price by creating artificial scarcity which can drive up prices. A WHO study of sixteen drugs in eighteen countries found an average tariff in the range of 4-10%.^{lxxvi}
 6. **Supply Chain Cost.** A significant portion of a drug's final cost is due to distribution, involving wholesalers, pharmacies, and other middlemen. This report assumes that when Bangladesh exports a drug, its supply chain cost in that country is the same as a domestic manufacturer's. This factor is therefore neutral in determining international competitiveness.

Square and Beximco represent 25% of the domestic market. Their costs in the areas discussed are shown in

Table 3. The table also indicates whether a cost is standardized globally or not, e.g., labor costs are not globally standardized, whereas equipment costs are more so.

Table 3: Square and Beximco expenditures

Factor	Square and Beximco Expenditures		Standard Cost Globally
	Absolute (Taka)	Percent of Revenue	
Cost of raw materials (APIs, excipients, packaging)	4.38B	46.63%	Mostly
Labor costs	743M	7.8%	No
Fixed costs of machines and factories ^{lxxviii}	379M	4.0%	Mostly
Power costs (including water, electricity, and gas)	92M	1.0%	No

Workforce Skills

Bangladesh has trained pharmacists for quality assurance and skilled engineers for reverse engineering and manufacturing. If Bangladesh wants to produce APIs, its workforce will need to acquire these skills as well. New research and innovation skills, while very important for innovative drugs, are not a realistic short-term goal as Bangladeshi pharmaceutical firms target mainly lower-end branded generics. However, if Bangladesh wants to develop capacities to manufacture innovative products in the long-term, it needs to start investing now. Bangladesh's current educational and institutional infrastructure to build such skills is weak.

- **University Enrollment.** Tertiary education levels are low, as shown in Table 4. The universities adequately train pharmacists for quality assurance and quality control activities, but they are not prepared to train students with the skills necessary for APIs. Laboratory facilities for biotechnology are inadequate to produce results required by industry.

Table 4: Gross Enrollment Ratios in Selected Countries^{lxxix}

Country	Bangladesh	India	China	Global Average
Secondary	51.3%	53.5%	72.5%	61.4%
Tertiary	6.5%	11.8%	19.1%	18.6%

- **Industry Investment.** The pharmaceutical industry in Bangladesh currently invests about 1% in R&D—about the same as the agro-processing and textile firms invest in Bangladesh. This is a low percentage for pharmaceutical R&D.^{lxxx}
- **Government Participation.** University and government research is currently underfunded. The government allots 12 crore Taka (US\$1.73 million) for public sector research.^{lxxxi}

Government and Regulatory Environment

The pharmaceutical sector is at the intersection of health and industrial policy. Careful consideration is necessary to balance potential tensions between the two sectors. For health policy, the government wants to ensure a predictable supply of high-quality, low-cost medicines. For industrial policy, the government wants to build a thriving domestic pharmaceutical industry. Historically, Bangladesh's drug policy has probably succeeded more clearly as industrial policy than as health policy.^{lxxxii} [Historically, Bangladesh's drug policy has tended to support the country's industry rather than the health.

There are five mechanisms in place to regulate the quality of Bangladeshi drugs: drug legislation, the Drug Directorate Administration (DDA), the drug testing laboratories (DTL), bioequivalence laboratories and manufacturing certifications.

Drug Legislation

Bangladesh's domestic market is highly protected and virtually all imports are effectively blocked (only 5% of the drugs sold in the country are imports). With an average gross profit margin of 18%,^{lxxxiii} the domestic industry is succeeding in the protected and under-regulated market. However, a recent World Bank study found that the Bangladesh pharmaceutical industry inefficiently allocates resources to less productive firms which have a higher share of total industry output than expected. The study hypothesized that this inefficiency is due to two factors. The first factor is related to the lack of competition, especially import competition. Unproductive firms have been shielded from competition in Bangladesh and remain in business. For efficiency purposes, the industry would be better off selling those firms' assets and reallocating their market share to more productive firms. The second factor involves Bangladesh's bankruptcy rules and a lack of markets for used capital, which prevents the exit of less productive firms.^{lxxxiv}

The Drugs Act of 1940 and the Drug Control Ordinance (DCO) of 1982 (updated in 2005) regulate the process of registration, manufacture, distribution, sale, import and export of drugs in Bangladesh. In 1982, the Government of Bangladesh released the radical and far-reaching DCO, which is based on the country's self-reliance. This policy, while causing much international concern, was symbolic to Bangladeshis. Nationalist sentiment attached to this policy remains. The DCO included:

1. **Import restrictions.** The 1982 DCO states, "No drug shall...be manufactured in Bangladesh under license granted by a foreign company having no manufacturing plant in Bangladesh if such drug or its substitute is produced in Bangladesh." Due to the relative small size of the market and the trend toward large centralized manufacturing facilities with excellent logistics, few MNCs want to invest in production in Bangladesh. Thus, the law blocked many imports. This resulted in local companies increasing their share of production from 35% in 1970 to 67% by 1998. The domestic pharmaceutical industry grew at 14% per year from 1981-1986. These economic benefits created an important source of political support for the government.
2. **Limited drugs.** The policy banned approximately 1,700 drugs that were deemed harmful or non-essential.

3. **Price controls.** The government implemented price controls to stop transfer pricing, which resulted in a price drop of up to 40 times for some drugs.^{lxxxv}

On March 5, 1994, the new government released circular number 18/93/2364. Item two on the circular states: “The drugs and medicines that are locally manufactured in adequate numbers will not be imported.” The circular mentions “adequate quantity” but does not qualify that domestically manufactured drugs should have “adequate quality.” Because this circular is an executive order of the Ministry of Health and not an ordinance or a law, its legal ramifications and whether drugs can be imported are unclear. Apparently, firms can import a drug if the Ministry of Health gives it a “no objection certification” (NOC).^{lxxxvi} Three organizations, UNICEF, ICDDR, and GSK tried to import drugs but were unsuccessful. Each was told the requested drugs were already manufactured in sufficient quantity in Bangladesh. Other organizations did succeed. Médecins Sans Frontières (MSF), under the Prime Minister office’s NGO Affairs Bureau, has an exemption for humanitarian action and can import drugs.^{lxxxvii} And Abbott Pharmaceuticals, an MNC, apparently imports Klaricid even though Square and Beximco manufacture it.^{lxxxviii}

On April 18, 2005, the Government of Bangladesh updated the National Drug Policy (NDP). The amended NDP states, “Another main objective of the NDP is to ensure self-sufficiency in all types of drugs. Therefore, all necessary measures should be undertaken to ensure that the current trend of increased rate of local production of drugs is sustained and further improved.” The new National Drug Policy also allows both domestic and foreign companies with manufacturing capacity in Bangladesh to contract manufacture with domestic firms. Firms may also manufacture drugs for export that meet the importing country’s standards and not Bangladesh’s standards.

Drug Directorate Administration

The Drug Directorate Administration (DDA) has been charged with ensuring the safety, efficacy, and quality of drugs in Bangladesh, as well as the relevance and accuracy of product information.^{lxxxix} While extensive rules for regulating the market exist on paper, the market remains, in essence, a significantly under-regulated market due to poor governance, vested interests, the power of the pharmaceutical industry, and the weakness of the regulating authorities.

The DDA is significantly under-resourced. It has 44 inspectors, 16 located in Dhaka and approximately one per district (30 districts). The inspectors on average inspect manufacturing facilities for license renewal once every two years.^{xc} Some firms consider that visit as nothing more than a courtesy visit. The DDA has only one government car. Inspectors are required therefore to take a bus or have the pharmaceutical firm they are inspecting provide a ride. The DDA staff is also under-trained. Local inspectors shadow international inspectors doing site visits to learn from them. WHO has held numerous training sessions but this provides insufficient training for the local inspectors.

The DDA has a budget of 90 million Taka (approximately \$1.3 million). One-third is allocated by the government and the remainder is from registration fees. The DDA has requested an upgrade from directorate to directorate-general status, which would result in an increased budget allocation. The government is considering the request. The current drug registration fee in Bangladesh is approximately \$100 per drug. The DDA requested an increase in the drug regulation fee to 100,000 Taka (\$1,450), but the ministry did not approve this request.^{xci}

The DDA is also reputed to have corruption and low morale issues. Because of a lack of accountability, drug inspectors suffer no consequence for not taking action. Without significant restructuring of the DDA, further resource allocation to the agency will likely result in uncertain improvements in the quality of its services.

Drug Testing Laboratories

Drug testing is the most expensive tool in the drug regulatory process, but the only means to verify if a product is counterfeit or substandard. There are two drug-testing laboratories in Bangladesh, each reporting to different parts of the government. The one in Dhaka reports to the Director of Public Health in the Ministry of Health. The other in Chittagong reports to the DDA. Although the Dhaka laboratory has the status of directorate general, both laboratories are significantly under-resourced. The difference between public and private laboratories is stark. Public laboratories lack an air control system, proper equipment, machines or reagents, and staffing is inadequate and suffers from lack of training, proper clothing and sanitation equipment. Laboratories vary from being merely under-resourced to being under-resourced and using available resources inefficiently.

The Dhaka laboratory has no legal capability to independently collect samples from manufacturers. It receives drug samples from DDA inspectors, police raids, and other groups.^{xcii} If a drug fails its tests, the laboratory reports to the DDA and has no further follow up. The laboratory does compile statistics on quality trends but has no knowledge of the reasons why a drug passes or fails, since it is not involved in sample collection. It is unaware, for example, why 22% of the drugs tested in 2005 failed compared to a historical average of 1%. The laboratories suspect that due to corruption they do not receive random drug samples drugs. Random sampling is crucial to overall testing quality.

Bioequivalence Laboratories

Bioequivalence laboratories test the availability of the drug in the blood. They determine drug absorption and elimination rates, and other in vivo effects. For a generic final formulation to be approved for import into a regulated market—and some moderately regulated markets such as Tanzania and Malaysia—the drug needs to be tested for bioequivalence. Bangladesh has no bioequivalence laboratory capabilities. Bangladeshi firms that want to export their products send drug samples to an internationally

recognized bioequivalence laboratory abroad [for testing? yes] at a cost of \$30,000-\$60,000 per drug.^{xciii}

Manufacturing Certification

Firms focus on ensuring quality manufacturing procedures and environment because testing each and every final product off the line could destroy or compromise it. There are several different manufacturing quality standards to which firms can adhere:

1. **World Health Organization (WHO).** The WHO promotes Good Manufacturing Practices (GMP) or Current Good Manufacturing Practices (cGMP) and produces the standards for these. Organizations such as UNICEF or governments then use these standards to certify a facility. WHO has no capacity to carry out itself the actual inspections. Thus, although many organizations are using the same WHO standards, there may be great differences amongst various inspecting agencies. A GMP certificate will be provided to a facility for a certain product if it meets standards for base materials, premises, equipment, processes, documentation, training, and personal staff hygiene. These standards are quite general; their implementation determines their actual stringency. Bangladeshi firms can be certified in two ways: (1) by the Government of Bangladesh through the DDA and (2) by international organizations, such as UNICEF. UNICEF requires GMP certification to pre-qualify a firm to sell products to UNICEF. However, local DDA inspectors are hampered by lack of training and political pressures and are therefore not as stringent as international inspectors, as demonstrated by the record. While the DDA certified 95% of the firms it inspected,^{xciv} UNICEF has globally passed 63% in the past four years.^{xcv} The DDA has currently certified 30 facilities for export.^{xcvi} In Bangladesh, UNICEF has fully GMP certified four companies and partially certified two (i.e., not all their facilities or products are certified).^{xcvii}
2. **United States.** The US Food and Drug Administration (USFDA) must approve a drug before it can be imported. USFDA approval is a valuable indicator of quality for companies seeking access to other markets. Its certification process is more rigorous than the WHO's GMP standards. To achieve USFDA approval, both API and final generic drug producers send samples to the USFDA for chemical analysis. They also undergo a full-scale plant, process, and production inspection based on the USFDA's version of GMP standards which differ from the WHO's. Generic drug producers must also have their product tested for bioequivalence. Successful applicants receive two types of approval: product approval (based on data submitted) and market approval (based on patent clearance from the USFDA's Orange Book).^{xcviii} This process can take several months and costs between \$150,000 and \$300,000. The USFDA averages 350-400 foreign inspections globally per year.^{xcix}
3. **Europe.** Because of European Union agreements (EU-15), certification in one country will grant a company access to all countries. The UK's Medicines and Healthcare Products Regulatory Agency (UKMHRA) approval process is similar to the USFDA's. It certifies facilities to permit product access to the UK market.

UKMHRA certification is also a useful indicator of quality in other markets. The UKMHRA charges firms for inspections.

4. **Australia.** The Therapeutic Goods Administration (TGA) is Australia's regulatory body. TGA adopts European standards unless a unique Australian standard is necessary. TGA approval is a global indicator of quality. It also charges firms for inspections.

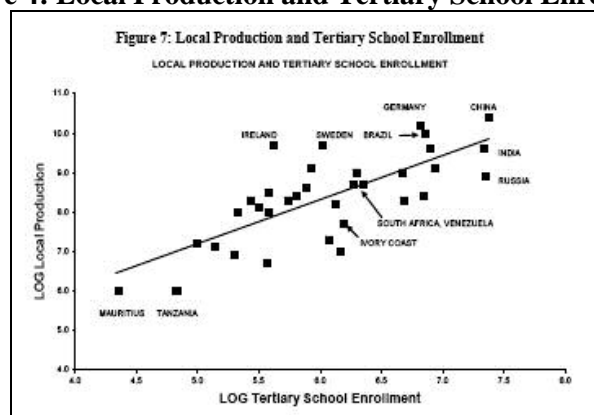
Macro Factors

The World Bank's global study on pharmaceutical production in the developing world concluded that local production of medicines is often not feasible due to a number of reasons including: realities of global trade, international economics of the pharmaceutical industry, national governments' need to balance industrial and health policy, and the business environment in many developing countries is not conducive to a successful domestic pharmaceutical industry. Furthermore, the study concluded that local production is often not reliable, and even when reliable, the cost of medicine for the end user are not necessarily reduced.^c

The study also correlated the strength of a local industry with independent variables to determine the factors that enable a country to have a viable domestic industry. This study (the entire study was exploratory) was exploratory research rather than an evidence-based examination of the issue. The resulting criteria listed below therefore represent statistical trends more than conclusive findings.^{ci}

1. **Sufficient percentage of the population enrolled in secondary and tertiary education.** The pharmaceutical industry requires a highly skilled employee base. The percent of the population in tertiary education is significantly correlated to local production of pharmaceuticals, but there are still some outliers, as shown in Figure 4. As previously discussed, Bangladesh's tertiary enrollment levels significantly lag Indian, Chinese, and global levels.

Figure 4: Local Production and Tertiary School Enrollment



2. **Gross Domestic Product (GDP) greater than about \$100 billion.** Countries with greater than \$5 billion dollars of pharmaceutical production (Sweden, Ireland, Korea,

Russian Federation, India, Brazil, Germany, and China) all have GDPs between \$100 billion and \$1 trillion. This data represent trends and not exclusive criteria, and there are exceptions. Cuba and Jordan, for example, both manage to maintain a viable pharmaceutical industry without the hypothesized required size.^{cii} The current GDP of Bangladesh is \$69.02 billion.^{ciii}

3. ***A population greater than about 100 million.*** Because the pharmaceutical industry is technology driven not labor driven, viable markets require large populations only to consume locally produced pharmaceuticals.^{civ} However, some Eastern European countries, with populations significantly less than 100 million, do have viable pharmaceutical industries. The current population of Bangladesh is 147 million.^{cv}
4. ***A UNIDO competitiveness index greater than about 0.15.*** In 2003, UNIDO released a competitive industrial performance index based on manufacturing value added (MVA) per capita, manufactured exports per capita, share of medium- and hi-tech activities in MVA, and share of medium- and hi-tech products in manufactured exports. Generally, as a country moves “upwards” on the competitiveness index scale, local production of pharmaceuticals increases. Bangladesh’s 1998 score was 0.011, India’s 0.054, and China’s 0.126.^{cvi}
5. ***A net positive pharmaceutical balance of trade.*** Countries with a positive pharmaceutical trade balance are more likely to have sustainable local production above \$1 billion. While no one country is completely self-sufficient in pharmaceutical drug production, some countries such as India, China, and Brazil are net exporters of medicines.^{cvii} Even though domestic firms generate 95% of domestic pharmaceutical sales, Bangladesh is currently a net pharmaceutical importer, importing an estimated \$100-\$110 million APIs^{cviii} and exporting \$27 million finished product. As more and more firms export, these figures will change.

Potential Approaches to Improving Quality of Pharmaceuticals in Bangladesh

Many developing countries face similar challenges to improve their domestic pharmaceutical quality. Five potential mechanisms to address these challenge are discussed below. These mechanisms are not exclusive of each other and some countries have used a combination of them.

1. ***Export-led quality improvement.*** Some countries focus on building the export industry and then take advantage of the high quality of exports to influence domestic drug quality. While a connection exists between the export market and domestic markets, firms tend to segment their production for different markets with higher quality drugs headed to export markets and lower quality drugs remaining in the less regulated domestic market. Higher quality drugs can often be too expensive to compete effectively in the cost-sensitive, less regulated markets. However, some trickle-down effects occur when management and production know-how is shared by a company targeting both markets. India, for example, views the pharmaceutical market from an industrial rather than a health policy viewpoint. Competition in the export market pushed Indian firms to become world leaders in high-quality, low-cost drugs. However, the quality of domestic medicines still varies significantly because firms segment production.
2. ***Regulatory-led quality improvements.*** Some countries take a strict regulatory approach to improving quality. Such an environment does result in higher drug quality, but also requires significant political will to enforce and does not motivate firms to improve cost competitiveness (in fact it may raise costs). Some examples of these mechanism include:
 - Throughout the 1990s, Nigeria was plagued with counterfeit drugs. In 2001, the WHO estimated that up to 50% of drugs in the country's hospitals and pharmacies were counterfeit or substandard.^{cx} Amidst a groundswell of public outrage over deaths and poor health outcomes due to counterfeit drugs, Professor Dora Akunyili became the Director of Nigeria's National Agency for Food, Drug Administration and Control (Nafdac). She clamped down on corruption, conducted nearly 800 raids on drug-distribution outlets, and held public awareness campaigns. The results were impressive—the level of counterfeit drugs in Nigeria dropped by 80%. Her one-woman war to rid Nigeria of substandard drugs was not without costs. Some economic contraction resulted as entire markets were shut down to pursue disreputable firms,^{cx} and \$16 million in counterfeit drugs were confiscated and destroyed.^{cx} Nigeria succeeded in its efforts to reduce counterfeits because its domestic drug quality had become so poor that enormous popular support backed the crack down.
 - In the 1990s, China wanted its firms to have GMP certification, but many firms resisted due to the costs. As of July 1, 2004, the Chinese government required all firms to use GMP standards to manufacture pharmaceuticals. The government stops production or even closes non-compliant facilities. The Chinese drug

regulatory agency established a weekly monitoring system for those firms compulsorily shut down. Although still plagued by many problems, this policy and its rigorous enforcement sped up GMP adoption. In 1998, there were only 70 GMP approved firms. By June 30, 2004, there were 3,200.^{cxii}

3. ***Competition-led improvement.*** In today's highly dynamic global markets, with much reduced protection levels, competition is increasingly shaped by firm-level, cost-competitiveness advantages. Firms operating in economies with liberal trade policies and greater openness show stronger economic growth and overall development performance in the long run. Import restrictions are globally associated with higher domestic prices and lower quality products for the local population. Firms rarely become world leaders from a protected market. Efforts to open the economy and increase competition could lead to cost reduction and quality improvement.
4. ***Private sector-led improvement.*** The private sector has often played a role in maintaining and monitoring quality. There are generally two types of private-sector initiatives: industry-backed (e.g., fair-trade coffee and sustainably harvested seafood) and NGO-backed (e.g., the Rugmark Foundation, which label rugs made without child labor). Research on private-sector initiatives for self-regulation shows that success depends on four factors: the design of the codes, who adopts them, whether and how compliance is monitored, and whether the rules actually achieve what they purport to achieve. Little evidence exists to show that these types of programs have led to significant improvements. And although codes are an important start, without third-party verification, a company's position may deteriorate if found to be non-compliant.^{cxiii}
5. ***Knowledge transfer-led improvement.*** Most firms in Bangladesh want to provide the highest quality drugs possible. They are hindered by either lack of capital or knowledge. Given access to knowledge and opportunities to improve, most firms will take them. There are two benchmarks for which firms should strive:
 - WHO's GMP certification. Some firms in Bangladesh are operating at a sub-GMP standard. The government and donors could work with these firms to raise them to this minimum level.
 - International certification. To bridge this gap, the best mechanism is to work with world experts in the global industry. The best way to motivate MNC staff to work with a Bangladeshi firm to improve its quality is through some form of joint venture, licensing agreement, or contract manufacturing situation.

Conclusions and Next Steps

The following is a list of several potential next steps for the Bangladeshi pharmaceutical sector to improve both the drug quality and industry's competitiveness in the global economy. These steps are organized around three areas: the domestic market, the export market, and TRIPS.

Improving Price and Quality on the Domestic Market

1. ***Increase competition.*** Bangladeshi pharmaceutical firms are operating in a domestically protected environment. They should excel in price and quality of products produced, not as a result of import restrictions. Whether Bangladeshi firms lag behind global standards for competitiveness is beyond the scope of this study. But if this were shown to be the case, the domestic protection of the market would be damaging the Bangladeshis' health by providing them with lower quality drugs than the global standard. If the government determines that the domestic pharmaceutical market should be opened to global competition, the only remaining question would be how to do so. The 1982 DCO, which resulted in the protection of the Bangladesh market, is supported by significant national sentiments. Considerable political tact would be required to modify or alter it. Before opening the market, however, the drug regulatory institutions need to be strengthened to prevent dumping of low-quality products from abroad. Issues of safety nets and transition costs also need to be addressed to ensure that increased competition from global providers does not destroy the domestic industry without giving it a fair chance to compete. Clearly, increased domestic competition would cause difficulties for some pharmaceutical manufacturers, especially those with lower quality / higher prices, and open markets would be resisted. But competition will also improve the overall cost and quality of drugs available in the domestic market, the overall competitiveness of the domestic industry, and the overall competitiveness of exporting firms.
2. ***Improve the government's regulatory function.*** Strict regulatory environments are associated with higher quality drugs. The Government of Bangladesh should investigate the financing and structure of the institutions used to regulate drugs in Bangladesh.
 - ***Financing.*** Resources for the DDA and DTL institutions need to be significantly increased to support the responsibilities required of them. Small incremental increases are insufficient for the task. Options to increase their resources include:
 - ***Increased regular budget.*** The DDA requested an upgrade from a directorate to a directorate-general, which would result in a corresponding increase in resources. The government is considering this request.
 - ***Increased fee revenue.*** The self-financing of drug regulatory agencies through higher fees used to exist only among industrialized countries such as France, Sweden, the United Kingdom, and United States. Many countries are now following their example, such as Zimbabwe's autonomous Drug Control

Council (DCC), which is entirely self-sustaining. For testing, DCC charges \$300 for imported drugs and less for drugs repacked or manufactured in Zimbabwe. As a result of its self-sufficiency, the DCC acts as an independent agency, although the Ministry of Health still appoints DCC staff.^{cxiv}

- **Donations.** International organizations and financing institutions or bilaterals could fill the gap through donations to the regulator agencies. The WHO, for example, has supported and trained regulatory institutions.
 - **Collaboration with the domestic pharmaceutical industry.** The domestic pharmaceutical industry has a vested interest in better quality drugs, is proactive, and willing to pay for improvements. However, the pharmaceutical industry is also reputed to have significant influence over the DDA. The government has hesitated to give industry more control because the government would like to maintain control over the regulatory function.
- **Structure.** The current regulatory system is not delivering adequate services, considering the amount of resources the institutions do have. Staff morale, accountability, transparency and quality of services delivered are all low. Corruption is allegedly rampant. Further investigation into the regulatory processes and agencies is necessary to determine how best to improve them. Some areas to consider are as follows:
 - **Reviewing regulatory procedures and incentives.** Institutional measures should be investigated to increase transparency and provide inspectors with incentives to find, report, and fine low-quality manufacturers. Of the 235 registered pharmaceutical firms, approximately only 85 are active. Most problems are reportedly with the smaller, less active firms. The criteria to approve an operating license and the monitoring to continue the license should be investigated.
 - **A reorganization of the regulatory authority.** Many governments have satisfactorily appointed a semi-autonomous regulatory authority. The authority's independence promotes a professional discharge of responsibilities.
 - **Cracking down on corruption.** The current government is targeting corruption and drug safety. Improving the drug inspection process is an important issue for the population's health. In the interim, international inspectors could train staff and complete inspections for a limited time period.
 - **Making strategic personnel choices.** The DDA's director should be selected transparently based on technical skills and proven managerial abilities.
 - **Increasing public involvement.** Public awareness campaigns have been very successful in improving drug quality in many countries. Bangladesh could investigate the possibility of undertaking such a campaign combined with providing consumers with a toll-free number to report bad drugs. The government would have to commit to responding to the public and taking action if such an initiative were enacted.
3. **Level the playing field.** Firms that make investments in quality are in a sense penalized as long as firms that produce substandard drugs are allowed to sell their

drugs on the marketplace, and the consumer is unable to differentiate between the drugs before purchasing them. Box 5 describes Medicines Transparency Alliance (MeTa), which is working with countries to address issues of transparency and accountability.

Box 5: Medicines Transparency Alliance (MeTA)

MeTA is a global alliance launched in mid-2007. It will work through national and international partners (including the World Bank, DFID, the World Health Organization, and Health Action International) to support national efforts to enhance transparency and build capacity in medicines policy, procurement and supply chain management. This initiative involves explicit commitments from international actors to support national efforts, coupled with focused technical and financial support to strengthen transparency and accountability. Such national efforts would seek to improve access to information about medicine quality and availability and pricing, with strong civil society and consumer involvement in scrutiny and debate.

The Government of Bangladesh could address this issue through a variety of mechanisms:

- *Regulatory Approach.* Use the regulatory function to remove low-quality drugs.
- *Transparency Approach.* Knowledge is power and if consumers and doctors knew which drugs were better, they would migrate to quality. If, for example, all the producers of one drug each month were tested and the results released to the public, this would increase drug quality transparency. The 2005 Drug Law already sets up a provision for such a measure by stating, "...any information on substandard, spurious, and counterfeit drugs should be made freely available to all concerns by wide publicity in both print and electronic media."^{cxv} A sample testing program would have to be designed to be as impervious to corruption as possible.

4. ***Involving the private sector in quality control.*** As a "police function," the regulation of an industry has traditionally remained a government function. While efforts to enhance enforcement (the stick) should be made, the industry may have incentives to have better regulation (the carrot). Because government regulatory agencies lack capacity and the pharmaceutical sector has a sincere interest in improving quality, mechanisms to include the private sector in some sort of quality control mechanisms should be explored. However, a duplicate system should not be created nor a system as susceptible to corruption as the current system. Further analysis is needed of private sector examples from other countries and an examination of the success rates of its involvement in quality improvement programs. BAPI would be interested in the following types of private sector involvement:

- BAPI-organized "peer reviews" to expose bad quality producers.
- A government-approved independent private testing laboratory to provide drug monitoring and quality services. BAPI proposed that this institution's board could include representatives from BAPI, international organizations, academics, NGOs, and the government. Initial investment could come from donations, but operation expenses could be covered through per-product charges.

5. **Work with firms to improve quality.** Some firms in Bangladesh operate at a sub-WHO, GMP standard. For them, simple inexpensive changes will improve quality. Achieving USFDA standards is not necessary to improve quality domestically.

Improving price and quality on the export market

Several possible mechanisms are available to raise the international competitiveness of Bangladesh firms, including:

1. **Encourage contract manufacturing.** As production of both patented and non-patented drugs moves to low-cost manufacturing areas, Bangladesh firms could build export experience in finished dosage manufacturing through contract manufacturing with foreign firms. Contract manufacturing is a good business opportunity, and if done well, it can also enable technology transfers to domestic firms.
2. **Technical Assistance.** One barrier to exporting that many firms face is a lack of knowledge. The government and the international community can help to bridge this information gap. Government training, however, can be slow and bureaucratic, and it often requires training itself. Other potential trainings could involve international organizations, exchanges with China and India and other mechanisms. Bangladeshi firms want information on the following specific topics.
 - *Inspections and GMP certification.* Both the government and firms need training in the necessary requirements to pass inspections, including what is required for the HVAC system, how the inspection process works, and what needs to be done to pass inspection.
 - *How to export products?* Firms want information on how to get USFDA, UKMHRA, or TGA approval, the regulation requirements of other countries, and how to manage the approval process. Also, firms need training in international marketing, sales and negotiations.
 - *Investment and Strategy.* Mid- and small-level firms need training and assistance on manufacturing and selecting products, investments, and export markets. Not all pharmaceutical production is the same. Some therapeutic areas are more niche; whereas others depend more on low-cost bulk APIs. All markets are not the same either. Markets vary in levels of regulation, product sophistication, drug quality on the market, and the size of market potential. Bangladeshi pharmaceutical firms need to analyze which markets would provide the maximum competitive advantage based on their current capabilities and cost structures.
 - *TRIPS.* How can TRIPS help them?
3. **Government support for firms that export.** Box 6 and 7 include examples of how the Governments of China and India support their domestic pharmaceutical industries. Although the market, and not government subsidies, should drive competitiveness for Bangladeshi firms, current government support levels should be analyzed to determine if they put Bangladeshi firms at a disadvantage vis-à-vis firms from India and China.

4. **Investigation into the feasibility of a bioequivalence laboratory.** In order to export a drug to a regulated market and to some moderately regulated markets, Bangladeshi products must undergo bioequivalence testing. No bioequivalence laboratories exist in Bangladesh currently. Additional analysis of laboratory construction and operational costs is required to determine if a domestic laboratory could offer financially comparable services. Furthermore, if this laboratory's purpose is for international approval and recognition, analysis is necessary to ascertain whether the international community would accept results from a bioequivalence laboratory located in Bangladesh, where corruption is rampant. If analysis supports a local laboratory, regional or private-sector alternatives should be considered as well, because a bioequivalence laboratory requires a significant investment.

5. **Investigation of API production.** Because API production requires scale economies, Bangladesh will find it difficult to compete internationally. Nevertheless, Bangladeshi pharmaceutical firms may need to acquire API skills if they are going to effectively compete in the global market for final formulations as API costs are a major determinant of final cost and profit. Further analysis is needed to determine which APIs Bangladesh could produce on a scale relevant to the Bangladesh environment and still be price competitive. If Bangladesh succeeds in API production at all, most likely only a few companies will be able to reach the necessary scale. The following areas should be fully supported if API production is pursued.
 - **The API park.** The government has promised the construction of an API park for many years, but little action has been taken. The potential value of the park declines each day that its creation is not realized and the TRIPS' 2016 deadline nears. Prioritizing the API park and starting construction is vital if Bangladesh chooses to manufacture APIs.
 - **API skill.** Skills in reverse engineering and chemical synthesis should begin to be locally developed in collaboration with local universities and other countries.
 - **Backward integration.** To develop the entire supply chain for pharmaceuticals, backward integration from the raw solvents should be considered.

Taking advantage of TRIPS

The TRIPS exemptions offer potential opportunities for increasing exports, but these are limited, time-bound, must be undertaken in a very competitive environment, and need significant investments by both government and industry over a short period of time. Investing in exports does involve risk. Bangladesh has some of the underlying macroeconomic factors associated with pharmaceutical manufacturing success but not all. And, recouping any required upfront investments is limited to only a ten-year payback timeframe unless TRIPS is extended or the investment is structured to be successful post-TRIPS. Bangladesh therefore needs to strategically consider how to approach the advantages of TRIPS and should use this short-term period of opportunity to do the following:

Capitalize on any potential advantages now. Time is running out and manufacturers need to identify and take advantage of opportunities now.

Strategically choose which opportunities to pursue. Given the global cost structure of the industry and the advantages accrued to players with scale or niche skills, Bangladesh's opportunities may be narrowly focused on a few products and most likely finished products. Further analysis is needed to identify which products and partnerships it should focus on. This analysis should also include a "break-even point" below which investment in the industry is not deemed beneficial. In other words, if the investment return is inadequate before 2016 and cannot position the industry for long-term success post-2016 to justify its costs, then the investment should not be made.

Use this short-term opportunity to build long-term successful businesses. Investments made in quality manufacturing and forming partnerships should not be made for short-term benefits alone. Rather, they should be strategically chosen with post-2016 in mind, when Bangladesh will have to compete on the international marketplace.

Update the patent law. The current patent law was written in 1911 and needs to be updated to reflect flexibilities afforded Bangladesh under TRIPS. Changes need to be made regarding product and patent law legislation, parallel importation, and Bolar exceptions. In addition, the current compulsory license legislation is extremely cumbersome. The government should immediately pass legislation in this area. Institutional capacity to handle patent issues is also lacking. The Patent Office needs capacity building and training.

Box 6: China

China is a world leader for the pharmaceutical industry. In 2004, chemical drug manufacturing sales were \$24.27 billion and profits were \$1.9 billion.^{cxvi} China entered the pharmaceutical market with excipient manufacturing, moved into APIs five to seven years ago, then into final formulations, and most recently into innovative research. Today, China is the world's largest producer of APIs with \$4.4 billion in sales in 2005, much of it from exports.^{cxvii}

China's pharmaceutical industry is still considerably fragmented but consolidating. In 1996, there were 5,396 Chinese pharmaceutical firms. After the government initiated several efforts to increase industry concentration, the number of firms in 2002 was reduced to approximately 3,681 firms, which is still considered fragmented. China's top ten firms generated 15.48% of the industry's revenue in 2003.

By the end of 2003, 52 Chinese pharmaceutical ingredients firms passed FDA authentication.^{cxviii}

China founded its patent office in 1980 and passed its first patent law in March 1984. But the 1984 patent law did not cover pharmaceuticals, for which China was criticized internationally. China revised its patent law in 1992 to cover new pharmaceutical compounds, new uses for pharmaceutical compounds, and pharmaceutical compositions. Chinese patent law was further amended in 2000 to meet TRIPS' requirements.

Most of China's industry is currently focused on bulk production of me-too pharmaceuticals. Chinese firms currently lag behind Indian firms in sophisticated drug discovery capabilities. China is adapting rapidly to the new patent situation by moving upstream into innovative research. The government is supporting the industry's development of its innovative capacity. As a result,^{cxix} patents have been increasing. Chinese firms were awarded 224 patents in 1998. In 2002, the number more than doubled to 484. Patent applications increased even more rapidly. In 1998, 275 applications were filed; in 2002, 999 were filed.^{cxx} Local Chinese companies now account for seven out of ten patent applications in China, including gene therapy, antibodies, and peptides.

In China, there are many ties between the government and the pharmaceutical industry, including:

- China is still evolving from a communist system to a more capitalist system. Some pharmaceutical firms—operating under a Chinese accounting system (different from Generally Accepted Accounting Principles (GAAP) and with partial or full state ownership—often sell products at extremely low prices.
- The government's current five-year plan specified biotechnology and innovative drug discovery on its list of key focus area. From 2000-2005, public funds annually invested in China's biotech sector averaged \$600 million.
- Sixty Life Park zones have been created in China. They offer basic amenities and fiscal and regulatory incentives.^{cxxi}
- The government has been encouraging foreign investment through various incentives. Foreign-funded research centers may be exempt from import tariffs and custom taxes. And business taxes may be exempted if foreign companies transfer technology to China.
- Systematic efforts were taken to educate the bureaucrats, policy makers and the industry about the WTO and product patents in the pharmaceutical industry.^{cxxii}

Box 7: India

India is another world leader in pharmaceuticals. It has low development costs, complex synthesis capabilities, growing experience with GMP compliance, and a large local market in which to gain experience. Its robust pharmaceutical industry covers both final formulations and APIs. India gained its global foothold with its innovatively engineered generic drugs and APIs, and it is now seeking to become a leader in outsourced clinical research as well as contract manufacturing. Indian firms are becoming global MNCs in their own right.

In 2003, Indian pharmaceutical sales were approximately RS 300 billion (\$6.9 billion) with RS 141 billion (\$3.2 billion) of exports to over 90 countries. India is the third largest global API producer after China and Italy.^{cxxiii} In terms of the global pharmaceuticals market, India currently holds a modest 1-2% share, but it has been growing at approximately 10% per year.^{cxxiv}

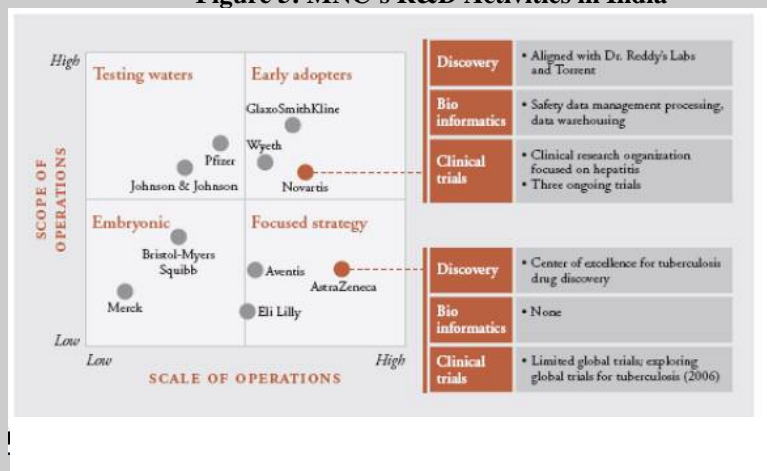
Two-hundred fifty of the largest companies control 70% of the Indian market. In 1999, 70% of the APIs and 80% of the formulations in India were domestically produced. India also supplies a large share of the world’s generic drugs, approximately 22% of the entire market.^{cxxv} MSF estimates that approximately 70% of all patients in their HIV/AIDS projects take generic ARV medicines made in India. Worldwide, an estimated 350,000 people on ARV treatment depend on Indian generic production, which is half of all those taking ARVs in developing countries.^{cxxvi} Indian companies also produce 50% of the essential drugs UNICEF provides to children worldwide.

India has a significant number of strong chemists, many with PhDs from the United States and Europe, who provide rapid and creative process development.^{cxxvii} India also has 445 institutes with an annual intake of 4,670 students for bachelor and doctorate of pharmaceuticals and 132 institutes for masters of pharmaceuticals with an annual intake of 2,680 students.^{cxxviii}

There are 74 USFDA-approved manufacturing facilities in India, more than in any other country outside the United States. In 2005, Indian companies expected to file almost 20% of all Abbreviated New Drug Applications (ANDA) to the USFDA.^{cxxix}

Foreign firms have significantly invested in India. Figure 7 shows some of their investment strategies.

Figure 5: MNC’s R&D Activities in India



The Indian government views the pharmaceutical industry under industrial rather than health policy. While there is considerable variation in access to medicine along with the quality and pricing of drugs throughout India, the government used industrial policy to jumpstart the industry in the 1970s.^{cxxx} It established an incentive scheme for domestic producers (price controls, local content laws, limitations on the importation of APIs), promoted research and development and legislated an enabling patent protection regime which

included process patents only for a short period of time. Foreign firms were also required to make minimum capital investments in R&D facilities in India, and to reinvest part of their turnover in local R&D facilities.^{cxv} In 1970, domestic firms generated only 15% of the Indian pharmaceutical market. These policies helped the domestic industry grow to 50% of the market by 1982 and 61% by 1999.^{cxvii} In the mid-eighties, the Indian government started encouraging exports through incentives such as upgrading exporters' facilities and undertaking R&D.^{cxviii}

The Indian government continues to support the pharmaceutical industry in many ways, some of which include:

- The government is significantly involved in setting up pharmaceutical parks, based on a public-private partnership model. Twenty-two Life Park zones have been created in India. They offer basic amenities and fiscal and regulatory incentives.^{cxix}
- The Government of India has been supporting research and innovation:
 - The Pharmaceutical Research & Development Support Fund (PRDSF) has Rupees 150 crore to support the development of new molecules.^{cxv}
 - India's Department of Biotechnology has funded more than 1,800 R&D projects, helped to develop twelve vaccines, and transferred 54 technologies to the biotech industry, seventeen of which have been commercialized.
 - R&D intensive companies receive price benefits (200% weighted deduction) for the drugs under India's Drug Price Control Order (DPCO).
 - Firms receive 150% weighted exemption for R&D activities in the tax code.
 - The government recently expanded the list of equipment that is exempt from import duty.^{cxvi}
- The Government of India is working with firms to improve quality. It has created a dedicated fund to provide an interest subsidy (5%) on borrowings to small- and medium-scale pharmaceutical firms making investments to meet Schedule M, the domestic Indian standard for GMP. The central and state governments also offer financial assistance for this.^{cxvii}
- The government has been encouraging foreign firms to invest in India. Foreign-funded research centers may be exempt from import tariffs and custom taxes. FDI up to 100% is now permitted for all bulk drugs, their intermediaries and formulations.^{cxviii}
- The Government of India encourages exports. Exporters are allowed to import inputs on a duty-free basis for export productions. Additionally, excise duties on pharmaceutical products are being lowered. An excise duty of 16% is levied on only 60% of the maximum retail drug price. There are plans to reduce the excise duty from 16% to 8%. The government also works with importing countries to reduce their tariffs for Indian pharmaceutical products.^{cxix} The National Pharmaceuticals Policy (2006) also sets six key policy objectives, four of which focus on increasing exports.^{cxl}
- The Small Business Innovation Research Initiative (SBIRI) has been set up to encourage public-private partnership in the biotechnology sector.^{cxli}
- Indian states have begun to vie with one another for biotech business by offering exemption from VAT and other fees, financial assistance with patents and subsidies on everything ranging from investment to land to utilities.
- India's Minister of Science launched a program that provides tax incentives and grants for biotechnology firms and to establish the Biotechnology Parks Society of India to support ten biotech parks by 2010.^{cxlii}
- The Pharmaceutical Advisory Forum was created to facility dialogue between industry and government.

In 1999 and 2002, the Government of India amended the Patent Act of 1970 to fulfill its TRIPS obligations, including the establishment of the mailbox facility. India started to assess mailbox applications in 2005. If an application meets the TRIPS' agreement standards of patentability, as interpreted and implemented under the national law, a patent will be granted for the remainder of the patent term, calculated from the date of the application's filing in India.^{cxliii}

India's new patent law will fully be interpreted through case law and trials. Indian patent law, for example, defines a patentable pharmaceutical substance as "any new entity involving one or more inventive steps."^{cxliv} What does "new" mean precisely in this definition? And what constitutes "an inventive step?"

In response to critics who wanted the patent law more precisely defined, the Minister of Commerce and Industry established a Technical Expert Group, led by Dr. R. A. Mashelkar. The task of these experts is to consider whether limiting the grant of patents for pharmaceutical substance to a “new chemical entity” or to a “new medical entity” involving one or more inventive steps is TRIPS compatible.^{cxlv} The committee’s February 2007 report to the Ministry of Commerce and Industry fueled the current patent argument raging in India when some of the report was discovered plagiarized from an industry-backed NGO’s report.

In 2005, the Indian Patent Office rejected Novartis’ application to patent the cancer drug Gleevec. The office reported that Novartis had not demonstrated that Gleevec is more efficacious than a different form of the drug already available on the Indian market, a requirement of India’s patent law. Instead of appealing, however, Novartis is challenging the law itself. Many activists argue that if Novartis is successful in its challenge, generic production across India would be affected and a global precedent would be set.^{cxlvi}

Many Indian companies that manufactured patented drugs off-patent are now being prevented from continuing this practice. Eli Lilly, for example, challenged four Indian companies which manufactured generic version of Cialis in India and won its case. Any Indian company that wants to manufacture Cialis now must do so under a licensing agreement with Eli Lilly and pay a royalty. A number of other patent suits are already under way in India.^{cxlvii}

The change in India’s patent law is driving an intense consolidation of the Indian pharmaceutical industry. Of the existing 24,000 companies, approximately 200 to 300 are expected to survive.^{cxlviii} As of 2004, the top ten pharmaceutical firms controlled 37% of the market.^{cxlix}

Endnotes

-
- ⁱ Health futures in Bangladesh: Some key issues and options. Report commissioned by the World Bank with assistance from DFID.
- ⁱⁱ Pharmaceutical industry overview. <http://web.csustan.edu/manage/harris/industry1.html>. Accessed on March 22, 2007.
- ⁱⁱⁱ IMS Data, 2006.
- ^{iv} Guidelines for the examination of Pharmaceutical Patents: Developing a Public Health Perspective. Carlos Correa, University of Buenos Aires. WHO-ICTSD-UNCTAD Working Paper. January 2007.
- ^v Interview with Mr. Jeff Gilbert, Global Pharmaceutical Industry Fellow at the World Bank. March 2007.
- ^{vi} Ibid.
- ^{vii} Contract Pharma. API Manufacturing: How will changes in India and China affect the outsourcing of APIs? George Karris. September 2002.
- ^{viii} IMS Health Study quoted in Congress, patients step up campaign for more generic drugs. Managed Healthcare Executive. December 1, 2006. Accessed in May 2007 at <http://www.managedhealthcareexecutive.com/mhe/article/articleDetail.jsp?id=389268>.
- ^{ix} Interview with Patty Eisenhour, Watson Pharmaceuticals, Director, Investor Relations. March 2007.
- ^x Ibid.
- ^{xi} Interview with Monique Mrazek, IFC. April 2007.
- ^{xii} As Drug Patents End, Costs for Generics Surge. Milt Freudenheim. New York Times. December 22, 2002.
- ^{xiii} Contract Pharma. API Manufacturing: How will changes in India and China affect the outsourcing of APIs? George Karris. September 2002.
- ^{xiv} In India a Little Lab Work and Lots of Lawyers. Business Week Online. July 14, 2003. http://www.businessweek.com/magazine/content/03_28/b3841144_mz033.htm. Accessed in March 2007.
- ^{xv} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{xvi} Contract Pharma. API Manufacturing: How will changes in India and China affect the outsourcing of APIs? George Karris. September 2002.
- ^{xvii} Interview with Nazmul Hassan, Beximco Pharmaceuticals CEO. February 2007.
- ^{xviii} Ibid.
- ^{xix} Interview with Samson Chowdhury, Chairman, Square Pharmaceuticals. May 2007.
- ^{xx} Intellectual Property and Innovation in Least Developed Countries: Pharmaceutical, Agro-Processing and Textiles and RMG in Bangladesh. Padmashree Gehl Sampath. United Nations University – MERIT. 2007.
- ^{xxi} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{xxii} IMS data, 2006.
- ^{xxiii} Interview with Nazmul Hassan, Beximco Pharmaceuticals CEO. February 2007.
- ^{xxiv} Interview with Square Pharmaceuticals. May 2007.
- ^{xxv} Data given to the writers of the Strategy for Establishing the API Park report. Industry members provided the figures. The authors note that obtaining current industry and firm information is difficult. They made their estimates based on statements from the industry and data from a 1999-2003 survey of 54 firms.
- ^{xxvi} Square Annual Report. 2005-2006.
- ^{xxvii} Interview with Dr. Charles Larson, Director Health Systems and Infectious Diseases Division. ICDDR,B. February 2007.
- ^{xxviii} Interview with UNICEF Supply & Procurement Section. February 2007.
- ^{xxix} Interview with Padmashree Gehl Sampath. United Nations University – MERIT. 2007.
- ^{xxx} Interview with Square Pharmaceuticals. February 2007.
- ^{xxxi} Interview with BAPI. May 2007.
- ^{xxxii} Interview with Bangladesh Pharmaceutical Society. February 2007.
- ^{xxxiii} Interview with BAPI. May 2007.
- ^{xxxiv} Interview with BAPI. February 2007.

-
- ^{xxxv} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{xxxvi} Bangladesh Export Statistics, EPB.
- ^{xxxvii} Interview with Ashfaque ur Rahman, Managing Director, Novartis Bangladesh. May 2007
- ^{xxxviii} Bangladesh Association of Pharmaceutical Industries quoted in Study on the Pharmaceuticals Sector of Bangladesh. Jetro. 2005.
- ^{xxxix} Interview with Farook Chowdhury, author of A Strategy for Establishing the API Park. February 2007.
- ^{xl} Firm Productivity in Bangladesh Manufacturing Industries. Ana M. Fernandes. The World Bank. August 2006.
- ^{xli} Beximco Annual Report. 2005. Conversion of Taka to Dollars at 1 BDT = 0.0144509 USD.
- ^{xlii} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{xliii} Ibid.
- ^{xliv} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{xlv} Ibid.
- ^{xlvi} Interview with Monique Mrazek, IFC. April 2007.
- ^{xlvii} Interview with Square Pharmaceuticals. February 2007
- ^{xlviii} Interview with Nazmul Hassan, Beximco Pharmaceuticals CEO. February 2007.
- ^{xlix} The Indian Pharmaceutical Industry: Collaboration for Growth. KPMG. 2006.
- ^l Square Pharmaceuticals. Annual Report. 2005-2006.
- ^{li} Interview with Samson Chowdhury. Chairman. Square Pharmaceuticals. May 2007.
- ^{lii} Beximco Pharmaceuticals. Annual Report. 2005.
- ^{liii} The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access To Medicines? Sisule Musungu, South Center. Cecilia Oh, World Health Organization. August 2005.
- ^{liv} Will the lifeline of affordable medicines for poor countries be cut? Consequences of Medicines Patenting in India. Médecins Sans Frontières. February 2005.
- ^{lv} WTO Agreements and Public Health: A joint study by the WHO and the WTO Secretariat. 2002.
- ^{lvi} United States Patent and Trademark Office Performance and Accountability Report. Fiscal Year 2006.
- ^{lvii} Utilizing TRIPS Flexibilities for Public Health Protection through South-South Regional Frameworks. Sisule Musungu, Susan Villanueva, and Roxana Blasetti. South Centre. April 2004
- ^{lviii} The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access To Medicines? Sisule Musungu, South Center. Cecilia Oh, World Health Organization. August 2005.
- ^{lix} Interview with Samson Chowdhury, Chairman, Square Pharmaceuticals. May 2007.
- ^{lx} The TRIPS Agreement and Pharmaceuticals. Report of an ASEAN Workshop on the TRIPS Agreement and Its Impact on Pharmaceuticals. World Health Organization. Jakarta, 2-4 May 2000.
- ^{lxi} Interview: Thailand Fed Up With High Drug Prices. The Star Online. Darren Schuettler. Feb 19 2007. Accessed via cpTech website: <http://www.cptech.org/ip/health/>
- ^{lxii} Compulsory Licensing of Pharmaceuticals and TRIPS. World Trade Organization. October 2005.
- ^{lxiii} Multinationals Patenting Drugs despite WTO Waiver (quoting a BAPI source). Jasim Uddin Khan. The Daily Star. February 10, 2006.
- ^{lxiv} The Bolar Provision allows organizations to use patented medicines for experimental purposes before the patent expiration. This is crucial for reverse engineering of a drug.
- ^{lxv} Parallel importation is when an organization imports a drug from another country. The importer does not have to pay a royalty as the exporter has already paid this royalty. Article 6 of the TRIPS Agreement allows this.
- ^{lxvi} TRIPS and the Pharmaceutical Industry in Bangladesh: Towards a National Strategy. Tony VanDuzer. Centre for Policy Dialogue. April 2003.
- ^{lxvii} Interview with Monique Mrazek, IFC. April 2007.
- ^{lxviii} Interview with Samson Chowdhury, Chairman, Square Pharmaceuticals. May 2007.
- ^{lxix} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{lxx} Interview with Bangladesh Association of Pharmaceutical Industries. February 2007.
- ^{lxxi} Boston Consulting Group.
- ^{lxxii} Square Annual Report. 2005-2006.

- ^{lxxiii} Interview with Professor Charles L. Cooney, MIT.
- ^{lxxiv} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{lxxv} Interview with Square Pharmaceuticals. February 2007.
- ^{lxxvi} Trade Barriers and Prices of Essential Health-Sector Inputs. David Woodward. World Health Organization. Commission on Macroeconomics and Health. June 2001.
- ^{lxxvii} Annual Reports. Square Pharmaceuticals (2005-2006) and Beximco (2005).
- ^{lxxviii} The fixed costs of machines and factories are estimated via their depreciation charge, an accounting term to represent the annualized PP&E expense. Please note that this is a non-cash expense reported on the income statement and can be influenced by, for example, depreciation schedules. Square has a ten-year span for depreciating buildings and seven for machinery. Beximco has a ten- to twenty-year span for buildings and a seven- to thirteen-year span for machines. In 2005-06, Square and Beximco had 4.42 billion Taka of PP&E (Plant, Property & Equipment) on their books.
- ^{lxxix} World Bank Group EdStats, 2004. Bangladesh numbers are from the nearest available year to 2004, within 2 years.
- ^{lxxx} Intellectual Property and Innovation in Least Developed Countries: Pharmaceutical, Agro-Processing and Textiles and RMG in Bangladesh. Padmashree Gehl Sampath. United Nations University – MERIT. 2007.
- ^{lxxxii} Ibid.
- ^{lxxxii} Bangladesh Pharmaceutical Policy and Politics. Health Policy and Planning. Michael R. Reich. Harvard School of Public Health. 1994.
- ^{lxxxiii} A Strategy for Establishing the API Park. Farook Chowdhury. June 2006.
- ^{lxxxiv} Firm Productivity in Bangladesh Manufacturing Industries. Ana M. Fernandes. The World Bank. August 2006.
- ^{lxxxv} Bangladesh Pharmaceutical Policy and Politics. Health Policy and Planning. Michael R. Reich. 1994.
- ^{lxxxvi} Interview with UNICEF Supply & Procurement Section. February 2007.
- ^{lxxxvii} Interview with MSF Country Director. February 2007.
- ^{lxxxviii} Interview with Nazmul Hassan, Beximco Pharmaceuticals CEO. February 2007.
- ^{lxxxix} Ratanawijitrasin & Wondemagegnehu. Effective Drug Regulation: A Multi-Country Study. World Health Organization 2002. referenced in Drug Regulation and Incentives of Innovation: The Case of ASEAN. Sauwakon Ratanawijitrasin.
- ^{xc} Interview with DDA. February 2007.
- ^{xcii} Ibid.
- ^{xcii} Interview with Drug Testing Laboratory. February 2007.
- ^{xciii} Interview with Square Pharmaceuticals. February 2007.
- ^{xciv} Interview with the DDA. February 2007.
- ^{xcv} Interview with UNICEF GMP inspector. February 2007.
- ^{xcvi} Interview with DDA. February 2007.
- ^{xcvii} Interview with UNICEF Drug Procurement Team. February 2007.
- ^{xcviii} Paper by Bill Haddad, Chairman and CEO of Biogenics. [wbln0018.worldbank.org/.../2adc484a5d57888f85256d350054080f/\\$FILE/Paper%20Bill%20Haddad.doc](http://wbln0018.worldbank.org/.../2adc484a5d57888f85256d350054080f/$FILE/Paper%20Bill%20Haddad.doc). Accessed on March 27, 2007.
- ^{xcix} Interview with Dr. Khadar. USFDA. March 2007.
- ^c Local Production: Industrial Policy and Access to Medicines: An Overview of Key Concepts, Issues and Opportunities for Future Research. Warren A Kaplan. Richard Laing. Health, Nutrition and Population Discussion Paper. The World Bank. June 2003.
- ^{ci} Ibid.
- ^{cii} Ibid.
- ^{ciii} CIA Factbook, <https://www.cia.gov/cia/publications/factbook/geos/bg.html>. Accessed on March 22, 2007
- ^{civ} Local Production: Industrial Policy and Access to Medicines: An Overview of Key Concepts, Issues and Opportunities for Future Research. Warren A Kaplan. Richard Laing. Health, Nutrition and Population Discussion Paper. The World Bank. June 2003.
- ^{cv} CIA Factbook, <https://www.cia.gov/cia/publications/factbook/geos/bg.html>. Accessed on March 22, 2007.

- ^{cvi} Industrial Development Report 2002/2003: Competing Through Innovation and Learning. UNIDO. 2002.
- ^{cvii} Local Production: Industrial Policy and Access to Medicines: An Overview of Key Concepts, Issues and Opportunities for Future Research. Warren A Kaplan. Richard Laing. Health, Nutrition and Population Discussion Paper. The World Bank. June 2003.
- ^{cviii} Interview with BAPI. May 2007. Please note that, according to Square's annual report, they import \$28.44 million of APIs. As Square generates 15% of total Bangladesh pharmaceutical sales, it can be assumed that the industry imported at least \$189 million of APIs.
- ^{cix} Counterfeit Drugs are Murder. Global Education.
<http://www.globaleducation.edna.edu.au/globaled/go/cache/offonce/pid/2296;jsessionid=8159785F92A736DDE4E0A5AB3E0FD94E>. Accessed in May 2007.
- ^{cx} The Independent. Dr Dora, the scourge of Nigeria's drug fakers, is honored. December 2005.
<http://news.independent.co.uk/world/africa/article331948.ece>. Accessed on March 27, 2007.
- ^{cxii} Transparency International Press Release. January 6, 2004.
- ^{cxiii} Developing Innovative Capacity in China to Meet Health Needs. Zezhong Li. April 2005. MIHR (Center for the Management of Intellectual Property in Health Research and Development) Paper prepared for the WHO's Commission on Intellectual Property Rights, Innovation, and Public Health.
- ^{cxiiii} Industry Self-Regulation: What's Working (and What's Not)? Harvard Business School Working Knowledge. Martha Lagace. April 9, 2007.
- ^{cxiv} Public-Private Roles in the Pharmaceutical Sector: Implications for equitable access and rational drug use. Sara Bennett, Jonathan Quick, and German Velasquez. World Health Organization. 1997.
- ^{cxv} National Drug Policy 2005. Ministry of Health & Family Welfare. Government of the People's Republic of Bangladesh.
- ^{cxvi} Review of China's Biopharmaceutical Industries in Recent Years. Asiabiotech. Vol 10, Number 16. 2006.
- ^{cxvii} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxviii} Developing Innovative Capacity in China to Meet Health Needs. Zezhong Li. April 2005. MIHR (Center for the Management of Intellectual Property in Health Research and Development) Paper prepared for the WHO's Commission on Intellectual Property Rights, Innovation, and Public Health.
- ^{cxix} Ibid.
- ^{cxx} Innovation in Developing Countries to Meet Health Needs. Experiences of China, Brazil, South Africa and India. Commission on Intellectual Property Rights, Innovation and Public Health. April 2004.
- ^{cxxi} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxxii} Impact of Product Patent on FDI in Indian Pharmaceutical Industry. Arvind Singhatiya. Accessed in May 2007. <http://ezinearticles.com/?Impact-of-Product-Patent-on-FDI-in-Indian-Pharmaceutical-Industry&id=89594>.
- ^{cxxiii} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxxiv} Wikipedia. Pharmaceuticals in India. http://en.wikipedia.org/wiki/Pharmaceuticals_in_India. Accessed March 2007.
- ^{cxxv} Verma. Then and Now. Nature, 436, 28 July 2005. P 478-479.
- ^{cxxvi} Prognosis: Short Term Relief, Long Term Pain. The Future of Generic Medicines Made In India. Médecins Sans Frontières Campaign for Access to Essential Medicines. Briefing Note. April 21, 2005.
- ^{cxxvii} Local Production: Industrial Policy and Access to Medicines: An Overview of Key Concepts, Issues and Opportunities for Future Research. Warren A Kaplan. Richard Laing. Health, Nutrition and Population Discussion Paper. The World Bank. June 2003.
- ^{cxxviii} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxxix} Wikipedia. Pharmaceuticals in India. http://en.wikipedia.org/wiki/Pharmaceuticals_in_India. Accessed March 2007
- ^{cxx} Local Production: Industrial Policy and Access to Medicines: An Overview of Key Concepts, Issues and Opportunities for Future Research. Warren A Kaplan. Richard Laing. Health, Nutrition and Population Discussion Paper. The World Bank. June 2003.

- ^{cxxx} The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access To Medicines? Sisule Musungu, South Center. Cecilia Oh, World Health Organization. August 2005.
- ^{cxxxii} Organization of Pharmaceutical Producers in India (OPPI). 38th Annual Report. 2003.
- ^{cxxxiii} Developing Innovative Capacity in China to Meet Health Needs. Zezhong Li. April 2005. MIHR (Center for the Management of Intellectual Property in Health Research and Development) paper prepared for the WHO's Commission on Intellectual Property Rights, Innovation, and Public Health.
- ^{cxxxiv} National Pharmaceuticals Policy, 2006. Government of India. Department of Chemicals and Petrochemicals.
- ^{cxxxv} Impact of Product Patent on FDI in Indian Pharmaceutical Industry. Arvind Singhatiya. Accessed in May 2007. <http://ezinearticles.com/?Impact-of-Product-Patent-on-FDI-in-Indian-Pharmaceutical-Industry&id=89594>.
- ^{cxxxvi} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxxxvii} National Pharmaceuticals Policy, 2006. Government of India. Department of Chemicals and Petrochemicals.
- ^{cxxxviii} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxxxix} National Pharmaceuticals Policy, 2006. Government of India. Department of Chemicals and Petrochemicals.
- ^{cxl} Ibid.
- ^{cxli} The Offshoring of Engineering: Facts, Myths, Unknowns and Implications. Offshoring in the Pharmaceutical Industry. Charles L. Cooney. MIT. October 24, 2006.
- ^{cxlii} [http://en.wikipedia.org/wiki/Pharmaceuticals_\(India\)](http://en.wikipedia.org/wiki/Pharmaceuticals_(India)). Accessed in May 2007.
- ^{cxliii} Taking TRIPS to India – Novartis, Patent Law, and Access to Medicines. The New England Journal of Medicine. Janice Mueller. February 8, 2007.
- ^{cxliv} Section 2h of the Patents Amendment Act 2005 inserting a new clause Section 2(ta) in the Patents Act 1970.
- ^{cxlv} The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access To Medicines? Sisule Musungu, South Center. Cecilia Oh, World Health Organization. August 2005.
- ^{cxlvi} Letter from US Representative Henry Waxman to Novartis. February 13, 2007. Accessed via cpTech website: <http://www.cptech.org/ip/health/>.
- ^{cxlvii} Interview with Nazmul Hassan, Beximco Pharmaceuticals CEO. February 2007.
- ^{cxlviii} Pharmaceutical Industrial Partnering Trends in India. Dr. Harvinder Popli, Ranbaxy Labs. Asia Biotech. Volume 10, Number 16. 2006.
- ^{cxlix} Developing Innovative Capacity in India to meet Health Needs. Dr. HR Bhojwani. April 2005. Paper prepared for the WHO's Commission on Intellectual Property Rights, Innovation, and Public Health.